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Association between long-term air pollution exposure and development of diabetes among community-dwelling adults: Modification of the associations by dietary nutrients

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ABSTRACT

Background: Studies on the modifying effects of dietary factors on the association between air pollution and diabetes-related outcomes are limited. We examined whether dietary nutrients could modify the association between long-term air pollution exposure and the development of diabetes.

Methods: We used data from the Cardiovascular Disease Association Study, which enrolled adults aged 40–69 years in Korea between 2005 and 2011 and followed them up until 2016 ($n = 14{,}667$). Annual concentrations of fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) at each participant's residence(s) were estimated using community multiscale air quality models. Intake of 22 dietary nutrients was assessed using a validated food frequency questionnaire during the baseline survey. We examined the product terms between air pollution levels (continuous) and each dietary nutrient (quartile) using Cox regression models, adjusted for potential confounders.

Results: $PM_{2.5}$ [hazard ratio (HR) = 1.49, 95 % confidence interval (CI): 1.11, 2.00] and NO_2 (HR = 1.29, 95 % CI: 1.12, 1.49) concentrations were found to be associated with incident diabetes. NO_2 levels interacted with dietary intake of retinol, vitamin A, and cholesterol (p-values for interaction < 0.05). Stronger associations were observed between NO_2 levels and the occurrence of diabetes among individuals with a lower intake of these nutrients compared to those with a higher intake. No interaction was found between $PM_{2.5}$ and the 22 investigated dietary nutrients.

Conclusions: Adequate intake of dietary nutrients, such as retinol, vitamin A, and cholesterol, from various food items in a balanced diet may prevent the occurrence of diabetes in a setting wherein reduction of air pollution levels cannot be achieved in a short time frame.

1. Introduction

Diabetes mellitus (hereafter, diabetes) is a prevalent chronic disease, increasing healthcare expenditure worldwide (Sun et al., 2022). Diabetes can result in severe and even life-threatening complications and disabilities involving several organs, including the heart, nerves, kidneys, and eyes, as well as lower life expectancy (Heald et al., 2020). In addition to genetic predisposition, smoking, obesity, and physical inactivity (Amarasinghe et al., 2015), air pollution has emerged as a risk factor for diabetes (Yang et al., 2020). Air pollution can induce oxidative stress and systemic inflammation, which may result in insulin resistance and impaired insulin secretion (Luc et al., 2019; Wang et al., 2014). Due to the involvement of these biological pathways, it is plausible that a diet rich in antioxidant and anti-inflammatory compounds can mitigate the adverse effects of air pollution on diabetes (Barthelemy et al., 2020). Few epidemiological studies have supported this hypothesis. For example, a cross-sectional study reported that the association between particulate matter with an aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$)

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; MDA, Mini Dietary Assessment; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay; NO_2, nitrogen dioxide; $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤2.5 μm; RNI, recommended nutrient intake; USD, United States dollars.

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levels and diabetes prevalence was weaker among individuals with higher fruit consumption than among those with lower fruit consumption (Yang et al., 2018). Another cohort study demonstrated attenuated associations of $PM_{2.5}$ and nitrogen dioxide (NO_2) levels with diabetes mortality among those with a higher intake of fruits (Lim et al., 2018).

Although the investigation of interaction with dietary nutrients can shed light on the underlying mechanisms of air pollution impacts and have implications on dietary guidelines among different cultures, to our knowledge, only one study has explored the potential interactions between air pollution and dietary nutrients on the development of diabetes (Li et al., 2022). In the previous study, the associations of $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 10 μm (PM_{10}), and NO_2 with incident diabetes were stronger among adults with insufficient intake of vitamin C, and the association between $PM_{2.5}$ and incident diabetes was stronger among those with insufficient intake of vitamin E. Since this previous study only considered vitamins A, C, and E and was conducted in a European population (United Kingdom), it is necessary to assess the interactions between air pollution exposure and a wide range of dietary nutrients in different cultural and geographical contexts (e.g., Asia).

Therefore, we performed a longitudinal study using a population-based cohort that enrolled participants from medium-sized cities and districts in Korea along with information regarding various dietary factors to evaluate the following hypotheses: a) Long-term exposure to air pollution may increase the risk of occurrence of diabetes. b) Dietary nutrients, especially those with antioxidant and anti-inflammatory functions, may modify the association between air pollution exposure and the development of diabetes.

2. Methods

2.1. Ethical considerations

The study design was reviewed and approved by the Institutional Review Board of Ajou University Hospital (AJIRB-MED-EXP-22–222). This study was conducted in accordance with the tenets of the Declaration of Helsinki. All study participants provided written informed consent before the commencement of the study.

2.2. Study population

We used data from the Cardiovascular Disease Association Study (CAVAS), a prospective cohort study conducted to identify risk factors for chronic diseases, including cardiovascular disease, and to provide a scientific evidence base for effective disease prevention and early screening. The details of the CAVAS cohort have been presented previously (Kim et al., 2017). Briefly, 28,337 (non-institutionalized and therefore relatively healthy) community-dwelling adults aged 40–69 years were recruited without any other explicit inclusion and exclusion criteria and followed up in Ganghwa (population in 2008: 67,387; area: 411.4 km^2), Goryeong (34,770; 384.0 km^2), Namwon (88,356; 752.6 km^2), Pyeongchang (43,706; 1,464.1 km^2), Wonju (303,975; 867.3 km^2), and Yangpyeong (89,812; 877.1 km^2) in Korea. The baseline survey was conducted between 2005 and 2011, and up to 4 follow-up surveys were performed by 2016. In every survey, trained interviewers acquired information regarding sociodemographic features, lifestyle, diet, disease and family history, and current health conditions and symptoms using structured questionnaires. Trained technicians also measured the anthropometric indices and collected blood and urine samples according to the standard procedures (Kim et al., 2017).

Among 28,337 enrolled participants, we subsequently excluded the following: 2,686 individuals who reported a previous diagnosis of diabetes during the baseline survey; 720 with 8-hour fasting plasma glucose levels $\geq$ 126 mg/dL during the baseline survey; 10,149 who did not participate in any of the follow-up surveys; 2 with missing data for body mass index (BMI); and 113 who reported an implausible total energy intake (<500 or > 5,000 kcal/day) during the baseline survey. Finally, a total of 14,667 individuals were included in the final analyses (Fig. S1).

2.3. Exposure assessment of air pollutants

We considered $PM_{2.5}$ and NO_2 exposures because previous studies have associated them with diabetes-related outcomes, such as the increased prevalence of diabetes and diabetes mortality (Lim et al., 2018; Yang et al., 2018). Air pollution concentrations in CAVAS were estimated using community multiscale air quality models, which combined the meteorological (generating a three-dimensional meteorological field), emission (processing emission data from various domestic and foreign sources), and chemical transport models (linking meteorological and emission models to estimate air pollution levels). For NO_2, data assimilation was conducted in a 9-km grid unit using data from monitoring stations across the Republic of Korea. Data assimilation for $PM_{2.5}$ was performed in a 1-km grid unit using satellite-derived aerosol optical depth data from the National Aeronautics and Space Administration Terra and Aqua satellites since nationwide monitoring for $PM_{2.5}$ began in 2015. Further adjustment for air pollution levels was made for normalized difference vegetation index and meteorological factors using multiple linear regression models. The root mean square errors of estimated $PM_{2.5}$ levels compared to measured levels were 8.31 $\mu g/m^3$, 6.26 $\mu g/m^3$, and 4.09 $\mu g/m^3$ on the daily, weekly, and annual scales, respectively. The root mean square errors of NO_2 levels were 6.9 ppb, 5.8 ppb, and 4.4 ppb on the daily, weekly, and annual scale, respectively. The full description of air pollution modeling methods can be found elsewhere (Woo et al., 2022).

Information regarding each study participant's residential address (es) was obtained during the baseline and follow-up surveys and geocoded using the GeoService-Xr software (Geoservice, Seoul, Republic of Korea). Air pollution data modeled for the study period (2004–2016) were merged with cohort data by matching the geocoded address(es) with 1 km grids ($PM_{2.5}$) or 9 km grids (NO_2) from the air pollution models.

2.4. Evaluation of dietary factors

Information regarding dietary intake was obtained using a validated food frequency questionnaire inquiring on the average intake frequency (nine categories; from 'never or rarely' to 'three times/day') and portion size per meal (three or four categories for each food item) of 106 food items during the previous year (Ahn et al., 2007). To reduce the concern that dietary patterns would change due to the occurrence of the outcome, we used dietary information collected during the baseline survey.

We estimated the intake of 22 dietary nutrients (vitamin A, retinol, β-carotene, vitamin B1, vitamin B2, Niacin, vitamin B6, folate, vitamin C, vitamin E, calcium, phosphate, iron, protein, fat, carbohydrate, sodium, potassium, zinc, fiber, ash, and cholesterol) based on the seventh edition of Korean Food Composition Table (Ahn et al., 2007). Nutrient intake for total energy intake was corrected by applying the residual method (Willett et al., 1997) and used for further analyses.

In addition, we evaluated the overall dietary quality of study participants using the Mini Dietary Assessment (MDA) index, which was developed considering Korea's nutritional guidelines and cultural backgrounds (Kim et al. 2003). MDA consists of 10 good (e.g., milk, meat, vegetable, and fruit intake) and unfavorable (e.g., sugar, salt, and fat intake) dietary habits and provides scores ranging from 10 to 50, with higher scores indicating better overall dietary quality. The MDA index score was assessed to demonstrate a high correlation with the Healthy Eating Index score (Kim et al. 2003).

Finally, we evaluated the study participants' milk and egg intake by estimating the average weight (g) of milk and eggs consumed per day, respectively. Dairy product intake was assessed by summing the weights of milk, yogurt, and cheese consumed per day. We also assessed

vegetable and fruit intake by summing the average weight of each vegetable consumed per day and that of each fruit consumed per day.

2.5. Diabetes identification and measurements of fasting glucose levels

Diabetes was identified if participants reported physician-diagnosed diabetes in response to a structured questionnaire or had an 8-hour fasting plasma glucose level $\geq$ 126 mg/dL. Plasma glucose levels were evaluated using the enzyme method (ADVIA 1650 and ADVIA 1800; Siemens Healthineers, IL, USA) in the core clinical laboratory, which participated in the quality assurance surveys conducted by the Korean Association of Quality Assurance for Clinical Laboratories.

2.6. Statistical analysis

We presented the baseline characteristics of the total study participants and those who developed and did not develop diabetes during the baseline survey, respectively. Time-dependent Cox regression models were used to assess the associations of annual $PM_{2.5}$ and NO_2 levels from 2005 to 2016 (or to the year of censoring when diabetes developed or follow-up loss occurred) as time-varying exposures with the development of diabetes, and their modification by dietary nutrients. Cox models used age as the time scale, had a random effect of survey sites (Gangwha, Goryeong, Namwon, Pyeongchang, Wonju, and Yangpyeong), and were adjusted for the following covariates which were selected based on previous studies (Lim et al., 2018; Yang et al., 2018): age (year, by using age as the time scale), sex, monthly household income [<100,000 won (701.9 US$), 100,000–300,000 won (701.9–2,105.5 US$), or $\geq$ 300,000 won (2,105.5 US$)], educational level (less than elementary school, elementary school, middle school, high school, or more than high school), cigarette smoking (never smoker, past smoker, or current smoker), alcohol consumption (never drinker, past drinker, or current drinker), regular physical activity (no or yes), MDA index score (quartile), and BMI (<18.5 kg/m^2, 18.5–22.9 kg/m^2, 23.0–24.9 kg/m^2, or $\geq$ 25.0 kg/m^2). Information regarding all the covariates was obtained from the questionnaire or anthropometric measurements during the baseline survey. Missing data were treated using a missing indicator category. After the main analyses, stratified analyses by sex and BMI (<23 kg/m^2 vs $\geq$ 23 kg/m^2) were also performed because the heterogeneity of associations between air pollution exposure and various health outcomes by these factors have been suggested (Barthelemy et al., 2020; Lim et al., 2018; Wang et al., 2022; Zhang et al., 2020; Zhu et al., 2022).

We examined the interactions between air pollution and dietary nutrients by testing the product terms between air pollution levels (continuous variables) and dietary nutrients (quartiles and categorical variables) added to the main models with lower-order terms. The Association between air pollution exposure and the development of diabetes was also explored in each quartile of dietary nutrients.

Analyses for associations between air pollution and diabetes were stratified according to the MDA index score (<median vs $\geq$ median), which is an index of the overall dietary quality. We also stratified the analyses according to the intake of milk, dairy products, eggs, vegetables, and fruits (<median vs $\geq$ median), which are common sources of dietary nutrients identified to interact with air pollution exposure in the present study (i.e., retinol, vitamin A, and cholesterol). Interactions between air pollution and MDA index score or intake of selected food items were also assessed by testing the corresponding product terms.

The robustness of the main results was confirmed by the following sensitivity analysis: First, instead of using time-varying exposures, we used baseline $PM_{2.5}$ and NO_2 concentrations averaged for one year before the date of enrollment as exposures. In this analysis, baseline air pollution levels were used as both continuous and categorical variables (quartiles) to assess the possibility of nonlinear associations. Second, since $PM_{2.5}$ and NO_2 levels were correlated, a two-pollutant model incorporating both air pollutant levels (as time-varying exposures) was constructed to confirm the independent association of $PM_{2.5}$ or NO_2 levels with the development of diabetes. Third, we further adjusted for survey sites (Fig. S1; Table S1) to evaluate whether the results changed due to unmeasured or unknown confounders inherent in the survey sites. Fourth, since data regarding the monthly household income variable was missing substantially (54.5 %), we created analytical models that were not adjusted for this variable and repeated the analyses. Fifth, to enhance the precision of nutrient intake estimation, we excluded participants who were taking nutritional supplements. Sixth, due to the concern of over-adjustment, we repeated analyses with analytical models not adjusted for BMI. Seventh, we re-assessed the results with models not adjusted for MDA index score to lower the possibility of over-adjustment induced by including both MDA index score and dietary nutrients.

The results were presented per 10 μg/m^3 for $PM_{2.5}$ and 10 ppb for NO_2 exposure. In addition to the main results from analyses not adjusted for multiple comparisons, we also presented the results from analyses adjusted for multiple comparisons (interactions of $PM_{2.5}$ and NO_2 with 22 dietary nutrients) using the Benjamini-Hochberg false discovery rate (FDR) method (Benjamini and Hochberg, 1995). All analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA), and plots were generated using R software (version 4.2.0; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

This study was conducted among 14,667 individuals without diabetes during the baseline survey, among whom 907 developed diabetes during the study period while 13,760 did not. The mean age at the time of enrollment was 58.6 years, and 62.3 % of the study participants were women. The majority of study participants had an education level of elementary school or less (55.5 %), never smoked (70.7 %), never consumed alcohol (52.0 %), and did not engage in regular physical activity (68.6 %). The mean MDA index score was 23.5, and the mean BMI was 24.4 kg/m^2. Individuals who developed diabetes were more likely to be men (42.6 % vs 37.4 %), have a lower education level (elementary school or less, 61.0 % vs 55.2 %), be current smokers (19.1 % vs 13.8 %), and have a higher BMI (25.7 kg/m^2 vs 24.3 kg/m^2) compared to those who did not develop diabetes during the study period (Table 1). Daily intake of dietary nutrients was generally lower than the dietary reference intakes for Koreans, while was comparable between those who did and did not develop diabetes during the study period (Table 2; Table S1; Table S2).

Long-term exposures to $PM_{2.5}$ and NO_2 were associated with an increased risk of incident diabetes [hazard ratio (HR) = 1.49, 95 % confidence interval (CI): 1.11, 2.00 per 10-μg/m^3 increase in $PM_{2.5}$; HR = 1.29, 95 % CI: 1.12, 1.49 per 10-ppb increase in NO_2]. Sex-stratified analyses revealed similar associations between men and women (p-values for interaction of 0.80 for $PM_{2.5}$ and 0.90 for NO_2), whereas the associations were stronger among those with BMI < 23 kg/m^2 (HR = 2.46, 95 % CI: 1.24, 4.90 for $PM_{2.5}$; HR = 2.04, 95 % CI: 1.42, 2.91 for NO_2) compared to those with BMI $\geq$ 23 kg/m^2 (HR = 1.17, 95 % CI: 0.89, 1.54 for $PM_{2.5}$; HR = 1.13, 95 % CI: 0.98, 1.30 for NO_2), with p-values for interaction being 0.24 for $PM_{2.5}$ and 0.01 for NO_2 (Table 3).

NO_2 levels interacted with dietary intakes of retinol (p-value for interaction of 0.01), vitamin A (p-value for interaction of 0.04), and cholesterol (p-value for interaction of 0.05) regarding the occurrence of diabetes, while $PM_{2.5}$ levels did not demonstrate any interactions with the 22 assessed dietary nutrients (all p-values for interaction > 0.05) (Fig. 1). After adjustments for multiple comparisons, statistically significant interactions of NO_2 and $PM_{2.5}$ with 22 dietary nutrients were not found (all FDR p-values for interaction > 0.05) (Table S3). In analyses stratified by quartiles of dietary nutrients, associations between NO_2 levels and diabetes were stronger among the individuals included in the first quartile (Q1) of dietary intake of retinol, vitamin A, and cholesterol compared to those in the second (Q2), third (Q3), or fourth

Table 1
Baseline characteristics of the study participants.

Variables	Total participants (n = 14,667)	No diabetes[a] (n = 13,760)	Diabetes[b] (n = 907)
Age (years)	58.6 ± 9.4	58.5 ± 9.5	59.9 ± 8.6
Sex			
Men	5,532 (37.7)	5,146 (37.4)	386 (42.6)
Women	9,135 (62.3)	8,614 (62.6)	521 (57.4)
Monthly household income (US$)			
<701.9	2,694 (18.4)	2,540 (18.5)	154 (17.0)
701.9–2,105.5	2,827 (19.3)	2,676 (19.5)	151 (16.7)
≥2,105.5	1,160 (7.9)	1,101 (8.0)	59 (6.5)
Missing	7,986 (54.5)	7,443 (54.1)	543 (59.9)
Educational levels			
<Elementary school	3,158 (21.5)	2,930 (21.3)	228 (25.1)
Elementary school	4,985 (34.0)	4,659 (33.9)	326 (35.9)
Middle school	2,508 (17.1)	2,366 (17.2)	142 (15.7)
High school	2,721 (18.6)	2,574 (18.7)	147 (16.2)
>high school	1,261 (8.6)	1,199 (8.7)	62 (6.8)
Missing	34 (0.2)	32 (0.2)	2 (0.2)
Cigarette smoking			
Never smoker	10,369 (70.7)	9,784 (71.1)	585 (64.5)
Past smoker	2,211 (15.1)	2,063 (15.0)	148 (16.3)
Current smoker	2,077 (14.2)	1,904 (13.8)	173 (19.1)
Missing	10 (0.1)	9 (0.1)	1 (0.1)
Alcohol consumption			
Never drinker	7,630 (52.0)	7,163 (52.1)	467 (51.5)
Past drinker	814 (5.6)	752 (5.5)	62 (6.8)
Current drinker	6,199 (42.3)	5,821 (42.3)	378 (41.7)
Missing	24 (0.2)	24 (0.2)	0 (0.0)
Regular physical activity			
No	10,068 (68.6)	9,432 (68.6)	636 (70.1)
Yes	4,584 (31.3)	4,315 (31.4)	26 (29.7)
Missing	15 (0.1)	13 (0.1)	2 (0.2)
Mini Dietary Assessment index score	23.5 ± 5.2	23.5 ± 5.2	23.9 ± 5.1
Body mass index (kg/m^2)	24.4 ± 3.1	24.3 ± 3.0	25.7 ± 3.3
Air pollution levels[c]			
$PM_{2.5}$ ($\mu g/m^3$)	27.4 ± 3.0	27.4 ± 3.0	27.6 ± 2.9
NO_2 (ppb)	15.4 ± 5.1	15.4 ± 5.1	15.6 ± 4.9
Daily intakes of selected food items (g)			
Egg	9.3 ± 15.0	9.4 ± 15.1	8.6 ± 13.2
Milk	57.2 ± 100.5	57.5 ± 100.3	53.6 ± 103.6
Dairy product	83.4 ± 125.3	83.8 ± 125.2	78.1 ± 128.1
Vegetable	252.3 ± 184.0	251.9 ± 183.1	258.3 ± 197.6
Fruit	175.9 ± 190.9	176.1 ± 190.7	172.8 ± 194.6

Values are presented as n (%) for categorical variables and mean ± standard deviation for continuous variables.
[a] Participants who did not develop diabetes during the study period.
[b] Participants who developed diabetes during the study period.
[c] Mean air pollution levels during the study period.

(Q4) quartiles (Fig. 2; Table S3).

The point estimates of associations between air pollution exposure and incident diabetes were larger in the strata with MDA index score < median (24), daily milk intake < median (6.7 g), daily vegetable intake < median (211.7 g), and daily fruit intake ≥ median (122.1 g) compared to the strata in the corresponding counterparts. However, these differences in the point estimates of association were not statistically significant (all p-values > 0.05) (Fig. 3; Table S4).

Six sensitivity analyses were performed. First, in analyses using baseline $PM_{2.5}$ and NO_2 levels as exposures, point estimates of associations between air pollution and diabetes remained positive, although

Table 2
Daily intake of dietary nutrients by the study participants.

Dietary nutrients	Total participants (n = 14,667)	Participants without diabetes[a] (n = 13,760)	Participants with diabetes[b] (n = 907)
Vitamin A (R.E.)	393.3 ± 273.7	393.0 ± 266.4	398.1 ± 367.0
Retinol (μg)	47.2 ± 50.1	47.4 ± 50.3	44.8 ± 46.7
β-carotene (μg)	2,023.1 ± 1,547.9	2,020.6 ± 1,512.3	2,061.0 ± 2,012.9
Vitamin B1 (μg)	885.0 ± 201.0	884.5 ± 198.0	893.5 ± 241.1
Vitamin B2 (μg)	746.7 ± 260.6	746.7 ± 258.3	745.6 ± 293.5
Niacin (mg)	12.4 ± 2.7	12.4 ± 2.7	12.5 ± 2.8
Vitamin B6 (μg)	1,407.9 ± 356.0	1,407.6 ± 352.8	1,412.2 ± 402.4
Folate (μg)	190.7 ± 86.6	190.7 ± 85.3	191.2 ± 104.6
Vitamin C (mg)	94.0 ± 54.7	93.9 ± 54.4	95.0 ± 59.3
Vitamin E (μg)	6,855.7 ± 2,649.0	6,856.7 ± 2,614.5	6,839.7 ± 3,128.0
Calcium (mg)	378.0 ± 185.3	378.3 ± 184.2	373.7 ± 201.2
Phosphate (mg)	795.6 ± 159.7	795.6 ± 159.1	796.4 ± 168.8
Iron (μg)	8,409.3 ± 2,765.7	8,410.1 ± 2,753.1	8,396.2 ± 2,951.1
Protein (g)	50.8 ± 9.7	50.8 ± 9.7	51.0 ± 10.2
Fat (g)	20.9 ± 9.4	20.9 ± 9.4	20.7 ± 10.1
Carbohydrate (g)	308.5 ± 25.4	308.5 ± 25.3	308.6 ± 27.2
Sodium (mg)	2,590.9 ± 1,372.3	2,587.2 ± 1,360.6	2,647.1 ± 1,539.3
Potassium (mg)	2,000.4 ± 722.3	1,999.6 ± 716.9	2,012.6 ± 799.4
Zinc (ng)	6,865.0 ± 1,739.4	6,865.3 ± 1,758.2	6,860.8 ± 1,424.3
Fiber (mg)	5,390.8 ± 2,154.6	5,387.8 ± 2,141.6	5,436.4 ± 2,344.9
Ash (mg)	15.5 ± 10.2	15.5 ± 10.1	16.0 ± 11.0
Cholesterol (mg)	121.9 ± 99.3	122.0 ± 99.4	119.4 ± 98.1

Abbreviation: R.E., retinol equivalent.
Values are presented as mean ± standard deviation.

Table 3
Associations[a] of $PM_{2.5}$ and NO_2 levels with the development of diabetes.

	Total	Sex[b]		Body mass index[c]	
		Men	Women	<23 kg/m^2	≥23 kg/m^2
	HR (95 % CI)	HR (95 % CI)	HR (95 % CI)	HR (95 % CI)	HR (95 % CI)
$PM_{2.5}$	1.49 (1.11, 2.00)	1.28 (0.88, 1.85)	1.43 (1.01, 2.03)	2.46 (1.24, 4.90)	1.17 (0.89, 1.54)
NO_2	1.29 (1.12, 1.49)	1.22 (1.00, 1.48)	1.32 (1.09, 1.59)	2.04 (1.42, 2.91)	1.13 (0.98, 1.30)

Abbreviations: HR, hazard ratio; CI, confidence interval.
The results are presented per 10 $\mu g/m^3$ for $PM_{2.5}$ exposure and 10 ppb for NO_2 exposure.
[a] Estimated from Cox regression models, adjusted for sex, monthly household income, educational levels, cigarette smoking, alcohol consumption, regular physical activity, Mini Dietary Assessment index score, and body mass index, with a random effect of survey sites. Sex was not adjusted in analyses stratified by sex. Body mass index was not adjusted in the analyses stratified by body mass index.
[b] p-values for interaction were 0.80 for $PM_{2.5}$ and 0.90 for NO_2.
[c] p-values for interaction were 0.24 for $PM_{2.5}$ and 0.01 for NO_2.

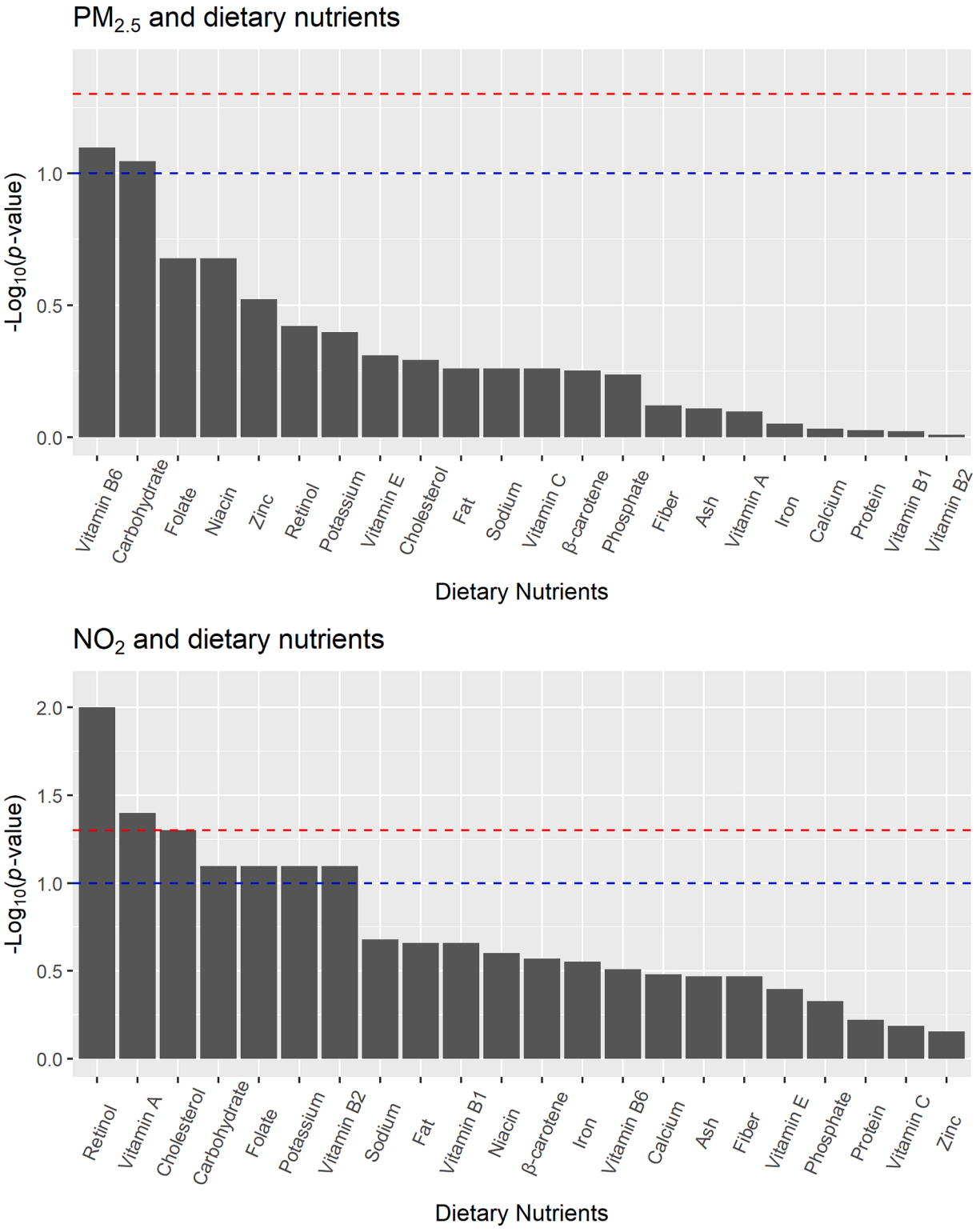

Fig. 1. *p*-values for interactions between air pollution and dietary nutrients. The red and blue lines indicate a *p*-value of 0.05 and 0.10, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

they were smaller than the main results (Table S5). In addition, these analyses identified the interactions between NO_2 levels and retinol or cholesterol, but not vitamin A, and a new interaction between $PM_{2.5}$ and vitamin A (Table S6). Second, in the two-pollutant model, NO_2 levels were found to be associated with the occurrence of diabetes (HR = 1.28, 95 % CI: 1.07, 1.54). However, although the point estimate of the association between $PM_{2.5}$ and diabetes was also positive, CI was wide and included 1 (HR = 1.28, 95 % CI: 0.93, 1.76). Third, the association between air pollution and diabetes was robust in analyses not adjusted for monthly household income (HR = 1.51, 95 % CI: 1.13, 2.02 for $PM_{2.5}$; HR = 1.30, 95 % CI: 1.13, 1.51 for NO_2). The results of the interaction analyses did not change appreciably (Table S7). Fourth, when we excluded 789 individuals who reported taking any nutritional supplements, the association between air pollution and diabetes

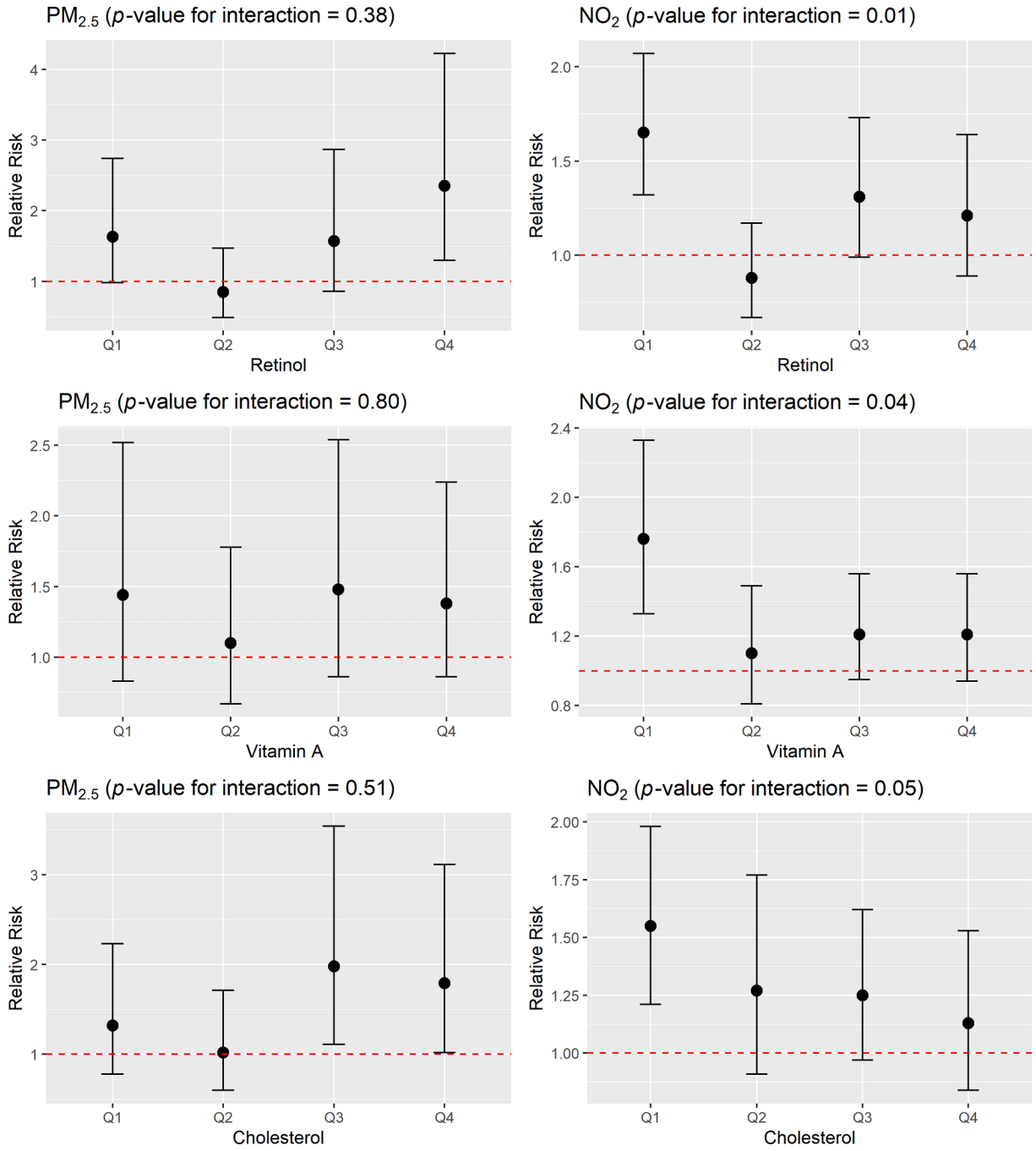

Fig. 2. Associations between air pollution exposure and development of diabetes in each quartile of dietary nutrients that demonstrated interactions with air pollution. The results were estimated from Cox regression models, adjusted for sex, monthly household income, educational levels, cigarette smoking, alcohol consumption, regular physical activity, Mini Dietary Assessment index score, and body mass index, with a random effect of survey sites. Abbreviation: Q, quartile.

remained unchanged (HR = 1.38, 95 % CI: 1.04, 1.84 for $PM_{2.5}$; HR = 1.23, 95 % CI: 1.08, 1.40 for NO_2). Interaction between NO_2 levels and retinol was still observed after excluding those taking nutritional supplements (p-value for interaction = 0.01). The interactions between NO_2 and vitamin A (p-value for interaction = 0.06) or cholesterol (p-value for interaction = 0.07) were identified as marginally significant, possibly due to reduced sample size (Table S8). Fifth, in analyses not adjusted for BMI, robust results were found for the associations between air pollution and diabetes (HR = 1.49, 95 % CI: 1.11, 2.01 for $PM_{2.5}$; HR = 1.29, 95 % CI: 1.11, 1.49 for NO_2) and their interactions with dietary nutrients (Table S9). Sixth, the results did not change appreciably in models not adjusted for MDA index score for the associations between air pollution and diabetes (HR = 1.49, 95 % CI: 1.12, 1.99 for $PM_{2.5}$; HR = 1.28, 95 % CI: 1.12, 1.47 for NO_2) and the interactions between air pollution and dietary nutrients (Table S10).

4. Discussion

Among 28,227 community-dwelling Korean adults aged 40–69 years, $PM_{2.5}$ and NO_2 levels were associated with an increased risk of diabetes development. We identified the interactions between NO_2 levels and dietary intake of retinol, vitamin A, and cholesterol for the development of diabetes. The association between NO_2 levels and diabetes occurrence was stronger among individuals with a lower intake of

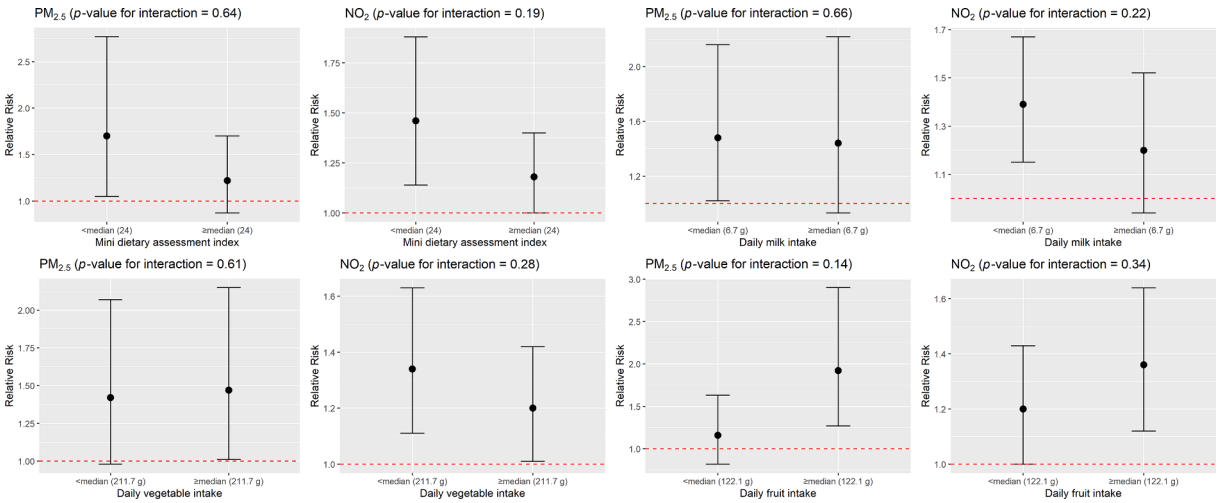

Fig. 3. Associations between air pollution exposure and development of diabetes according to the median values for daily intake of selected food items and median Mini Dietary Assessment index score. The results were estimated from Cox regression models, adjusted for sex, monthly household income, educational levels, cigarette smoking, alcohol consumption, regular physical activity, Mini Dietary Assessment index score (not included as a covariate in the analyses stratified by this score), and body mass index, with a random effect of survey sites.

these nutrients than those with a higher intake. However, no interaction was found between $PM_{2.5}$ and the 22 investigated dietary nutrients. Point estimates of the associations between air pollution and incident diabetes were larger among individuals with lower MDA index scores, lower milk and vegetable intake, and higher fruit intake compared to their counterparts.

In a study using data from the UK Biobank, the association between air pollution exposure (including $PM_{2.5}$ and NO_2) and diabetes development was reportedly stronger among study participants with insufficient dietary intake [<2 vitamins meeting the British Adult recommended nutrient intake (RNI)] of antioxidant vitamins (vitamins A, C, and E) (Li et al., 2022). This previous study also found that the point estimates of associations of $PM_{2.5}$ and NO_2 with diabetes development were larger among individuals with insufficient dietary intake (<RNI) of vitamin A, consistent with our findings. However, although we did not observe any evidence of interaction between air pollution and dietary intake of vitamin C or E in the present study, associations of $PM_{2.5}$ and NO_2 with diabetes were reported to be stronger among those with insufficient vitamin C intake (<RNI) in the previous study. The previous study also demonstrated that the association between $PM_{2.5}$ and diabetes was stronger among those with insufficient vitamin E intake (<RNI) (Li et al., 2022). Regarding this inconsistency, the UK Biobank study obtained the dietary information of the previous day of the survey using the 24-h recall method. In contrast, the present study obtained the dietary information during the one year using the food frequency questionnaire method, which may target different contexts of dietary factors. In addition, it is notable that dietary vitamin intake levels, especially vitamin A and retinol intake levels, were substantially lower among the study participants of the present study than those of the UK Biobank study (393.3 retinol equivalent vs 954.0 retinol equivalent for vitamin A; 47.2 μg vs 461.0 μg for retinol; 94.0 mg vs 127.0 mg for vitamin C; 6.9 mg vs 10.8 mg for vitamin E) (Perez-Cornago et al., 2021). These lower vitamin A and retinol intake levels compared to the UK Biobank study may be responsible for detecting the interaction of NO_2 with vitamin A and retinol in the present study, possibly due to non-optimal nutrient levels increasing susceptibility to outer insults. Meanwhile, air pollution profiles also differed between the present study and the UK Biobank study, with substantially higher $PM_{2.5}$ levels (27.4 μg/m^3 vs 9.9 μg/m^3) and lower NO_2 levels (15.4 ppb vs 29.4 ppb) in the present study compared to the UK Biobank study. These different air pollution levels might explain the results regarding the detection of interactions between NO_2, while not $PM_{2.5}$, and dietary factors in the present study if overwhelming adverse effects of $PM_{2.5}$ in the present study and NO_2 in the UK Biobank study due to high exposure levels deterred the interaction effects of dietary factors. This hypothesis needs to be explored in future studies with various air pollution exposure levels and comprehensive dietary information. Furthermore, differences in the genetic and cultural backgrounds of the study participants may also have contributed to the inconsistency in the results (non-detection of interactions of NO_2 with vitamin C and E). Finally, the possibility that residual confounding (especially by factors related to survey sites) and chance finding due to multiple testing may be responsible for the inconsistency in the results cannot be excluded.

Epidemiological evidence demonstrating the modifying effects of dietary factors, especially vegetable and fruit-rich diets and Mediterranean diets, on air pollution impacts is accumulating (Barthelemy et al., 2020). Adherence to healthy dietary patterns assessed using a healthy diet score attenuated the association between air pollution exposure and all-cause mortality (Wang et al., 2022). The association between long-term exposure to $PM_{2.5}$ and poor cognitive function was found to be weaker among individuals with vegetable and fruit-rich diets, assessed using a plant-based diet index (Zhu et al., 2022). Association between $PM_{2.5}$ exposure and decreased brain white matter volume was observed among women with a lower score of the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) dietary pattern, but was absent among those with a higher score (Chen et al., 2021).

Only a few studies have investigated the interaction between air pollution and dietary factors on diabetes-related outcomes (Li et al., 2022; Lim et al., 2018; Yang et al., 2018). Although previous studies have demonstrated weaker associations between air pollution exposure and diabetes prevalence or diabetes mortality among individuals with higher fruit consumption (Lim et al., 2018; Yang et al., 2018), we found that the point estimates of the association between air pollution and diabetes incidence were larger among those with daily fruit intake ≥ median (122.1 g) compared to those with daily fruit intake < median. The reason for this inconsistency remains unclear. However, this inconsistency might be explained, at least in part, by differences in the types of fruits commonly consumed (e.g., high glycemic index fruits, such as watermelons, pineapples, and bananas vs low glycemic index fruits, such as avocados, blackberries, and cherries) and related cultural and sociodemographic characteristics of the study populations. Since we could not further assess this possibility due to a lack of necessary information in previous studies and the insufficient power of this study, future studies should consider the types of specific fruits as well as the

amount of total fruit intake.

Vitamin A, a fat-soluble micronutrient including retinol, retinal, and retinoic acid, should be provided to humans through diet because it is not produced in the human body. Several rodent studies have demonstrated that vitamin A may reduce hepatic necrosis and fibrosis after liver damage due to outer insults (e.g., carbon tetrachloride), possibly by regulating immunological responses in the liver tissue and inhibiting the transformation of Ito cells into myofibroblasts (Freund and Gotthardt, 2017). However, the point estimates of the associations between air pollution and diabetes did not decrease monotonically as the intakes of retinol and vitamin A increased (they tend to be larger among individuals with both higher and lower intakes of retinol and vitamin A; Fig. 2), suggesting potential additional pathways not involving immunological responses. These non-monotonic changes in the associations between air pollution and diabetes by retinol and vitamin A intake levels might suggest optimal nutrient levels (around Q2 levels in the present study population) regarding homeostasis of body functions and resilience to outer insults, given the essential roles of these nutrients. Therefore, higher and lower nutrient intake levels than optimal levels might increase the susceptibility to air pollution exposure. Although the underlying mechanisms of the observed interactions remain unknown and should be elucidated in future studies, given the critical role of the liver in glucose homeostasis and diabetes development (Postic et al., 2004), the potentially beneficial effects of vitamin A (and retinol) on hepatic necrosis and fibrosis might explain the findings of this study, in part.

Although adequate cholesterol intake is important because of its role in constructing cell membranes and synthesizing steroid hormones, vitamin D, and bile acids (Lecerf and de Lorgeril, 2011), the cholesterol intake levels in the present study (121.9 mg/day) were substantially lower than the recommended dietary intake levels for Koreans (300 mg/day) (Health and Welfare, 2015). We speculate that participants with lower dietary cholesterol intake in this study may experience disturbances in the regulation of body functions, resulting in higher vulnerability to air pollution exposure and non-optimal glucose homeostasis (Seneff et al., 2011). In this vein, study participants with higher dietary cholesterol intake (closer to the recommended levels) may be more resilient to air pollution exposure than those with lower dietary cholesterol intake. However, the observed interaction between NO_2 and cholesterol intake might be driven by the interaction between NO_2 and retinol or vitamin A intake due to the dietary sources being common to cholesterol and retinol (or vitamin A) (e.g., eggs, dairy products, and liver) (Tanumihardjo et al., 2016; Zhong, 2019). In addition, because a statistically significant interaction was not found after adjustment for multiple comparisons (FDR p-value > 0.05), we should also consider the possibility that these results regarding cholesterol intake might be chance findings. Therefore, these results should be interpreted with caution and confirmed in future studies before drawing any conclusions.

Although we found stronger associations between air pollution and diabetes among individuals with BMI < 23 kg/m^2 compared to those with BMI ≥ 23 kg/m^2, many previous studies have reported that the associations between air pollution exposure and diabetes-related outcomes are stronger among overweight or obese individuals (Li et al., 2021; Yang et al., 2020). The reason for this inconsistency is not apparent. However, first, the findings of this study may be due to a random chance, given that we performed many statistical analyses. Second, this inconsistency may also be explained by the overwhelming adverse effects of higher BMI in this study population (Table 1), resulting in no further increase (saturation) in diabetes risk due to air pollution exposure. Third, because this study is an observational study, the possibility that unknown or unmeasured factors closely related to BMI (e.g., socioeconomic status, contextual factors, and health-seeking behaviors) rather than BMI per se may be responsible for these findings cannot be excluded, although a range of covariates was considered.

This study has a few limitations. First, exposure misclassification may have occurred because individual air pollution exposure was estimated without considering time-activity patterns and indoor air pollution levels (Woo et al., 2022). In addition, because this study employed air pollution data adjusted for normalized difference vegetation index, which measures the portion of private greenery and is generally considered to be related to socioeconomic status; the results of this study should be interpreted to capture the air pollution impact per se independent of the impact of greenness and indirectly socioeconomic status. Because adjusting for normalized difference vegetation index is not a common practice for air pollution modeling, the results of this study should be cautiously compared to those of other air pollution epidemiology literature. Furthermore, although traffic-related air pollution, which is reflected more directly by NO_2 than $PM_{2.5}$, has been associated with a higher risk of diabetes-related outcomes in several studies (Brook et al., 2008; Krämer et al., 2010; Teichert et al., 2013), more prominent interactions between NO_2 exposure and dietary factors on diabetes observed in the present study were unexpected. Notably, a recent Korean study using a nationally representative sample found that fasting glucose levels increased more greatly by an interquartile range increase in NO_2 than $PM_{2.5}$ or PM_{10} (Hwang et al., 2020), which might be explained by heterogeneity of particulate matter chemical composition and resulting health effects across different areas at least in part (Dominici et al., 2015). Alternatively, since prediction models and leveraged data were different for $PM_{2.5}$ and NO_2 (Woo et al., 2022), exposure misclassification levels and patterns may differ by air pollutants. Therefore, the findings of more prominent interactions of dietary nutrients with NO_2 compared to $PM_{2.5}$ should be elaborated more cautiously and further assessed in other contexts. Second, data limitations made it impossible to differentiate between type 1 and type 2 diabetes in this study. However, because the prevalence of type 1 diabetes is estimated to be 0.017–0.021 % of the entire population and < 1 % of all diabetes patients in Korea (Song et al., 2016), we assumed that majority of the cases in this study were of type 2 diabetes. Third, diet can reflect multiple facets of socioeconomic status and lifestyle. Therefore, to control for possible confounding by socioeconomic status and lifestyle and to assess the dietary nutrient effects per se, we adjusted the models for extensive potential confounders, including monthly household income, educational levels, cigarette smoking, alcohol consumption, regular physical activity, and MDA index. Fourth, however, concerns regarding residual confounding by traffic noise and pollutants possibly included in foods and/or packages, like pesticides, heavy metals, per- and polyfluoroalkyl substances, and phthalates remain (Thompson and Darwish, 2019). Fifth, the present study was conducted among adults residing in medium-sized cities and districts of Korea whose socioeconomic status was relatively low. Therefore, these results may not be generalizable to individuals with higher socioeconomic status and different dietary patterns. Sixth, because statistically significant interactions were not found after multiple testing correction, some of the observed associations (e.g., protective effects of cholesterol intake on the adverse air pollution impact) might be due to chance finding. Therefore, the results of this study should be interpreted in light of this inflated alpha error and possible false findings. However, we presented the results from analyses not adjusted for multiple comparisons as the main results, following an epidemiological view advocating non-adjustment of multiple comparisons in empirical research due to reasons including concern of increased type II error (Rothman, 1990).

However, the present study also has the following notable merits. First, this study provides one of the first pieces of evidence on the modifying effects of dietary factors on the association between air pollution and diabetes-related outcomes (Li et al., 2022; Lim et al., 2018; Yang et al., 2018). Furthermore, to our knowledge, only one other study has investigated the interaction between air pollution exposure and dietary nutrients on the development of diabetes (Li et al., 2022). Second, the cohort study design (and the usage of dietary information during the baseline survey) is an important strength of this study, given that diabetic patients are likely to change their dietary patterns and habits. Third, among studies assessing the interactions between air pollution

and dietary factors on diabetes-related outcomes, this investigation considered the most comprehensive dietary factors to date (22 dietary nutrients, MDA index, and dietary intake of milk, dairy products, eggs, vegetables, and fruits).

5. Conclusions

Long-term exposure to $PM_{2.5}$ and NO_2 was associated with an increased risk of diabetes among community-dwelling adults. NO_2 levels interacted with dietary intake of retinol, vitamin A, and cholesterol in the context of diabetes development. Associations between NO_2 levels and incident diabetes were stronger among individuals with a lower dietary intake of these nutrients compared to those with a higher intake. The results of this study suggest the possibility of complementary population (air quality control policies) and individual-level (diet interventions) prevention strategies, which might be particularly beneficial to susceptible populations, such as individuals with underlying diseases and the elderly. If future studies confirm the findings of this study, adequate intake of dietary nutrients, such as retinol, vitamin A, and cholesterol, from various food items in a balanced diet, might be suggested as an individual-level dietary intervention to prevent diabetes in a setting wherein the reduction of air pollution levels cannot be achieved in a short time frame.

Data availability

The authors do not have permission to share the data used in this study.

CRediT authorship contribution statement

Moon-Kyung Shin: Conceptualization, Data curation, Investigation, Methodology, Validation, Writing – original draft. **Kyoung-Nam Kim:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Software, Supervision, Visualization, Writing – review & editing.

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.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.107908.

References

Ahn, Y., Kwon, E., Shim, J.E., Park, M.K., Joo, Y., Kimm, K., Park, C., Kim, D.H., 2007. Validation and reproducibility of food frequency questionnaire for Korean genome epidemiologic study. Eur. J. Clin. Nutr. 61, 1435–1441. https://doi.org/10.1038/sj.ejcn.1602657.

Amarasinghe, S., Balakumar, S., Arasaratnam, V., 2015. Prevalence and risk factors of diabetes mellitus among adults in Jaffna District. Ceylon Med. J. 60, 107–110. https://doi.org/10.4038/cmj.v60i3.8191.

Barthelemy, J., Sanchez, K., Miller, M.R., Khreis, H., 2020. New opportunities to mitigate the burden of disease caused by traffic related air pollution: antioxidant-rich diets and supplements. Int. J. Environ. Res. Public Health 17, E630. https://doi.org/10.3390/ijerph17020630.

Benjamini, Y., Hochberg, Y., 1995. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. J. Roy. Stat. Soc.: Ser. B (Methodol.) 57, 289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x.

Brook, R.D., Jerrett, M., Brook, J.R., Bard, R.L., Finkelstein, M.M., 2008. The relationship between diabetes mellitus and traffic-related air pollution. J. Occup. Enviro.n Med. 50, 32–38. https://doi.org/10.1097/JOM.0b013e31815dba70.

Chen, C., Hayden, K.M., Kaufman, J.D., Espeland, M.A., Whitsel, E.A., Serre, M.L., Vizuete, W., Orchard, T.S., Wang, X., Chui, H.C., D'Alton, M.E., Chen, J.-C., Kahe, K., 2021. Adherence to a MIND-Like Dietary Pattern, Long-Term Exposure to Fine Particulate Matter Air Pollution, and MRI-Based Measures of Brain Volume: the Women's Health Initiative Memory Study-MRI. Environ.. Health Perspect. 129, 127008 https://doi.org/10.1289/EHP8036.

Dominici, F., Wang, Y., Correia, A.W., Ezzati, M., Pope, C.A., Dockery, D.W., 2015. Chemical Composition of Fine Particulate Matter and Life Expectancy: In 95 US Counties Between 2002 and 2007. Epidemiology 26, 556–564. https://doi.org/10.1097/EDE.0000000000000297.

Freund, C., Gotthardt, D.N., 2017. Vitamin A deficiency in chronic cholestatic liver disease: Is vitamin A therapy beneficial? Liver Int.. 37, 1752–1758. https://doi.org/10.1111/liv.13433.

Heald, A.H., Stedman, M., Davies, M., Livingston, M., Alshames, R., Lunt, M., Rayman, G., Gadsby, R., 2020. Estimating life years lost to diabetes: outcomes from analysis of national diabetes audit and office of national statistics data. Cardiovasc. Endocrinol. Metab. 9, 183–185. https://doi.org/10.1097/XCE.0000000000000210.

Health, M. of, Welfare, T.K.N.S., 2015. Dietary reference intakes for Koreans 2015.

Hwang, M.-J., Kim, J.-H., Koo, Y.-S., Yun, H.-Y., Cheong, H.-K., 2020. Impacts of ambient air pollution on glucose metabolism in Korean adults: a Korea National Health and Nutrition Examination Survey study. Environ.. Health 19, 70. https://doi.org/10.1186/s12940-020-00623-9.

Kim, W.-Y., Cho, M.-S., Lee, H.-S., 2003. Development and validation of mini dietary assessment index for Koreans. The Korean J. Nutrition 83–92.

Kim, Y., Han, B.-G., KoGES group, 2017. Cohort Profile: The Korean Genome and Epidemiology Study (KoGES) Consortium. Int J Epidemiol 46, 1350. https://doi.org/10.1093/ije/dyx105.

Krämer, U., Herder, C., Sugiri, D., Strassburger, K., Schikowski, T., Ranft, U., Rathmann, W., 2010. Traffic-related air pollution and incident type 2 diabetes: results from the SALIA cohort study. Environ.. Health Perspect 118, 1273–1279. https://doi.org/10.1289/ehp.0901689.

Lecerf, J.-M., de Lorgeril, M., 2011. Dietary cholesterol: from physiology to cardiovascular risk. Br J. Nutr. 106, 6–14. https://doi.org/10.1017/S0007114511000237.

Li, H., Cai, M., Li, H., Qian, Z.M., Stamatakis, K., McMillin, S.E., Zhang, Z., Hu, Q., Lin, H., 2022. Is dietary intake of antioxidant vitamins associated with reduced adverse effects of air pollution on diabetes? Findings from a large cohort study. Ecotoxicol. Environ. Saf. 246, 114182 https://doi.org/10.1016/j.ecoenv.2022.114182.

Li, X., Wang, M., Song, Y., Ma, H., Zhou, T., Liang, Z., Qi, L., 2021. Obesity and the relation between joint exposure to ambient air pollutants and incident type 2 diabetes: a cohort study in UK Biobank. PLoS Med. 18, e1003767.

Lim, C.C., Hayes, R.B., Ahn, J., Shao, Y., Silverman, D.T., Jones, R.R., Garcia, C., Thurston, G.D., 2018. Association between long-term exposure to ambient air pollution and diabetes mortality in the US. Environ. Res. 165, 330–336. https://doi.org/10.1016/j.envres.2018.04.011.

Luc, K., Schramm-Luc, A., Guzik, T.J., Mikolajczyk, T.P., 2019. Oxidative stress and inflammatory markers in prediabetes and diabetes. J. Physiol. Pharmacol. 70 https://doi.org/10.26402/jpp.2019.6.01.

Perez-Cornago, A., Pollard, Z., Young, H., van Uden, M., Andrews, C., Piernas, C., Key, T.J., Mulligan, A., Lentjes, M., 2021. Description of the updated nutrition calculation of the Oxford WebQ questionnaire and comparison with the previous version among 207,144 participants in UK Biobank. Eur. J. Nutr. 60, 4019–4030. https://doi.org/10.1007/s00394-021-02558-4.

Postic, C., Dentin, R., Girard, J., 2004. Role of the liver in the control of carbohydrate and lipid homeostasis. Diabetes Metab. 30, 398–408. https://doi.org/10.1016/s1262-3636(07)70133-7.

Rothman, K.J., 1990. No adjustments are needed for multiple comparisons. Epidemiology 1, 43–46.

Seneff, S., Wainwright, G., Mascitelli, L., 2011. Is the metabolic syndrome caused by a high fructose, and relatively low fat, low cholesterol diet? Arch. Med. Sci. 7, 8–20. https://doi.org/10.5114/aoms.2011.20598.

Song, S.O., Song, Y.D., Nam, J.Y., Park, K.H., Yoon, J.H., Son, K.M., Ko, Y., Lim, D.H., 2016. Epidemiology of Type 1 Diabetes Mellitus in Korea through an Investigation of the National Registration Project of Type 1 diabetes for the reimbursement of glucometer strips with additional analyses using claims data. Diabetes Metab. J. 40, 35–45. https://doi.org/10.4093/dmj.2016.40.1.35.

Sun, H., Saeedi, P., Karuranga, S., Pinkepank, M., Ogurtsova, K., Duncan, B.B., Stein, C., Basit, A., Chan, J.C.N., Mbanya, J.C., Pavkov, M.E., Ramachandaran, A., Wild, S.H., James, S., Herman, W.H., Zhang, P., Bommer, C., Kuo, S., Boyko, E.J., Magliano, D.J., 2022. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res. Clin. Pract. 183, 109119 https://doi.org/10.1016/j.diabres.2021.109119.

Tanumihardjo, S.A., Russell, R.M., Stephensen, C.B., Gannon, B.M., Craft, N.E., Haskell, M.J., Lietz, G., Schulze, K., Raiten, D.J., 2016. Biomarkers of Nutrition for Development (BOND)-Vitamin A Review. J. Nutr. 146, 1816S–S1848. https://doi.org/10.3945/jn.115.229708.

Teichert, T., Vossoughi, M., Vierkötter, A., Sugiri, D., Schikowski, T., Schulte, T., Roden, M., Luckhaus, C., Herder, C., Krämer, U., 2013. Association between traffic-related air pollution, subclinical inflammation and impaired glucose metabolism: results from the SALIA study. PLoS One 8, e83042.

Thompson, L.A., Darwish, W.S., 2019. Environmental chemical contaminants in food: review of a global problem. J. Toxicol. 2345283. https://doi.org/10.1155/2019/2345283.

Wang, B., Xu, D., Jing, Z., Liu, D., Yan, S., Wang, Y., 2014. Effect of long-term exposure to air pollution on type 2 diabetes mellitus risk: a systemic review and meta-analysis of cohort studies. Eur. J. Endocrinol. 171, R173–R182. https://doi.org/10.1530/EJE-14-0365.

Wang, M., Zhou, T., Song, Q., Ma, H., Hu, Y., Heianza, Y., Qi, L., 2022. Ambient air pollution, healthy diet and vegetable intakes, and mortality: a prospective UK Biobank study. Int. J. Epidemiol. 51, 1243–1253. https://doi.org/10.1093/ije/dyac022.

Willett, W.C., Howe, G.R., Kushi, L.H., 1997. Adjustment for total energy intake in epidemiologic studies. Am J Clin Nutr 65, 1220S-1228S; discussion 1229S-1231S. https://doi.org/10.1093/ajcn/65.4.1220S.

Woo, H.D., Song, D.S., Choi, S.H., Park, J.K., Lee, K., Yun, H.-Y., Choi, D.-R., Koo, Y.-S., Park, H.-Y., 2022. Integrated dataset of the Korean Genome and Epidemiology Study cohort with estimated air pollution data. Epidemiol. Health, e2022071. https://doi.org/10.4178/epih.e2022071.

Yang, B.-Y., Fan, S., Thiering, E., Seissler, J., Nowak, D., Dong, G.-H., Heinrich, J., 2020. Ambient air pollution and diabetes: a systematic review and meta-analysis. Environ. Res. 180, 108817 https://doi.org/10.1016/j.envres.2019.108817.

Yang, Y., Guo, Y., Qian, Z.M., Ruan, Z., Zheng, Y., Woodward, A., Ai, S., Howard, S.W., Vaughn, M.G., Ma, W., Wu, F., Lin, H., 2018. Ambient fine particulate pollution associated with diabetes mellitus among the elderly aged 50 years and older in China. Environ. Pollut. 243, 815–823. https://doi.org/10.1016/j.envpol.2018.09.056.

Zhang, J., Cai, L., Gui, Z., Wang, S., Zeng, X., Lai, L., Lv, Y., Tan, K., Wang, H., Huang, C., Chen, Y., 2020. Air pollution-associated blood pressure may be modified by diet among children in Guangzhou, China. J. Hypertens. 38, 2215–2222. https://doi.org/10.1097/HJH.0000000000002521.

Zhong, V.W., 2019. Eggs, dietary cholesterol, and cardiovascular disease: the debate continues. J. Thorac. Dis. 11, E148–E150. https://doi.org/10.21037/jtd.2019.09.40.

Zhu, A., Chen, H., Shen, J., Wang, X., Li, Z., Zhao, A., Shi, X., Yan, L., Zeng, Y., Yuan, C., Ji, J.S., 2022. Interaction between plant-based dietary pattern and air pollution on cognitive function: a prospective cohort analysis of Chinese older adults. Lancet Reg. Health West Pac. 20, 100372 https://doi.org/10.1016/j.lanwpc.2021.100372.