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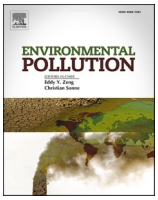

Long-term air pollution exposure and diabetes risk in American older adults: A national secondary data-based cohort study.☆

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ABSTRACT

Type 2 diabetes is a major public health concern. Several studies have found an increased diabetes risk associated with long-term air pollution exposure. However, most current studies are limited in their generalizability, exposure assessment, or the ability to differentiate incidence and prevalence cases. We assessed the association between air pollution and first documented diabetes occurrence in a national U.S. cohort of older adults to estimate diabetes risk. We included all Medicare enrollees 65 years and older in the fee-for-service program, part A and part B, in the contiguous United States (2000–2016). Participants were followed annually until the first recorded diabetes diagnosis, end of enrollment, or death (264, 869, 458 person-years). We obtained annual estimates of fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), and warm-months ozone (O_3) exposures from highly spatiotemporally resolved prediction models. We assessed the simultaneous effects of the pollutants on diabetes risk using survival analyses. We repeated the models in cohorts restricted to ZIP codes with air pollution levels not exceeding the national ambient air quality standards (NAAQS) during the study period. We identified 10, 024, 879 diabetes cases of 41, 780, 637 people (3.8% of person-years). The hazard ratio (HR) for first diabetes occurrence was 1.074 (95% CI 1.058; 1.089) for 5 $\mu g/m^3$ increase in $PM_{2.5}$, 1.055 (95% CI 1.050; 1.060) for 5 ppb increase in NO_2, and 0.999 (95% CI 0.993; 1.004) for 5 ppb increase in O_3. Both for NO_2 and $PM_{2.5}$ there was evidence of non-linear exposure-response curves with stronger associations at lower levels ($NO_2 \leq 36$ ppb, $PM_{2.5} \leq 8.2$ $\mu g/m^3$). Furthermore, associations remained in the restricted low-level cohorts. The O_3-diabetes exposure-response relationship differed greatly between models and require further investigation. In conclusion, exposures to $PM_{2.5}$ and NO_2 are associated with increased diabetes risk, even when restricting the exposure to levels below the NAAQS set by the U.S. EPA.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a major public health concern rising rapidly, with the number of people diagnosed with the disease worldwide more than doubling in the past 20 years (Zimmet et al., 2014). T2DM may cause major complications, including blindness, cardiovascular damage, and premature mortality (Papatheodorou et al., 2016), it is therefore important to identify determinants of the disease.

Like many chronic conditions, type I diabetes mellitus (T1DM) and T2DM have a genetic component, but genetics alone explains only a small portion of the variance. Studies show that in T2D, which represents over 99% of diabetes cases globally (Rajagopalan and Brook, 2012), genetics and environmental exposures play a significant role (Kaprio et al., 1992). In the last few decades, environmental research focused primarily on behavioral factors, such as inactivity and diet. However, in recent years, cardiometabolic risk was linked to various

Abbreviations: CCW, Chronic Conditions Warehouse; NAAQS, national ambient air quality standards; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus.

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environmental components, including the social environment (Basile Ibrahim et al., 2021; Khan et al., 2021), environmental pollutants (Dendup et al., 2018; Rajagopalan and Brook, 2012), and, more specifically, air pollution (Andersen et al., 2012; Brook, 2008; Brook et al., 2010; Chandrabose et al., 2019; Y Li et al., 2019; Park and Wang, 2014).

Several studies have found an increased diabetes risk associated with air pollution exposure, with most studies focusing on fine particulate matter ($PM_{2.5}$) exposure (Yang et al., 2020). A study of 4.5 million US veterans have found $PM_{2.5}$ exposure to be associated with excess burden of death due to T2DM (Bowe et al., 2019). Another study in the UK have found higher risk for T2DM incidence and complications associated with $PM_{2.5}$ exposure (Zou et al., 2022). Finally, a 2020 meta-analysis of 11 studies concluded that each ten $\mu g/m^3$ difference in long-term $PM_{2.5}$ exposure was associated with 10% higher T2DM incidence risk and 8% higher T2DM prevalence risk (Yang et al., 2020).

Fewer studies have investigated the association between nitrogen dioxide (NO_2) exposure and diabetes. For example, a US study among the National Institutes of Health American Association of Retired Persons Diet and Health Study found increased diabetes mortality risk associated with long term NO_2 exposure (Lim et al., 2018). Additionally, a 2020 meta-analysis of 7 studies have found a 7% increase in T2DM prevalence associated with ten $\mu g/m^3$ increase in long-term NO_2 exposure. No significant association was observed with diabetes incidence (Yang et al., 2020). Diabetes, $PM_{2.5}$, and NO_2 associations were observed in other systematic reviews as well (Eze et al., 2015; Liu et al., 2019). However, evidence regarding ozone (O_3) is scarce, with studies showing inconsistent results (LaKind et al., 2021; Yang et al., 2020).

In this study, we aim to assess the association between long-term air pollution exposure and first documented diabetes occurrence. Our study combines the benefits of a national large-scale study with the ability to measure disease incidence. Studies of long-term exposures to air pollution have generally relied either on large administrative datasets using hospital admissions data to identify chronic diseases (Zanobetti et al., 2009), or on cohort studies, with detailed information on personal predictors but with participant numbers only in the thousands (Puett et al., 2011). These smaller cohorts are generally limited to a sample of volunteers and are therefore less representative of the total population (Grundy et al., 1998). In this national analysis, we use the Medicare Chronic Conditions Warehouse (CCW) data to approximate disease incidence. Unlike previous studies that did not capture diagnoses of non-emergent visits, in CCW, the first occurrence of chronic conditions can be identified using an algorithm that incorporates information from inpatient, outpatient, skilled nursing facility, home health, and carrier (physician) claims (warehouse 2015). With this information, we will approximate incidence cases in a population-based cohort with tens of millions of older adults in the U.S.

Additionally, our use of highly spatiotemporally resolved exposure models reduces bias due to exposure misclassification. In addition, unlike most national studies or chronic air pollution effects, we use comprehensive chronic conditions data on Medicare enrollees across the U.S. Finally, we focus on the effect of air pollution exposure below the U.S. Environmental Protection Agency (EPA) national ambient air quality standards (NAAQS) and provide robust scientific evidence for decision-makers to use in the review of air quality standards (Di et al., 2020).

2. Methods

2.1. Study population

Medicare is the largest health insurance provider in the U.S., covering over 95% of the population over 65 years of age. It is an open cohort that enrolls new members every year and contains a representative sample of older adult population in the U.S. We included all Medicare enrollees who were 65 years and older in the fee-for-service (FFS) program, part A and part B, in the contiguous U.S. between the years 2000–2016. Medicare part A provides inpatient (i.e., hospital) coverage and Medicare part B provides outpatient coverage. Most beneficiaries receive these services through the FFS program offered through the federal government. We limited the data to person-years included in these programs because the algorithm used to identify chronic conditions utilizes claims covered by these three programs. We entered participants into the cohort on January 1 after they became Medicare participants and followed participants for each calendar year within the observation period until the first recorded diabetes diagnosis, end of enrollment in either of the mentioned Medicare programs, or death – whichever came first. Medicare coverage is renewed annually and annual enrollment in these three programs is documented for each participant, allowing us to identify individuals who are no longer enrolled. To avoid gaps in follow-up, once enrollment in the FFS, Medicare part A or B programs was terminated, those participants were no longer included in the cohort even if they renewed their enrollment in later years within the observation period.

This study was approved by the Center for Medicare and Medicade services, 2015 (CMS) under the data use agreement (#RSCH-2020-55, 733), the Institutional Review Board of Emory University (#STUDY00000316), and the Institutional Review Board of Mount Sinai (STUDY 20–01344), and a waiver of informed consent was granted. The Medicare dataset was stored and analyzed in the Rollins High-Performance Computing (HPC) Cluster at Emory University, in compliance with Health Insurance Portability and Accountability Act (HIPAA).

2.2. Outcome

We obtained information on diabetes status from the CCW database. This database has been used in many studies evaluating chronic conditions among the older adult population in the U.S (Lochner et al., 2013; Shi et al., 2020; Shi et al., 2021b). The CCW algorithms were developed based on prior research using Medicare claims data to identify various chronic conditions. Diabetes is identified using an algorithm that incorporates claims indicating that an individual received a healthcare service for diabetes. The algorithm combines inpatient, outpatient, skilled nursing facilities, home health claims, or carrier claims (primarily doctor visits) (warehouse 2015). To be diagnosed with diabetes, beneficiaries must have at least one claim with the international classification of disease codes of diabetes (ICD-9 or ICD-10) from either inpatient, skilled nursing facility, home health, or part B services within two years. This algorithm was found to have 71.5% sensitivity and 97.8% specificity (Hebert et al., 1999). To better approximate incident cases, we excluded individuals diagnosed with diabetes before or in their first year of enrollment.

2.3. Exposures

Our study was focused on three principal air pollutants linked to cardiometabolic health: $PM_{2.5}$, O_3, and NO_2. $PM_{2.5}$ are fine inhalable particles, smaller than 2.5 μm, comprising a mixture of solids and liquids. NO_2 is an air pollutant that originates mostly from traffic and high-temperature combustion processes (Lim et al., 2013). O_3 at the ground level is formed naturally and following a chemical reaction - where air pollutants emitted from sources such as traffic, industry, and wildfires (i.e., nitrogen oxides and volatile organic compounds) react with sunlight and organic gases, principally from vegetation (Lange et al., 2018).

We obtained predictions of $PM_{2.5}$ (24-h average, $\mu g/m^3$), NO_2 (daily 1-h maximum, ppb) and ozone (daily maximum of 8-h average, ppb) exposures from validated prediction models calibrated to measurements at approximately 2000 monitoring stations using an ensemble of three machine learners (neural network, random forest, and gradient boosting) that provided daily estimates for a 1 km^2 grid of the contiguous U.S. (Di et al., 2019, 2020; Requia et al., 2020). In brief, each machine learning algorithm incorporated more than 100 predictor variables from satellite data, land-use information, weather data, and chemical

transport model simulations. The predictions of the three learners were then integrated using a generalized additive model-based geographically weighted-averaging technique. The model was calibrated using daily pollutants concentrations measured at EPA monitoring sites and demonstrated excellent model performance (average cross-validation $R^2 = 0.89$, 0.84, and 0.86 for annual predictions of $PM_{2.5}$, NO_2, and O_3, respectively). To align with the Medicare data, we aggregated gridded exposures to ZIP codes by averaging daily predictions of grid cells within each ZIP code annually. For ozone, we averaged the exposure only during the warmer months of each year (May–October), a commonly specified time window to examine associations with health outcomes (Wei et al., 2021). We selected this window because ozone formation is increased in warmer months due to its reaction with sunlight.

2.4. Covariates

The Medicare data is a dynamic cohort that includes individual-level information on the participants' sex, race, age, Medicaid eligibility, and date of death. Medicaid is a joint federal and state program that provides health coverage to eligible low-income individuals. This was used in many studies as an indicator for low socioeconomic status (Schwartz et al., 2021; Yitshak-Sade et al., 2019a; Yitshak-Sade et al., 2019b; M. Yitshak-Sade et al., 2020; Yitshak-Sade et al., 2021). We additionally obtained the following ZIP code level covariates from the U.S. Census: median household income, population density, percent home renters, percent of residents with no high school education, and percent of the population self-identified as Black and Hispanic. We obtained data from available U.S. Census years and the annual American Community Survey, and extrapolated values for missing years. We aggregated annual summer, and winter temperature ZIP code means from gridded Daymet 1- km models (DAAC) 2020).

2.5. Statistical analysis

In a secondary data-based study, we investigated the effect of the three air pollutants simultaneously using a cox-equivalent re-parameterized Poisson survival approach (Shi et al., 2020). To allow for strata-specific baseline hazard functions, we stratified the models by follow-up year, calendar year, ZIP code, sex, race (White, Black, other), age, and Medicaid insurance. We calculated diabetes counts in each follow-up year, calendar year, and ZIP code within strata specified by these individual characteristics, using the log of the corresponding total person-time as an offset. This approach is proven to be equivalent to a time-varying cox survival model using the Anderson-Gill formulation (Shi et al., 2020). We used the m-out-n bootstrap method to account for spatial autocorrelation of neighboring ZIP codes. This methods samples ZIP codes randomly for each bootstrap replicate, and estimates statistically robust confidence intervals (Bickel and Götze, 2012). First, we fit a multi-pollutant model using linear terms for the three pollutants. Then, to allow for nonlinear exposure-response curves, we used penalized spline functions for each of the pollutants. We fit three multi-pollutant models in which we used a penalized spline to estimate the exposure-response curve for one pollutant, and linear terms for the adjusted pollutants. We adjusted the models for annual summer and winter mean temperatures, population density, median household income, percent home renters, percent of residents without a high school diploma, and percent of the population self-identified as Black and Hispanic.

To assess the effect of air pollution concentrations below the NAAQS, we created three restricted low-exposure subsets comprised of individuals who were always exposed to exposure levels lower than the national standards within the study period. The first cohort was restricted to individuals only exposed to $PM_{2.5}$ <12 μg/m. The second cohort was restricted to individuals only exposed to $NO_2 < 53$ ppb. The third cohort was restricted to individuals only exposed to $O_3 < 50$ ppb. As there is no annual standard for O_3, we selected 50 ppb as a threshold to approximate the current World Health Organization global interim target 1 for peak-season average O_3 concentration (WHO, 2005).

2.6. Sensitivity analyses

The exclusion of individuals who are not enrolled in the FFS, part A, and Part B programs can potentially induce a selection bias in the study. Biased results can also occur due to competing mortality risks. To avoid selection bias, we used inverse probability weights. Probabilities of enrollment in the cohort and probability of not dying were modeled, accounting for the subjects' age, sex, race, Medicaid eligibility, and the ZIP code population density, percent population under the poverty line, percent population without a high school diploma, percent self-identify as Black and Hispanic. We calculated these probabilities using pooled logistic regressions. We then calculated the weight by multiplying the inverse probability of enrolling in the three programs with the inverse probability of being alive and calculated the averaged weight within each stratum of follow up year, calendar year, ZIP code, and individual characteristics. We then repeated the models incorporating the weights and compared the exposure-response curves with and without weights.

3. Results

We have included 264, 869, 458 person-years of 41, 780, 637 people. The mean age was approximately 76 years, 60% were women, and 90% were white. We observed 10, 024, 879 diabetes cases (3.8% of person-years) (Table 1). The mean and IQR values of the air pollutants were as follows: $PM_{2.5}$ 10.1 μg/m^3 (4.2 μg/m^3), O_3 43.2 ppb (7.0 ppb), and NO_2 18.9 ppb (13.7 ppb). The correlations with temperature and among the air pollutants were low to moderate (Supplementary Table 1), with the highest correlation observed between $PM_{2.5}$ and NO_2 (r = 0.44).

Using linear terms, we observed an increased diabetes risk associated with 5 μg/m^3 increase in $PM_{2.5}$ (HR = 1.074, 95% CI 1.058; 1.089) and 5 ppb increase in NO_2 (HR = 1.055, 95% CI 1.050; 1.060). No linear association was observed with O_3 (HR 0.999,95% CI 0.993; 1.004). We then used penalized spline functions to allow for nonlinear exposure-response curves and found evidence of nonlinear associations with the three pollutants (Fig. 1). Both for NO_2 and $PM_{2.5}$ we observed linear associations at the lower ends of the pollutants' distributions. For $PM_{2.5}$ the associations were linear for levels<8.2 μg/m^3 (the 25th percentile), followed by a plateaued association. For NO_2 the associations were

Table 1
Population characteristics (264,869,458 person years).

	Summary statistics
Individual characteristics	
Age, Mean (S.D.)	75.97 (7.7)
Female sex, n (%)	158,138,886 (59.7)
Race, n (%)	
White	238,995,206 (90.2)
Black	14,986,036 (5.7)
Other	10,888,216 (4.1)
Medicaid insurance, n (%)	24,986,082 (9.4)
Diabetes, n (%)	10,024,879 (3.8)
Hypertension, n (%)	96,411,807 (36.4)
Ischemic heart disease, n (%)	57,842,331 (21.8)
Death, n (%)	1,125,608 (0.4)
ZIP code characteristics	
Percent poverty, Mean (SD)	0.1 (0.1)
[a] Population density, Mean (SD)	2650.1 (7854.1)
[b] Median house value, Mean (SD)	195,301.5 (159,465.5)
Percent Black population, Mean (SD)	0.1 (0.2)
[b] Median household income, Mean (SD)	53,618.0 (22,608.6)
Percent Hispanic population, Mean (SD)	0.3 (0.1)

[a] Number of persons per square kilometer.
[b] Median house worth value and median household income are presented in dollars.

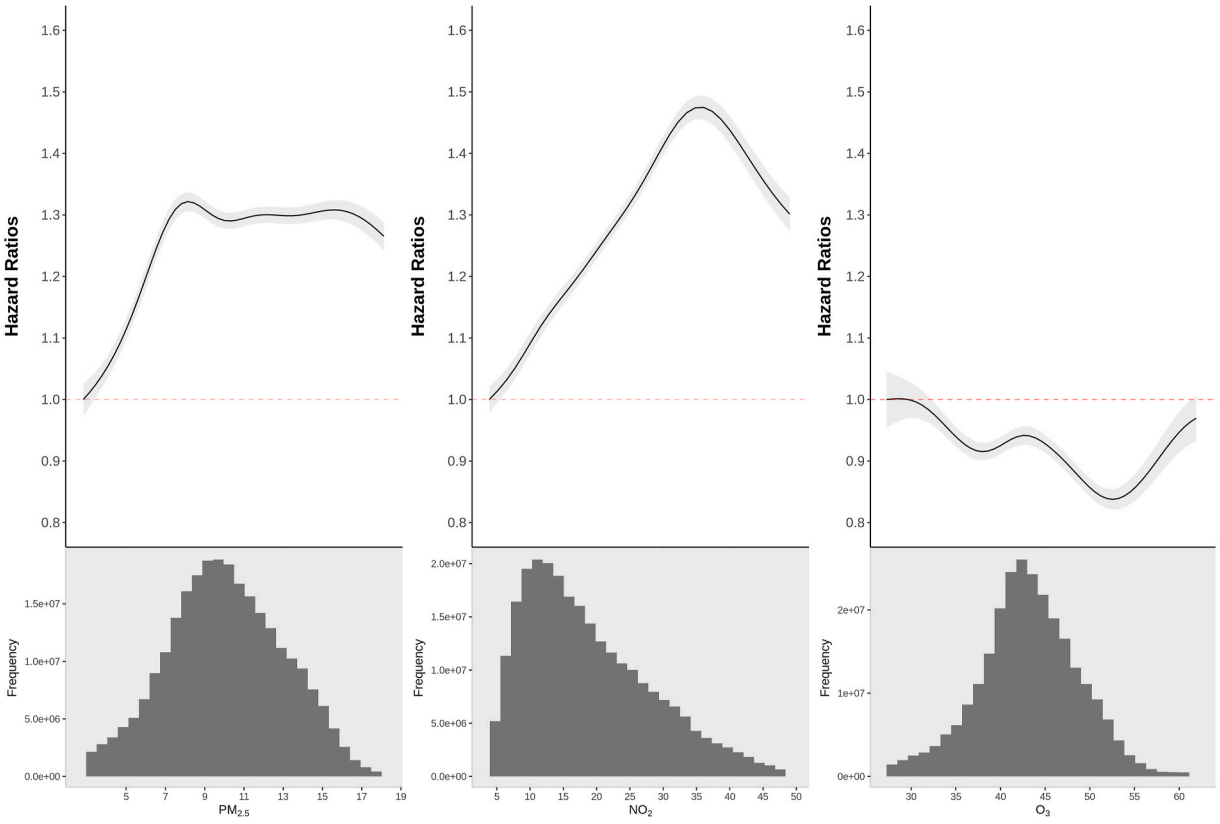

Fig. 1. The association between $PM_{2.5}$, NO_2, and warm-months O_3 exposure and diabetes occurrence. Fig. 1 shows the exposure-response curves for the association between $PM_{2.5}$, NO_2, and warm-months O_3 and diabetes occurrence. We show the curve from the 0.5th percentile of $PM_{2.5}$, i.e., with 0.5% poorly constrained extreme values excluded. Results are obtained from a multivariate model, adjusted for age, race, sex, Medicaid insurance, annual ZIP code means of summer and winter temperature, and annual ZIP code level sociodemographic variables. The model also includes a random intercept for each ZIP code and a spline function of year.

linear for levels <36 ppb (94th percentile), followed by attenuated associations. The O_3 exposure-response curve was highly nonlinear with mostly negative associations. The association with NO_2 was similar in the single pollutant and the multivariate models. For $PM_{2.5}$, the associations were mostly similar between the single pollutant and multivariate models, except for the plateaued association observed more clearly in the multivariate model. The O_3 exposure-response curve differed greatly between the single and multipollutant models. Unlike the negative associations seen in the multivariate model, there was no clear trend in the association with the pollutant in the single pollutant model (Supplementary Fig. 1).

Of the analytical dataset, 33.7% (89, 519, 417 person-years), 96.4% (255, 575, 750 person-years), and 54.4% (144, 225, 079 person-years) were only exposed to low-level annual $PM_{2.5}$, annual NO_2, and warm-season O_3 during the study period, respectively. High-pollution ZIP codes excluded from the restricted datasets were mostly located in the mid-west, southeast, and the mid-Atlantic U.S. regions. We estimated the nonlinear exposure-response curves for the three pollutants in multivariate regressions in these restricted cohorts, and the associations with $PM_{2.5}$ and NO_2 remained similar and significant. For O_3, there was no clear association with diabetes and the direction of the associations differed across the distribution of the pollutant (Fig. 2).

Supplementary Table 2 shows the baseline characteristics of those included and excluded from the analytical dataset. Person-years included in the analytical dataset were of older people. In addition, the proportion of whites and women was larger, and the proportion of death was much smaller. We conducted a sensitivity analysis and repeated the models including inverse probability weights accounting for the probability of being enrolled in the cohort and alive. The results of the two models were very similar (Supplementary Fig. 2).

4. Discussion

In a large-scale, national cohort, we observed higher risks for diabetes associated with increases in NO_2 and $PM_{2.5}$ exposures, even when restricting the data to exposure levels below the NAAQS set by the U.S. EPA. Results regarding the association with O_3 were inconclusive.

T2DM is characterized by high blood glucose levels and increased insulin resistance leading to vascular damage and metabolic dysfunctions (Cooper-DeHoff and Pepine, 2007). A growing body of literature links ambient air pollution exposure to diabetes risk, as concluded in several systematic reviews (Eze et al., 2015; Liu et al., 2019; Yang et al., 2020). Studies also found associations between air pollution exposure and markers of potential underlying pathways of this association: lower insulin sensitivity (Wolf et al., 2016), and higher fasting glucose (Wolf et al., 2016; Yitshak Sade et al., 2016). Different mechanisms were proposed to explain the links between air pollution exposure and T2D. Oxidative stress is considered a major pathway to this association (Rajagopalan and Brook, 2012). PM exposure is associated with oxidative stress, which can lead to lipid peroxidation, reduction of antioxidants, and activation of pro-inflammatory processes (Birben et al., 2012; Brook et al., 2010). These, in turn, have a major role in the development and progression of metabolic syndrome and diabetes in particular (Hutcheson and Rocic, 2012; Lim and Thurston, 2019). Another suggested pathways are endothelial dysfunction (Hahad et al., 2019; Lederer et al., 2021), and air pollution-induced mitochondrial dysfunction (Alderete et al., 2018; Schooneman et al., 2013; Sourij et al., 2011; Zhao et al., 2015), which decreases brown adipose tissue (Xu et al., 2011) and impairs glucose homeostasis and insulin sensitivity (Bartelt et al., 2011; Cannon and Nedergaard, 2004).

We found higher diabetes risk associated with higher long-term

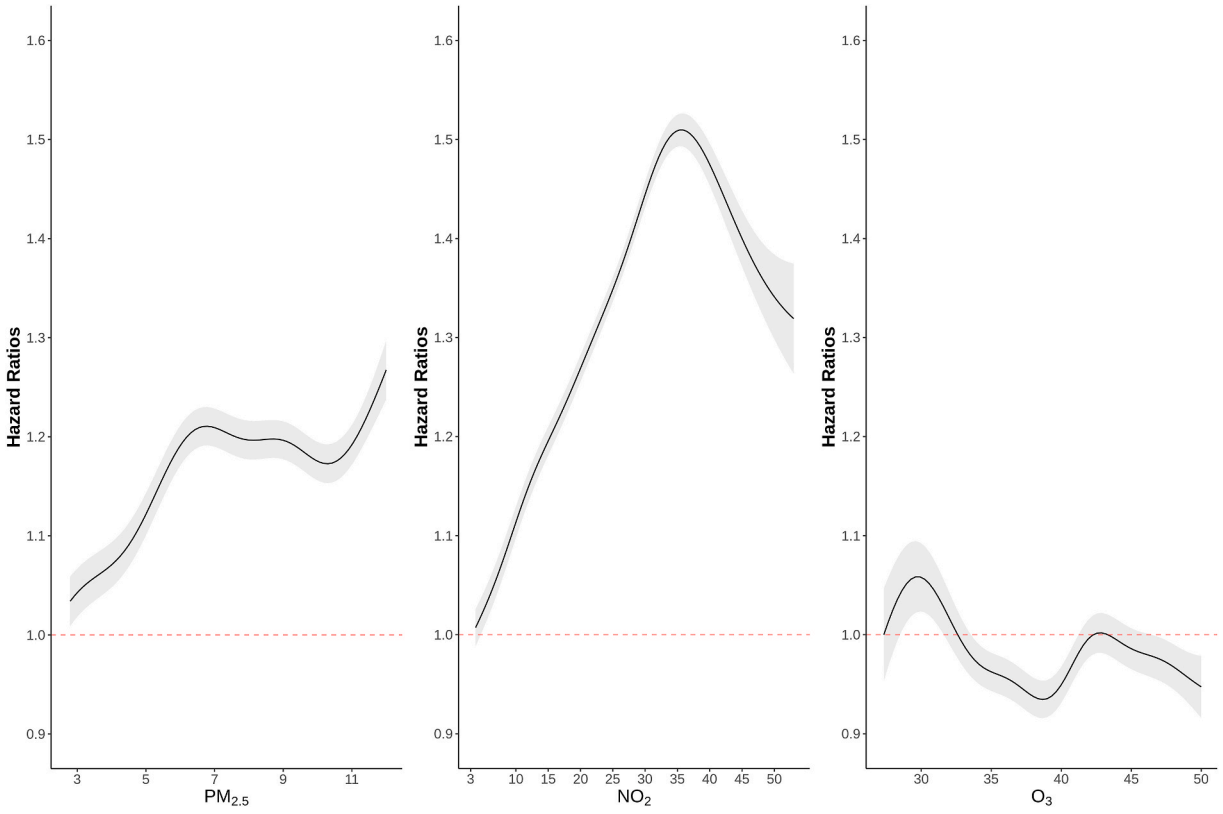

Fig. 2. The association between low-levels air pollutants exposure and diabetes occurrence. Fig. 2 shows the exposure-response curves for the association between $PM_{2.5}$, NO_2, and warm-months O_3 and diabetes occurrence, in subsets, restricted to ZIP codes in which the annual exposures levels have not exceeded the national ambient air quality standards during the study period (i.e., $PM_{2.5}$<12 μg/m^3, NO_2 < 35 ppb, or O_3 < 50 ppb). We show the curves from the 0.5th percentile of NO_2, i.e., with 0.5% poorly constrained extreme values excluded. Results are obtained from a multivariate model, adjusted for age, race, sex, Medicaid insurance, annual ZIP code means of summer and winter temperature, and annual ZIP code level sociodemographic variables. The model also includes a random intercept for each ZIP code and a spline function of year.

$PM_{2.5}$ and NO_2 exposures. Like our findings, a 2019 meta-analysis concluded that the odds for T2DM were 1.03 and 1.05 times higher for incremental increases of 10 μg/m^3 in $PM_{2.5}$ and NO_2 exposures, respectively (Liu et al., 2019). We observed nonlinear associations with the pollutants. Like our findings, Paul et al., (2020) also observed nonlinear associations between $PM_{2.5}$ and diabetes incidence and the changes in risk plateaued at higher $PM_{2.5}$ concentrations. Additionally, as in our study, they observed a nearly linear association with NO_2 exposure up to approximately 35 ppb. The exposure range in our study was larger, with attenuated associations observed for NO_2 levels higher than 36 ppb. This might be attributed to larger measurement error at these higher concentrations.

Our study was conducted among the older adult population. Older adults, who already face higher rates of chronic diseases as well as underlying social and economic factors, were found to be particularly vulnerable to air pollution health effects in several studies (Honda et al., 2017; Yang et al., 2020; Yang et al., 2018). The higher vulnerability among older individuals may be attributed to biologic susceptibility (Yang et al., 2020) and compromised physiological capacity to cope with air pollution exposure (Makri and Stilianakis, 2008). Studies conducted among younger populations also observed higher diabetes risk associated with $PM_{2.5}$ and NO_2 exposures (Bai et al., 2018; Hansen et al., 2016; Renzi et al., 2018), suggesting that air pollution poses a cardiometabolic risk for younger populations as well.

Studies assessing the association between O_3, and diabetes are much more limited, and the direction of the observed associations is inconsistent and varies greatly depending on the model covariates (LaKind et al., 2021). For example, a longitudinal cohort of 13,548 individuals in China found a 5.7% increase in diabetes incidence hazard associated with a ten μg/m^3 increase in annual O_3 exposure (Wang et al., 2022). However, two recent long-term studies did not find a significantly increased diabetes risk associated with O_3 exposure in multipollutant models accounting for particulate matter (Jerrett et al., 2017; H Li et al., 2019) and NO_2 (Jerrett et al., 2017) exposures. Moreover, a 2021 review concluded that evidence on the association between O_3 exposure and diabetes is insufficient to infer causality (LaKind et al., 2021). Our study also showed inconclusive results, possibly related to residual confounding, exposure measurement error, or the complexities of simultaneously estimating the effects of multiple air pollutants.

The major findings of our study are the harmful air NO_2, and $PM_{2.5}$ exposures cardiometabolic effects observed even from levels below the NAAQS set by the EPA. The Clean Air Act was last amended in 1990 and requires the U.S. EPA to set NAAQS that mitigate any harmful consequences of air pollution to human health and the environment (EPA, 2021). However, recent studies suggest that these thresholds are insufficient to protect human health. There is evidence of increased mortality risk associated with air pollution levels below the NAAQS (Danesh Yazdi et al., 2021; Di et al., 2017; Shi et al., 2016; Shi et al., 2021a; Wei et al., 2020; Maayan Yitshak-Sade et al., 2020). In some previous analyses, the associations observed at the lower exposure distribution range were stronger than the higher range of the exposure distribution (Di et al., 2017; Wei et al., 2020). This may be attributed to larger measurement error at the rarer higher exposure concentrations that is likely to attenuate the overall effect observed when considering the full ranges of the pollutant exposures in the analysis (Steenland et al., 2015). Regarding $PM_{2.5}$, it is also possible that the composition of the particles is different for low and high pollution days (Shi et al., 2021a).

Our study has several limitations. First, there are differences between people included and excluded from the cohort. This is a limitation of all studies that analyze claims data of the Medicare cohort. However, our

sensitivity analysis suggests that our results were not biased due to differential probabilities of enrollment or death. Second, the Medicare data does not provide information on subtypes of diabetes or prediabetes state. However, because we assess incident cases among older adults, we are more likely to identify type II diabetes rather than type I. Additionally, the Medicare data does not provide data on individual confounders such as BMI, smoking, physical activity, or lifestyle. However, since exposure is assigned on a ZIP code level, neighborhood factors are more likely to confound the associations in our study. These neighborhood factors were accounted for in our models. Finally, we might have had exposure misclassification errors like other air pollution studies. However, the use of highly spatiotemporally resolved exposure models reduces this error.

5. Conclusions

In conclusion, assessing the simultaneous effects of particulate and gaseous air pollutants in a national cohort of older adults, we found increased diabetes risk associated with $PM_{2.5}$ and NO_2 exposure. The observed effects remained when restricting the data to exposure levels below the NAAQS. For ozone, the effects were inconclusive and require further investigation. Since current studies of the link between air pollution and diabetes are scarce and often limited in quality or sample size, this national study may add robust evidence important for inferring the causal link between air pollution exposure and the development of diabetes.

Credit author statement

MYS: Formal analysis, Investigation, and Writing – original draft; LS: Funding acquisition, Data curation, and Writing – review & editing; EC: Conceptualization, Methodology, and Writing – review & editing; HA and QD: Investigation, and Writing – review & editing; JS and RW: Supervision, Funding acquisition, and Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Maayan Yitshak Sade, Liuhua Shi, Robert Wright, Elena Colicino, Joel Schwartz reports financial support was provided by National Institute of Environmental Health Sciences. Liuhua Shi reports financial support was provided by the national institute of aging. Joel Schwartz reports financial support was provided by United States Environmental Protection Agency. Heresh Amini reports financial support was provided by Novo Nordisk Foundation Challenge Programme.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2023.121056.

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