

Examining the effect of air pollutants on hospitalization with Parkinson’s disease among Medicare beneficiaries using traditional and causal inference approaches

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BACKGROUND

- Parkinson’s disease (PD) is an age-related central nervous system disorder characterized by the degeneration of dopaminergic neurons¹
- ~1 million people in the US are affected by PD, with the prevalence expected to increase to 1.2 million by 2030²
- Since the average age of PD onset is 60 years old, the Medicare program, which offers near universal overage for the US elderly, carries the brunt of the directed costs³
- Given prior evidence that air pollution may play a role in the development and exacerbation of PD^{4,5}, we aimed to examine the effect of air pollution exposure on hospitalizations among those with PD in Medicare

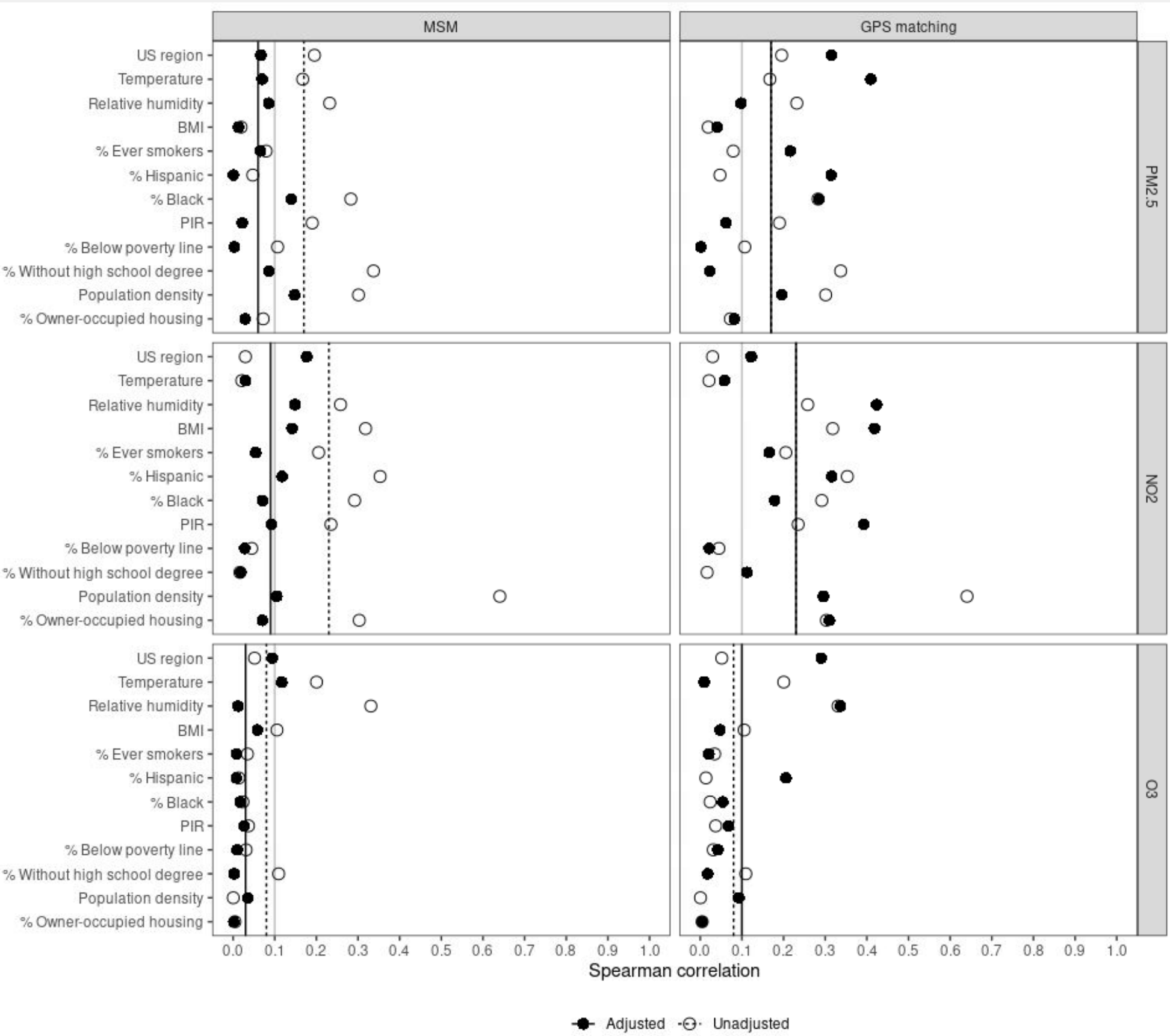


Figure 1. Covariate balance with and without adjusting for confounding in generalized propensity score (GPS)-based models. For PM_{2.5}, NO₂, and O₃ (rows top to bottom), the white- and black- filled points represent the Spearman correlation calculated in the unadjusted population and weighted (marginal structural model [MSM]) or matched (generalized propensity score [GPS] matching model) pseudo-populations, respectively, for each air pollution-confounder pair. The black dotted and solid lines denote the mean unadjusted and adjusted Spearman correlation, respectively, in each panel. The grey line represents our correlation threshold for covariate balance (i.e., 0.1).

Table 1. Model specification of each statistical approach.

Statistical approach	Model specification ^{1,2}	Model weights ³
Traditional outcome stratification	$\log[E(\text{hospitalization with PD counts})] = \text{air pollution} + \text{area-level confounders} + \text{strata}(\text{individual-level variables}) + \text{offset}[\log(\text{person year})]$	None
Marginal structural	$\log[E(\text{hospitalization with PD counts})] = \text{air pollution} + \text{strata}(\text{individual-level variables}) + \text{offset}[\log(\text{person year})]$	$f(\text{air pollutant})/\text{GPS}$
Doubly robust	$\log[E(\text{hospitalization with PD counts})] = \text{air pollution} + \text{area-level confounders} + \text{strata}(\text{individual-level variables}) + \text{offset}[\log(\text{person year})]$	$f(\text{air pollutant})/\text{GPS}$
GPS matching	$\log[E(\text{hospitalization with PD counts})] = \text{air pollution} + \text{strata}(\text{individual-level variables}) + \text{offset}[\log(\text{person year})]$	Matching counter

¹Area-level confounders include county body mass index, % county ever smokers, % Hispanic, % Black, price-income ratio, % below poverty line, % without high school degree, % owner-occupied housing, population density, summer maximum temperature, and summer maximum relative humidity. Each area-level covariate was parameterized using a linear and a quadratic term.
²Individual-level variables include age, sex, race/ethnicity, Medicaid eligibility, and year.
³ $f(\text{air pollutant})$ is the marginal density function of air pollution exposure.

METHODS

Study population & hospitalization with PD definition

- 2001-2016 Medicare Fee-For-Service beneficiaries aged ≥65 years residing in the contiguous US
- ‘hospitalization with PD’ = first recorded hospital admission accompanied with a PD diagnosis code (ICD-9 332;ICD-10 G20) from Medicare Part A
- Excluded those who experienced a hospitalization with PD during initial 2 years of follow-up to minimize inclusion of those further along in disease progression

Air pollution exposure

- Daily ambient PM_{2.5}, NO₂, and summer O₃ concentrations were obtained from state-of-the-art spatiotemporal models with 1 km grid resolution that were averaged to the ZIP code level and linked to each beneficiary

Covariates

- Individual: age, sex, race/ethnicity, Medicaid eligibility
- Area: % Hispanic, % Black, house-price-to-income ratio, % poverty, % <high school, % owner-occupied housing, population density, mean BMI, % smokers, maximum daily summer temperature and humidity

Statistical analyses

- For each air pollutant, used four different models to estimate the effect of exposure on hospitalization with PD
- Model specifications can be found in **Table 1**

RESULTS & CONCLUSIONS

- Covariate balance was achieved in the weighted pseudo-population but did not meet the threshold ($p < 0.1$) in the matched pseudo-population, so effects were estimated only under traditional and weighting approaches (**Figure 1**)
- Incidence rate ratios under the doubly robust approach were 1.08 (95% CI 1.07, 1.10), 1.07 (95% CI: 1.05, 1.08), and 1.03 (95% CI: 1.02, 1.05) for an IQR increase of PM_{2.5} (3.7 µg/m³), NO₂ (13.8 ppb), and O₃ (10.1 ppb), respectively (**Figure 2**)
- **In this national retrospective cohort study among 49,121,026 beneficiaries with >425 million person-years of follow-up, air pollution increased the rate of hospitalizations with PD**
- **Confidence in our findings is bolstered by our use of several causal inference methods**

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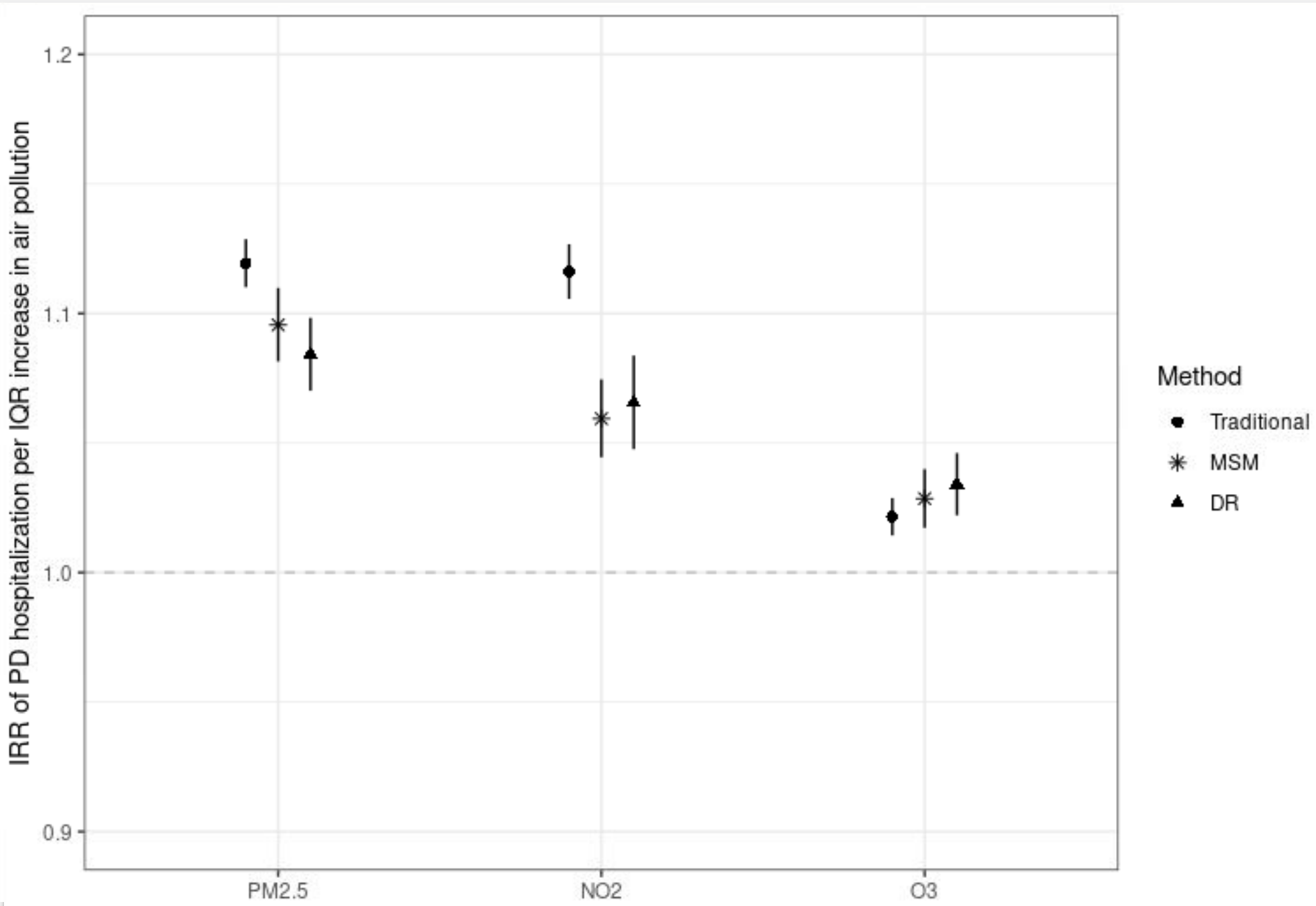


Figure 2. Effect of air pollution on Parkinson’s disease (PD) hospitalization among Medicare Fee-For-Service beneficiaries. The estimated incidence rate ratio (IRR) of hospitalization with PD for an interquartile range (IQR) increase in particulate matter ≤2.5 µm (PM_{2.5}) (3.7 µg/m³), nitrogen dioxide (NO₂) (13.8 ppb), and summer ozone (O₃) (10.1 ppb) is indicated by a black-filled point for traditional models; an asterisk for marginal structural models; and a black-filled triangle for doubly robust (DR) models. The error bars represent the corresponding 95% m-out-of-n bootstrapped confidence intervals. All models were adjusted for area- and individual-level characteristics and year.

¹National Institute of Aging. Parkinson’s Disease: Causes, Symptoms, and Treatments. *National Institute on Aging* <https://www.nia.nih.gov/health/parkinsons-disease>; ²Marras, C. *et al.* Prevalence of Parkinson’s disease across North America. *NPJ Parkinsons Dis* **4**, 21 (2018); ³Albarmawi, H. *et al.* The economic burden of Parkinson disease among Medicare beneficiaries. *JMCP* **28**, 405–414 (2022); ⁴Kasdagli, M.-I., Katsouyanni, K., Dimakopoulou, K. & Samoli, E. Air pollution and Parkinson’s disease: A systematic review and meta-analysis up to 2018. *International Journal of Hygiene and Environmental Health* **222**, 402–409 (2019); ⁵Ai, B. *et al.* Causal association between long-term exposure to air pollution and incident Parkinson’s disease. *Journal of Hazardous Materials* **469**, 133944 (2024).