Title

Role of air pollution and socioeconomic position on cognition over six years in older adults in the United States

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Role of air pollution and socioeconomic position on cognition over six years in older adults in the United States

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Dedication and Acknowledgements

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Kristina Van Dang

Abstract

As our population ages, mounting interest lies in alleviating the illnesses of our older populations. Alzheimer's Disease and related dementias affect 5.8 million Americans as of 2019, and this figure is set to grow to 7.1 million by 2050. This translates to current annual healthcare costs in excess of $1 trillion. There are 12 identified modifiable risk factors for dementia that could prevent up to 40% of dementia incidence, including air pollution, which was added in 2020. This objective of this dissertation was to examine the role of air pollution and socioeconomic position on cognition over six years in the National Health and Aging Trends Study (NHATS). As air pollution is socially patterned, there is a need to evaluate its interaction with social factors on cognition and cognitive decline. Chapter 1 of this dissertation compares racial and socioeconomic measures, from 2000 to 2015, across the conterminous US in exposure to outdoor nitrogen dioxide (NO_2) and fine particulate matter ($PM_{2.5}$). Chapter 2 builds upon Chapter 1 by using the individual and area-level metrics at the census tract level to examine their interaction with air pollution exposure on cognition in NHATS. Finally, the temporal pattern of air pollution exposure may be relevant to risk of cognitive decline in older adulthood. In Chapter 3, we characterized 10-year trajectories of $PM_{2.5}$ and NO_2 exposure at the census-tract level using sequence analysis and cluster analysis, and evaluated their association with cognition among a cohort of older adults.

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Chapter 1: Area-level Inequities in air pollution reduction across the United States: A 15-year comparison of $PM_{2.5}$ and NO_2 air quality improvements

INTRODUCTION

Exposures to nitrogen dioxide (NO_2) and fine particulate matter (PM with an aerodynamic diameter ≤2.5 μm ; $PM_{2.5}$) are associated with numerous adverse health effects(1–3), including cardiovascular and respiratory morbidity(4,5), excess mortality(6–9), increased hospital admissions(10–12), and higher odds of preterm birth(13). Several geographically localized, cross-sectional studies suggest that exposure to air pollutants is not uniform across all communities and subpopulations(14–17). Ambient air pollution levels have been decreasing since the passage of the 1970 Clean Air Act(18). Prior studies have documented continued inequities across the US in exposure to air pollution, including to federally regulated criteria pollutants such as NO_2 and $PM_{2.5}$ (14,16,17,19–24). However, prior studies often focused on subsets of the U.S. population, either urban areas, specific metropolitan areas, or single states. Additionally, there has been limited research incorporating spatiotemporal patterns of these air pollutants with area-level measures of structural racism, even though structural racism has strongly influenced where people from historically marginalized groups live, along with the degree of environmental hazard in those residential areas. To date, we lack longitudinal, nationwide evidence on how the geographic clustering of air pollution leads to social inequalities in exposure.

Previous work has examined the perpetuation of environmental injustice over time among communities of racial and ethnic minority people(25,26). Understanding and addressing the structural drivers of racial/ethnic inequities in air pollution exposure requires evaluating how the geography of air pollution corresponds with measures of structural racism and racially patterned economic and political power. For example, Clark et. al(24) found that excess exposure to traffic-related air pollution NO_2 in non-White populations has persisted from 2000 to 2010. Liu et. al(22) observed differing associations by census block-level race/ethnicity and income strata with criteria pollutants for the U.S. Environmental Protection Agency (EPA) National Ambient Air Quality Standards (NAAQS). Neither study evaluated area-level measures of racism. Bravo et. al(17) observed air pollution disparities using measures of racial isolation of Black individuals in North Carolina. Structural racism manifests at the local level as systematic neighborhood disinvestment in infrastructure where racial and ethnic minorities reside. Industry practices and residential zoning decisions downstream from this disinvestment and racial segregation leave marginalized communities vulnerable to excess air pollution exposure.

We advanced the inquiry into injustices in air pollution exposure with an investigation of differences from 2000 to 2015 in exposure to $PM_{2.5}$ and NO_2 as experienced by subpopulations in the conterminous U.S., defined by race/ethnicity, education, income, and neighborhood-level racial and economic segregation. We also used integrated empirical geographic regression models to predict ambient concentrations at a resolution of ~0.1km for each pollutant at each U.S. census tract, as opposed to focusing only on urban areas or near monitor exposures. Further, we use the Index of Concentration at the Extremes as a proxy for local level disinvestment in infrastructure and Dissimilarity Index as a proxy for structural racism to evaluate potential area-level factors that account for disparities in air pollution exposure.

METHODS

Our analyses included all residents of the conterminous U.S. in 2000 and 2015. This included 72,539 census tracts representing approximately 280 million people in 2000 and 314 million in 2015.

Air Pollution Data. Annual average values of $PM_{2.5}$ ($\mu g/m^3$) and NO_2 (ppb) at the census tract level from 2000 to 2015 were based on previously published prediction models from the Center for Air, Climate and Energy Solutions (CACES), using v1 empirical models as described in Kim et. al(27). Briefly, these models use regulatory monitoring data and a limited number of geographic characteristics with universal kriging to produce predictions of concentration estimates for all criteria air pollutants for each census tract.

To estimate each of the *k* group-specific average air pollution exposure levels in 2000 and 2015 for US residents in a group (e.g. non-Hispanic Black individuals) we computed the population-weighted concentrations of $PM_{2.5}$ and NO_2 for each group *k*, averaged over all *j* census tracts, defined as:

$$PWE_k = \frac{\sum_{i=1}^{j} AP_i l_i}{\sum_{i=1}^{j} l_i} \quad (1)$$

where AP_i is the concentration of $PM_{2.5}$ or NO_2 in census tract *i*, and l_i is the number of people living in census tract *i* who are members of that population subgroup (e.g., if looking at those with less than a high school degree, the number of people in that census-tract with less than a high school degree) summed across all census tracts in the United States. This is the group-specific average air pollution exposure for all US residents in each group calculated based on each census tract's pollution level and the population composition of that census tract. The denominator for these analyses is the Census or ACS reported population size for that subgroup *k*.

Decennial Census and American Community Survey Data. Census tract-level variables related to demographics, segregation, and socioeconomic status were derived from the 2000 Decennial Census (SF3) and 2015 American Community Survey. Race/ethnicity was categorized as individuals who self-identified as non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, or Hispanic (Census variable P007001; ACS variable B03002). Annual household income in the past 12 months in 2010-inflation adjusted dollars was categorized as less than $20,000 or more than $125,000 (Census variable P05200; ACS variable B19001). Educational attainment was categorized as the population over 25 with: less than high school degree; high school degree, General Educational Development (GED), or equivalent credential; some college or Associate's degree; Bachelor's degree; or any graduate education (e.g., Master's Degree, Professional School, Doctorate)(Census variable B15002; ACS variable P037003).

We dichotomized urban and non-urban areas according to the USDA Rural-Urban Commuting Area Codes(28) updated in 2019, with "1" representing urban populations, and all other values (2-10) representing non-urban populations.

Measures of Residential Segregation. Existing indicators of racial residential segregation and spatial social polarization have been developed to both reflect the consequences of structural racism due to *de jure* (formally legislated) and *de facto* (in practice) housing discrimination. This discrimination serves as a structural mechanism of racism by diminishing political, economic, and social power in predominantly Black or Latino neighborhoods. Segregation and spatial social polarization (29) should be evaluated at the regional and local levels as larger spatial units may mask true associations (30,31). At the regional level, the Dissimilarity Index(32) is defined as the proportion of people of a given race or ethnicity (e.g., Non-Hispanic Black) that would have to move from their census tract (or subarea) to match the distribution at the regional (higher) level. Massey(32) offers the Dissimilarity Index as a formal measure of segregation which links how a socially and economically cohesive region relates to each of its subareas. In this conceptualization, the larger economic region, e.g., a Metropolitan Statistical Area, is conceptualized as the entity that makes decisions for siting of industry, housing/zoning regulations, roads, etc. The Dissimilarity Index for region *j* measures the evenness distribution of individuals within that region's constituent subareas (census tracts) compared to the region as a whole (Metropolitan Statistical Area).

The Dissimilarity Index for each region j is defined as:

$$Dj = \frac{1}{2}\sum_{i=1}^{n}\left|\frac{P_{1i}}{P_1} - \frac{P_{2i}}{P_2}\right|, \quad (2)$$

where P_1 is the metropolitan-wide population of group 1, P_2 is the metropolitan-wide population of group 2, P_{1i} is censustract i population of group 1, P_{2i} is census tract i population of group 2, and n is the number of census tracts in the metropolitan area j.

At the local level, the Index of Concentration at the Extremes (ICE) (33) can be defined with respect to any characteristic thought to correspond with social privilege. ICE is hypothesized to influence health through inequitable spatial access to resources, such as schools, employment opportunities, environmental hazards, and violence(34). The ICE tells us how spatially integrated a census tract is using the distributions of the most advantaged (non-Hispanic White and/or high income) and disadvantaged group (non-Hispanic Black and/or low-income). ICE is meant to distinguish census tracts that contain populations of well mixed demographic and socioeconomic characteristics from those that are isolated trending towards the extremes of -1 and 1 which would quality of social and economic resources in the census tract likely differ.

As these two concepts are closely related, using one index measure minimizes issues of correlated independent variables(35). Together, these measures capture local and regional features of the composition, and, based on the correlates of these compositional features, these measures also imply variations in quality of local neighborhood resources that influence health, such as schools, safety, medical care, occupational opportunities, and retail outlets.

Our measure of local social polarization, the Index of Concentration at the Extremes (ICE)(36), was calculated as:

$$ICE = (A_i - P_i)/T_i, \quad (3)$$

where A_i is the number of people in the census tract *i* in the most privileged extreme, P_i is the number of people in the census tract *i* in the most deprived extreme, and T_i is the total number of people living in that census tract *i*. The ICEi is summed across all conterminous census tracts *n* in the US for this analysis. We calculated an ICE for racialized economic segregation. This variable defines the privileged group as high-income non-Hispanic White people and the disadvantaged group as low-income non-Hispanic Black people. High income is defined as \$100K and greater, and low income as \$25K and less(37) for this study period. ICE for each census tract ranges from -1 (concentrated with low-income non-Hispanic Black individuals) to 1 (concentrated with high-income non-Hispanic White individuals).

Given the historical structural racism specifically experienced by African Americans, The Dissimilarity Index and ICE were calculated to contrast non-Hispanic Black and non-Hispanic White (i.e., the privileged race/ethnicity for ICE measures, and the reference group from relative measures of inequality) subpopulations.

Statistical analysis. We calculated PWEs for race/ethnicity, education, and income and area-level measures of segregation (Black-White Dissimilarity Index) and racial composition (ICE). Census tracts with <100 people were excluded (17,38) due to the possibility of unstable estimates. Due to variation in air pollution components and sources, stratification by urban/rural was conducted. Finally, the Dissimilarity Index was categorized by the number of people that would have to move out of a census tract to match of the composition of the larger regional level; a census tract that is the most similar (lowest Dissimilarity Index score) would imply that a census tract is representative at the regional level. The Dissimilarity Index was categorized at 0.4, 0.5, and 0.6, consistent with the literature (39). We used quintiles of each ICE measure from 2000, and set the least exposed/most advantaged quintile as the reference group. These cutoffs are listed in the Supplement.

RESULTS

Nationwide, the absolute levels of air pollution decreased from 2000 to 2015 (Figure 1.1).

NO_2. Over this period, the mean (standard deviation) NO_2 concentration fell from 13.2 (SD 7.5) ppb to 7.2 (SD 4.3) ppb (Table 2), an approximately 45% drop over 15 years.
Over the study period, Hispanic populations experienced the greatest reduction, at 49% (or 8.85 ppb), and non-Hispanic Black populations experienced the least reduction , at 46.5% (or 7.02 ppb). Comparing quintiles of ICE, those in the greatest quintile (most advantaged census tracts) experienced the largest percentage decrease in NO_2 over time, at 53.4% (from 8.4 to 3.9 ppb). Those in the most disinvested census tracts, as indicated by being in the lowest quintile experienced the smallest percentage decrease over time, at 47.9% (from 17.7 to 9.2 ppb). Similarly, communities scoring lowest on the Dissimilarity Index (least dissimilar = referent) experienced a 38.9% (8.2 to 5.9 ppb) reduction, and those who scored highest were still exposed absolutely to the highest NO_2 (16.4 to 9.3 ppb).

In examining inequalities of exposure to NO_2, on the relative (ratio) and absolute (difference) scale, we used the least exposed group in 2000 as the reference group (non-Hispanic

White populations, those in the highest ICE quintile, and those in the least dissimilar communities D1) and sought to determine if and to what extent these inequalities persisted over time. In 2000, each non-White racial/ethnic group was exposed to a higher excess percentage of NO_2, and this excess remained in 2015 (Table 1.1). Non-Hispanic Black populations were exposed to 29% higher exposure (provide absolute levels) compared to non-Hispanic White populations in 2000, and 35% excess exposure in 2015, representing an increase in 6% excess exposure over the study period. Hispanic populations were exposed to 55% (6.37 ppb) more NO_2 compared to non-Hispanic White populations in 2000, and 54% (3.21 ppb) more than non-Hispanic White populations more in 2015. During both 2000 and 2015, we also observed an inverse dose-response effect of decreasing NO_2 exposure with increasing quintile of ICE, ranging from excess of 30% to 111% in 2000, and 24% to 136% in 2015; these estimates correspond with an absolute excess of 2.47 ppb to 9.32 ppb in 2000, and 0.95 to 5.32 ppb in 2015. Those in the census tracts whose racial composition varied most from their surrounding region, as operationalized by the Dissimilarity Index, similarly had a relative excess exposure of 100% in 2000 and 86% in 2015, corresponding to, respectively, differences of 8.23 ppb and 4.33 ppb excess NO_2 exposure (Figure 1.2.).

$PM_{2.5}$. Ambient mean $PM_{2.5}$ was 13.0 (3.4) $\mu g/m^3$ in 2000 and 8.0 (1.7) in 2015 (Table 1.2). Average exposure to $PM_{2.5}$ decreased by 4.98 $\mu g/m^3$ from 13.0 $\mu g/m^3$to 8 $\mu g/m^3$, a 38.3% reduction over the 15-year study period. Non-Hispanic Black populations were exposed to 14.4 $\mu g/m^3$ in 2000 and 7.8 $\mu g/m^3$ in 2015, representing a 40.2% decrease. Conversely, non-Hispanic White populations were exposed to 12.6 $\mu g/m^3$ in 2000 and 7.8 $\mu g/m^3$ in 2015 (a 38.4% decrease). We observed a similar magnitude in exposure and trend across racial-ethnic ICE quintiles; those in the most disinvested census tracts had the greatest absolute decrease, from

14.5 μg/m^3 in 2000 to 8.7 μg/m^3 in 2015, a 40.1% reduction, similar to those in the most advantaged communities (12.1 μg/m^3 in 2000 to 7.4 μg/m^3 in 2015). Using the lowest Dissimilarity Index score as a reference, these census tracts were exposed to the least $PM_{2.5}$ in 2000 (11.6 μg/m^3) and 2015 (7.2 μg/m^3), representing a 37.6% reduction over the study period. In contrast, those in the most dissimilar census tracts had the highest exposure to $PM_{2.5}$ in 2000 (14.2 μg/m^3) and 2015 (8.7 μg/m^3), experiencing a 38.8% decrease.

Inequalities in exposure to $PM_{2.5}$ over time were examined on the relative and absolute scale using non-Hispanic White populations, census tracts with the most privileged extreme for the ICE race/ethnicity measure, and those living in the least dissimilar neighborhoods as the reference populations. Non-Hispanic Black populations were exposed to 14% more $PM_{2.5}$ compared to non-Hispanic White populations in 2000 and 11% more in 2015 this represents a 4% decrease in excess exposure. In other words, there would have to be an additional 11% decrease in exposure to non-Hispanic Black populations to make their exposure equivalent to non-Hispanic White populations. ICE by race/ethnicity demonstrates a dose-response relationship in exposure to NO_2, in which we see the highest relative and absolute exposures in the most disadvantaged communities. In 2000, those in the most disadvantaged census tracts were exposed to 23% more $PM_{2.5}$ than those in the most advantaged census tracts. In 2015, the comparable disadvantaged versus advantaged excess $PM_{2.5}$ exposure was 20%; this represents a differential of 2.69 μg/m^3 in 2000 and 1.44 μg/m^3 in 2015 excess $PM_{2.5}$ exposure. By quintiles of the Dissimilarity Index, those in the most regionally dissimilar census tracts had a 23% excess exposure in 2000 and 20% in 2015, indicating a differential of 2.66 μg/m^3 in 2000 and 1.49 μg/m^3 in 2015 (Figure 1.3).

By contrast, exposure to $PM_{2.5}$ and NO_2 differed much less across categories of educational attainment, median household income, or age.

DISCUSSION

Annual average $PM_{2.5}$ and NO_2 concentrations have substantially declined in the United States since the 1990s, which has led to improved health and well-being. We examined temporal trends in $PM_{2.5}$ and NO_2 concentrations across the conterminous U.S from 2000-2015 at the census-tract level related to race/ethnicity and socioeconomic status, along with community measures of racialized economic segregation and dissimilarity. We also evaluated differentials in these factors by urban and rural classification. Compared to non-Hispanic White populations, we observed higher relative excess exposure to $PM_{2.5}$ (ranging from 8-14% excess in 2000, and 9-11% in 2015) and NO_2 (ranging from 29-61% excess in 2000 , and 35-62% in 2015) in all non-White racial/ethnic groups . The unequal distribution of $PM_{2.5}$ and NO_2 exposures was elevated in urban compared to rural areas for most of our disparity metrics. This indicates that while there has been substantial progress to decrease air pollution nationally over this 15-year study period, inequitable distribution of exposure to air pollution persists.

Recent studies by Bravo et al.(17) and Anenberg et al.(5) have shown that focusing on absolute reductions in air pollutants could obscure persistent or even increased disparities based on race/ethnicity, urban/rural and other socio-demographic factors. In the year 2000, census tracts with a majority non-Hispanic Black population had a mean excess exposure to $PM_{2.5}$ of 1.77 $\mu g/m^3$ compared to majority Non-Hispanic White census tracts. Census tracts with higher $PM_{2.5}$ concentrations in 2000 had greater improvements in air quality in 2015 than lower-exposure areas. Areas where the population was majority-Non-Hispanic Black were exposed to

14% more $PM_{2.5}$ in 2000 and 11% more in 2015 than their majority-Non-Hispanic White counterparts, indicating a decrease of only 3% in excess exposure.

We document that areas with greater segregation, as operationalized via the Black-White Dissimilarity Index, experienced an excess exposure to $PM_{2.5}$ and NO_2. Based on the legacy of slavery, followed by Jim Crow laws and legalized residential segregation (e.g., redlining, restricted covenants),White-Black dynamics represent the cumulative historical and social inequities that a socially dominant group have inflicted on their marginalized counterparts. Further, environmental justice literature documents from the 1980s the inequitable exposure of Black Americans to hazardous materials(40). The ICE measures also showed a dose-response relationship when comparing the highest to lowest quintile, although these patterns were less clear for the ICE with median household income. Historically, poor, minority communities have disproportionately shouldered the burden of excess exposure (41,42), while disparities by income have become less pronounced with time, possibly due to gentrification(43).

The use of area-level measures of socioeconomic position, specifically at a local and regional level, highlights that air pollution exposure profiles are not merely a reflection of individual characteristics. Area-level composite measures tell us more about the quality of a neighborhood, above the individual characteristics, which is where policies should be targeted. The magnitude of these differences is significant, as Wei et. al(44) find changes in mortality rate by less than 1 $\mu g/m^3$ difference in $PM_{2.5}$ exposure, and about 3 ppb in NO_2 exposure. Finally, using area-level characteristics would imply that interventions should target the area-level (e.g., changes in the NAAQS standards), and not individuals (e.g., personal air filters).

Strengths of this study include longitudinal assessment of air pollution exposure disparities over a 15-year period, which allowed us to track inequities in exposure that persisted with national reduction in air pollution. Further, by using a national sample, our methods apply to the entire United States, while also providing context to urban, rural, and regional subsets. Finally, our use of socioeconomic measures at the individual, local, and regional level allow us to evaluate the social patterning of air pollution above individual characteristics, such as race/ethnicity. Accordingly, interventions and policies to combat excess air pollution exposure should not focus on individual characteristics, but on community-level changes.

Our study has some limitations. The Dissimilarity Index does not cover rural areas, and its values are restricted to micropolitan and metropolitan areas as defined by the Census Bureau in 2010. Additionally, we focused only on Black-White Dissimilarity, instead of other races and ethnicities. Although other dimensions of the Index of Concentration at the Extremes may also capture area-level inequities in area pollution trends, e.g. the educational and income segregation that comprises gentrification, residential racial segregation remains a root cause of these economic disparities. Finally, due to stark racial differences in integrational wealth and earning potential(45), it is difficult to actualize an intervention to alter socioeconomic position as operationalized in this analysis. Changes in the NAAQS standards have decreased overall levels of air pollution, however, the relative excess exposure still persists.

We observe improvements in overall levels of exposure to ambient $PM_{2.5}$ and NO_2 over the 15-year study period. Even though the average concentrations of NO_2 and $PM_{2.5}$ have decreased over time, the relative percentage difference in inequitable exposures between the different racial/ethnic groups has remained the same, or in some cases increased. We found greater inequitable exposure in urban compared to rural areas. Examination of the relative change in addition to the absolute by traditional health disparities and segregation measures can identify sustained environmental justice issues as air pollution overall is decreasing.

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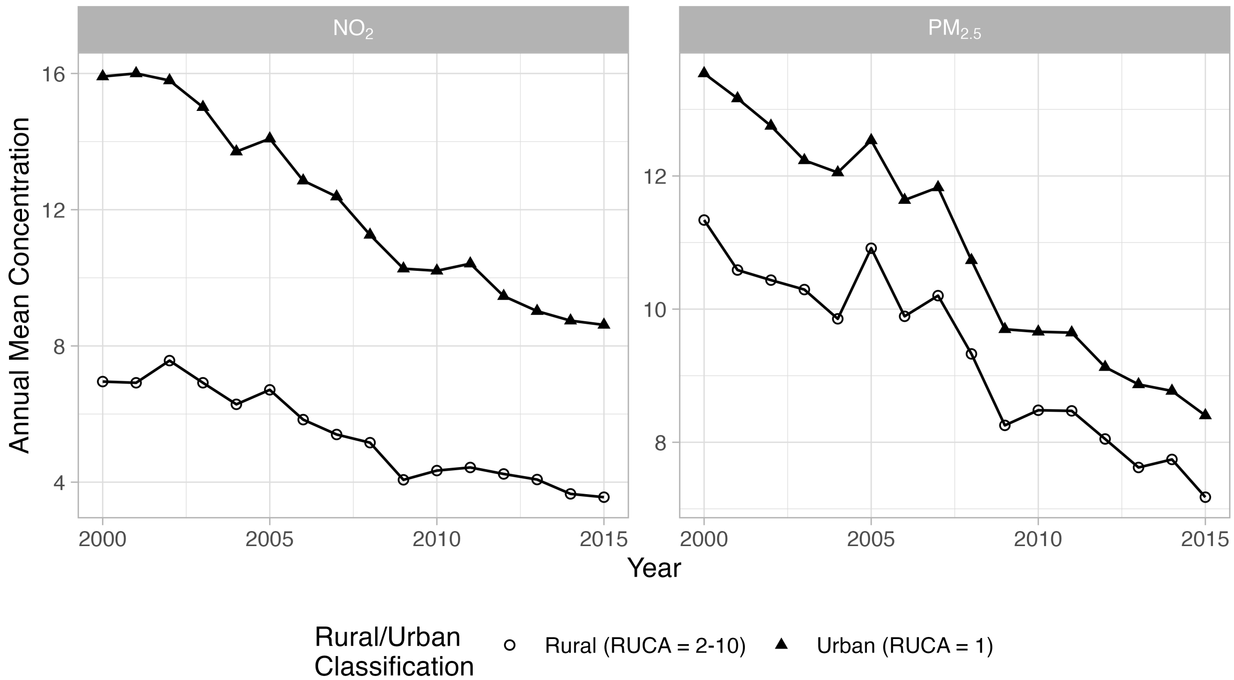

Figure 1.1. Annual Average Concentration Estimates of NO_2 and $PM_{2.5}$ in the conterminous United States, 2000-2015.

Table 1.1. Population-weighted annual average NO_2 concentration (2000 and 2015), by race/ethnicity, education, household income, age, and indices of residential segregation

			Group-specific change in NO_2 from 2000 to 2015		Year-specific difference in NO_2 concentration between group and reference group			
			Absolute Change	Relative Change	Relative ratio		Absolute difference	
Year	2000	2015			2000	2015	2000	2015
Total	13.2	7.2	-5.99	-45.4%				
Race/ethnicity								
White	11.7	6.0	-5.68	-48.7%	Ref.	Ref.	Ref.	Ref.
Black	15.1	8.1	-7.02	-46.5%	1.29	1.35	3.42	2.08
Asian	18.8	9.7	-9.11	-48.4%	1.61	1.62	7.17	3.74
Hispanic	18.0	9.2	-8.85	-49.0%	1.55	1.54	6.37	3.21
Educational Attainment								
Less than High School	14.1	7.8	-6.25	-44.4%	1.02	1.06	0.31	0.45
High School	12.3	6.6	-5.72	-46.5%	0.89	0.89	-1.47	-0.79
Some college	12.8	6.7	-6.16	-48.0%	0.93	0.90	-0.95	-0.72
Bachelors' Degree	13.4	7.2	-6.22	-46.3%	0.97	0.98	-0.36	-0.18
Graduate Degree	13.8	7.4	-6.39	-46.4%	Ref.	Ref.	Ref.	Ref.
Median Household Income								
Less than $20,000	13.4	7.3	-6.10	-45.6%	0.97	1.01	-0.39	0.09
Greater/equal than $125,000	13.8	7.2	-6.58	-47.8%	Ref.	Ref.	Ref.	Ref.
Racialized economic ICE[a]								
Q1	15.2	8.9	-6.39	-41.9%	1.14	1.37	1.83	2.38
Q2	13.9	8.4	-5.51	-39.7%	1.03	1.29	0.47	1.90
Q3	11.4	6.9	-4.47	-39.2%	0.85	1.07	-2.02	0.45
Q4	12.3	6.0	-6.27	-51.1%	0.91	0.92	-1.16	-0.49
Q5	13.4	6.5	-6.94	-51.7%	Ref.	Ref.	Ref.	Ref.
Black-White Dissimilarity[b]								
D1	8.2	5.0	-3.18	-38.9%	Ref.	Ref.	Ref.	Ref.
D2	12.4	5.6	-6.79	-54.7%	1.52	1.13	4.24	0.63
D3	11.1	5.8	-5.30	-47.7%	1.36	1.16	2.92	0.80
D4	16.4	9.3	-7.08	-43.1%	2.00	1.86	8.23	4.33

[a] Racialized Economic ICE cutoffs: -0.030, 0.012, 0.033, 0.085
[b]Black-White Dissimilarity (and therefore exposure to air pollution) was calculated for metropolitan and micropolitan areas only

Table 1.2. Population-weighted annual average $PM_{2.5}$ concentration (2000 and 2015), by race/ethnicity, education, household income, age, and indices of residential segregation

			Group-specific change in $PM_{2.5}$ from 2000 to 2015		Year-specific difference in $PM_{2.5}$ concentration between group and reference group			
			Absolute Change	Relative Change	Relative ratio		Absolute difference	
Year	2000	2015			2000	2015	2000	2015
TOTAL	13.0	8.0	-4.98	-38.3%				
Race/ethnicity								
White	12.6	7.8	-4.85	-38.4%	Ref.	Ref.	Ref.	Ref.
Black	14.4	8.6	-5.79	-40.2%	1.14	1.11	1.77	0.83
Asian	14.3	8.6	-5.77	-40.3%	1.14	1.10	1.71	0.79
Hispanic	13.6	8.5	-5.18	-38.0%	1.08	1.09	1.03	0.69
Educational Attainment								
Less than High School	13.4	8.3	-5.10	-38.0%	1.04	1.04	0.46	0.35
High School Diploma	12.9	8.0	-4.88	-37.9%	0.99	1.00	-0.08	0.03
Some college	12.8	7.9	-4.86	-38.1%	0.99	0.99	-0.19	-0.06
Bachelors' Degree	12.9	8.0	-4.99	-38.5%	1.00	1.00	-0.01	-0.01
Graduate Degree	13.0	8.0	-4.99	-38.5%	Ref.	Ref.	Ref.	Ref.
Median Household Income								
Less than $20,000	13.0	8.1	-4.91	-37.6%	1.00	1.02	0.01	0.20
Greater/equal than $125,000	13.0	7.9	-5.10	-39.1%	Ref.	Ref.	Ref.	Ref.
Racialized economic ICE[a]								
Q1	14.4	8.8	-5.58	-38.8%	1.14	1.16	1.81	1.20
Q2	13.2	8.4	-4.81	-36.4%	1.03	1.09	0.38	0.66
Q3	12.3	8.0	-4.27	-34.8%	0.95	1.03	-0.61	0.24
Q4	12.5	7.8	-4.73	-37.7%	0.98	1.00	-0.27	0.03
Q5	12.8	7.8	-5.05	-39.5%	Ref.	Ref.	Ref.	Ref.
Black-White Dissimilarity[b]								
D1	11.6	7.2	-4.35	-37.6%	Ref.	Ref.	Ref.	Ref.
D2	12.0	7.4	-4.57	-38.1%	1.04	1.03	0.44	0.23
D3	12.4	7.9	-4.51	-36.4%	1.07	1.09	0.83	0.67
D4	14.2	8.7	-5.52	-38.8%	1.23	1.21	2.66	1.49

[a] Racialized Economic ICE cutoffs: -0.030, 0.012, 0.033, 0.085
[b] Black-White Dissimilarity (and therefore exposure to air pollution) was calculated for metropolitan and micropolitan areas only

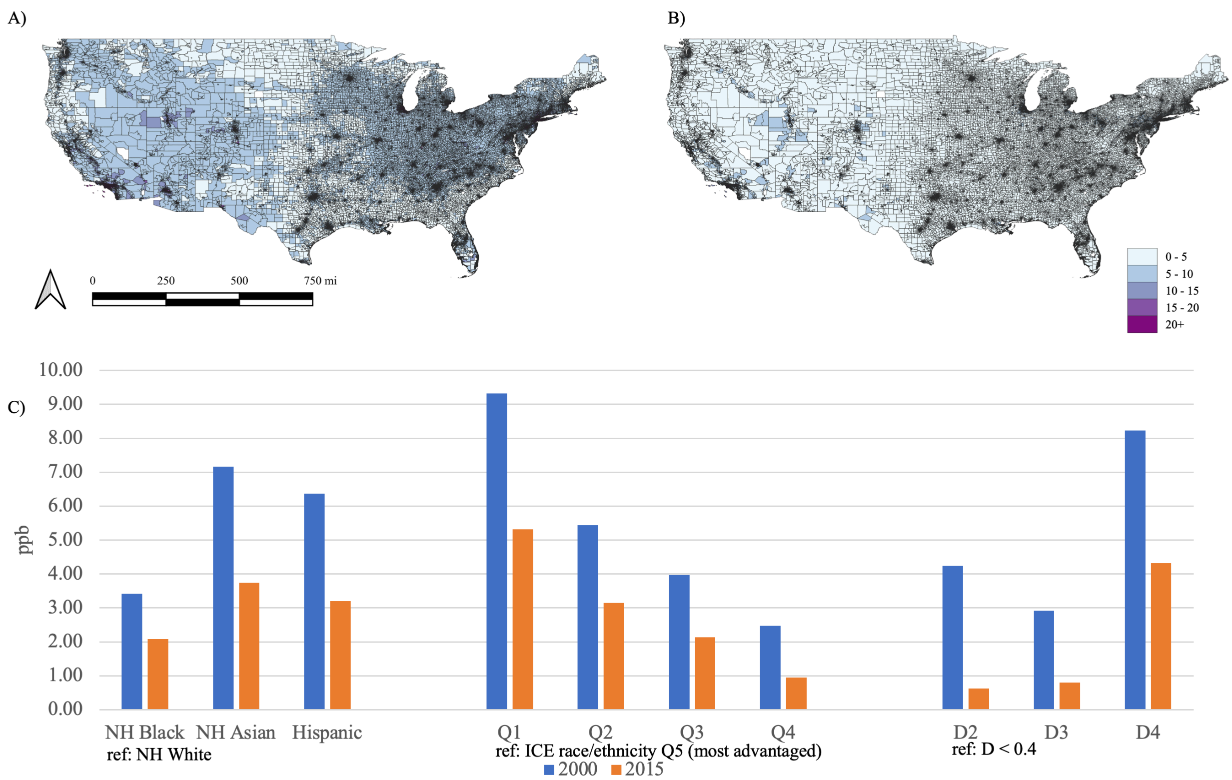

Figure 1.2. Distribution of NO_2 by census tracts for the United States in A) 2000 and B) 2015. C) Absolute difference in exposure to NO_2 by race/ethnicity, ICE for race/ethnicity, and Black-White Dissimilarity Index.

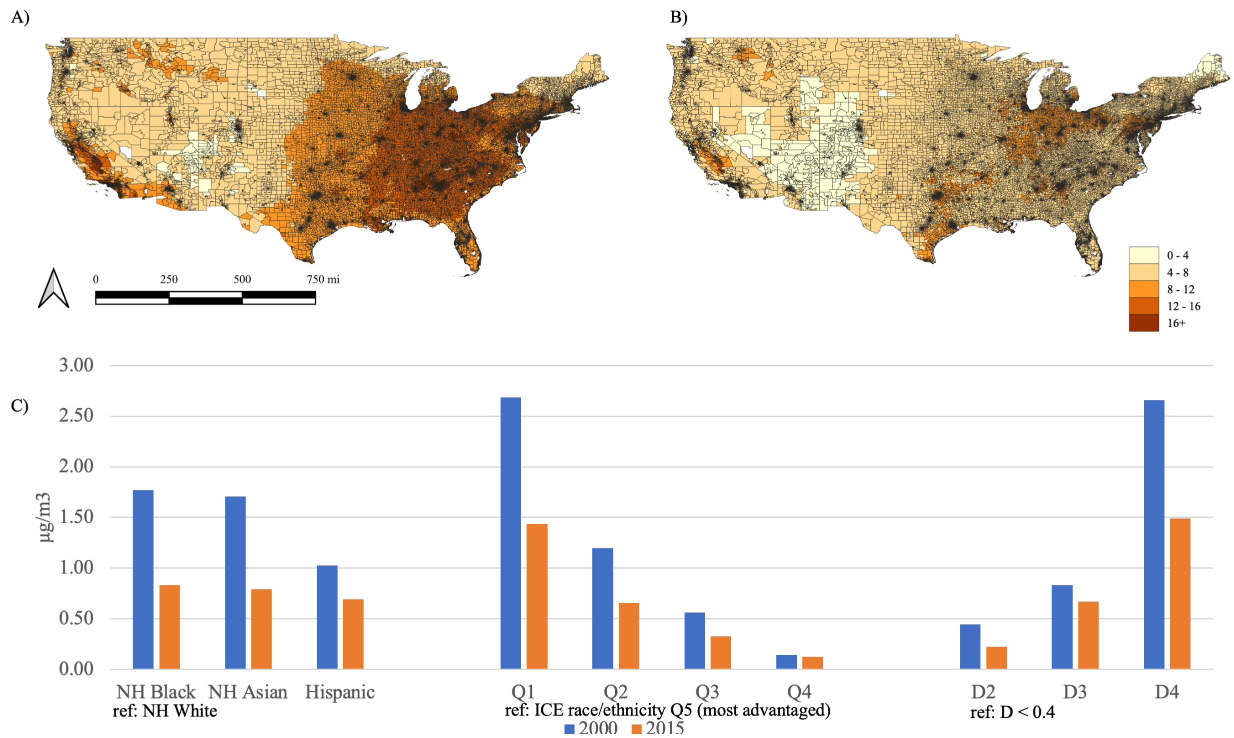

Figure 1.3. Distribution of $PM_{2.5}$ by census tracts for the United States in A) 2000 and B) 2015. C) Absolute difference in exposure to $PM_{2.5}$ by race/ethnicity, ICE for race/ethnicity, and Black-White Dissimilarity Index.

Chapter 2: Association of exposure to air pollution, segregation, and neighborhood racial composition with memory and memory decline in NHATS

INTRODUCTION

As our population ages(1), mounting interest lies in alleviating the illnesses of our older populations. Alzheimer's Disease and related dementias affect 5.8 million Americans as of 2019, and this figure is set to grow to 7.1 million by 2050(2). This translates to current annual healthcare costs in excess of $1 trillion. There are 12 identified modifiable risk factors for dementia that could prevent up to 40% of dementia incidence (3), including air pollution. As air pollution is socially patterned, there is a need to evaluate its interaction with social factors on cognition and cognitive decline.

Emerging research over the last decade has addressed the potential impact of air pollution on cognition(4,5). While studies generally show an adverse effect on cognition, there is less information on intra-individual changes in cognition over time. From a prevention perspective, it is important to study cognitive change compared to a downstream outcome such as dementia because of the typically late diagnostic timeline would not preclude reverse causation. Cognitive changes are utilized prior to a dementia diagnosis, and there can be significant misclassification of dementia based on factors such as race/ethnicity, education, and subjective diagnostic judgement(6). Furthermore, studies have shown a weighted positive predictive value of 56% in Medicare data when compared to clinical evaluation of dementia(7). Recent studies of exposure to some air pollutants (NO_2) and cognitive outcomes have shown inconsistent effects, or have been restricted to smaller geographic areas. Finally, as air pollution is socially patterned, few studies have focused on the specific interaction of area-level residential segregation and racial economic composition and air pollution on cognition and decline. Our understanding is that educational opportunities (and therefore educational attainment) is the product of neighborhood economic investment. Further, segregation as a policy implies that there is a political power dynamic between an immediate neighborhood, and a larger area, presumably the area involved in political decisions. We have chosen to utilize the Dissimilarity Index (D), one of the oldest and most popular formal measures of segregation(8,9). Dissimilarity will influence an immediate neighborhood's resources, which we've chosen to operationalize as the Index of Concentration at the Extremes for race/ethnicity and income combined(10–12). Segregated areas will have high disinvestment in neighborhood economic resources, worse housing quality, worse infrastructure to promote healthy behaviors, and worse access to medical care (and less likely to receive the appropriate medical even after access)(13,14), which will then in turn affect the racial and economic composition of a neighborhood (ICE).

This study aims to examine the relationship between the Dissimilarity Index (D), Index of Concentration at the Extremes (ICE) for race/ethnicity and income, and exposure to air pollution ($PM_{2.5}$ and NO_2), on memory and memory decline in the National Health and Aging Trends Study (NHATS). More specifically, the cross-sectional relationship between our D, ICE, air pollutant ($PM_{2.5}$ and NO_2) and episodic memory; if the association differs by D or ICE, by pollutant; if there is an interaction between pollutant and ICE (or D); and if this association is related to cognitive decline. By utilizing the entire United States, we leverage heterogeneity in our segregation, neighborhood composition, and air pollution measures. Our study oversamples African Americans, which compromise 22% of our analytic sample. We hypothesized that living in areas with higher segregation and high community disinvestment and worse air pollution will be negatively associated with episodic memory in the National Health and Aging Trends Study (NHATS).

METHODS

Study Population. The National Health and Aging Trends Study (NHATS) is a representative sample of 8,245 Medicare beneficiaries aged 65+ at baseline in 2011(15). Persons at older ages and African Americans are oversampled within geographic clusters in a stratified, multistage sampling design. Annual, in-person interviews collected data related to aging and disability, independent functioning, and quality of life. Respondent data was obtained from NHATS (nhats.org), which is sponsored by the Division of Behavioral and Social Research, a division of the National Institutes on Aging; we utilized the Public Use files, Sensitive Data files, and the restricted Geographic files. Using data from the 2011 cohort (enrolled as of September 30, 2010), we excluded those with dementia/AD at baseline (n=457), nursing home residents (n=468) or those who only completed a Facility Questionnaire (n=168), those who used proxy respondents (n=314), and those who refused the Cognitive Section at baseline (n=88), resulting in a final analytic sample size of 6,750. A study flow diagram (Figure 1) and comparison based on key characteristics is included. Selection into the analytic sample is discussed in more detail in the results and discussion section. Finally, the census tract in which each participant resided at baseline was used to link with air pollution exposure.

Assessment of air pollution exposure. This article includes concentration estimates developed by the Center for Air, Climate and Energy Solutions using v1 empirical models as described in Kim et al., 2018(16). Briefly, these models were built from U.S. EPA regulatory monitors, land use maps, and satellite images to predict ambient concentrations at locations without monitors of seven pollutants throughout the contiguous United States. Annual average concentrations of outdoor $PM_{2.5}$ ($\mu g/m^3$) and NO_2 (ppb) for residential Census Block centroid were predicted and population weighted to the census tract in the contiguous United States were obtained for the baseline year of this analysis, 2011.

Assessment of segregation. D, as a regional measure of segregation, can affect local compositional measures, like ICE. Together, D and ICE may influence the concentration of political and social power leading to changes in neighborhood resources that will affect health. Multiple measures of racial residential segregation and spatial social polarization have been developed. These indicators of segregation are thought to both reflect the consequences of structural racism due to *de jure* and *de facto* housing discrimination and serve as a structural mechanism of racism as political power is diminished in predominantly Black or Latino neighborhoods. Segregation and spatial social polarization (13) should be evaluated at the regional and local levels(17). At the regional level, the Dissimilarity Index (D)(8) is defined as the proportion of non-Hispanic Black people (or White) that would have to move from their census tract (or subarea) to match the distribution at the metropolitan (higher) level. Massey(8) offers D as a formal measure of segregation which links how a socially and economically cohesive region relates to each of its units, manifesting with policies on industrial siting and construction of major roadways(18). The D compares the proportion of individuals (e.g. non-Hispanic Black) in a census tract i compared to the proportion in metropolitan area j, defined as:

$$Dj = \frac{1}{2}\sum_{i=1}^{n}\left|\frac{P_{1i}}{P_1} - \frac{P_{2i}}{P_2}\right|, \quad (2)$$

where P_1 is the metropolitan-wide population of group 1, P_2 is the metropolitan-wide population of group 2, P_{1i} is census-tract i population of group 1, P_{2i} is census tract i population of group 2, and n is the number of census tracts in the metropolitan area j. A value of 0 for D suggests that no one would have to relocate to another census tract to match that census tract's proportion of a population to the metropolitan area. A high value, such as 0.70, indicates that 70% of non-Hispanic White or non-Hispanic Black residents of a census tract would have to relocate to match that census tract's proportions to that of the metropolitan area.

The Index of Concentration at the Extremes (ICE) quantifies how much two social extremes are mixed within a spatial unit(10). Advantages of ICE are that it can be defined at any geographic level (we are using the census tract) and with respect to any social characteristic (income, race/ethnicity, education)(11). We use non-Hispanic Black and non-Hispanic White people as one dimension of our ICE calculation, reflecting the United States' history of systemic racism and oppression of one race on another. And as with other residential composition measures, the presence of affluent may benefit all members of the community. We combine median household income and race/ethnicity for our measure of ICE. We computed ICE(19) for each census tract, calculated as:

$$ICE_i = \frac{A_i - P_i}{T_i}, (3)$$

where A_i is the number of people in the census tract *i* in the most privileged extreme, P_i is the number of people in the census tract *i* in the most deprived extreme, and T_i is the total number of people living in that census tract *i*. The ICE_i is summed across all census tracts *n* in the US for the estimates presented in Table 1. A distinct advantage of using ICE is the ability to combine multiple dimensions of social advantage, and for this analysis, we use racialized economic segregation(11). This variable defines the privilege group as high-income non-Hispanic White people and disadvantage as low-income non-Hispanic Black people. High income is defined as the 80th percentile, \$100K and greater, and low income as \$25K and less(11) for this study period. ICE ranges from -1 (concentrated with low-income non-Hispanic Black individuals) to 1 (concentrated with high-income non-Hispanic White individuals), and was computed for each census tract. We trichotomized continuous ICE at -0.5 and 0.5 for the marginal analysis. Data for this variable was obtained from American Community Survey 5-year survey for 2011, the baseline enrollment year for NHATS, for each census tract. The American Community Survey and Census variables used for this analysis are available in the Appendix.

Assessment of memory. NHATS collects annual memory assessments: immediate and delayed recall of a 10-word list(15). We standardized each measure to the baseline mean and standard deviation, and averaged the two for a composite measure of memory.

Statistical analysis. The effects of exposure to each air pollutant ($PM_{2.5}$, NO_2), D, and ICE on memory and memory decline were estimated with linear mixed effects model with random intercepts for participant and census tract. Our models included covariates according to our DAG (Figure 2), and those with statistical difference between our exposed and unexposed groups. Thus, our final model adjusted for education, race/ethnicity, smoking status, gender, census region, and urbanicity. Education was a 4-category variable (less than a high school degree, high school graduate, some college, and Bachelor's Degree and higher). Race/ethnicity was self-reported and combined into White, African American, Hispanic/Latino, and Other. Census regions were either Northeast, Midwest, South, or West. Urbanicity corresponded to USDA 2010 rural-urban commuting area (RUCA)(20) codes, with "1" corresponding to urban, and all else classified as rural. Smoking was defined as current, former, and never. Diabetes was coded as an indicator for those who reported being diabetic at baseline. Air pollution estimates were centered on their respective means (9.49 $\mu g/m^3$ $PM_{2.5}$ and 8.17 ppb NO_2) and scaled by 5 for $PM_{2.5}$ and 10 for NO_2 for ease of interpretability. We modeled each air pollutant in a separate model, and considered specifications of air pollution as a linear term and as inter-quartile range

(IQR) categories. The ICE was multiplied by -1 for these models so that higher values would correspond to a more disadvantaged neighborhood. We are interested in the total effects, so we did not adjust for mediators that may be affected by air pollution, D, or ICE. To understand longitudinal effects, we included a three-way cross-product between each air pollutant (in separate models), ICE (or D), and time. Time was modeled/parameterized as years since baseline, a continuous variable. For longitudinal models, we also included a term for practice effects, coded as an indicator for the baseline test. In sensitivity analyses, we adjusted for body mass index, smoking status, and diabetes, as the values for these variables were different between exposure groups at baseline. We tested for nonlinear effects of air pollution and ICE (or D) over time. The marginal (population averaged) effect of air pollution and ICE (and their interaction) was estimated by predicting outcomes of cognitive function for counterfactual levels of exposure for each subject under low, average, or high exposure to air pollution, and low, average, or high ICE (or D).

RESULTS

Our analytic sample consisted of 6,750 individuals with a mean age at baseline of 77.06 (SD = 7.66) years, 42% male, and 74% self-reporting as White for primary race (See Table 2.1). NHATS, by design, oversamples African Americans (22% of analytic sample). Most (27%) participants had a high school degree. A comparison of the full NHATS sample compared to the analytic sample is presented in the Appendix. At baseline, participants had lived in their current residence on average for 23 years, and 3,048 unique census tracts are represented in the analytic sample. At baseline, mean immediate word recall was 4.66 (SD = 1.65) and mean delayed word recall was 3.21 (SD = 2.00). Each follow-up year, 4% of the cohort died (Appendix Table). On average, participants returned for 4.2 visits over the six-year study period.

Black-White Dissimilarity was 0.60 (0.11) at baseline, which is consistent with published research(9). This number is interpreted as 60% of black (or white) people would have to move from their census tract to another census tract in their metro area in order for the overall black/white composition to match of the metropolitan or micropolitan area (areas that were metropolitan or micropolitan as defined by Office and Management and Budget(21)).

The average ICE value defining non-Hispanic Black as the disadvantaged group and non-Hispanic White as the privileged group ethnicity was 0.48 (sd=0.54), indicating a sample skewed towards the privileged (non-Hispanic White) group at the census-tract level. The average ICE for income (20^{th} versus 80^{th} percentile corresponding to 25K and 100K) was -0.06 (0.23), and the average ICE defined jointly based on race/ethnicity and income for our sample was 0.05 (0.19). The value of ICE race/ethnicity varied based on the race/ethnicity of the respondent. For example, non-Hispanic White participants lived in census tracts with an average ICE of 0.70; for non-Hispanic Black participants, the average ICE was -0.20. Further, ICE for race/ethnicity and census tract racial composition were highly correlated (correlation ICE with percent non-Hispanic Black was 0.92).

The average $PM_{2.5}$ was 9.49 (SD = 1.84) $\mu g/m^3$ at baseline; for NO_2 this was 8.17 (4.97) ppb. The EPA establishes National Ambient Air Quality Standards (NAAQS) for criteria pollutants; 468 (6.9%) of participants exceeded the $PM_{2.5}$ standards at baseline. NO_2 standards were not exceeded. Those who were living in census tracts with NAAQS exceedances were disproportionately female, non-White, African American, less educated, urban residents, living in more disadvantaged neighborhoods (according to ICE), and exposed to more NO_2.

Results from linear mixed models examining the relationship between our measures of segregation (D and ICE) and exposure to air pollution ($PM_{2.5}$ and NO_2) are shown in Table 2.2 and 2.3. A 1-unit higher D (i.e., contrasting the maximum dissimilarity of 1 to the minimum dissimilarity of 0) was associated with .061 SD (95%CI: -0.14, 0.26; Table 3, Model 1) SD higher episodic memory. A 5-unit higher $PM_{2.5}$ was associated with 0.046 (95%CI:-0.10, 0.013) SD-units lower memory, which is roughly similar to the estimated effect of a year of aging on episodic memory.

In models with $PM_{2.5}$ and the joint race/ethnicity-income ICE predicting baseline episodic memory, the estimated effect of a unit-difference in ICE (beta = -0.28 95%CI: -0.13, -0.02) was about six times larger than the coefficient for a single year of age (beta = -0.045 95%CI: -0.048, -0.043). Each 5-unit ($\mu g/m^3$) higher $PM_{2.5}$ was associated with 0.027 SD-units (95%CI: -0.042, 0.012) worse episodic memory score.

For NO_2, the coefficient for D was 0.122 SD units (-0.08, 0.33) increase for episodic memory. For every 10-unit increase in NO_2, episodic memory averaged 0.056 SD (-0.19, -0.002) lower. Each unit higher score on the joint race/ethnicity-income ICE was associated with 0.28 SD-units (-0.41, -0.15) lower episodic memory, and a 10-unit increase in $NO_2$was associated with 0.028 SD-units (-0.08, 0.023) worse episodic memory score. Generally, exposure to air pollution showed a small, adverse effect, with confidence intervals consistent with either small harms or small benefits.

Figures 2.3-2.6 show marginal predicted cognitive changes over time for individual with low or high levels of exposure to each air pollutant, stratified by low, medium, or high D or ICE values. We find little evidence that either $PM_{2.5}$ or NO_2 were robustly associated with rate of memory decline, regardless of D or ICE, and similarly little evidence of differences in rate of memory change by D or ICE. Effect estimates and CIs are provided in the Appendix.

DISCUSSION

In this longitudinal study of older US adults, higher exposure to $PM_{2.5}$ and NO_2 was weakly associated with worse episodic memory, and did not show a relationship with memory decline. Our two measures of neighborhood context, D and ICE, allow us to examine formal measures of racial residential segregation and racial and economic neighborhood composition on memory. We found a consistent relationship of worse racial economic polarization and memory, and the relationship was not modified by time. We did not find evidence of an interaction of either air pollutant with D or ICE when predicting memory or rate of memory decline.

Prior studies of air pollution and cognitive decline have been mixed(5,22), consistent with our findings. To our knowledge, no prior work has examined the interaction of air pollution and neighborhood segregation on memory and memory decline.

The literature on segregation and ICE with cognitive aging is less consistent. Using the Getis-Ord G_i* statistic as a measure of neighborhood racial/ethnic segregation, Meyer et. al(23) showed an association between highly clustered Black and Latino neighborhoods and cognition, but did not observe one for cognitive change. Pohl et. al(14) found that non-Hispanic Black adults were more likely to experience negative effects of neighborhood segregation on cognition (language and memory domains only) and dementia, but their findings were less pronounced for other cognitive domains and incident dementia. Both studies did not examine effects nationally; Meyer et. al(23) was a sample of 452 participants in an Alzheimer's Disease Research Center in Davis, and study participants in Pohl et. al.(14) were located in Northern Manhattan, New York.

Several studies have been recently published that add to the body of evidence looking at air pollution and dementia(24–27). However, none of these studies include a theoretical framework to test the social patterning of air pollutants using D and ICE.

This study has some limitations. The baseline age for this population was 77 years. Many participants will have experienced memory decline prior to the study and the cognitive assessment may not be sensitive to further decline, given the floor. Additionally, our analytic sample included those who did not have dementia at baseline. This could introduce selection bias that would attenuate effect estimates toward the null. We only considered non-Hispanic Black and non-Hispanic White populations in our measures of structural racism (D) and local racial and economic composition (ICE). Calculating it this way adheres to the historical structural racism that has shaped the United States' residential neighborhoods, but does not capture dynamics affecting other groups often targeted for discrimination, such as Asian and Hispanic individuals. Further, this study was limited to $PM_{2.5}$ and NO_2, the criteria air pollutants that have the strongest biological evidence to suggest a neurological effect. Ideally, multiple pollutants would be examined in the same model, and methods to deal with the high correlation between pollutants is a further direction in this work. Finally, we used baseline air pollutant concentrations as a proxy for long-term exposure. As air pollution levels have been decreasing since the passage of the Clean Air Act, using the baseline value is an underestimate of cumulative long-term exposure. Future work will include validating the use of ICE for this question in a larger sample. We believe that the concept of ICE as a downstream effect of racist policies would be strengthened if neighborhood ICE levels were adjusted for regional differences in race composition to reflect the relative power a neighborhood had with siting decisions (presumably source of air pollution) made at the regional/metropolitan statistical area. However, this study found no evidence that the

Dissimilarity Index was associated with cognitive aging. This could be due to only metropolitan and micropolitan areas being included in the sample.

The continued significant effect of neighborhood on cognitive function and decline necessitates a greater understanding of the historical and social patterning of air pollution. This is the first study to examine the effects of exposure to $PM_{2.5}$ and NO_2 and their interaction with neighborhood quality on cognition and cognitive decline in this sample of Medicare beneficiaries.

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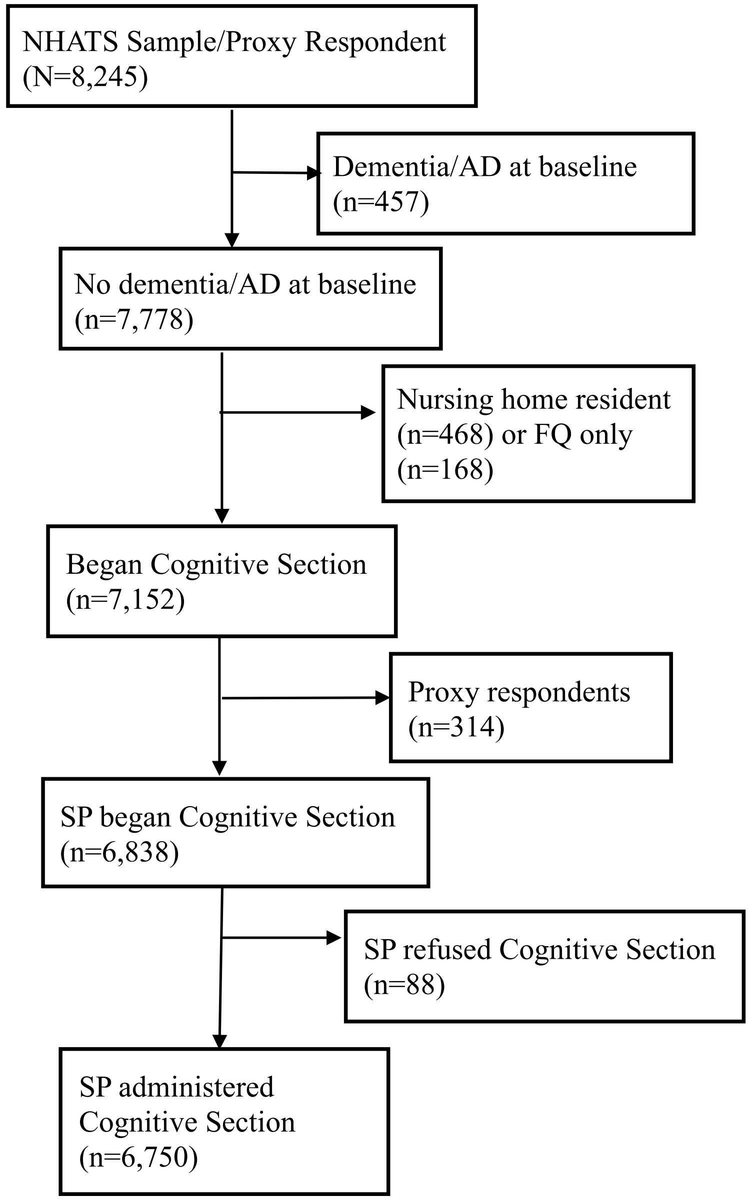

Figure 2.1. Study Flow Diagram for Analytic Sample in NHATS. We excluded those with dementia/AD at baseline in order to preclude reverse causation. Nursing home residents and those who completed a Facility Questionnaire were excluded because they did not complete a Sample Person (SP) Questionnaire. Those who used Proxy Respondents were excluded because we concluded this sample has a higher prevalence of dementia/AD and a majority did not complete the Cognitive Section of the SP Questionnaire. Finally, we excluded those who refused the Cognitive Section of the SP Questionnaire (as they would not provide values for any cognitive items at baseline).

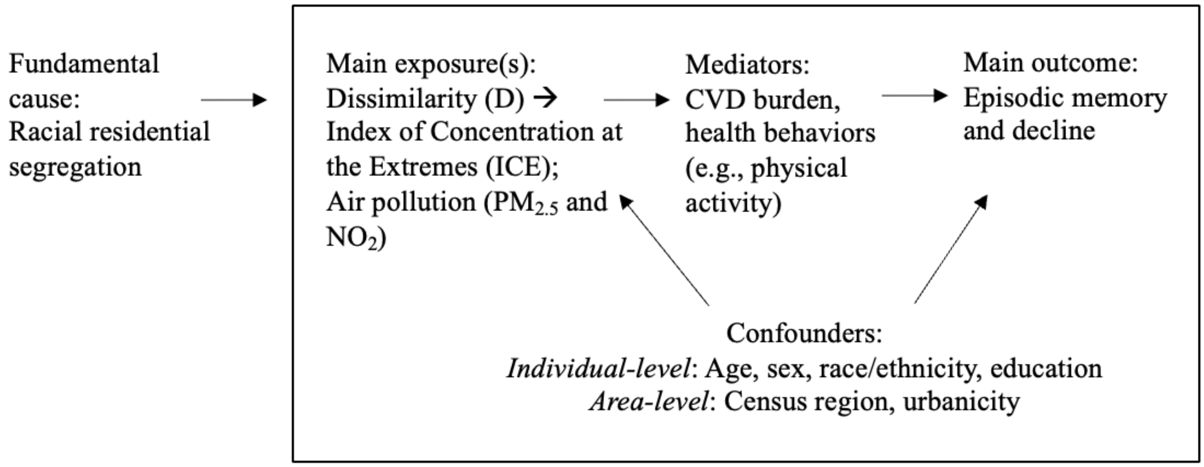

Figure 2.2. DAG Directed Acyclic Graph of the relationship between racial residential segregation, Dissimilarity, Index of Concentration at the Extremes, air pollution ($PM_{2.5}$ and NO_2), and episodic memory and decline, NHATS, 2011 cohort

Table 2.1. Baseline characteristics of participants by racialized economic Index of Concentration at the Extremes (ICE) (n=6,750)

	ICE <= -0.3	-0.3< ICE <= 0.3	ICE > 0.3
n	386	5825	538
Age at baseline, years	77.01 (7.15)	77.05 (7.69)	77.17 (7.72)
Male	135 (35.0%)	2447 (42.0%)	258 (48.0%)
Race/ethnicity			
White	24 (6.2%)	4509 (77.4%)	467 (86.8%)
African American	353 (91.5%)	1071 (18.4%)	40 (7.4%)
Hispanic	3 (0.8%)	357 (6.1%)	10 (1.9%)
Other race	12 (3.1%)	349 (6.0%)	35 (6.5%)
Education			
Less than High School	194 (50.3%)	1477 (25.4%)	53 (9.9%)
High School Diploma	91 (23.6%)	1664 (28.6%)	90 (16.7%)
Some College	57 (14.8%)	1509 (25.9%)	129 (24.0%)
Bachelor's Plus	44 (11.4%)	1175 (20.2%)	266 (49.4%)
Health measures			
Heart Attack	48 (12.4%)	878 (15.1%)	64 (11.9%)
Stroke	44 (11.4%)	589 (10.1%)	43 (8.0%)
Diabetes	146 (37.8%)	1454 (25.0%)	91 (16.9%)
Heart Disease	53 (13.7%)	1041 (17.9%)	91 (16.9%)
Lung Disease	67 (17.4%)	891 (15.3%)	62 (11.5%)
High blood pressure	297 (76.9%)	3886 (66.7%)	319 (59.3%)
Current smoker	50 (13.0%)	466 (8.0%)	25 (4.6%)
Former smoker	177 (45.9%)	3025 (51.9%)	279 (51.9%)
BMI	28.68 (7.07)	27.53 (5.83)	26.59 (4.93)
Neighborhood measures			
Black-White Dissimilarity	0.60 (0.13)	0.58 (0.11)	0.66 (0.09)
Racialized economic ICE	-0.42 (0.09)	0.05 (0.11)	0.41 (0.10)
$PM_{2.5}$ ($\mu g/m^3$)	10.82 (1.26)	9.41 (1.87)	9.35 (1.43)
NO_2 (ppb)	10.27 (4.68)	7.96 (5.00)	8.86 (4.42)
Urban	317 (82.1%)	3758 (64.5%)	526 (97.8%)

Table 2.2. Regression coefficients (b) to describe the association between fine particulate matter ($PM_{2.5}$), Black-White Dissimilarity Index (D), racialized economic Index of Concentration at the Extremes (ICE), and episodic memory (standardized z-scores) from mixed linear effects models

Covariate	Estimate	2.50%	97.50%
(Intercept)	3.585	3.358	3.811
$PM_{2.5}$	-0.306	-0.658	0.046
ICE	-0.560	-1.171	0.050
D	-0.049	-0.268	0.171
Baseline age	-0.051	-0.054	-0.049
Female sex	0.226	0.191	0.260
High school graduate	0.280	0.232	0.328
Some college	0.396	0.347	0.446
Bachelors' degree+	0.652	0.600	0.705
Black	-0.291	-0.342	-0.239
Hispanic	-0.239	-0.318	-0.160
Other race	-0.141	-0.215	-0.067
Midwest	0.045	-0.013	0.104
South	-0.046	-0.105	0.013
West	-0.042	-0.105	0.022
Urban	0.026	-0.022	0.073
$PM_{2.5}$*ICE	-0.248	-2.205	1.708
$PM_{2.5}$*D	0.463	-0.128	1.052
ICE*D	0.432	-0.526	1.392
$PM_{2.5}$*ICE*D	0.415	-2.708	3.536

Table 2.3. Regression coefficients (b) to describe the association between nitrogen dioxide (NO_2), Black-White Dissimilarity Index (D), racialized economic Index of Concentration at the Extremes (ICE), and episodic memory (standardized z-scores) from mixed linear effects models

Effect	Estimate	2.50%	97.50%
(Intercept)	3.563	3.331	3.792
NO_2	-0.072	-0.339	0.194
ICE	-0.391	-1.027	0.246
D	-0.027	-0.250	0.197
Baseline age	-0.051	-0.053	-0.049
Female sex	0.226	0.192	0.260
High school graduate	0.282	0.234	0.330
Some college	0.397	0.348	0.446
Bachelors' degree+	0.655	0.603	0.707
Black	-0.291	-0.343	-0.239
Hispanic	-0.236	-0.317	-0.155
Other race	-0.144	-0.218	-0.071
Midwest	0.039	-0.021	0.100
South	-0.050	-0.111	0.011
West	-0.025	-0.090	0.041
Urban	0.023	-0.029	0.075
NO_2*ICE	1.436	-0.155	3.029
NO_2*D	0.102	-0.266	0.471
ICE*D	0.166	-0.848	1.181
NO_2*ICE*D	-1.743	-3.895	0.405

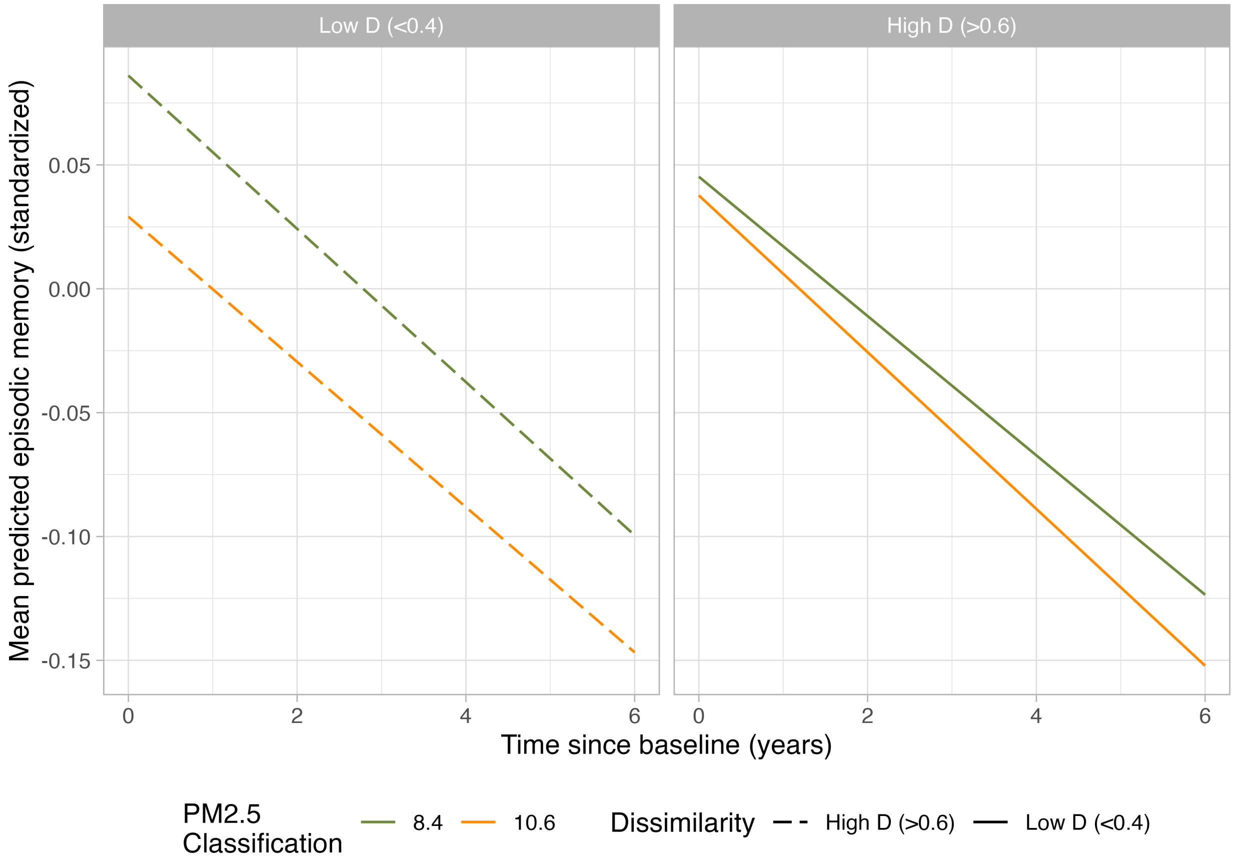

Figure 2.3. Marginal estimates of Black-White Dissimilarity (D) and exposure to $PM_{2.5}$

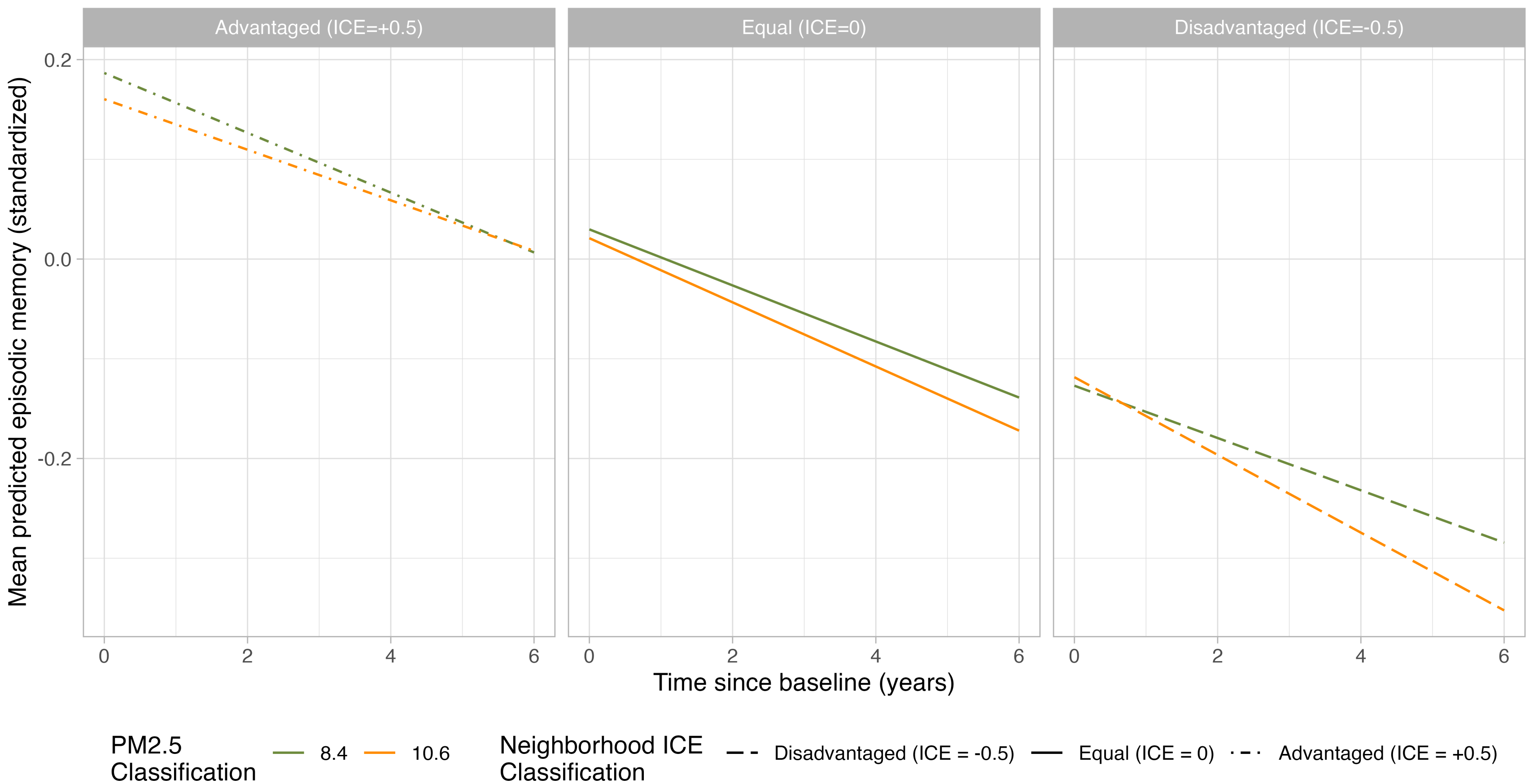

Figure 2.4. Marginal estimates of racialized economic Index of Concentration at the Extremes (ICE) and exposure to $PM_{2.5}$

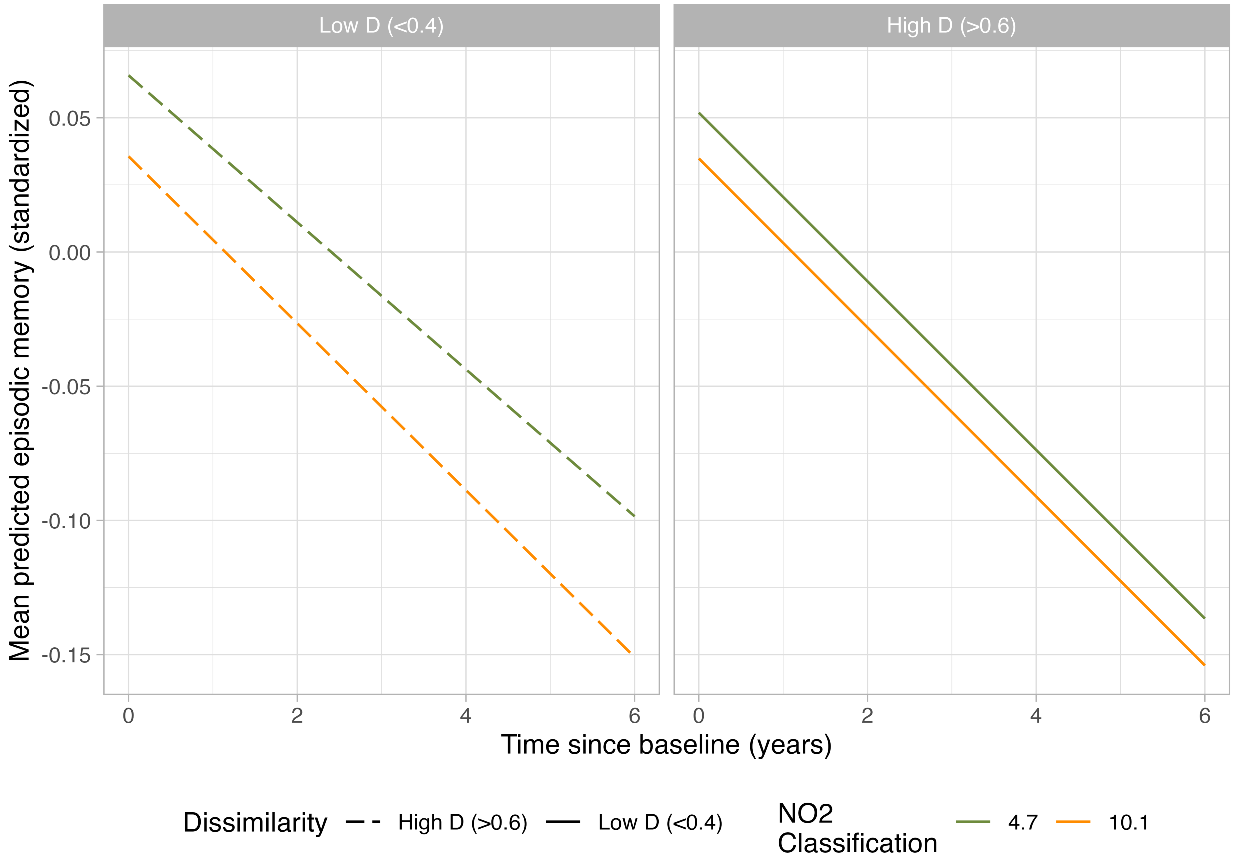

Figure 2.5. Marginal estimates of Black-White Dissimilarity (D) and exposure to NO_2

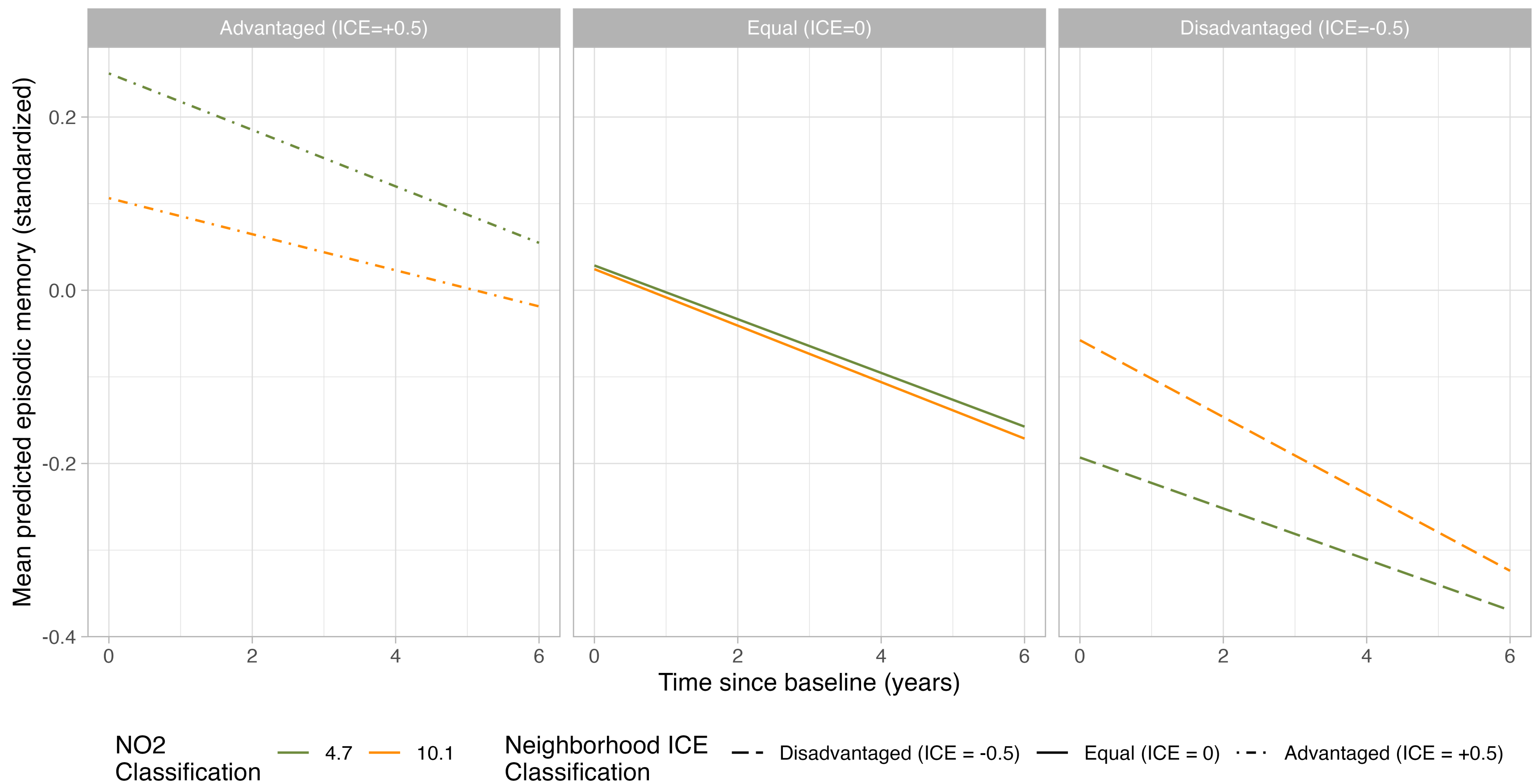

Figure 2.6. Marginal estimates of racialized economic Index of Concentration at the Extremes (ICE) and exposure to NO_2

Chapter 3: Do 10-year trajectories of ambient air pollutant ($PM_{2.5}$ and NO_2) exposure influence memory? Examining co-pollutant changes using sequence analysis

INTRODUCTION

As our population ages(1), mounting interest lies in alleviating the illnesses of our older populations. Alzheimer's Disease and related dementias affect 5.8 million Americans as of 2019, and this figure is set to grow to 7.1 million by 2050(2). Currently, this translates to healthcare costs in excess of $1 trillion annually. There are 12 known modifiable risk factors for dementia that could prevent up to 40% of dementia incidence (3). Air pollution was added as a risk factor in 2020 and its adverse effects on cognition, and more distally, Alzheimer's Disease and related dementias, has been an active area of research(3–5).

However, the literature continues to struggle with documenting past exposure to air pollution over a period longer than a few years; this is a concern when evaluating with cognition, specifically, as AD/ADRD develops over decades(4) . With changing exposure to air pollution over time, it is important to consider longer time frames of air pollution exposure. Alzheimer's Disease and related dementia develop over the course of decades in a process that is still largely unknown. Using exposure data that reflects the longest possible exposure period will more likely reflect the true biological process (and the estimate). In addition, the evaluation of co-occurrence of multiple pollutants has been constrained to reporting of correlations between them and dropping highly correlated ones. Air pollution is a complex mixture of particulate and gaseous components, and as such, it is incomplete to look at one component in isolation. Recently, more methods have been developed to include multiple correlated pollutants without having to sacrifice highly correlated ones in the model, but none of them in one model with the outcome.

Sequence analysis is a data-driven approach that summarizes sequences of ordered events or "states" that are set in time or position. Originating in evolutionary biology to deduce the function of DNA sequences(6), it was first adapted to the social sciences in the 1990s to examine musicians' careers(7,8). More recently, it has been used to characterize exposures that unfold over time (e.g., educational or occupational trajectories) to identify distinct exposure groups; these groups are then used subgroups at higher risk of adverse health outcomes(9,10). In an innovation, we will apply sequence analysis and cluster analysis to characterize 10-year air pollution trajectories. The sequence analysis of air pollutant ($PM_{2.5}$ and NO_2) trajectories for the 10 years preceding baseline in a nationally-representative cohort of Medicare beneficiaries will allow us to better characterize exposure histories and understand the role of air pollution on adverse cognitive effects.

METHODS

Study population. The National Health and Aging Trends Study (NHATS) is a representative sample of 8,245 Medicare beneficiaries aged 65+ at baseline in 2011. Design, sampling, and response rates are described elsewhere(11). We excluded those with dementia or Alzheimer's disease at baseline, nursing home residents or those who only completed a Facility Questionnaire (this group did not complete the Cognitive Section), those who used proxy respondents, and those who refused the Cognitive Section at baseline, resulting in a final analytic sample size of 6,750. A study flow diagram is included (Supplement Figure 1).

Assessment of air pollution exposure. Our exposure was census-tract level air pollution trajectories from 2000 to 2010. Air pollution concentration estimates were developed by the Center for Air, Climate and Energy Solutions using v1 empirical models as described in Kim et al., 2018(12). Briefly, these models were built from U.S. EPA regulatory monitors, land use maps, and satellite images to predict ambient concentrations at locations without monitors of seven pollutants throughout the contiguous United States. Annual average concentrations of outdoor $PM_{2.5}$ ($\mu g/m^3$) and NO_2 (ppb) for residential Census Block centroid were predicted and population weighted to the census tract in the contiguous United States were obtained for the 10 years prior to baseline, creating an exposure window from 2000 to 2010. Individual air pollution trajectories that incorporate 10 years of prior exposure data could yield thousands of unique exposure sequences. To operationalize thousands of air pollution trajectories from 2000-2010 into an analytically tractable number of distinct trajectory clusters, we applied sequence analysis, an innovation in air pollution trajectory data. This was accomplished in three steps: [1] creation of census-tract level air pollution trajectories; [2] sequence analysis to quantitatively evaluate how similar each trajectory was to all other trajectories in the data; [3] cluster analysis to group similar trajectories.

First, we created census-tract level air pollution trajectories, by categorizing data on two pollutants ($PM_{2.5}$, NO_2) into low (<25th percentile), medium (25 – 75th percentile), and high (>75th percentile) categories using 2010 data for percentile cut offs. For $PM_{2.5}$, cut points were 7.9 $\mu g/m^3$ and 10.8 $\mu g/m^3$, and for NO_2 cut points were 4.8 ppb and 10.8 ppb). For each year between 2000 and 2010, nine mutually exclusive categories are possible (e.g. low $PM_{2.5}$, low NO_2; medium $PM_{2.5}$, low $N0_2$; high $PM_{2.5}$, low NO_2, etc.).

Second, we used the optimal matching algorithm to evaluate quantitatively how trajectories differed from each other. Optimal matching calculates dissimilarities (distances) between each pair of sequences as the minimum total "cost" to transform one sequence into another, obtained as a combination of edit operations (substitutions, insertions and deletions). For our specific application, we utilized dynamic hamming, a variation of the optimal matching algorithm that calculates time-varying substitution costs and does not allow insertion and deletion operations, therefore prioritizing timing over duration and order of events (13). Substitution costs between pollution categories were based on observed transition rates at each time point such that more rare transitions were assigned higher substitution costs. A substitution cost matrix was generated from the transition rates at each time point in the study period. Next, single substitution costs were summed to calculate the dissimilarity between each sequence and all the other sequences in the data, resulting into a symmetric, square distance matrix.

Finally, we applied agglomerative hierarchical clustering to group similar air pollution trajectories together on the basis of the distance matrix obtained from the sequence analysis. We used Ward's linkage(14), which iteratively compares the error sum of squares of a cluster solution with the error sum of squares of a cluster solution with one less cluster. The final number of clusters was determined using Duda-Hart stopping rules(15). With additional assessments based on cluster heterogeneity, 10-year air pollution trajectories with a 9-cluster solution was selected.

Outcome ascertainment. The outcome was a composite measure of episodic memory calculated from the immediate and delayed word list recall from the Cognitive Section assessed in-person annually. These measures ask participants to read a list of 10 words. For the immediate word recall, participants are asked to recall as many words as possible immediately after reading the list. After 5-minutes, the participant is asked to recall as many of the 10 words as possible for the delayed word list recall measure. Scores on each test were standardized to baseline mean and standard deviation, and then averaged.

Covariates. We included the following potential confounders in our final model: baseline age (years), sex (female, male), education (less than high school, high school diploma, some college, Bachelor's degree and higher), race/ethnicity (Black, Hispanic, White, other), Census region (Midwest, South, West, Northeast), urban census tract (Rural-Urban Commuting Area Code(16) = 1 indicator), and neighborhood Index of Concentration at the Extremes (ICE). The Index of Concentration (ICE) at the Extremes measures the concentration of privilege (non-Hispanic White with high incomes) and disadvantage (non-Hispanic Black with low income) in a census tract(17,18). We computed ICE(19) for each census tract, calculated as:

$$ICE_i = \frac{A_i - P_i}{T_i},$$

where A_i is the number of people in the census tract *i* in the most privileged extreme, P_i is the number of people in the census tract *i* in the most deprived extreme, and T_i is the total number of people living in that census tract *i*. The ICE_i is summed across all census tracts *n* in the US for the estimates presented in Table 1. A distinct advantage of using ICE is the ability to combine multiple dimensions of social advantage, and for this analysis, we use racialized economic segregation. This variable defines the privilege group as high-income non-Hispanic White people and disadvantage as low-income non-Hispanic Black people. High income is defined as the 80^{th} percentile, \$100K and greater, and low income as \$25K and less(17,19). ICE ranges from -1 (concentrated with low-income non-Hispanic Black individuals) to 1 (concentrated with high-income non-Hispanic White individuals), and was computed for each census tract.

Statistical analysis. Our primary goal was to investigate the relationship between air pollution trajectories generated from sequence and cluster analysis and memory. We used a linear mixed model to evaluate the effect of air pollution trajectories on memory, adjusted for confounders, with random intercepts for census tract.

We conducted several robustness checks to compare estimates using sequence and cluster analysis to more traditional measures of the effect between exposure to air pollution and episodic memory. We compared separate models of $PM_{2.5}$ and NO_2 in 2010 as a continuous variable representing long-term exposure to air pollution. We also categorized $PM_{2.5}$ and NO_2 at the 25th and 75th percentiles in 2010 to create categories of low, medium, and high exposure, and tested each pollutant in separate models.

All analyses were weighted to be nationally representative, and all standard errors were adjusted for the sampling design of the National Health and Aging Trends Study, 2011 cohort. Data cleaning and analyses were conducted using R, version 2022.12.0+353. All data cleaning and analysis code was reviewed by the second author, who was not involved in the initial programming(20).

RESULTS

Our sample included 6,750 NHATS participants living in 3,048 different census tracts. Using the 25th and 75th percentiles for $PM_{2.5}$ (7.9 and 10.8 μg/m^3) and NO_2 (4.8 and 10.8 ppb) for all US census tracts in 2010, our sample contained 1,080 unique sequences (Figure 3.1 Index Plot). After implementing sequence and cluster analysis, air pollution sequences were clustered into 9 groups using Duda-Hart stopping rules (Supplement Table 3.3S) considering cluster heterogeneity. We described these groups based on the timing, duration, and order of air pollution states. We refer to these groups descriptively as: (1) high $PM_{2.5}$ and NO_2 with decreasing NO_2, (2) those with high exposure to $PM_{2.5}$ and NO_2 for the duration of the study period, (3) those with a mix of high/medium exposure, (4) those with a mix of medium exposure, (5) high $PM_{2.5}$ and medium NO_2 exposure, (6) low $PM_{2.5}$ and NO_2 exposure—designated as the reference group, (7) low exposure mixture with some medium at the start of the study period, (8) medium $PM_{2.5}$ and NO_2 exposure, and (9) medium exposure mixture (Figure 3.2).

Cluster Characteristics. The number of NHATS participants' census tracts in each cluster ranged from 205 (Cluster 6 to 2185 (Cluster 2) (Table 3.1). Those living in higher exposure pollution trajectories (Clusters 1 and 2) had a greater than 25% African American individuals. Unsurprisingly, Clusters 1 and 2 had the greatest percentage of NAAQS PM2.5 exceedances, 15% and 18%, respectively. Clusters 6-8 had greater than 90% White people. Cluster 4 had the highest percentage (14.3%) of Hispanic populations. Clusters 1-4 had greater than 90% urban census tracts; conversely Cluster 6, our reference cluster, was comprised completely of rural census tracts. We did not observe large differences by age, gender, health conditions, or measures of neighborhood socioeconomic conditions.

Ten-year Air Pollution Trajectories and Memory. Generally, higher exposure to air pollution and longer duration of exposure over the 10-year period predicted worse episodic memory (See Table 3.2). Compared to those with the lowest exposure trajectory over the 10-year exposure period (Cluster 6), all groups reported worse episodic memory at baseline. Those in Cluster 1, with high $PM_{2.5}$ and NO_2 and decreasing NO_2 towards the latter half of 2010, had a 0.217 (95% CI: -0.369, -0.065) SD worse cognitive score than those who experienced the least exposure to $PM_{2.5}$ and NO_2 for the study period (Cluster 6). For context, a year of aging in this sample was associated with an estimated effect of -0.045 (95% CI: -0.048, -0.043); therefore, compared to the low exposure referent group, all other air pollution trajectory clusters represent excess cognitive aging between 2 and 5 years.

Robustness Checks. Our sensitivity analyses showed consistent, albeit weaker and non-statistically significant associations with episodic memory at baseline (Supplement Tables 3.4S-3.7S). Using NO_2 in 2010 as a continuous measure, we observed that every-unit increase in NO_2 was associated with a 0.003 SD (95% CI: -0.008, 0.002) worse memory score; for $PM_{2.5}$, -0.005 (-0.016, 0.006) SD worse score. Comparing the highest category of NO_2 exposure to the lowest in 2010, we observed a 0.017 (-0.089, 0.056) SD worse memory score, and for the highest tertile of $PM_{2.5}$ we observed a 0.023 (-0.041, 0.087) SD better episodic memory score.

DISCUSSION

Higher exposure to air pollutants ($PM_{2.5}$ and NO_2) was generally associated with worse episodic memory in the National Health and Aging Trends Study in participants enrolled in 2011; however, memory at baseline was associated more strongly with trajectory cluster of participant than most recent exposure serving as a proxy for long-term exposure. Our results suggest that sequence analysis offers a more nuanced operationalization of the exposure, simultaneously incorporating exposure level, duration, and timing of air pollution over ten years.

Future research could incorporate more pollutants than the ones used here. We plan to use multi-channel sequence analysis to allow flexibility in multiple pollutants, other neighborhood factors, and their interaction. The definition of costs has been a point of contention with the application of sequence analysis to the social sciences. Another future direction of our work is to help validate this work.

There are limitations to these analyses. We were only able to examine the 10 years of exposure to air pollution history due to air pollution model changes and residential living patterns. Ideally, we would have residential and air pollution data for the entire life course;

however, we were able to detect meaningful differences in memory given our data, and our approach represents an important advance over prior work in this area. Sequence analysis is not able to address time-varying confounding that occur during exposure trajectories, only pre-trajectory confounders (occurring before 2000). Residual confounding is a concern in all observational analyses; although our substantive research questions are clearly causal, strong, untestable assumptions are needed for causal inference. Contemporaneous exposures (like increases in area level poverty due to plant closure) were not incorporated in these analyses and represent an important area to address in future work. These results may not generalize to more recent, or younger, cohorts, as air pollution has generally decreased since its measurement in the United States (1970), however, detecting health effects even at these lower levels is important to inform national standards for air pollution (NAAQS).

To our knowledge, this is the first analysis to rigorously examine the combined consequences of both $PM_{2.5}$ and NO_2 using sequence analysis.

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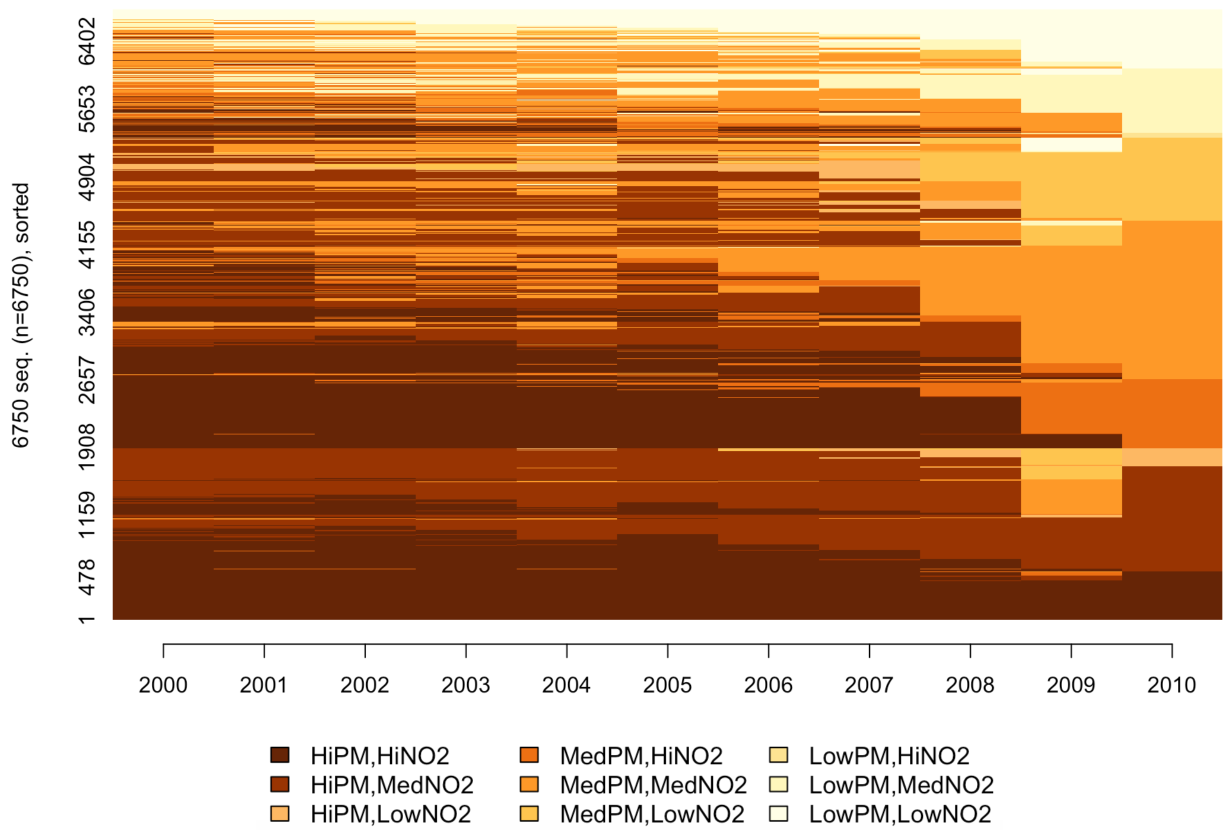

Figure 3.1. Sequence index plot showing the individual-level air pollution trajectories (2000-2010) represented in the National Health and Aging Trends Study 2011 cohort. Each individual's air pollution trajectory is a row on the y-axis; each year of exposure to air pollution is represented on the x-axis. There were 6,750 individuals followed for 10 years included in the sequence analysis. We categorized each year of exposure into 1 of 9 mutually exclusive states based on the 25th and 75th percentiles of $PM_{2.5}$ and NO_2 in 2010. Of a total possible 9^{10} air pollution trajectories, there were 1,080 unique air pollution trajectories.

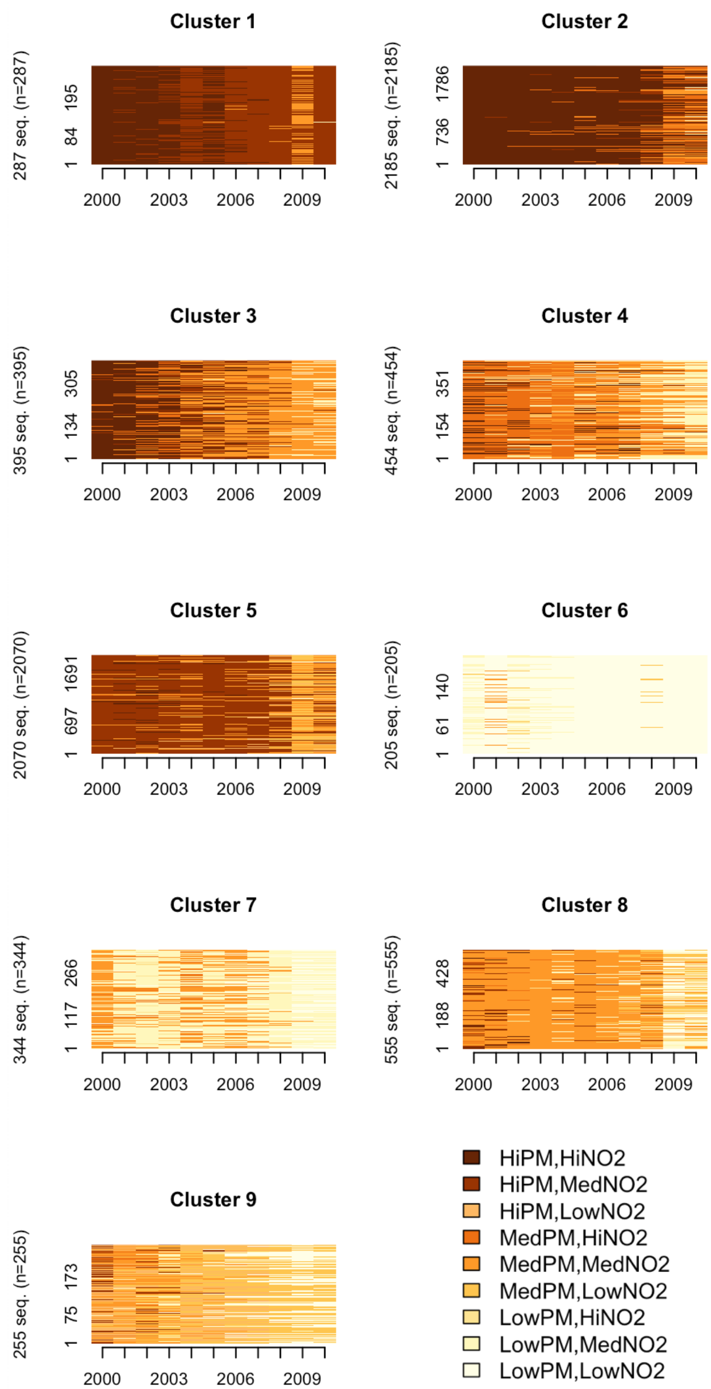

Figure 3.2. Sequence index plots of the 9 prototypical air pollution sequences from 2000-2010 used to predict memory in NHATS. We refer to these groups descriptively as: (1) high $PM_{2.5}$ and NO_2 with decreasing NO_2, (2) high $PM_{2.5}$ and NO_2 throughout the study period, (3) a mix of high/medium exposures, (4) a mix of medium exposures, (5) high $PM_{2.5}$ and medium NO_2 exposure, (6) low $PM_{2.5}$ and NO_2 exposure—designated as the reference group, (7) low exposure with some medium at the start of the study period, (8) medium $PM_{2.5}$ and NO_2 exposure, and (9) medium exposure mixture.

Table 3.1. Baseline (2011) characteristics of participants by air pollution trajectories' cluster in the National Health and Aging Trends Study (NHATS) 2011 cohort

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Cluster 8	Cluster 9
n	287	2185	395	454	2070	205	344	555	255
Age at baseline, years	77.31 (7.52)	77.41 (7.70)	77.37 (7.78)	77.77 (7.73)	76.49 (7.53)	76.06 (7.31)	77.79 (8.09)	77.22 (7.72)	76.09 (7.28)
Male	116 (40.4%)	892 (40.8%)	164 (41.5%)	195 (43.0%)	886 (42.8%)	110 (53.7%)	146 (42.4%)	224 (40.4%)	108 (42.4%)
White	203 (70.7%)	1257 (57.5%)	311 (78.7%)	387 (85.2%)	1636 (79.0%)	193 (94.1%)	312 (90.7%)	514 (92.6%)	188 (73.7%)
African American	77 (26.8%)	751 (34.4%)	66 (16.7%)	46 (10.1%)	410 (19.8%)	3 (1.5%)	17 (4.9%)	33 (5.9%)	61 (23.9%)
Hispanic	2 (0.7%)	185 (8.5%)	19 (4.8%)	65 (14.3%)	46 (2.2%)	1 (0.5%)	13 (3.8%)	30 (5.4%)	10 (3.9%)
Other race	8 (2.8%)	193 (8.8%)	23 (5.8%)	25 (5.5%)	84 (4.1%)	15 (7.3%)	21 (6.1%)	16 (2.9%)	11 (4.3%)
Less than High School	72 (25.1%)	623 (28.5%)	72 (18.2%)	93 (20.5%)	591 (28.6%)	26 (12.7%)	65 (18.9%)	108 (19.5%)	75 (29.4%)
High School Diploma	79 (27.5%)	551 (25.2%)	99 (25.1%)	116 (25.6%)	608 (29.4%)	67 (32.7%)	97 (28.2%)	154 (27.7%)	74 (29.0%)
Some College	68 (23.7%)	514 (23.5%)	112 (28.4%)	134 (29.5%)	497 (24.0%)	51 (24.9%)	109 (31.7%)	145 (26.1%)	65 (25.5%)
Bachelor's Plus	68 (23.7%)	497 (22.7%)	112 (28.4%)	111 (24.4%)	374 (18.1%)	61 (29.8%)	73 (21.2%)	148 (26.7%)	41 (16.1%)
Heart Attack	43 (15.0%)	293 (13.4%)	61 (15.4%)	71 (15.6%)	332 (16.0%)	35 (17.1%)	43 (12.5%)	74 (13.3%)	39 (15.3%)
Stroke	37 (12.9%)	187 (8.6%)	41 (10.4%)	50 (11.0%)	225 (10.9%)	26 (12.7%)	38 (11.0%)	47 (8.5%)	26 (10.2%)
Diabetes	71 (24.7%)	596 (27.3%)	100 (25.3%)	107 (23.6%)	518 (25.0%)	39 (19.0%)	71 (20.6%)	113 (20.4%)	77 (30.2%)

	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Cluster 5	Cluster 6	Cluster 7	Cluster 8	Cluster 9
Heart Disease	51 (17.8%)	346 (15.8%)	71 (18.0%)	86 (18.9%)	390 (18.8%)	27 (13.2%)	57 (16.6%)	96 (17.3%)	62 (24.3%)
Lung Disease	54 (18.8%)	320 (14.6%)	59 (14.9%)	62 (13.7%)	330 (15.9%)	42 (20.5%)	45 (13.1%)	71 (12.8%)	38 (14.9%)
High blood pressure	192 (66.9%)	1483 (67.9%)	267 (67.6%)	284 (62.6%)	1411 (68.2%)	113 (55.1%)	223 (64.8%)	349 (62.9%)	181 (71.0%)
Current smoker	26 (9.1%)	164 (7.5%)	27 (6.8%)	32 (7.0%)	197 (9.5%)	24 (11.7%)	24 (7.0%)	27 (4.9%)	20 (7.8%)
Former smoker	156 (54.4%)	1100 (50.3%)	202 (51.1%)	236 (52.0%)	1047 (50.6%)	123 (60.0%)	194 (56.4%)	291 (52.4%)	132 (51.8%)
BMI	27.54 (6.31)	27.56 (6.04)	27.14 (5.68)	27.00 (5.08)	27.86 (5.91)	27.22 (5.04)	26.93 (5.48)	27.18 (5.72)	27.70 (6.07)
Black-White Dissimilarity	0.56 (0.09)	0.66 (0.10)	0.59 (0.07)	0.58 (0.08)	0.53 (0.10)	0.59 (0.09)	0.54 (0.09)	0.55 (0.09)	0.50 (0.12)
Racialized economic ICE	0.01 (0.22)	0.04 (0.23)	0.10 (0.18)	0.06 (0.14)	0.03 (0.17)	0.06 (0.05)	0.10 (0.14)	0.12 (0.12)	0.04 (0.12)
$PM_{2.5}$ ($\mu g/m^3$)	11.09 (0.86)	10.65 (1.31)	8.89 (0.99)	8.13 (1.37)	9.96 (0.97)	5.15 (0.91)	6.35 (0.83)	8.01 (1.01)	8.11 (1.42)
NO_2 (ppb)	7.61 (0.82)	13.52 (4.99)	7.31 (1.18)	8.79 (2.44)	5.16 (1.21)	2.32 (0.58)	5.20 (1.44)	5.13 (1.30)	2.89 (0.78)
Exceeds NAAQS $PM_{2.5}$	43 (15.0%)	394 (18.0%)	1 (0.3%)	0 (0.0%)	30 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Urban	253 (88.2%)	2169 (99.3%)	379 (95.9%)	417 (91.9%)	855 (41.3%)	0 (0.0%)	143 (41.6%)	303 (54.6%)	83 (32.5%)

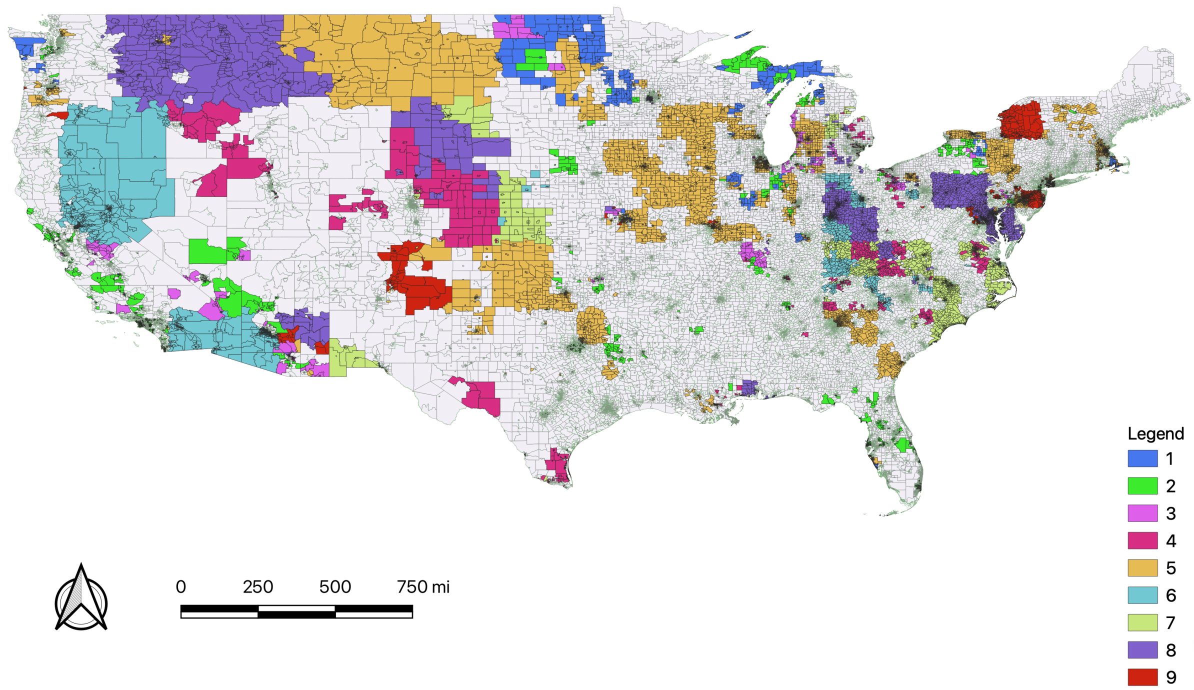

Figure 3.3. Geographic distribution of NHATS participant's baseline census tract 10-year air pollution trajectory clusters. Cluster 6 served as the reference for this analysis; Cluster 1 and 2 had the highest concentrations during the 10-year exposure window. Clusters 1-4 had a greater proportion of urban census tracts; Cluster 6 was comprised entirely of rural census tracts (urban defined according to RUCA code = 1)

Table 3.2. Regression coefficients (b) for the association of cluster of air pollution trajectories and memory score in the NHATS 2011 cohort (weighted)

Effect	Estimate	2.50%	97.50%
(Intercept)	3.320	3.077	3.562
Cluster 7	-0.103	-0.239	0.033
Cluster 8	-0.109	-0.240	0.022
Cluster 9	-0.119	-0.269	0.030
Cluster 4	-0.208	-0.344	-0.071
Cluster 3	-0.279	-0.419	-0.138
Cluster 5	-0.155	-0.274	-0.036
Cluster 2	-0.181	-0.307	-0.055
Cluster 1	-0.200	-0.353	-0.046
Baseline age	-0.047	-0.050	-0.044
Female sex	0.269	0.230	0.307
High school graduate	0.306	0.249	0.363
Some college	0.413	0.355	0.471
Bachelors' degree +	0.690	0.629	0.751
Black	-0.305	-0.382	-0.227
Hispanic	-0.152	-0.236	-0.068
Other race	-0.223	-0.302	-0.144
ICE	-0.300	-0.437	-0.162
Midwest	0.079	0.017	0.140
South	-0.018	-0.076	0.041
West	-0.018	-0.085	0.049
Urban	0.046	-0.009	0.100

Table 3.3S Duda-Hart Cluster Stopping Rules, Dynamic Hamming

Number of Clusters	Je(2)/Je(1)	pseudo T-squared
1	0.7500	2249.17
2	0.8312	916.16
3	0.8426	478.06
4	0.8303	314.45
5	0.7475	344.58
6	0.8623	207.74
7	0.7924	585.15
8	0.8474	351.05
9	0.8131	199.05
10	0.7877	382.52
11	0.5337	1106.29
12	0.7448	148.35
13	0.8463	108.77
14	0.8229	207.90
15	0.8705	101.78
16	0.7953	187.87
17	0.6864	244.93
18	0.8377	102.53
19	0.6306	105.46
20	0.7399	241.47

Table 3.4S Regression coefficients for categories (by IQR) for $PM_{2.5}$ in 2010 with memory score in NHATS 2011 cohort

Effect	Estimate	2.50%	97.50%
(Intercept)	3.104	2.892	3.317
ICE	-0.299	-0.425	-0.173
$PM_{2.5}$ IQR 2	-0.014	-0.070	0.042
$PM_{2.5}$ IQR 3	0.023	-0.041	0.087
Baseline age	-0.046	-0.048	-0.043
Female sex	0.235	0.197	0.274
High school graduate	0.312	0.259	0.365
Some college	0.409	0.354	0.464
Bachelor's degree +	0.672	0.613	0.731
Black	-0.284	-0.340	-0.227
Hispanic	-0.160	-0.249	-0.072
Other race	-0.177	-0.259	-0.095
Midwest	0.065	0.004	0.127
South	-0.049	-0.104	0.006
West	-0.026	-0.092	0.040
Urban	0.008	-0.036	0.052

Table 3.5S Regression coefficients for categories (by IQR) for NO_2 in 2010 with memory score in NHATS 2011 cohort

Effect	Estimate	2.50%	97.50%
(Intercept)	3.104	2.895	3.312
ICE	-0.292	-0.418	-0.167
NO_2 IQR 2	**-0.041**	**-0.093**	**0.011**
NO_2 IQR 3	**-0.017**	**-0.089**	**0.056**
Baseline age	-0.045	-0.048	-0.043
Female sex	0.236	0.198	0.275
High school graduate	0.311	0.258	0.365
Some college	0.408	0.353	0.463
Bachelor’s degree +	0.671	0.612	0.730
Black	-0.284	-0.341	-0.227
Hispanic	-0.158	-0.247	-0.069
Other race	-0.180	-0.262	-0.098
Midwest	0.083	0.023	0.144
South	-0.042	-0.100	0.015
West	-0.016	-0.079	0.046
Urban	0.027	-0.024	0.079

Table 3.6S Regression coefficients for continuous (by IQR) for $PM_{2.5}$ in 2010 with memory score in NHATS 2011 cohort

Effect	Estimate	2.50%	97.50%
(Intercept)	3.146	2.916	3.375
ICE	-0.281	-0.408	-0.155
$PM_{2.5}$	-0.005	-0.016	0.006
Baseline age	-0.046	-0.048	-0.043
Female sex	0.236	0.197	0.274
High school graduate	0.310	0.257	0.363
Some college	0.406	0.351	0.461
Bachelor’s degree +	0.669	0.610	0.728
Black	-0.280	-0.336	-0.223
Hispanic	-0.160	-0.248	-0.071
Other race	-0.175	-0.257	-0.093
Midwest	0.083	0.021	0.145
South	-0.044	-0.099	0.011
West	-0.029	-0.094	0.035
Urban	0.019	-0.025	0.064

Table 3.7S Regression coefficients for continuous (by IQR) for NO_2 in 2010 with memory score in NHATS 2011 cohort

Effect	Estimate	2.50%	97.50%
(Intercept)	3.117	2.907	3.327
ICE	-0.283	-0.408	-0.157
NO_2	-0.003	-0.008	0.002
Baseline age	-0.045	-0.048	-0.043
Female sex	0.236	0.197	0.274
High school graduate	0.310	0.257	0.363
Some college	0.407	0.352	0.462
Bachelor's degree +	0.671	0.612	0.729
Black	-0.276	-0.333	-0.218
Hispanic	-0.151	-0.240	-0.061
Other race	-0.172	-0.255	-0.090
Midwest	0.069	0.008	0.129
South	-0.060	-0.119	-0.001
West	-0.026	-0.088	0.037
Urban	0.028	-0.021	0.077

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