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Ambient Fine Particulate Matter ($PM_{2.5}$) Exposure and Incident Mild Cognitive Impairment and Dementia

Kevin J Sullivan, PhD[a,g], **Xinhui Ran, MS**[b], **Fan Wu, MS**[c], **Chung-Chou H Chang, PhD**[b,d], **Ravi Sharma, PhD**[a], **Erin Jacobsen, MS**[e], **Sarah Berman, MD PhD**[f], **Beth E Snitz, PhD**[f], **Akira Sekikawa, MD PhD**[a], **Evelyn O Talbott, DrPH**[a], **Mary Ganguli, MD, MPH**[a,d]

[a.]Department of Epidemiology, University of Pittsburgh;

[b.]Department of Biostatistics, University of Pittsburgh;

[c.]Department of Environmental and Occupational Health, University of Pittsburgh;

[d.]Department of Medicine, University of Pittsburgh;

[e.]Department of Psychiatry, University of Pittsburgh;

[f.]Department of Neurology, University of Pittsburgh;

[g.]Department of Medicine, University of Mississippi Medical Center

Abstract

Background/Objective: Poor air quality is implicated as a risk factor for cognitive impairment and dementia. Few studies have examined these associations longitudinally in well-characterized population-based cohorts with standardized annual assessment of both mild cognitive impairment (MCI) and dementia. We investigated the association between estimated ambient fine particulate matter ($PM_{2.5}$) and risk of incident MCI and dementia in a post-industrial region known for historically poor air quality.

Setting/Participants: Adults aged 65+ years in a population-based cohort (n=1572).

Measurements: Census tract level $PM_{2.5}$ from Environmental Protection Agency (EPA) air quality monitors; Clinical Dementia Rating(CDR)®.

Design: We estimated ambient $PM_{2.5}$ exposure ($\mu g/m^3$, single-year and five-year averages) by geocoding participants' residential addresses to census tracts with daily EPA $PM_{2.5}$ measurements

Corresponding author: Kevin J Sullivan, PhD, MPH, 2500 North State Street, Jackson, MS 39216. Phone: 601-815-7759, ksullivan3@umc.edu.

Author Contributions

KJS: study design and conceptualization, analysis and interpretation of data, drafting of manuscript. XR, FW, CCHC, RS: analysis and interpretation of data, figure design, critical revision of manuscript for intellectual content. EJ, SB, BES, AS: interpretation of data, critical revision of manuscript for intellectual content. EOT, MG: study design and conceptualization, interpretation of data, critical revision of manuscript for intellectual content, study supervision.

Conflicts of Interest

The authors have no conflicts.

Supplemental Material: Description of included and excluded participants (Table S1); Description of retained sample at each follow-up visit (Table S2); Bayesian spatial survival time-dependent models with and without frailty (Table S3); Primary spatial regression models additionally adjusted for household income (Table S4); Supplemental Methods detailing the assumptions of the frailty term in the Bayesian spatial survival models.

from 2002–2014. Using Bayesian spatial regression modeling adjusted for age, sex, education, smoking history, and household income, we examined the association between estimated $PM_{2.5}$ exposure and risk of incident mild cognitive impairment (CDR=0.5) and incident dementia (CDR≥1.0).

Results: Modeling estimated single-year exposure, each 1 μg/m^3 higher ambient $PM_{2.5}$ was associated with 67% higher adjusted risk of incident dementia (Hazard Ratio[HR]=1.669, 95% Credible Interval[CI]: 1.298, 2.136) and 75% higher adjusted risk of incident MCI (HR=1.746, 95% CI: 1.518, 2.032). Estimates were higher when modeling five-year ambient $PM_{2.5}$ exposure for incident dementia (HR=2.082, 95% CI:1.528, 3.015) and incident MCI (HR=3.419, 95% CI:2.806, 4.164).

Conclusions: Higher estimated ambient $PM_{2.5}$ was associated with higher risk of incident MCI and dementia, particularly when considering longer term exposure, and independent of demographic characteristics and smoking history. Targeting poor air quality may be a reasonable population-wide intervention to reduce risk of cognitive impairment in older adults, particularly in regions exceeding current recommendations for safe exposure to $PM_{2.5}$.

Keywords

fine particulate matter; air pollution; dementia; cognitive impairment; epidemiology

INTRODUCTION

Efforts to address the public health crisis of dementia, which affects nearly 50 million older adults worldwide and threatens to worsen with population aging, focus increasingly on prevention.[1] While behavioral and pharmacological interventions will likely play a role in delaying or preventing the onset of dementia, these interventions function at an individual level and have generally demonstrated mixed evidence as to their effectiveness.[2, 3] Regulatory public health preventative interventions that scale to the population level could potentially provide wide scale benefits towards reducing the dementia burden in the older adult population. Air pollution, now recognized as one of the primary contributors to disease worldwide,[4] has been strongly implicated as a modifiable factor that could prove a sensible policy target in efforts to reduce dementia risk at the population level.[5]

Ambient particulate matter with an aero diameter <2.5 μm ($PM_{2.5}$) is a ubiquitous air pollutant. It consists of a mixture of solid and liquid particles of organic and inorganic substances suspended in the air, with local and regional variation in ambient levels. Primary sources of $PM_{2.5}$ include motor vehicle emissions, industrial combustion, and road dust. Major chemicals detected in $PM_{2.5}$ include nitrates, sulfates, and carbon. Because of its very small size, $PM_{2.5}$ can potentially access the bloodstream and the central nervous system directly through the olfactory bulb or across the blood-brain barrier.[6, 7] Growing evidence suggests an association between $PM_{2.5}$ exposure and cognitive function,[8] cognitive decline,[9, 10] and dementia.[11, 12] The exact mechanisms behind these relationships remain unclear, but exposure to $PM_{2.5}$ has been associated with both cardiovascular and neurological damage,[13–18] two potential pathways relevant to dementia pathogenesis.

Investigating air pollution in the context of dementia prevention also requires the systematic study of the entire spectrum of cognitive functioning. Mild cognitive impairment (MCI) is an intermediary, but not necessarily transitional, state of cognitive decline between normal cognitive function and dementia. While MCI does not always progress to dementia,[19] it represents cognitive changes in excess of normal aging and is associated with an elevated probability of future dementia. Presently, there is a lack of studies investigating the relationship between MCI and $PM_{2.5}$ exposure. While it has been reported that exposure is related to cognitive decline below the threshold of dementia,[9, 10] it is unknown if this translates to higher risk of the clinically relevant state of MCI.

Focused epidemiologic investigations of incident dementia and MCI in regions known for poor air quality could be insightful. The Monongahela Valley of southwestern Pennsylvania, an industrial region and part of the “Rust Belt,” is one such area. The area was a major hub of the steel industry from the 1900s to 1960s. The region’s industrial background and topography, consisting of deep river valleys housing these industries,[20] subjected residents to historically high air pollutant exposure over the life course. Unfortunately, reliable measurements from peak industrial time periods are lacking, especially for the more recently recognized $PM_{2.5}$. The collapse of the United States steel industry and the closing of foundries in the 1970s has reduced air pollution in the region since that time. Even so, Pittsburgh, the county seat of Allegheny County, continues to make regular top ten appearances on the American Lung Association’s “State of the Air” list of worst cities for particulate air pollution.[21]

The Monongahela-Youghiogheny Healthy Aging Team (MYHAT) is an ongoing prospective cohort study of MCI and dementia in a community-based sample of older adults in this region. The cohort consists primarily of life-long residents of the area, who likely had high lifelong exposures to air pollution. We aimed to investigate the relationship between late-life $PM_{2.5}$ exposure, sourced from the Environmental Protection Agency (EPA) data for Allegheny County, and incidence of MCI and dementia in this cohort. We hypothesized that participants living within census tracts with higher estimated $PM_{2.5}$ exposure would have significantly higher risk of developing MCI and dementia.

METHODS

Participants

The ongoing MYHAT study recruited an initial sample of 1982 participants from 2006–2008 using age-stratified random sampling from publicly available voter registration lists. Inclusion criteria were age ≥65, no severe vision or hearing impairment, not institutionalized, and having decisional capacity. Additionally, being a study focused on MCI, MYHAT entry required a score of ≥21 on an age-education corrected Mini-Mental State Exam (MMSE).[22, 23] Participants were assessed in detail at study entry and reassessed annually. Assessments were conducted preferentially at participants’ residences or, alternatively, at the MYHAT project office within the study area. The current analyses used the following covariates: age, sex, education (<High School, High School or equivalent, >High School), and smoking status (ever vs. never). We also examined self-reported annual household income (<$40,000 or ≥$40,000), acknowledging that many

participants declined to answer this question. Further details of sampling, recruitment, and assessment protocols have been reported previously.[24, 25] All MYHAT study participants provided written informed consent, and the study was approved by the University of Pittsburgh Institutional Review Board.

MCI and Dementia Diagnosis

Every participant in MYHAT is annually assessed with the Clinical Dementia Rating (CDR)® Staging Instrument, performed by trained interviewers. The CDR evaluates everyday functioning across the following cognitively driven functional domains: memory, orientation, judgement and problem-solving, community affairs, home and hobbies, and personal care.[23,26] For the purposes of this report, MCI and dementia diagnosis was based on the CDR, which is explicitly not informed by neuropsychological test performance. Dementia was operationally defined as a CDR ≥1.0 and MCI was operationally defined as CDR=0.5, as we have done previously.[19, 27] Incident dementia cases were identified as participants with CDR<1.0 at baseline who were rated at CDR≥1.0 at a later study visit. Classification date was determined as the date of the first study visit at which a participant scored CDR≥1.0. Likewise, incident MCI cases were identified as participants with CDR=0 at baseline who scored CDR=0.5 at a later study visit, with classification date being the date of the first study visit at which a participant scored CDR=0.5.

Fine Particulate Matter Exposure

Daily exposure to fine particulate matter ($PM_{2.5}$; $\mu g/m^3$) was derived from publicly available Environmental Protection Agency (EPA) air quality data by census tract for years 2002–2014. Predictions of daily ambient 24-hour average PM2.5 obtained from the EPA used a downscaling modeling approach.[28–30] This downscaling approach uses Bayesian space-time modeling, combining air monitoring data and gridded numerical output from the Community Multi-Scale Air Quality Model (CMAQ), to produce point-level, daily, air pollution predictions. This method of exposure assessment is well-validated as an accurate estimation of ambient particulate matter.[31]

At the baseline study visit, MYHAT participants provided residential addresses which were geocoded to census tract using the geocoding tool from the United States Census Bureau (https://geocoding.geo.census.gov/). All 59 census tracts represented in MYHAT are located in southwestern Pennsylvania's Allegheny County, where 75.8% of the MYHAT cohort was born. Each participant's census tract was used to estimate annual $PM_{2.5}$ exposure, including up to four years preceding MYHAT study entry (2006–2008).

Study sample

The incident dementia analysis sample included 1572 participants, excluding persons with prevalent dementia (n=23; CDR≥1.0 at study baseline), those lost to follow-up before attending a second visit (n=258), those missing baseline covariate values and those missing census tract data due to failure of the geocoding tool to map their addresses to coordinates (n=129). The average follow-up time for this sample was 6.17 ± 3.42 years from study entry. The incident MCI analysis sample included 1163 participants, excluding individuals with prevalent MCI or dementia (n=569; CDR≥0.5 at study baseline), those lost to follow-up

before attending a second visit (n=154), missing baseline covariate values and missing census tract data (n=96). The average follow-up time for this sample was 5.66 ± 3.52 years from study entry. A comparison of included and excluded participants for each analysis sample is presented in Table S1. The included and excluded participants were largely similar regarding age and sex, but included participants had slightly higher education and were less likely to have smoked. A brief description of the remaining sample at each follow-up cycle for the incident dementia and incident MCI models is presented in Table S2.

Statistical Analyses

We fit Bayesian spatial survival time-dependent models to assess the effect of $PM_{2.5}$ on time to dementia classification, and on time to MCI classification (modeled separately), adjusting for age, sex, education, and tobacco smoking history. These frailty models are semiparametric, each frailty being associated with a distinct spatial location. In the statistical context, the term “frailty” refers to random effects in the survival model, and is distinct from the clinical geriatric frailty syndrome. Considering that we have georeferenced data (latitude and longitude) for each individual, unobserved frailty is assumed to arise from a Gaussian random field. [See supplemental methods for further details of the frailty assumptions and citations for additional detailed information.]

We characterized $PM_{2.5}$ exposure in two different ways in our modeling: (i) an estimated single-year running average of the $PM_{2.5}$ exposure (each participant’s assessment year for each cycle; model 1; (ii) an estimated five-year running average of the $PM_{2.5}$ exposure (each participant’s assessment year and previous 4 years for each cycle; model 2. The statistical significance of each covariate effect on the incident event (MCI or dementia) is suggested by the 95% credible interval (CI) of the posterior mean of a hazard ratio (HR) that does not include 1.

The estimated single- and five- year running average of the $PM_{2.5}$ exposures were relative to the incident dementia or incident MCI event date for cases or the censoring date for non-cases (including death before observing incident dementia or MCI). For example, for a participant classified as an incident dementia case in 2007, the predictor in model 1 includes estimated $PM_{2.5}$ exposure in Year 2007; the predictor in model 2, is the average estimated $PM_{2.5}$ exposure in the 5 years from Year 2003 to Year 2007. We excluded incident events after 2014 (the last available $PM_{2.5}$ data in this sample), from the current analysis to ensure that all participants had a full five-year estimated average $PM_{2.5}$ immediately preceding outcome events.

We conducted the following sensitivity analyses. First, we tested the primary models with and without a frailty assumption. Second, we repeated the primary incident dementia and MCI models with additional adjustment for annual household income (excluding participants with missing income data: n=288 for the incident dementia model and n=187 for the incident MCI model). Bayesian spatial survival time-dependent models were fit using the *survregbayes* function in the R package “spBayesSurv” version 1.1.4.

To generate an area density map for estimated $PM_{2.5}$ exposure (Figure 1), average ambient $PM_{2.5}$ level was determined from 2002–2007, which included the two initial years of the

MYHAT study and the 3 previous years. Note that this average is a static calculation used for visualization purposes only; it does not correspond to the participant-specific running five-year average used in the spatial regressions (model 2) described earlier. To protect confidential information, individual residential addresses were masked by offsetting 30m – 600m through an online masking tool called MaskMy.XYZ (https://maskmy.xyz/). The map was generated by ArcMap 10.7.1.

RESULTS

The current analysis samples include 108 incident dementia cases and 354 incident MCI cases. The average time to event from baseline (study entry) for these cases was 5.36 ± 2.94 years for incident dementia and 3.94 ± 2.82 years for incident MCI. Table 1 displays baseline descriptive statistics for the incident dementia analysis sample (n=1572, average age 77.4 ± 7.32 years, 62% women) and the incident MCI analysis sample (n=1163, average age 76.7 ± 7.23 years, 64% women.

Figure 1 displays a map of estimated $PM_{2.5}$ exposure from 2002–2007 in census tracts represented in MYHAT participants, with cognitively normal, incident MCI and incident dementia cases indicated.

Table 2 displays the average estimated ambient $PM_{2.5}$ across all 59 census tracts represented in the current study by year from 2002–2014.

Table 3 presents the adjusted model results relating $PM_{2.5}$ exposure to incident dementia and MCI using single-year and five-year estimated $PM_{2.5}$ exposure averages. Every 1 $\mu g/m^3$ increase in single-year average $PM_{2.5}$ was associated with a 67% higher hazard rate of incident dementia (HR=1.67, 95% [CI]: 1.30, 2.14) and a 75% higher hazard rate of incident MCI (HR=1.75, 95% CI: 1.52, 2.03). Every 1 $\mu g/m^3$ increase in five-year average $PM_{2.5}$ was associated with over a two-fold higher hazard rate of incident dementia (HR=2.08, 95% CI: 1.53, 3.02) and over a three-fold higher hazard rate of incident MCI (HR=3.42, 95% CI: 2.81, 4.16).

In the sensitivity analyses, results were consistent between primary models with and without frailty, although model comparison criteria (deviance information criterion (DIC, smaller is better) and log pseudo marginal likelihood (LPML, larger is better)) favored the frailty model in the incident MCI survival analysis (Table S3). Results were also consistent between primary models for incident MCI and incident dementia with and without adjustment for household income (Table S4).

DISCUSSION

We observed a significant association between higher estimated $PM_{2.5}$ exposure and higher risk of development of both dementia and MCI in this population-based cohort. Notably, associations were stronger using a five-year estimated $PM_{2.5}$ exposure compared to a single-year estimated $PM_{2.5}$ exposure. Specifically, each one $\mu g/m^3$ increase in five-year estimated $PM_{2.5}$ exposure was associated with a two times higher hazard of incident dementia and

three times higher hazard of incident MCI. These associations were independent of age, sex, education, and smoking history, and household income.

Our findings are particularly relevant in the context of the industrial history of the study area. The MYHAT participants represent a survivor cohort of older adults who have lived through historically high exposure to air pollutants. The Monongahela Valley was a major hub of the industrial revolution in the United States. Lifelong residents of the area benefited materially and socially from the vibrant economy generated by the coal and steel industries. However, they were exposed to the resulting emissions by working in these industries and/or by daily indirect exposure to ambient air. A widely publicized environmental disaster event, the "Donora Smog" was a 1948 air quality crisis, caused by a temperature inversion that sickened thousands of residents of the town of Donora, PA, and served as a catalyst for clean air reform in the United States.[32] Air quality began to recover in the southwestern PA region following the collapse of the United States steel industry in the 1970s, but at the cost of a significant economic downturn and dramatic population decrease. Notably, the region remains subject to nationally poor $PM_{2.5}$ levels attributed to the remaining industries.[21] The mean estimated $PM_{2.5}$ exposure in this sample in 2006 (study index visit; 15.8 ± 0.16 $\mu g/m^3$) was considerably higher than in other studies which have reported $PM_{2.5}$ exposure around a similar time period.[33–35] Even among the lowest exposure census tracts we examined from 2002–2014, levels far exceeded current recommendations from the World Health Organization, which set a guideline of 10 $\mu g/m^3$ annual average in a 2005 update.[36] It is notable that even within this limited spatial range of $PM_{2.5}$ exposure we still detected strong associations with incident cognitive impairment.

Our results are consistent with a growing consensus that $PM_{2.5}$ is related to cognitive impairment in older adults,[12] including diagnosis of dementia.[8, 11, 37, 38] However, not all investigations have reported these associations,[33, 34] with some of the heterogeneity in reported effects likely due to methodological differences. In comparison to several previous studies which used passive surveillance (e.g. medical record based determinations) of dementia diagnosis, to our knowledge this is the first population-based longitudinal study to model $PM_{2.5}$ exposure with both incident MCI and incident dementia classification determined by direct and detailed annual assessment.

The finding that $PM_{2.5}$ exposure was related to higher MCI incidence, an intermediary state of cognitive impairment often but not always preceding dementia,[19] has implications for prevention and early intervention. A previous cross-sectional study reported an association between estimated $PM_{2.5}$ exposure and prevalent MCI, particularly amnestic MCI.[39] Indeed delaying, not necessarily preventing, dementia onset by even a few years has the potential to make impactful reductions in prevalence and health-care costs.[40] Further reductions in $PM_{2.5}$ exposure could prove a viable and widespread intervention to delay onset. It has already been demonstrated that wide-scale reduction in $PM_{2.5}$ resulted in benefit regarding cardiovascular disease related mortality.[41, 42] Like in other regions, ambient $PM_{2.5}$ measurements in the Pittsburgh region have generally declined from early 2000s levels.[43] Although data are not available, it is reasonable to speculate that these measures also declined steadily in the latter quarter of the 20th century[44] as the region transitioned out of heavy industrial activity, perhaps not coincidentally corresponding with a reduction

in dementia incidence rates in this population over the past 30 years.[27] However, current residents of the region, including our study participants, were exposed to previously even higher levels of $PM_{2.5}$ and the associations reported here likely reflect cumulative exposures preceding the available data. Thus, air pollution remains a public health issue in the region, and a potentially viable intervention target to continue to lower the dementia burden, and improve other health outcomes, in this population. Our findings further suggest that prolonged cumulative exposure to $PM_{2.5}$, represented as a five-year average in our study, is more strongly associated with MCI and dementia risk compared to a single-year average estimated exposure.

Although directly examining mechanisms underlying the relationship of $PM_{2.5}$ exposure to cognitive impairment is beyond the scope of the MYHAT study, there are several relevant pathological pathways to consider. Air pollutant exposure has been associated with several pathological processes relevant to dementia, including but not limited to: cardiovascular disease,[45] oxidative stress,[46, 47] neuroinflammation,[15, 48, 49] cerebrovascular disease,[17, 50] and with both lower white and gray matter brain volume.[16, 17, 51, 52] A recent investigation in a population-based cohort in Sweden estimated that stroke explained nearly half of observed $PM_{2.5}$ and ozone related dementia cases.[18] Additionally, recent evidence suggests $PM_{2.5}$ exposure may exacerbate accumulation of toxic amyloid-beta oligomers in the brain,[53–56] and hyperphosphorylation of tau protein,[57] the primary neuropathological bases for Alzheimer's disease.[58] It remains to be determined whether the association between $PM_{2.5}$ and cognitive impairment is directly mediated by these processes, or whether the deleterious effects of $PM_{2.5}$ on the central nervous system, which it readily accesses,[15] creates an exploitable vulnerability to these pathologies.[59]

Strengths and limitations of our study are closely intertwined. The MYHAT cohort is large, population-based, and has been richly characterized over many years. Further, the stable demographics in the area, including low in- and out-migration rates, facilitates focused longitudinal research of environmental exposures. However, the sample is predominantly white, reflecting the demographics of the older adult population in the region, and therefore our findings need to be replicated in other older populations with greater ethnic diversity. Although we reported significant associations between late-life $PM_{2.5}$ exposure and cognitive impairment during the years 2006–2014, lifetime data on cumulative exposure to these pollutants among our participants would have been even more informative had such data been available. Although most of our participants are life-long residents of the area, reliable $PM_{2.5}$ measurements before 2002 are not available. We could not address the question of competing risks with mortality as the spatial regression models used do not lend themselves to joint modeling or subdistribution competing risk modeling. However, $PM_{2.5}$ exposure is associated with mortality in our sample (data not shown) so we anticipate unmeasured competing risk would only bias our results towards the null. While our single-region focused study is limited in scope and $PM_{2.5}$ exposure variability compared to multi-center and health-record studies, it has considerable strengths in limiting residual confounding through a focused investigation of a relatively homogeneous population with standardized assessment of MCI and dementia. Furthermore, even comparisons across an elevated range of $PM_{2.5}$ exposure suggested association with MCI and dementia risk. As we continue to follow the MYHAT cohort, we will be able to track concurrent changes in $PM_{2.5}$

and other pollutants and examine their relationships to other factors including cardiovascular and cerebrovascular measures and other disease biomarkers.

In conclusion, participants living in southwestern Pennsylvania census tracts with higher estimated $PM_{2.5}$ exposure were more likely than participants with lower estimated exposure to develop MCI and dementia. Reducing ambient air pollution levels has the potential to make impactful reductions in the incidence rate of dementia and deserves attention as a public health priority.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points:

1. Higher estimated exposure to ambient $PM_{2.5}$ is associated with higher incidence of cognitive impairment in older adults.
2. These associations were observed within an already high range of $PM_{2.5}$ exposure in a post-industrial region known for historically poor air quality.

Why does this paper matter?

This paper addresses the relationship of air pollution to cognition in a population-based cohort using active annual assessment of dementia and mild cognitive impairment rather than passive surveillance. These findings have public health implications regarding modifiable risk factors for dementia.

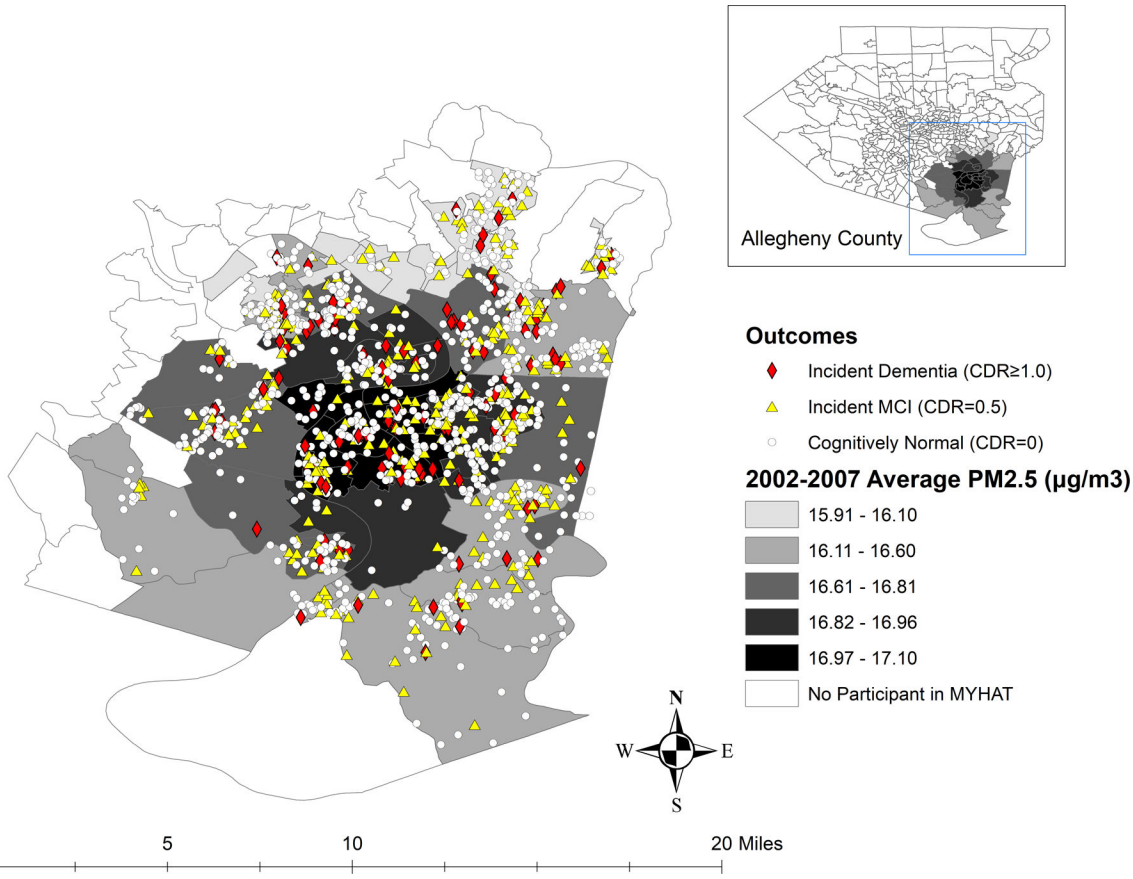

Figure 1.

Spatial distribution of incident mild cognitive impairment (MCI) and dementia cases within census tracts in relation to 5-year average estimated PM2.5 level (µg/m3) from 2002 to 2007

Table 1.

Incident Dementia and MCI Sample Characteristics at Study Baseline

	Incident Dementia Sample (n=1572)	Incident MCI Sample (n=1163)
Age in years, mean (SD)	77.4 (7.32)	76.7 (7.23)
Female Sex, n (%)	974 (62.0%)	743 (63.9%)
Education, n (%)		
<High School	200 (12.7%)	124 (10.7%)
High School	703 (44.7%)	530 (45.6%)
>High School	669 (42.6%)	509 (43.8%)
Ever Smoker, n (%)	825 (52.5%)	589 (50.6%)
Baseline CDR category, n (%)		
0	1163 (74.0%)	1163 (100%)
0.5	409 (26.0%)	0 (0%)
Annual household income, n(%)	(n*=1284)	(n*=976)
<$40,000	1000 (78.4%)	748 (76.6%)
>=$40,000	284 (21.6%)	228 (23.4%)

Note. MCI = Mild Cognitive Impairment; CDR = Clinical Dementia Rating.

Table 2.

Average Estimated Ambient $PM_{2.5}$ ($\mu g/m^3$) Across All 59 Census Tracts in the MYHAT Study

Year	Annual $PM_{2.5}$ Average (ug/m3)	Standard deviation
2002	17.04	0.19
2003	16.72	0.19
2004	16.70	0.19
2005	17.54	0.19
2006	15.93	0.16
2007	16.35	0.14
2008	14.28	0.13
2009	12.92	0.11
2010	13.78	0.13
2011	12.32	0.13
2012	11.79	0.11
2013	10.72	0.10
2014	11.91	0.08

Note: $PM_{2.5}$ = Fine Particulate Matter; MYHAT=Monongahela-Youghiogheny Healthy Aging Team.

Table 3.

Spatial Regression Models Associating $PM_{2.5}$ Exposure with Incident Dementia and Incident MCI

	Incident Dementia		Incident MCI	
	HR	**95% CI HR**	**HR**	**95% CI HR**
Model 1: Single-Year $PM_{2.5}$				
$PM_{2.5}$ Single-Year Average	1.669	(1.298,2.136)	1.746	(1.518,2.032)
Age (in years)	1.132	(1.094,1.170)	1.092	(1.073,1.111)
Female Sex	0.809	(0.507,1.239)	1.212	(0.942,1.575)
Ever Smoked	0.884	(0.567,1.376)	0.878	(0.699,1.098)
High School Education	0.597	(0.369,0.974)	0.739	(0.538,1.009)
>High School Education	0.586	(0.335,1.003)	0.525	(0.368,0.751)
Model 2: Five-Year $PM_{2.5}$				
$PM_{2.5}$ Five-Year Average	2.082	(1.528, 3.015)	3.419	(2.806, 4.164)
Age (in years)	1.133	(1.095, 1.175)	1.102	(1.079, 1.126)
Female Sex	0.805	(0.530, 1.278)	1.228	(0.950, 1.639)
Ever Smoked	0.885	(0.564, 1.382)	0.888	(0.675, 1.148)
High School Education	0.614	(0.341, 1.048)	0.721	(0.502, 1.015)
>High School Education	0.618	(0.344, 1.096)	0.521	(0.348, 0.758)

Note: $PM_{2.5}$ = Fine Particulate Matter; MCI=Mild Cognitive Impairment; HR=Hazard Ratio; CI=Credible Interval. Incident Dementia and MCI outcomes were modeled separately.

$PM_{2.5}$ estimates correspond to a 1 $\mu g/m^3$ increase.