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An Examination of the Joint Effect of the Social Environment and Air Pollution on Dementia Among US Older Adults

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Background: Evidence suggests exposure to air pollution increases the risk of dementia. Cognitively stimulating activities and social interactions, made available through the social environment, may slow cognitive decline. We examined whether the social environment buffers the adverse effect of air pollution on dementia in a cohort of older adults.

Methods: This study draws from the Ginkgo Evaluation of Memory Study. Participants aged 75 years and older were enrolled between 2000 and 2002 and evaluated for dementia semi-annually through 2008. Long-term exposure to particulate matter and nitrogen dioxide was assigned from spatial and spatiotemporal models. Census tract-level measures of the social environment and individual measures of social activity were used as measures of the social environment. We generated Cox proportional hazard models with census tract as a random effect and adjusted for demographic and study visit characteristics. Relative excess risk due to interaction was estimated as a qualitative measure of additive interaction.

Results: This study included 2,564 individuals. We observed associations between increased risk of dementia and fine particulate matter (µg/m³), coarse particulate matter (µg/m³), and nitrogen dioxide (ppb); HRs per 5 unit increase were 1.55 (1.01, 2.18), 1.31 (1.07, 1.60), and 1.18 (1.02, 1.37), respectively. We found no evidence of additive interaction between air pollution and the neighborhood social environment. **Conclusions:** We found no consistent evidence to suggest a synergistic effect between exposure to air pollution and measures of the social environment. Given the many qualities of the social environment that may reduce dementia pathology, further examination is encouraged.

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The authors declare that they have no conflicts of interest with regard to the content of this report.

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SDC Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.environepidem.com).

*Corresponding Author. Address: Department of Epidemiology, University of Washington, 3980 15th Ave NE, Seattle, WA 98195. E-mail: silango@uw.edu (S.D. Ilango). Copyright © 2023 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The Environmental Epidemiology. All rights reserved. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

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Introduction

Dementia is a chronic, progressive condition where cognitive functions (e.g., memory, orientation, comprehension, and reasoning) are impaired and affect daily living.¹ In 2018, an estimated 5.5 million Americans, ages 65 years and older, were living with the most common subtype, Alzheimer's dementia.² As the proportion of older adults grows worldwide, there is an increasing concern about dementia; in addition to impaired daily living, dementia places a substantial and long-term emotional and financial burden on both the affected individuals and their caregivers. The lack of effective therapy to slow the progression or reverse cognitive decline suggests the need for a shift in research to identify widespread, modifiable risk factors for dementia.³ Modifiable risk factors that impact an entire population are effective targets for population-level intervention strategies.

Exposure to air pollution is a well-documented population-level modifiable risk factor linked to several adverse health outcomes.^{4,5} Recent evidence suggests that air pollution may also affect the brain.⁶⁻¹³ Animal studies have shown that fine particulate matter (PM_{2.5}) can move from the nose via the olfactory nerve and into the brain; nitrogen dioxide (NO₂) can impair synapses and induce neuronal damage.^{6,7} Neuroimaging

What this study adds

This study advances research on air pollution and dementia by conducting the first examination of the interplay between air pollution and the social environment and their potentially joint effect on dementia risk in a cohort of US older adults. We hypothesized that neighborhood and individual-level measures of the social environment may offer some cognitive resilience to the adverse effects of air pollution on dementia. However, we found no consistent or robust evidence to suggest a synergistic effect between air pollution and measures of the social environment. studies have similarly observed an adverse effect of $PM_{2.5}$, coarse particulate matter (PM_{10}), and traffic-related pollutants on brain volume,^{9,10} suggesting that air pollution may accelerate structural brain changes resulting in worse cognitive health. Finally, there is a growing evidence base from epidemiologic studies that suggest a link between air pollution and dementia risk.¹⁴⁺¹⁶ For example, in a previous study from our research group, an interquartile range increase in 20-year exposure to $PM_{2.5}$ was associated with a 20% higher risk of dementia in a cohort study of 3,069 older adults from four US communities.¹⁷ A decade of research suggesting that increased exposure to air pollution may increase the risk of dementia^{14,15} resulted in the addition of air pollution as a modifiable risk factor for dementia in the 2020 Lancet Commission on Dementia.¹⁸

Despite the evidence suggesting a link between air pollution and structural brain damage and dementia risk, results from studies on air pollution and other cognitive outcomes (e.g., cognitive decline) are less consistent.¹⁴ This could be explained by the cognitive reserve hypothesis, where mental stimulation offers individuals a neural reserve or compensation that offers some resilience to air-pollution-related cognitive decline and dementia.^{19,20}

We hypothesize that the social environment, which we define as opportunities for social engagement at both the neighborhood and individual levels, contributes to resilience to air pollution-related dementia. The social environment can be modified through both neighborhood-level change (e.g., accessible community centers) and individual-level behaviors (e.g., social interactions and attending community events).²¹ On the contextual level, living in a neighborhood with more social opportunities has been linked to a reduced risk of cognitive impairment and dementia, potentially through mechanisms of reduced stress, access to healthier lifestyles, and improved psychological state.^{21,22} Individually, more frequent social engagement can result in less loneliness and more mental stimulation, thus reducing the risk of dementia.²² An examination of multiple aspects of the neighborhood environment and how they interact in relation to cognitive outcomes can improve our understanding of the biological mechanism, identify vulnerable populations, and inform intervention efforts for dementia. For example, if the adverse effect of air pollution on dementia is reduced by access to social environments, local governments can prioritize enhancing the social environment and the opportunity for social interaction in areas of high pollution to reduce the risk of dementia. This is important because the inequities in both air pollution and dementia are not evenly distributed across populations and geographies.²³⁻²⁵ Modifying the social environment may help rectify these inequities.

Dementia is a complex set of conditions with no single cause; understanding the synergistic effect of multiple exposures, for example, air pollution and the social environment, is critical to devising effective intervention strategies.²⁶ Our study examines the joint effect of air pollution and the social environment (both neighborhood- and individual-level measures) on incident dementia in a multi-site study of older adults from four US communities.

Methods

Study design and participants

Study participants were drawn from the Ginkgo Evaluation of Memory Study (GEMS), a randomized trial of older adults (>75 years) from four US communities (Hagerstown, Maryland; Pittsburgh, Pennsylvania; Sacramento, California; and Winston-Salem and Greensboro, North Carolina) designed to study the effect of the herbal supplement, *Ginkgo biloba*, on dementia prevention.²⁷ Although the initial trial concluded no protective effect of *Ginkgo biloba* on dementia,²⁸ the study has since been repurposed as an observational study to examine the effects

of air pollution on dementia and related cognitive outcomes.¹⁷ GEMS participants (n = 3,069) were evaluated every 6 months for dementia from 2000 to 2008 until dementia was diagnosed or study drop-out. We excluded those with prevalent dementia or mild cognitive impairment measured at baseline (n = 482) and those without air pollution data (n = 23). Signed informed consent was obtained from participants and their proxies for the original randomized control trial. The Institutional Review Board at the University of Washington approved this study.

Outcome classification

All-cause dementia was the outcome of interest of this study. GEMS participants visited their assigned academic clinic semi-annually from the date of randomization (i.e., study baseline) through the end of the study, dementia diagnosis, or attrition. At each visit, clinicians administered three dementia screening examinations to participants: the Modified Mini-Mental State Examination, the cognitive subscale of the Alzheimer Disease Assessment Scale, and the Clinical Dementia Rating Scale.²⁹⁻³¹ A decline in cognitive performance over two or more screening examinations, a self- or proxy-reported memory or cognitive concern, a dementia diagnosis, or a prescribed dementia medication triggered an extensive neuropsychological battery of 12 tests to determine dementia status. Final dementia status was determined after a complete neurological evaluation and brain magnetic resonance imaging and was adjudicated by a panel of neurologists, neuropsychologists, and a psychometrician according to diagnostic criteria from the National Institute of Neurological and Communication Disorders and Stroke, Alzheimer's Disease and Related Disorders Association, the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences, and the Alzheimer's Disease Diagnostic and Treatment Centers.32-35

Air pollution exposure classification

Long-term exposure to $PM_{2.5}$, PM_{10} , and NO_2 were the exposures of interest for this study. Details on exposure measurement have been previously described in detail.¹⁷ Briefly, exposures were assigned to study participants at their residential address reported at the initial study visit. We accounted for residential movement before the study baseline by reconstructing address history from 1980 using data from LexisNexis, a commercial credit reporting company.^{17,36} We used validated spatiotemporal models to estimate annual $PM_{2.5}$ and PM_{10} exposure at each residential address and a validated national spatial model to estimate annual NO, exposure.³⁷⁻³⁹ These models use measurements from regulatory monitoring stations and more than 300 spatiotemporal geographic predictors of air pollution. External validation statistics show good performance of the prediction models, with R² ranging from 0.84 to 0.91 for $PM_{2.5}$ and 0.78 to 0.88 for NO_2 .^{37,38} We selected the longest available exposure periods in support of the hypothesis that cumulative lifetime exposure to air pollution is best represented with longer averaging periods and is most relevant to adverse aging-related health outcomes.¹⁵ The exposure period was determined depending on data availability from regulatory monitoring stations; participants were assigned a 20-year exposure to PM2.5 and 10-year exposures to PM₁₀ and NO₂ for the period prior to the initial study visit.

Social environment measures

Neighborhood- and individual-level measures of the social environment were considered in this study jointly with air pollution to determine whether the social environment modified the effect of air pollution on dementia. Neighborhood contextual

measures were retrieved from the publicly available National Neighborhood Data Archive.⁴⁰⁻⁴³ These data assign an annual density (number of buildings per 10,000 people) of several components of the social environment to each US census tract drawing from the North American Industry Classification System.⁴⁰⁻⁴³ Census tracts are statistical subdivisions of a county or equivalent entity. They generally have population sizes between 1,200 and 8,000 people. The spatial size varies depending on the population density.44 Addresses recorded during the GEMS study belonged to census tracts with areas ranging mostly from 1.46 km² to 400 km², with outliers up to 4420 km². We selected the following measures of social environment: (1) arts, entertainment, and recreational organizations; (2) eating and drinking places; (3) religious, civic, and social organizations; and (4) social services; these reflect opportunities of social engagement that have been previously linked to measures of cognitive performance, specifically, a composite index of cognitive function including domains of verbal learning, memory, and executive function.^{45,46} Measures from 2003 were linked to participants residential address reported at baseline and were updated with any residential movement through the end of the follow-up to account for lifestyle transitions and infrastructural changes.

We also considered three self-reported individual-measures of the social environment from the baseline study visit questionnaire that paralleled the contextual measures we selected: Regular attendance at (1) clubs or organizations, (2) religious services, and (3) plays or concerts. First, participants were asked: "How often do you participate in a club or organization (church, social, or civic)" and selected from the following responses: every day, 2-3 times a week, once a week, 2-3 times a month, once a month, or less than once a month. Responses were dichotomized into regular participation or not, with regular participation defined as at least once a month. Second, participants were asked "How often do you attend church or religious services?"; the same response options and dichotomization used for clubs or organizations were applied. Finally, participants were asked "How often do you go to plays or concerts?"; the same response options and dichotomization as the two previous measures were applied.

Covariates

We considered the following covariates in our analyses, all recorded at study baseline: sex (female or male), race/ethnicity (white or non-white), education (high school or less, some college, college graduate, or postgraduate), smoking status (never or ever smoker), living situation (alone, with spouse or partner, or other (i.e., with other family or assisted living), GEMS site (Hagerstown, Pittsburgh, Sacramento, or Winston-Salem/ Greensboro), and original treatment assignment (G. biloba or placebo). We also created an index for neighborhood deprivation 1980–1999, measured at the census tract level from a principal components analysis that combined information from the following 2000 US Census variables: (1) percent with bachelor's degree, (2) percent in managerial occupations, (3) median home value, (4) percent with at least a high school education, (5) percent interest, dividend, or rental income, (6) median household income, and (7) percent with annual household income greater than \$50,000.4

Statistical analysis

Demographic and lifestyle characteristics, measures of social environment, dementia outcome, and study follow-up details were described for GEMS participants with means and standard deviation for continuous variables, frequencies and percentages for categorical variables, and median and interquartile ranges for neighborhood measures of the social environment.

We first estimated the individual effects of air pollution and measures of the social environment (seven measures evaluated separately) on incident dementia. We also estimated the correlation between individual and neighborhood measures of the social environment. As our main analysis, we examined the joint effect of air pollution and measures of social environment on incident dementia on the additive scale. For all models, we generated multi-level Cox proportional hazard models. Follow-up began at the age at randomization and, for individuals diagnosed with dementia, ended at the age halfway between the last examination without dementia and the examination that triggered the dementia screening. Dementia-free participants were censored at the age of last contact or death. Models included a minimal set of covariates decided a priori that may confound the relationship between exposure to air pollution and dementia: race/ethnicity, sex, education, living situation, and neighborhood deprivation and census tract as a random effect. We also included the study site and treatment assignment (Ginkgo biloba or placebo) as fixed effects to account for spatial clustering and the potential effect the treatment had on the outcome.

To evaluate the joint effect on the additive scale, we included an interaction between the pollutant and measure of the social environment in the previously described Cox proportional hazard models and evaluated whether the effect of air pollution and (lack of) social environment is larger than the sum of the individual effects of the two exposures on dementia risk.⁴⁷ This qualitative measure of effect modification was estimated with the relative excess risk due to interaction (RERI), where a positive additive interaction was characterized by RERI >0, no additive interaction was characterized by RERI = 0, and negative additive interaction was characterized with RERI <0. This measure can be applied to survival analyses and can identify a departure from additive interaction, which is a priority when prioritizing public health efforts.48-50 For this joint effect analysis, measures of the social environment were re-coded; higher values suggested a lack of social environment.⁴⁹ Confidence intervals were estimated using the delta method.⁵¹

In supplementary analyses, we evaluated the independent effect of air pollution on incident dementia. We also examined the joint effect of air pollution and (lack of) social environment on the multiplicative scale, in contrast to our main assessment of interaction on the additive scale, by running Cox proportional hazard models to estimate the effect of each social environment measure on incident dementia stratified by high and low levels of air pollution, indicated by measurements dichotomized at the median. We also estimated the effect of each pollutant on incident dementia stratified by dichotomized measures of the social environment. All data management and analyses were performed using SAS 9.4.

Results

After the exclusions described above, our study population consisted of 2,564 GEMS participants. The mean age of participants at baseline was 78.4 years. Over the study follow-up period (5.7 years on average), approximately 13% of participants were diagnosed with dementia (Table 1). Median 20-year exposure to PM_{25} was 18.41 (IQR = 2.44) µg/m³. Median 10-year exposure to PM_{10} was 24.78 (IQR = 4.44) µg/m³ and NO₂ was 16.62 (IQR = 6.67) ppb.

Less than half of the participants were female (46%) and most participants were White (96.7%). About 64% of participants had at least a high school degree. On average, the median number of neighborhood measures of social environment ranged from three to eight in a census tract. Between 40 and 63% of GEMS participants reported regularly attending clubs or organizations, religious services, and attending plays or concerts (Table 1).

Table 1.

Selected characteristics of study participants from the Ginkgo Evaluation of Memory Study, 2000–2008

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	Follow-up, years (mean [SD])	5.7 (1.5)

aVariable distributions are reported as n (%) unless otherwise specified.

^bMedian count per census tract (IQR).

SD indicates standard deviation; SES, socioeconomic status.

Table 2.

Associations between air pollution, measures of social environment and incident dementia^a

Exposure	HR (95% CI)
Air pollutant ^b	
PM ₂₅	1.55 (1.01, 2.18)
PM ₁₀	1.31 (1.07, 1.60)
NO ₂	1.18 (1.02, 1.37)
Neighborhood Measures of Social Environment ^c	
Arts, entertainment, and recreation organizations	0.98 (0.78, 1.23)
Eating and drinking places	0.90 (0.72, 1.13)
Religious, civic, and social organizations	1.05 (0.84, 1.31)
Social services	1.05 (0.83, 1.31)
Individual Measures of Social Environment	
Regularly attends clubs or organizations	0.87 (0.69, 1.10)
Regularly attends religious services	1.02 (0.79, 1.30)
Regularly attends plays or concerts	0.87 (0.68, 1.12)

^aModels adjusted for sex, education, race/ethnicity, living situation, study site, and treatment assignment.

^bPM_{2.5} and PM₁₀ per 5µg/m³, NO₂ per 5ppb.

Neighborhood measures are dichotomized at the median value for each site.

Cl indicates confidence interval; HR, hazard ratio.

We observed associations between increased risk of dementia for every 5 units higher exposure to air pollution 1.55 (1.01, 2.18), 1.31 (1.07, 1.60), and 1.18 (1.02, 1.37) for PM_{2.5} (μ g/m³), PM₁₀ (μ g/m³), and NO₂ (ppb), respectively (Table 2). A protective effect against dementia was suggested by living in a neighborhood with eating and drinking places, however, confidence intervals for hazard ratios were imprecise (Table 2). We also found a protective effect of individual measures of social environment, specifically regularly attending clubs or organizations and plays or concerts; these results were also imprecise (Table 2). The correlation between individual and neighborhood-level measures was low (r² < 0.10 for all measures).

We observed suggestions of a joint effect of exposure to $PM_{2.5}$ and PM_{10} and all three individual measures of social environment (regularly attending clubs or organizations, religious services, and plays or concerts), as indicated by the RERI values greater than zero, however, these RERI values are close to zero and confidence intervals contained the null. We found no consistent evidence of additive interaction with NO₂ for individual measures of social environment or for any neighborhood measures, as indicated by the approximately null RERI values (Table 3).

In supplementary analyses, we found no evidence of a joint effect between air pollution and measures of social environment on the multiplicative scale. Specifically, the association between social environment and dementia stratified by high and low exposure to $PM_{2.5}$, PM_{10} , and NO_2 , and PM_{10} yielded no consistent pattern (eTables 1–3; http://links.lww.com/EE/A220). Hazard ratios between air pollution and dementia stratified by neighborhood measures of the social environment suggest that air pollution may have a stronger effect among individuals living in neighborhoods with fewer social amenities, however, estimates were imprecise and confidence intervals overlap (eTable 4; http://links.lww.com/EE/A220). Finally, we found no consistent pattern for hazard ratios between air pollution and dementia stratified by individual measures of the social environment (eTable 5; http://links.lww.com/EE/A220).

Discussion

This research builds upon previous research in GEMS and other cohorts that found an association between air pollution and incident dementia.^{14,15,17} In this study, we estimated the joint effect of air pollution and individual- and neighborhood- measures of social environment on incident dementia. We hypothesized that access to a social environment, on both neighborhood- and individual- levels, would reduce the adverse effects of air pollution on incident dementia. Although we found that regularly attending clubs, organizations, plays, and concerts were marginally associated with reduced risk of dementia, we did not find consistent or robust evidence for a synergistic effect between air pollution and measures of the social environment in this cohort of older adults from four US communities.

Researchers have recently coined the term "cognability" to conceptualize how neighborhood contexts, including the built and social environment, can provide opportunities for and create barriers to cognitive health among older adults.⁴⁶ One study found that access to civic and social organizations, recreation centers, fast-food and coffee establishments, and art centers/ museums was associated with improved cognitive function.46 These types of establishments can be considered "third places" because they are where people spend large amounts of time outside of the home and work and have been linked to improved cognitive function and cognitive decline.^{20,45,52,53} The neighborhood social environment captures opportunities for social engagement at these third places and can encourage mental stimulation, support networks, and creative and complex activities.⁴⁶ These neuroprotective pathways strengthen brain function and may buffer cognitive function from the harmful effects of air pollution. Together, these findings and hypotheses motivated our evaluation of the selected neighborhood measures of social engagement.

Table 3.

Qualitative assessment of additive interaction between air pollution and individual and neighborhood measures of social environment on incident dementia^a

Measure of social environment ^b	RERI° (95% CI)		
	PM _{2.5}	PM ₁₀	NO ₂
Neighborhood measures ^d			
Arts, entertainment, and recreation organizations	-0.05 (-0.30, 0.19)	0.01 (-0.13, 0.15)	0.07 (-0.04, 0.18)
Eating and drinking places	0.02 (-0.31, 0.35)	0.20 (-0.40, 0.79)	0.01 (-0.15, 0.17)
Religious, civic, and social organizations	-0.07 (-0.32, 0.19)	-0.004 (-0.13, 0.12)	0.02 (-0.11, 0.15)
Social services	0.01 (-0.35, 0.36)	-0.004 (-0.13, 0.12)	0.02 (-0.12, 0.16)
Individual measures			
Regularly attends clubs or organizations	0.19 (-0.66, 1.04)	0.06 (-0.17, 0.29)	-0.07 (-0.33, 0.18)
Regularly attends religious services	0.18 (-0.67, 1.03)	0.02 (-0.27, 0.30)	-0.08 (-0.33, 0.17)
Regularly attends plays or concerts	0.30 (-0.93, 1.54)	0.01 (-0.12, 0.14)	0.05 (-0.09, 0.19)

^aPM_{2.5} and PM₁₀ per 5µg/m³, NO₂ per 5 ppb.

^bMeasures of social environment are reverse-coded; higher value = less social engagement.

 $RERI = HR_{10} + HR_{10}$

Cl indicates confidence interval; NO2, nitrogen dioxide; PM, o, coarse particulate matter; PM2 e, fine particulate matter; RERI, Relative excess risk due to interaction;

We also included self-reported individual measures that corresponded with the neighborhood measures to capture the frequency of social engagement. These more direct measures of social engagement have overlapping and distinct mechanisms that can contribute to increased cognitive reserve. Self-reported social engagement captures actual engagement and social activities both within and outside of the neighborhood, although individuals tend to spend more time in their neighborhood as they age.⁵⁴

To our knowledge, this is the first study that examined the joint effect of air pollution and social environment on dementia outcomes. Previous studies have evaluated the interplay between PM22.5 and neighborhood socioeconomic status and neighborhood conditions (e.g., neighborhood disorder and decay) and found that the adverse effect of air pollution on cognitive function and the decline was worse among older adults living in neighborhoods with worse conditions or with lower socioeconomic status.55-57 Our research expands the literature on joint effects of air pollution and the social environment by presenting findings on both additive and multiplicative scales. The interpretation of the interaction is scale-dependent. Our primary aim was to measure interaction on the additive scale because it is more appropriate for public health priorities; it can be qualitatively assessed from multiplicative models (e.g., Cox proportional hazard models) by calculating RERI.47,48

Despite the previous literature and our hypothesis that the social environment would modify the effect of air pollution on dementia, our study yielded primarily null results. These null findings may be explained by limited data to capture the frequency or quality of engagement which may have relevant contributions for dementia development in older adults. Additionally, social engagement earlier in the life course may have a more substantial contribution to cognitive resilience. However, our study does not have any information on mid-life social networks or environments. Finally, this study has limited statistical power to examine the hypothesized joint associations and we encourage future researchers with increased sample size and variability in the social environment to replicate this analysis. This study includes several strengths, including air pollution estimates that account for residential movement, well-characterized dementia data, and a long follow-up of up to 8 years. We acknowledge the limitations in this study and encourage future researchers to fill these gaps. First, we assumed that the neighborhood social environment measures in 2000-2002 were equivalent to measures in 2003 due to data availability. Second, our contextual measures do not account for proximity to social facilities. Next, there are several ways to quantify the

social environment, many of which were not explored in this analysis. Although we selected a subset of variables that have been found to predict healthy cognitive aging,^{45,58-60} we encourage other measures, including more nuanced measures such as frequency and quality of social engagement, to be explored. We also encourage future researchers to repeat this study in a cohort with more geographic variation.

In conclusion, this study contributes to the literature on air pollution and dementia by evaluating whether social engagement buffers the adverse effects of air pollution. Although we did not find evidence to support a joint effect of air pollution and social engagement on dementia, we encourage future research on this topic. Such research aims to promote equitable healthy aging through multiple avenues for large-scale interventions.

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