Associations of Air Pollution and Gait Speed in Older Adults

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Abstract

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Background: Air pollution is widely recognized as a threat to public health. The impact of long-term exposure to air pollution on gait speed trajectories over time have not been fully explored among US older adults. The specific aims of this study were to 1) examine the relationship between long-term exposure to air pollution and decline in gait speed among older adults, and 2) explore effect modification by cardiovascular disease status on the association.

Methods: We analyzed data from 3,022 older adults in a prospective cohort study conducted from 2000 to 2008. Long term exposure to fine particulate matter ($PM_{2.5}$) and nitrogen dioxide (NO_2) prior to study enrollment was estimated using state of the art prediction models. Gait speed at usual and rapid pace was assessed annually using a 15-feet timed walk test. Mixed effect models with random intercepts and slopes were fitted, adjusting for demographic and socioeconomic factors.

Results: Greater long-term $PM_{2.5}$ exposure was related to faster gait speed decline at usual pace: one interquartile range higher 5-year average $PM_{2.5}$ exposure was related to 0.048 m/s decline in gait speed (95% CI: -0.084, -0.024) over a 6-year study period adjusted for age, gender, race and ethnicity,

education, smoking status, alcohol consumption, study site, and year since enrollment. Greater long-term NO_2 exposure was associated with faster gait speed decline at both usual and rapid pace: one interquartile range higher 5-year average NO_2 was associated with 0.078 m/s decline in usual pace gait (95% CI: -0.120, -0.042) and 0.042 m/s decline in rapid pace gait speed (95% CI: -0.078, -0.006) over 6-year period in adjusted models. The longitudinal association between air pollution and rapid gait speed decline was significant only in individuals with cardiovascular disease.

Conclusions: Long-term exposure to air pollution appears to be associated with faster progression in gait speed decline among older adults in four different locations in the US. Older adults with cardiovascular disease are more susceptible to the adverse effects of long-term exposure of air pollution and the progression in gait speed decline may be even faster among those with cardiovascular disease. Policies to reduce emission of air pollutants and interventions of avoid air pollution exposure or manage cardiovascular disease could contribute to the reduction in the burden of preventable institutionalization and hospitalization.

Background

Aging is associated with a decline in physical function that can alter independence and quality of life at older ages.[1] Gait speed is a reliable, noninvasive, and quick assessment of estimating older adults' functional capacity.[2-4] Gait control involves complex processes, integrating musculoskeletal, neurological, respiratory and cardiovascular systems.[5,6] Thus, decline in gait speed has been shown to be associated with a range of adverse health outcomes, such as disability, cognitive impairment, institutionalization, falls, and mortality.[7-9] Gait speed decline could be used to predict and identify individuals at high risk of these adverse outcomes.[7,10,11] Additionally, gait speed assessment can provide objective and sensitive results of capturing changes over time.[12] Low educational attainment, depressive symptoms, physical inactivity, and obesity were known as risk factors for slow gait speed.[13] However, little is known about other environmental factors that may increase the risk of slow gait speed or declining gait speed.

Air pollution is widely recognized as a threat to public health.[14] Exposure to air pollution, particularly long-term exposure, has been associated with multiple health outcomes, including cardiovascular mortality, cardiovascular diseases (through inflammation, oxidative stress, activation of the abnormal hemostatic system, and disturbance of the autonomic nervous system),[15-17] diabetes,[18] cognitive decline, dementia,[19] and reduction of life expectancy.[20] Given strong associations between these health conditions and gait speed[21-24], air pollution may be a determinant of declines in gait speed in older adults. Older adults, particularly those with neurocognitive, cardiovascular and respiratory disease, can be susceptible to the adverse health effects of air pollutants due to diminished capacity to withstand the hazardous effects of environmental pollutants.[25]

A few studies have investigated air pollution as a potential risk factor for physical functioning, disability, and frailty which are highly related to gait speed.[20,26-28] A longitudinal study examined annual

average outdoor air pollution concentrations at participants' the home addresses with performance-based physical functioning among 1,762 older adults in the Netherlands.[28] The physical functioning score was created based on multiple tests, including gait speed, balance, ability to stand up and sit down in a chair, and capacity to put on and take off a cardigan.[28] The authors found significant associations between annual concentration of nitrogen dioxide (NO_2) and physical functioning at baseline but not over a 6-year study period.[28] This study also did not find the link between particulate matter (less than 2.5 μm in diameter, $PM_{2.5}$) and physical functioning score.[28] Another longitudinal study was conducted to evaluate the association between long-term exposure to traffic-related air pollution (i.e., nitrogen oxides, NO_X) and physical disability score consisting of balance, gait speed, and lower-extremity strength tests among 5,708 older populations in Chicago, the United States (US).[27] The authors found that higher long-term NO_X exposure (i.e., 5-year averaged ambient concentrations at residential location) was related to faster progression in disability.[27] A longitudinal study conducted in China did not find a significant association between annual average exposure to $PM_{2.5}$ and gait speed among 10,823 middle-aged and older adults.[29] Another longitudinal study in China found that city-level 1-year exposure to poorer air quality measured by air quality index was associated with greater frailty over a 3-year study period among 6,570 older adults.[30]

These studies showed mixed findings on the association between air pollution (NO_2 and $PM_{2.5}$) and physical functioning although comparison is limited because they applied different physical functioning tests, geographic levels, and populations. The impacts of long-term exposure to air pollution on gait speed trajectories over time have not been fully explored among US older adults. Moreover, it has not been examined if the hazardous effects from the air pollution is larger among older adults with cardiovascular disease which is known to be strongly associated with air pollution.[31]

In this present study, we studied the relationship between long-term exposure to air pollution (NO_2 and $PM_{2.5}$) and decline in gait speed among older adults and examined effect modification by cardiovascular disease status on this association. We hypothesized that greater long-term exposure to ambient air pollution would be associated with faster decline in gait speed and older adults with cardiovascular disease would show faster decline in gait speed compared to those without comorbidities.

Methods

Study design and participants

We conducted a prospective cohort study of 3,069 participants enrolled in the "Air Pollution, the Social Environment, and Alzheimer's Disease: risk and resilience in the Ginkgo Evaluation Memory Study (GEMS)". The study was designed to evaluate the associations of air pollution and the social environment with Alzheimer's disease (AD) in a well characterized cohort of older adults. The GEMS was a randomized controlled trial, initially designed to determine the effectiveness of *Ginkgo biloba* for the prevention of all-cause dementia and AD in healthy older adults. [32,33] However, robust dedication of data collection between 2000 and 2008 provides an extraordinary opportunity for investigating trajectories of gait speed in association with air pollution exposure. Participants aged 72 years or older were recruited from four study sites in the US: Winston-Salem/Greensboro, North Carolina; Sacramento, California; Hagerstown, Maryland; and Pittsburgh, Pennsylvania between 2000 and 2002. Potential participants were contacted through various modes. All candidate participants underwent comprehensive screening tests before enrollment. Individuals with prevalent neurological or neurodegenerative diseases (e.g., dementia, Parkinson's disease, mental disorders using antipsychotic agents), contraindications for the use of *G. biloba* (e.g., use of anticoagulants), and health conditions that might lead to study dropout (e.g., heart failure with disability) were excluded from the trial.

Participants were followed up via clinic visits every six months through 2008. The current study was approved by the Institutional Review Board at the University of Washington.

Gait speed assessment

Gait speed was measured annually over 6 years using a 15 feet (4.57 m) timed walk protocol which is a valid, reliable, and sensitive measure of physical function.[21,22] The walking course for this test was marked with tape, and time was counted using a stopwatch (timed to 0.1 seconds). The time in seconds were transformed into meters per second. Participants were instructed to walk a 3 feet course first as a practice prior to the 15 feet walk test. Participants were asked to walk at their usual pace and then to walk at a rapid pace by asking them to walk as fast as possible.

Long-term exposure to air pollution

Long-term exposure to air pollution was measured using two criteria of air pollutants, including fine particulate matter (less than 2.5 μm in diameter, $PM_{2.5}$) and nitrogen dioxide (NO_2) at the participant's residential area. The details of geocoding and ambient air pollution assessment at the residential location were previously described.[34] The residential history of participants from 1980 to 1999 (prior to study entry) was constructed using commercial credit reporting data (i.e., LexisNexis).[35] The participants' home addresses were geocoded using parcel-based geocoding methods based on the TeleAtlas Dynamap 2000 v.16.1 road network (Boston, Massachusetts) with the Business Analyst tool in ArcGIS10.6.1 (ESRI, Redlands, California). Residential addresses with an 80% matching accuracy were automatically geocoded, and the rest of the addresses matched with at least 80% accuracy were manually geocoded to the exact location if possible.

Averaged annual $PM_{2.5}$ exposure at each residential location from 1980 through 1999 was estimated using a validated historical prediction model based on approximately 300 geographic

parameters (e.g., traffic, land use categories, vegetation, and emission).[36] To examine the long-term exposure to air pollution, the annual concentration of $PM_{2.5}$ were averaged in 5, 10, 15, and 20 years prior to study enrollment. For instance, 5-year exposure to $PM_{2.5}$ would be the mean value of annual estimates of $PM_{2.5}$ concentration between 1995 to 1999. Averaged NO_2 exposure at each year and geocoded location between 1990 and 1999 was estimated with a national land-use regression model with universal kriging based on 418 geographic parameters (e.g., distance to roadway).[37,38] Due to data availability, averaged estimates of NO_2 exposure over 5 and 10 years will be included as a measure of long-term exposure to NO_2.

Other covariates

Demographic factors and health behaviors at baseline included age (year), education (less than high school, high school graduate, some college or graduate, postgraduate), race and ethnicity (White, people of color), gender (female, male), smoking status (never, former, current), alcohol consumption[39] (none, less than 1 drink per week, 1 to 7 drinks per week, 7 to 14 drinks per week, and more than 14 drinks per week), and study site (Winston-Salem/Greensboro, NC; Sacramento, CA; Hagerstown, MD; Pittsburgh, PA). Cardiovascular disease indicator was generated based on self-reported medical history of myocardial infarction, angina pectoris, stroke, atrial fibrillation, transient ischemic attack (TIA), heart failure, deep vein thrombosis, pulmonary embolus, hypertension, and rheumatic fever or heart valve (having at least one of the diseases).

Data analysis

Descriptive analyses for study variables and mean of gait speed (m/s) were calculated by demographic and health-related factors. The associations between air pollution and decline in gait speed, both at usual and rapid paces, were evaluated by fitting a mixed-effect model to account for correlations of observations within an individual. Participant specific random intercepts and random

slopes for year since enrollment were added to the model. Separate models were fitted for each pollutant (i.e., $PM_{2.5}$ in 5-, 10-, 15-, and 20-year and NO_2 in 5- and 10-year) with gait speed. The main effect of air pollutants was included to analyze the association at baseline. Interaction effects of year since enrollment with air pollution metrics were added to examine the average annual decline of gait speed for different levels of air pollution over the study period. Age, gender, education, race and ethnicity, smoking status, alcohol consumption, study sites, and year since study enrollment were adjusted in all models. The models were fitted again by subgroups based on having or not having cardiovascular disease at baseline. We calculated interquartile range (IQR) for each air pollution metric with different averaging periods and used own IQR change in air pollution to interpret the point estimates. All analyses were conducted using STATA version 16 (StataCorp, College Station, Texas) or R statistical computing software (R Core Team).

Results

Baseline characteristics

Of 3,069 participants at baseline, 47 cases (1.5%) were excluded due to missing either gait speed or air pollution metrics, leaving 3,022 participants (12,676 observations) as an analytic sample. Participants completed an average of 4.2 annual research assessments (minimum of one to maximum of seven). All other missing items in other covariates were less than 3%. Descriptive statistics of study variables with missing (%) are presented in Table 1. Mean (standard deviation) age of participants was 78.6 (3.3) and 1,630 (53.9%) participants were male. Average gait speed (m/s) decreased with age and male participants showed faster gait speed compared to female participants. Mean gait speed was faster among individuals reporting high educational attainment (postgraduate level) and without cardiovascular disease (Table 1).

Table 2 shows the distribution of air pollution metrics by study site. Figure 1 and 2 depict distribution of air pollutants over different averaging periods and study site. Median air pollution metrics varied across study regions with Pittsburgh reporting poorer air pollution compared to other sites. The median 20-year average $PM_{2.5}$ and 10-year average NO_2 were the highest for all study regions, indicating improved air quality over time.

Long-term exposure to air pollution and gait speed

Table 3 reports findings on air pollution prior to the study entry in association with gait speed at baseline as well as annual change in gait speed over the study period. Long-term exposure to $PM_{2.5}$ prior to the enrollment was not associated with gait speed at baseline (cross-sectional association) for both usual and fast paces. Greater long-term exposure to $PM_{2.5}$ was related to a faster decline in gait speed at a usual pace regardless of exposure averaging period; one IQR higher 5-year average $PM_{2.5}$ exposure (2.00 $\mu m/m^3$) was related to 0.048 m/s decline in gait speed (95% CI: -0.084, -0.024) at a usual pace over 6-year study period, controlling for age, gender, race and ethnicity, education, smoking status, alcohol consumption, study site, and year since enrollment. Higher average $PM_{2.5}$ was not associated with a faster gait speed decline at a rapid pace regardless of exposure averaging period.

Long-term exposure to NO_2 prior to study entry was associated with gait speed at usual pace at baseline (cross-sectional association), adjusting for all potential confounders. One IQR higher 5-year average NO_2 (6.53 ppb) was associated with 0.026 m/s increase in usual pace gait on average at baseline (95% CI: 0.002, 0.046). Long-term exposure to NO_2 was associated with a faster decline in gait speed at both usual and rapid paces regardless of exposure averaging period; one IQR higher 5-year average NO_2 (6.53 ppb) was associated with 0.078 m/s decline in usual pace gait (95% CI: -0.120, -0.042) and 0.042 m/s decline in rapid pace gait speed (95% CI: -0.078, -0.006) over 6-year period, controlling for all potential confounders.

Long-term exposure to air pollution and gait speed by cardiovascular disease status

Table 4 demonstrates the association between air pollution and gait speed among individuals with and without cardiovascular disease. For usual gait speed, greater 5-year, 10-year, and 15-year average long-term exposure to $PM_{2.5}$ was associated with a decline in gait speed for both individuals with and without cardiovascular disease. For example, one IQR higher 5-year average $PM_{2.5}$ exposure (2.00 $\mu m/m^3$) was related to 0.036 m/s gait speed decline (95% CI: -0.060, -0.012) among individuals without cardiovascular disease and 0.072 m/s gait speed decline (95% CI: -0.132, -0.024) among those with cardiovascular disease over 6-year study period. For rapid pace gait, greater 5-year and 10-year average $PM_{2.5}$ were associated with a gait speed decline over time among individuals with cardiovascular disease but not those without cardiovascular disease.

Similarly, the longitudinal association between usual gait speed and long-term NO_2 exposure was significant among both individuals with and without cardiovascular disease: one IQR higher 5-year average NO_2 exposure (6.53 ppb) was associated with 0.060 m/s decline in usual gait speed (95% CI: -0.090, -0.030) among individuals without cardiovascular disease and 0.120 m/s usual gait speed decline (95% CI: -0.198, -0.042) among those with cardiovascular disease over 6-year study period. For rapid pace gait speed, the longitudinal association between long-term NO2 exposure and gait speed decline was observed among individuals with cardiovascular disease but not those without the disease. For example, one IQR higher 5-year average NO_2 exposure (6.53 ppb) was related to 0.078 m/s rapid pace gait decline (95% CI: -0.120, -0.012) over 6-year study period among people with cardiovascular disease.

Discussion

This longitudinal study found robust association between long-term exposure to air pollution and gait speed decline in a large cohort of older adults in four different locations in the US. Resident specific long-term concentrations of $PM_{2.5}$ and NO_2, taking account of residential mobility, were

estimated over the 20-year period prior to study entry using a spatio-temporal prediction model.[36,38] The air pollution metrics indicated that air quality improved over the estimated period, but magnitude of the association between air pollution and gait speed decline was similar regardless of exposure averaging periods. Gait speed is the result of a complex integration of multiple body functions such as aerobic capacity, proprioceptive control, and brain networks.[40-42] Exposure to air pollution has been reported to be adversely associated with a range of body function and health outcomes such as brain function, risk of developing dementia, diabetes incidence, and cardiovascular disease mortality.[43-46] Development or progression of these diseases by air pollution exposure may contribute to faster decline of gait speed. Additionally, air pollution may directly lead to dysfunction in multiple body structures and functions that control gait speed.

Previous studies mostly investigated annual average concentration of air pollutants in relation to performance-based physical functioning.[28,29] Unlike our study, the authors did not find a faster decline in performance-based physical functinioing[28] and gait speed among individuals who were exposed to higher level concentration of air pollution.[29] On the other hand, another study showed consistent results with our study. The authors found a significant association between 5-year ambient concentration of air pollution and faster progression in physical functioning among older adults.[27] The previous studies that did not find significant associations[28,29] assessed air pollution in a relatively short period of time (1-year annual average) compared to the study by Weuve et al.[27] and ours. This indicates that longer exposure to air pollution may have more harmful and stronger impacts on physical functioning; in other words, one year annual average air pollutant concentrations may be too short to capture the hazardous impacts of air pollution on progression in physical function decline.

We found the significant association of $PM_{2.5}$ exposure with decline of gait speed at the usual, but not at a rapid pace. Usual gait speed and rapid gait speed tests capture a slightly different aspect of functionality. Both usual and rapid gait speed tests together can provide a more complete picture of

individuals' current physical functioning and health status.[4] Usual gait speed is indicative of physical functioning, frailty, and health status.[7,47] Rapid gait speed, required more efforts and physical strength, is suggestive of capabilities in the community such as safely cross the street in the time of a signal.[48] The difference may partially explain the variation in the association of air pollution with usual and rapid gait speed. However, further studies are required to understand the nuance of how $PM_{2.5}$ exposure differently affect usual gait speed and rapid gait speed.

The association between long-term exposure to air pollution prior to study entry and faster gait speed decline varied by cardiovascular status at study enrollment. The longitudinal association between air pollution (5-year and 10-year average $PM_{2.5}$ and NO_2) and rapid gait speed decline was significant only in individuals with cardiovascular disease. The magnitude of harmful impacts of air pollution on rapid pace gait may be greater for individuals with cardiovascular disease than in those without cardiovascular disease. Air pollution is a well-known risk factor for cardiovascular disease.[31] Presence of cardiovascular disease may aggregates the adverse impacts of long-term exposure to rapid pace gait speed decline.

This study has several limitations. First, we included only past exposure to air pollution prior to the initial gait speed measure to ensure the temporality that the exposure precedes the outcome. However, levels of air pollution are changing over time. Gait speed may be affected by not only long-term exposure to air pollution in the past but also current air pollution exposure. Second, air pollution was disaggregated into specific types of air pollutants ($PM_{2.5}$ and NO_2) because each measure may differentially impact health in terms of effect size or direction. It is still unclear which air pollutant has the most hazardous impacts on health among older adults.[49] However, in real life, air pollutants may interact with each other and have synergetic effects on health. Future study should explore the interplay of multiple air pollutants on older adults' health outcomes. Third, the study population primarily consists of self-identified White individuals age 75 years and older and highly educated even though the

study team made efforts to recruit diverse people. The application of the findings to other settings with diverse people may be limited. However, we analyzed rigorously collected data over 6-year and the association between long-term air pollution exposure and gait speed we found in this study was robust, not changing much depending on covariates or models. The findings still add to the literature and increase knowledge on the impacts of long-term air pollution on the gait speed alteration with aging.

Conclusion

Gait speed alteration indicates the risk of development or progression of physical disability, frailty, or chronic diseases which are essential for independent living in later life. Long-term exposure to air pollution appears to be associated with faster progression in gait speed decline among older adults in four different locations in the US. Older adults with cardiovascular disease appear more susceptible from the adverse effects of long-term exposure to air pollution and the progression in gait speed decline could be even faster among those with cardiovascular disease. Policies to reduce emission of air pollutants and interventions of avoid air pollution exposure or manage cardiovascular disease could contribute to the reduction in the burden of preventable institutionalization and hospitalization.

Table 1. Gait speed at usual and fast pace by selected participants' characteristics at baseline (*N* = 3,022)

		Gait speed (m/s)[a]	
		Usual gait	Fast gait
Selected Measure	*N* (%)	Mean (*SD*)	Mean (*SD*)
Age (year)			
72-79	2,004 (66.31)	0.97 (0.22)	1.39 (0.65)
80-84	839 (27.76)	0.92 (0.26)	1.30 (0.41)
85+	179 (5.92)	0.83 (0.22)	1.17 (0.32)
Mean (*SD*)	78.59 (3.25)		
Gender			
Female	1,392 (46.06)	0.92 (0.23)	1.28 (0.53)
Male	1,630 (53.94)	0.97 (0.23)	1.41 (0.62)
Race			
White	2,888 (95.57)	0.95 (0.23)	1.35 (0.59)
People of color	134 (4.43)	0.91 (0.22)	1.26 (0.35)
Education			
Less than high school	336 (11.12)	0.89 (0.20)	1.27 (0.47)
High school graduate	753 (24.92)	0.92 (0.22)	1.30 (0.32)
Some college or graduate	1,233 (40.80)	0.95 (0.23)	1.35 (0.69)
Postgraduate	700 (23.16)	0.99 (0.26)	1.43 (0.63)
Smoking			
Never	1,210 (40.04)	0.94 (0.24)	1.33 (0.35)
Former	1,620 (53.61)	0.95 (0.22)	1.37 (0.73)
Current	134 (4.43)	0.90 (0.20)	1.28 (0.31)
Missing	58 (1.92)		
Alcohol consumption (drinks/week)			
Nondrinkers	1,267 (41.93)	0.91 (0.24)	1.31 (0.71)
0.1-0.9	461 (15.25)	0.96 (0.22)	1.36 (0.32)
1.0-7.0	677 (22.40)	0.96 (0.20)	1.36 (0.33)
7.1-14.0	284 (9.40)	1.01 (0.27)	1.42 (0.34)
> 14.0	287 (9.50)	0.98 (0.20)	1.44 (0.88)
Mean (*SD*)	3.52 (6.48)		
Missing	46 (1.52)		
Cardiovascular disease[b]			
Yes	1,751 (57.94)	0.93 (0.22)	1.32 (0.61)
No	1,271 (42.06)	0.97 (0.24)	1.39 (0.54)
Study site			
Winston-Salem/Greensboro, North Carolina	725 (23.99)	0.92 (0.19)	1.30 (0.64)
Sacramento, California	894 (29.58)	0.94 (0.23)	1.35 (0.31)
Hagerstown, Maryland	447 (14.79)	0.86 (0.17)	1.29 (0.31)
Pittsburgh, Pennsylvania	956 (31.63)	1.01 (0.26)	1.42 (0.79)

[a] The number of seconds to complete the 15 feet (4.57m) timed walk assessed, then converted to meter per second (m/s).

[b] Presence of cardiovascular disease was defined as having at least one of the following diseases: myocardial infarction, angina pectoris, stroke, atrial fibrillation, transient ischemic attack, heart failure, deep vein thrombosis, pulmonary embolus, hypertension, rheumatic fever or heart valve

Table 2. Long-term air pollution exposure prior to study enrollment by study site

	Winston-Salem/ Greensboro, NC (*N* = 725)	Sacramento, CA (*N* = 894)	Hagerstown, MD (*N* = 447)	Pittsburgh, PA (*N* = 956)	Overall (*N* = 3,022)
	Median (*IQR*)				
5-year average $PM_{2.5}$ ($\mu m/m^3$)	15.69 (1.17)	15.14 (3.29)	15.32 (1.62)	17.12 (0.93)	16.11 (2.00)
10-year average $PM_{2.5}$ ($\mu m/m^3$)	16.45 (1.29)	15.63 (3.36)	16.02 (1.66)	18.01 (1.01)	16.81 (2.14)
15-year average $PM_{2.5}$ ($\mu m/m^3$)	17.32 (1.39)	16.34 (3.51)	16.82 (1.76)	18.91 (1.08)	17.62 (2.26)
20-year average $PM_{2.5}$ ($\mu m/m^3$)	18.12 (1.52)	17.06 (3.50)	17.58 (1.88)	19.83 (1.12)	18.43 (2.38)
5-year average NO_2 (ppb)	13.28 (4.33)	15.82 (6.23)	11.83 (4.53)	19.82 (4.56)	15.69 (6.53)
10-year average NO_2 (ppb)	13.69 (4.20)	17.14 (6.42)	13.70 (4.61)	20.42 (4.41)	16.43 (6.54)

Abbreviation: IQR, interquartile range

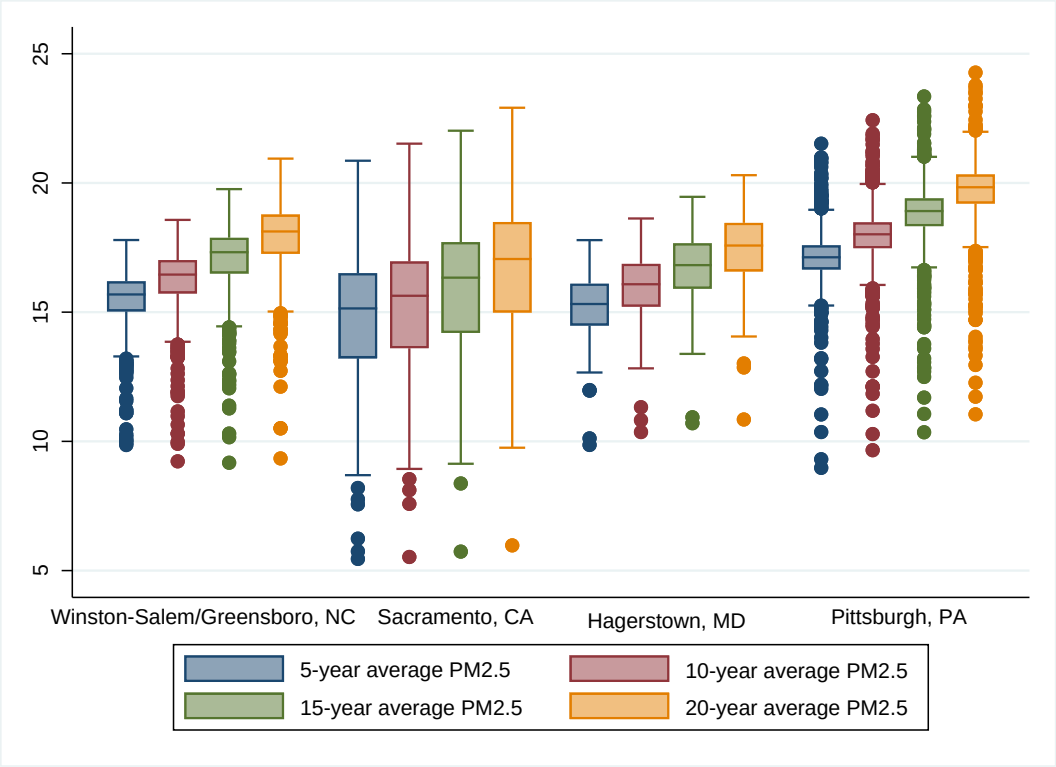

Figure 1. Distribution of $PM_{2.5}$ ($\mu m/m^3$) exposure before study enrollment by study site

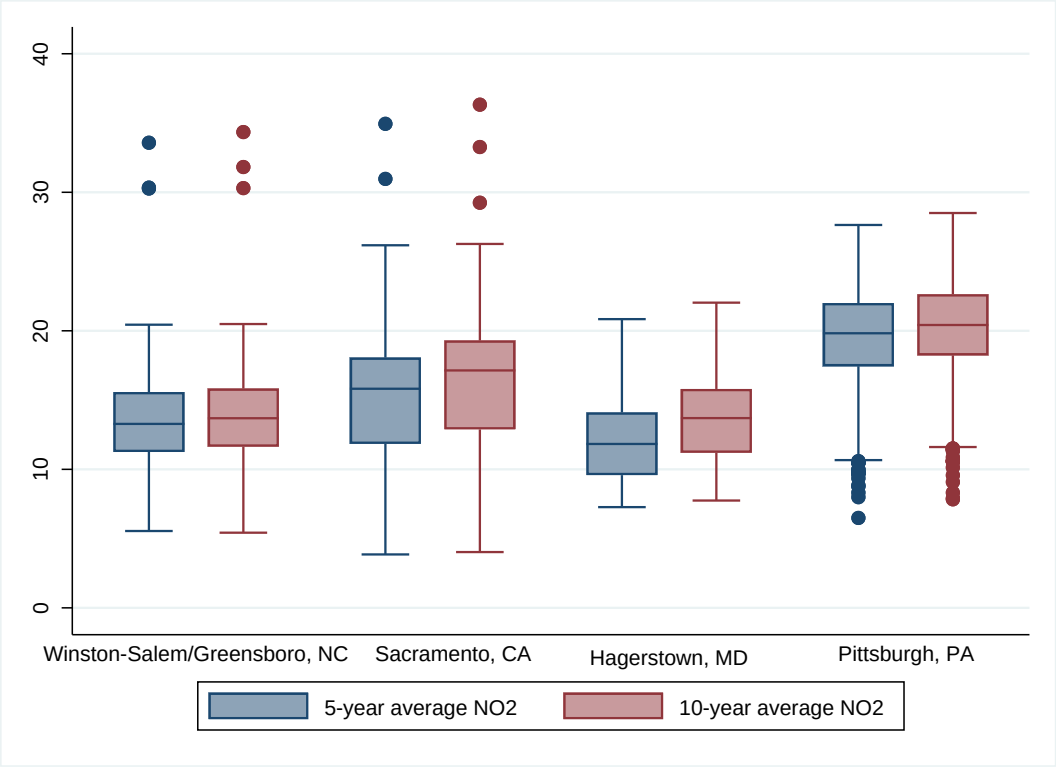

Figure 2. Distribution of NO_2 (ppb) exposure before study enrollment by study site

Table 3. Selected coefficients from linear mixed-effect models for gait speed on air pollution (N = 2,933)

	Gait speed (m/s)	
	Usual pace	Rapid pace
Air pollutants	Coefficient (95% CI)	
5-year average $PM_{2.5}$		
Mean difference in gait speed at baseline[a]	0.008 (-0.010, 0.024)	-0.008 (-0.024, 0.010)
Mean annual decline in gait speed[b]	-0.008 (-0.014, -0.004)**	-0.004 (-0.010, 0.000)
10-year average $PM_{2.5}$		
Mean difference in gait speed at baseline[a]	0.006 (-0.011, 0.024)	-0.009 (-0.028, 0.009)
Mean annual decline in gait speed[b]	-0.009 (-0.013, -0.002)**	-0.004 (-0.009, 0.001)
15-year average $PM_{2.5}$		
Mean difference in gait speed at baseline[a]	0.007 (-0.011, 0.025)	-0.009 (-0.027, 0.009)
Mean annual decline in gait speed[b]	-0.007 (-0.014, -0.002)**	-0.005 (-0.009, 0.002)
20-year average $PM_{2.5}$		
Mean difference in gait speed at baseline[a]	0.007 (-0.012, 0.026)	-0.010 (-0.029, 0.010)
Mean annual decline in gait speed[b]	-0.007 (-0.012, -0.002)*	-0.005 (-0.010, 0.002)
5-year average NO_2		
Mean difference in gait speed at baseline[a]	0.026 (0.002, 0.046)*	-0.007 (-0.026, 0.020)
Mean annual decline in gait speed[b]	-0.013 (-0.020, -0.007)***	-0.007 (-0.013, -0.001)*
10-year average NO_2		
Mean difference in gait speed at baseline[a]	0.026 (0.002, 0.046)*	0.003 (-0.020, 0.026)
Mean annual decline in gait speed[b]	-0.013 (-0.020, -0.007)***	-0.007 (-0.013, -0.003)**

[a] Mean difference in gait speed (m/sec) at baseline for every one additional interquartile change ($\mu m/m^3$) in air pollutant

[b] Mean annual decline in gait speed (m/sec) overtime for every one additional interquartile change ($\mu m/m^3$) in air pollutant

Linear mixed-effect models with random intercept (participant) and random slope (year since enrollment) were fitted, adjusting for age, gender, race and ethnicity, education, smoking status, alcohol consumption, study site, and year since enrollment. *p<0.05 **p<0.01 ***p<0.001

Table 4. Selected coefficients from linear mixed-effect models for gait speed on air pollution by cardiovascular disease (CVD) status (N = 2,933)

	Gait speed (m/s)			
	Usual pace		Fast pace	
	Without CVD (*N* = 1,230)	With CVD (*N* = 1,703)	Without CVD (*N* = 1,230)	With CVD (*N* = 1,703)
Air pollutants	Coefficient (95% CI)		Coefficient (95% CI)	
5-year average $PM_{2.5}$				
Mean difference in gait speed at baseline[a]	-0.001 (-0.016, 0.014)	0.014 (-0.014, 0.042)	-0.012 (-0.042, 0.020)	-0.006 (-0.026, 0.016)
Mean annual decline in gait speed[b]	-0.006** (-0.010, -0.002)	-0.012** (-0.022, -0.004)	-0.002 (-0.010, 0.008)	-0.006* (-0.012, -0.001)
10-year average $PM_{2.5}$				
Mean difference in gait speed at baseline[a]	-0.001 (-0.015, 0.013)	0.0013 (-0.017, 0.041)	-0.011 (-0.041, 0.021)	-0.011 (-0.032, 0.011)
Mean annual decline in gait speed[b]	-0.004** (-0.009, -0.001)	-0.011* (-0.019, -0.002)	-0.002 (-0.011, 0.006)	-0.006* (-0.013, 0.000)
15-year average $PM_{2.5}$				
Mean difference in gait speed at baseline[a]	0.000 (-0.016, 0.016)	0.011 (-0.018, 0.041)	-0.007 (-0.041, 0.025)	-0.011 (-0.034, 0.009)
Mean annual decline in gait speed[b]	-0.005* (-0.009, -0.001)	-0.009* (-0.018, 0.000)	-0.002 (-0.011, 0.007)	-0.007 (-0.011, 0.000)
20-year average $PM_{2.5}$				
Mean difference in gait speed at baseline[a]	0.002 (-0.014, 0.017)	0.012 (-0.019, 0.040)	-0.007 (-0.040, 0.026)	-0.012 (-0.034, 0.010)
Mean annual decline in gait speed[b]	-0.005* (-0.010, -0.001)	-0.010 (-0.019, 0.000)	-0.002 (-0.012, 0.007)	-0.007 (-0.012, 0.000)
5-year average NO_2				
Mean difference in gait speed at baseline [a]	0.007 (-0.013, 0.026)	0.039* (0.001, 0.078)	-0.007 (-0.046, 0.033)	-0.007 (-0.033, 0.026)
Mean annual decline in gait speed [b]	-0.010*** (-0.015, -0.005)	-0.020** (-0.033, -0.007)	-0.007 (-0.020, 0.007)	-0.013* (-0.020, -0.002)
10-year average NO_2				
Mean difference in gait speed at baseline [a]	0.007 (-0.013, 0.026)	0.039* (0.002, 0.078)	0.013 (-0.033, 0.052)	-0.007 (-0.033, 0.026)

	Gait speed (m/s)			
	Usual pace		Fast pace	
	Without CVD (*N* = 1,230)	With CVD (*N* = 1,703)	Without CVD (*N* = 1,230)	With CVD (*N* = 1,703)
Air pollutants	Coefficient (95% CI)		Coefficient (95% CI)	
Mean annual decline in gait speed [b]	-0.007*** (-0.013, -0.007)	-0.020** (-0.033, -0.007)	-0.007 (-0.020, 0.007)	-0.013** (-0.020, -0.007)

[a] Mean difference in gait speed (m/sec) at baseline for every additional interquartile change ($\mu m/m^3$) in air pollutant

[b] Mean annual decline in gait speed (m/sec) overtime for every additional interquartile change ($\mu m/m^3$) in air pollutant

Presence of cardiovascular disease was defined as having at least one of the following diseases: myocardial infarction, angina pectoris, stroke, atrial fibrillation, transient ischemic attack, heart failure, deep vein thrombosis, pulmonary embolus, hypertension, rheumatic fever or heart valve

Linear mixed-effect models with random intercept (participant) and random slope (year since enrollment) were fitted. Age, gender, race and ethnicity, education, smoking status, alcohol consumption, study site, and year since enrollment were controlled. *p<0.05 **p<0.01 ***p<0.001

References

1. Cruz-Jimenez M. Normal Changes in Gait and Mobility Problems in the Elderly. *Phys Med Rehabil Clin N Am*. 2017;28(4):713-725. doi:10.1016/j.pmr.2017.06.005

2. Peters DM, Fritz SL, Krotish DE. Assessing the Reliability and Validity of a Shorter Walk Test Compared With the 10-Meter Walk Test for Measurements of Gait Speed in Healthy, Older Adults. *J Geriatr Phys Ther*. 2013;36(1):24-30. doi:10.1519/JPT.0b013e318248e20d

3. Rasmussen LJH, Caspi A, Ambler A, et al. Association of Neurocognitive and Physical Function With Gait Speed in Midlife. *JAMA Network Open*. 2019;2(10):e1913123-e1913123. doi:10.1001/jamanetworkopen.2019.13123

4. Middleton A, Fritz SL, Lusardi M. Walking speed: the functional vital sign. *J Aging Phys Act*. Apr 2015;23(2):314-22. doi:10.1123/japa.2013-0236

5. Peel NM, Alapatt LJ, Jones LV, Hubbard RE. The Association Between Gait Speed and Cognitive Status in Community-Dwelling Older People: A Systematic Review and Meta-analysis. *The Journals of Gerontology: Series A*. 2018;74(6):943-948. doi:10.1093/gerona/gly140

6. Studenski S. Bradypedia: is gait speed ready for clinical use? *J Nutr Health Aging*. 2009;13(10):878-880.

7. Abellan van Kan G, Rolland Y, Andrieu S, et al. Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people an International Academy on Nutrition and Aging (IANA) Task Force. *J Nutr Health Aging*. 2009;13(10):881-9. doi:10.1007/s12603-009-0246-z

8. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA*. 2011;305(1):50-8. doi:10.1001/jama.2010.1923

9. den Ouden ME, Schuurmans MJ, Arts IE, van der Schouw YT. Physical performance characteristics related to disability in older persons: a systematic review. *Maturitas*. 2011;69(3):208-219. doi:10.1016/j.maturitas.2011.04.008

10. Ferrucci L, Levine ME, Kuo PL, Simonsick EM. Time and the Metrics of Aging. *Circ Res*. 2018;123(7):740-744. doi:10.1161/circresaha.118.312816

11. Fitzpatrick AL, Buchanan CK, Nahin RL, et al. Associations of gait speed and other measures of physical function with cognition in a healthy cohort of elderly persons. *J Gerontol A Biol Sci Med Sci*. 2007;62(11):1244-51. doi:10.1093/gerona/62.11.1244

12. Patrizio E, Calvani R, Marzetti E, Cesari M. Physical Functional Assessment in Older Adults. *J Frailty Aging*. 2021;10(2):141-149. doi:10.14283/jfa.2020.61

13. Figgins E, Pieruccini-Faria F, Speechley M, Montero-Odasso M. Potentially modifiable risk factors for slow gait in community-dwelling older adults: A systematic review. *Ageing Res Rev*. 2021;66:101253. doi:10.1016/j.arr.2020.101253

14. Kelly FJ, Fussell JC. Air pollution and public health: emerging hazards and improved understanding of risk. *Environ Geochem Health*. 2015;37(4):631-49. doi:10.1007/s10653-015-9720-1

15. Liu Z, Wang F, Li W, et al. Does utilizing WHO's interim targets further reduce the risk - meta-analysis on ambient particulate matter pollution and mortality of cardiovascular diseases? *Environ Pollut*. 2018;242(Pt B):1299-1307. doi:10.1016/j.envpol.2018.07.041

16. Kaufman JD, Spalt EW, Curl CL, et al. Advances in Understanding Air Pollution and CVD. *Glob Heart*. 2016;11(3):343-352. doi:10.1016/j.gheart.2016.07.004

17. Wang C, Tu Y, Yu Z, Lu R. PM2.5 and Cardiovascular Diseases in the Elderly: An Overview. *Int J Environ Res Public Health*. 2015;12(7):8187-97. doi:10.3390/ijerph120708187

18. Choi HS, Kim JT, Seo JY, Linkov F, Shubnikov E, Lee HK. Correlation between total air pollutant emissions and incidence of type 1 diabetes in the Russian Federation. *Clin Exp Pediatr*. 2021;64(10):525-530. doi:10.3345/cep.2020.01501

19. Delgado-Saborit JM, Guercio V, Gowers AM, Shaddick G, Fox NC, Love S. A critical review of the epidemiological evidence of effects of air pollution on dementia, cognitive function and cognitive decline in adult population. *Sci Total Environ*. 2021;757:143734. doi:10.1016/j.scitotenv.2020.143734

20. Wen M, Gu D. Air pollution shortens life expectancy and health expectancy for older adults: the case of China. *J Gerontol A Biol Sci Med Sci*. 2012;67(11):1219-29. doi:10.1093/gerona/gls094

21. Veronese N, Stubbs B, Volpato S, et al. Association Between Gait Speed With Mortality, Cardiovascular Disease and Cancer: A Systematic Review and Meta-analysis of Prospective Cohort Studies. *J Am Med Dir Assoc*. 2018;19(11):981-988.e7. doi:10.1016/j.jamda.2018.06.007

22. Alenazi AM, Alshehri MM, Alqahtani BA, Alanazi AD, Bindawas SM. Combined diabetes and arthritis are associated with declined gait speed. *Clin Rheumatol*. 2021;40(4):1593-1598. doi:10.1007/s10067-020-05370-3

23. Chou MY, Nishita Y, Nakagawa T, et al. Role of gait speed and grip strength in predicting 10-year cognitive decline among community-dwelling older people. *BMC Geriatr*. 2019;19(1):186. doi:10.1186/s12877-019-1199-7

24. Dumurgier J, Artaud F, Touraine C, et al. Gait Speed and Decline in Gait Speed as Predictors of Incident Dementia. *J Gerontol A Biol Sci Med Sci*. 2017;72(5):655-661. doi:10.1093/gerona/glw110

25. Shumake KL, Sacks JD, Lee JS, Johns DO. Susceptibility of older adults to health effects induced by ambient air pollutants regulated by the European Union and the United States. *Aging Clin Exp Res*. 2013;25(1):3-8. doi:10.1007/s40520-013-0001-5

26. Lin H, Guo Y, Zheng Y, et al. Exposure to ambient PM(2.5) associated with overall and domain-specific disability among adults in six low- and middle-income countries. *Environ Int*. 2017;104:69-75. doi:10.1016/j.envint.2017.04.004

27. Weuve J, Kaufman JD, Szpiro AA, et al. Exposure to Traffic-Related Air Pollution in Relation to Progression in Physical Disability among Older Adults. *Environ Health Perspect*. 2016;124(7):1000-8. doi:10.1289/ehp.1510089

28. de Zwart F, Brunekreef B, Timmermans E, Deeg D, Gehring U. Air Pollution and Performance-Based Physical Functioning in Dutch Older Adults. *Environ Health Perspect*. 2018;126(1):017009. doi:10.1289/ehp2239

29. Wang H, Liu H, Guo F, et al. Association between Ambient Fine Particulate Matter and Physical Functioning in Middle-aged and Older Chinese Adults: A Nationwide Longitudinal Study. *J Gerontol A Biol Sci Med Sci*. 2021;doi:10.1093/gerona/glab370

30. Hu K, Keenan K, Hale JM, Börger T. The association between city-level air pollution and frailty among the elderly population in China. *Health Place*. 2020;64:102362. doi:10.1016/j.healthplace.2020.102362

31. Mannucci PM, Harari S, Franchini M. Novel evidence for a greater burden of ambient air pollution on cardiovascular disease. *Haematologica*. 2019;104(12):2349-2357. doi:10.3324/haematol.2019.225086

32. DeKosky ST, Fitzpatrick A, Ives DG, et al. The Ginkgo Evaluation of Memory (GEM) study: design and baseline data of a randomized trial of Ginkgo biloba extract in prevention of dementia. *Contemp Clin Trials*. 2006;27(3):238-53. doi:10.1016/j.cct.2006.02.007

33. Fitzpatrick AL, Fried LP, Williamson J, et al. Recruitment of the elderly into a pharmacologic prevention trial: the Ginkgo Evaluation of Memory Study experience. *Contemp Clin Trials*. 2006;27(6):541-53. doi:10.1016/j.cct.2006.06.007

34. Semmens E et al. Air pollution and incident dementia in older adults in four communities in the USA: the Gingko Evaluation of Memory Study. Under review.

35. Hurley S, Hertz A, Nelson DO, et al. Tracing a Path to the Past: Exploring the Use of Commercial Credit Reporting Data to Construct Residential Histories for Epidemiologic Studies of Environmental Exposures. *Am J Epidemiol*. 2017;185(3):238-246. doi:10.1093/aje/kww108

36. Kim SY, Olives C, Sheppard L, et al. Historical Prediction Modeling Approach for Estimating Long-Term Concentrations of PM2.5 in Cohort Studies before the 1999 Implementation of Widespread Monitoring. *Environ Health Perspect*. 2017;125(1):38-46. doi:10.1289/ehp131

37. Sampson PD, Richards M, Szpiro AA, et al. A regionalized national universal kriging model using Partial Least Squares regression for estimating annual PM(2.5) concentrations in epidemiology. *Atmos Environ (1994)*. 2013;75:383-392. doi:10.1016/j.atmosenv.2013.04.015

38. Young MT, Bechle MJ, Sampson PD, et al. Satellite-Based NO2 and Model Validation in a National Prediction Model Based on Universal Kriging and Land-Use Regression. *Environ Sci Technol*. 2016;50(7):3686-94. doi:10.1021/acs.est.5b05099

39. Koch M, Fitzpatrick AL, Rapp SR, et al. Alcohol Consumption and Risk of Dementia and Cognitive Decline Among Older Adults With or Without Mild Cognitive Impairment. *JAMA Netw Open*. 2019;2(9):e1910319. doi:10.1001/jamanetworkopen.2019.10319

40. Fiser WM, Hays NP, Rogers SC, et al. Energetics of walking in elderly people: factors related to gait speed. *J Gerontol A Biol Sci Med Sci*. 2010;65(12):1332-7. doi:10.1093/gerona/glq137

41. Park YH, Kim YM, Lee BH. An ankle proprioceptive control program improves balance, gait ability of chronic stroke patients. *J Phys Ther Sci*. 2013;25(10):1321-4. doi:10.1589/jpts.25.1321

42. Allali G, Montembeault M, Brambati SM, et al. Brain Structure Covariance Associated With Gait Control in Aging. *J Gerontol A Biol Sci Med Sci*. 23 2019;74(5):705-713. doi:10.1093/gerona/gly123

43. Costa LG, Cole TB, Dao K, Chang YC, Garrick JM. Developmental impact of air pollution on brain function. *Neurochem Int*. 2019;131:104580. doi:10.1016/j.neuint.2019.104580

44. Paul KC, Haan M, Yu Y, et al. Traffic-Related Air Pollution and Incident Dementia: Direct and Indirect Pathways Through Metabolic Dysfunction. *J Alzheimers Dis*. 2020;76(4):1477-1491. doi:10.3233/jad-200320

45. Hayes RB, Lim C, Zhang Y, et al. PM2.5 air pollution and cause-specific cardiovascular disease mortality. *Int J Epidemiol*. 2020;49(1):25-35. doi:10.1093/ije/dyz114

46. Lin Y, Zhou S, Liu H, et al. Risk Analysis of Air Pollution and Meteorological Factors Affecting the Incidence of Diabetes in the Elderly Population in Northern China. *J Diabetes Res*. 2020;2020:3673980. doi:10.1155/2020/3673980

47. Castell MV, Sánchez M, Julián R, Queipo R, Martín S, Otero Á. Frailty prevalence and slow walking speed in persons age 65 and older: implications for primary care. *BMC Fam Pract*. 2013;14:86. doi:10.1186/1471-2296-14-86

48. Salbach NM, O'Brien K, Brooks D, et al. Speed and distance requirements for community ambulation: a systematic review. *Arch Phys Med Rehabil*. 2014;95(1):117-128.e11. doi:10.1016/j.apmr.2013.06.017

49. Simoni M, Baldacci S, Maio S, Cerrai S, Sarno G, Viegi G. Adverse effects of outdoor pollution in the elderly. *J Thorac Dis*. 2015;7(1):34-45. doi:10.3978/j.issn.2072-1439.2014.12.10