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Fine particulate matter and nonaccidental and cause-specific mortality

Do associations vary by exposure assessment method?

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Background: There is considerable heterogeneity in fine particulate matter ($PM_{2.5}$)–mortality associations between studies, potentially due to differences in exposure assessment methods. Our aim was to evaluate associations of $PM_{2.5}$ predicted from different models with nonaccidental and cause-specific mortality.

Methods: We followed 107,906 participants of the Nurses' Health Study cohort from 2001 to 2016. $PM_{2.5}$ concentrations were estimated from spatiotemporal models developed by researchers at the University of Washington (UW), Pennsylvania State University (PSU), and Harvard TH Chan School of Public Health (HSPH). We calculated 12-month moving average concentrations and we used time-varying Cox proportional hazard ratios (HRs).

Results: There were 30,242 nonaccidental deaths in 1,435,098 person-years. We observed high correlations and similar temporal trends between the $PM_{2.5}$ predictions. We found no associations of UW, PSU, or HSPH $PM_{2.5}$ with nonaccidental mortality, but suggestive positive associations with cancer, cardiovascular, and respiratory disease mortality. There were small differences in HRs between the $PM_{2.5}$ predictions. All three predictions showed the strongest associations with cancer mortality: HRs (95% confidence interval, expressed per 5 μg/m^3 increase) were 1.06 (1.01, 1.12) for UW, 1.08 (1.03, 1.13) for PSU, and 1.05 (1.00, 1.10) for HSPH. In a subset restricted to participants who were always exposed to $PM_{2.5}$ below 12 μg/m^3, we observed positive associations with nonaccidental mortality.

Conclusion: We found that differences between $PM_{2.5}$ exposure assessment methods could lead to minor differences in strengths of associations between $PM_{2.5}$ and cause-specific mortality in a population of US female nurses.

Keywords: Air pollution; Exposure assessment; Mortality; Particulate matter; Spatiotemporal models

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This study used confidential data from the Nurses' Health Study that cannot be made publicly available. A detailed analysis plan and computing code are available upon reasonable request.

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Introduction

Fine particulate matter ($PM_{2.5}$) is a complex mixture of small particles and is regulated in many countries.[1] Inhalation of $PM_{2.5}$ can lead to systemic inflammation and oxidative stress.[2] A recent study of more than 81 million participants showed positive associations of $PM_{2.5}$ with all-cause mortality in Canada, Europe, and the United States.[3] A meta-analysis reported that $PM_{2.5}$ was also associated with nonaccidental, lung cancer, cardiovascular disease (CVD), and respiratory disease mortality.[1] The majority of the studies included in this meta-analysis observed positive associations; however, there was considerable heterogeneity in the magnitude of associations.[1] This could be due to various factors, including differences in PM composition, demographics, adjustment for potential confounders, and exposure assessment methods.[1]

Predicting $PM_{2.5}$ at a fine spatial scale has been a major challenge for epidemiological studies. Over the past decade,

What this study adds:

We observed high correlations and similar temporal trends between $PM_{2.5}$ predictions from different spatiotemporal models. We found no associations of $PM_{2.5}$ with nonaccidental mortality, but suggestive positive associations with cause-specific disease mortality. There were small differences in hazard ratios between the $PM_{2.5}$ predictions. All three predictions showed the strongest associations with cancer mortality and weaker suggestive associations with respiratory disease mortality. In a low-level population of US female nurses, we found suggestive associations between $PM_{2.5}$ and nonaccidental and cause-specific mortality. Differences between $PM_{2.5}$ exposure assessment methods could lead to minor differences in strengths of associations.

Table 1.

A brief overview of the three different US-based spatiotemporal $PM_{2.5}$ models

Model	Temporal resolution	Spatial resolution	Statistical methods	Potential predictors	$PM_{2.5}$ monitoring stations
UW	2-week average	Exact address	Hierarchical land use regression model in a universal kriging framework (regional models)	Geographic covariates Annual NO_x, SO_2, CO, $PM_{2.5}$, and PM_{10} averages of emissions sources Satellite-measured ground-level NO_2	US EPA Air Quality System Cohort-specific residential and fixed-site monitoring data
PSU	Daily	Exact address	Generalized additive mixed model	Geographic covariates Dispersion model $PM_{2.5}$ predictions Chemical transport model $PM_{2.5}$ predictions Meteorological covariates	US EPA Air Quality System SEARCH (Southern Aerosol Research and Characterization Study) network
HSPH	Daily	1 km	Ensemble model combining gradient boosting, random forest, and neural network algorithm predictions	Geographic covariates Aerosol optical depth measurements Aerosol estimations Chemical transport model $PM_{2.5}$ predictions Meteorological covariates	US EPA Air Quality System Other regional or local monitoring data

exposure assessment methods have improved considerably due to advances in statistical methods, computational power, $PM_{2.5}$ monitoring, and increased availability of potential predictors (e.g., land use data, satellite measurements, and dispersion model outputs).[4,5] The variety in statistical methods and increasing availability of potential predictors may drive different $PM_{2.5}$ assessment models and predictions and could contribute to heterogeneity in the magnitude of the associations of $PM_{2.5}$ with health outcomes between studies. There are only a few studies that have systematically compared potential heterogeneity in health effect estimates using $PM_{2.5}$ predictions from different exposure models.[6–10] In general, these studies observed strong to very strong correlations between $PM_{2.5}$ estimates (Pearson $r >$ 0.60). However, for some health outcomes, differences in effect estimates of $PM_{2.5}$ generated from different exposure assessment models were observed.[6–9]

In the United States, several exposure assessment models to predict $PM_{2.5}$ have been developed.[11–13] Our aim was to compare three different spatiotemporal models previously used in impactful US studies of health effects of $PM_{2.5}$. We linked $PM_{2.5}$ predictions obtained from each model to a nationwide cohort of 107,906 participants from the US-based Nurses' Health Study (NHS) and followed them from 2001 through 2016. We evaluated associations of 12-month moving average $PM_{2.5}$ exposures with nonaccidental, cancer, CVD, and respiratory disease mortality.

Methods

Study population

The NHS is a prospective cohort study of 121,701 female registered nurses who were between 30 and 55 years of age at the start of the study in 1976. Nurses were enrolled from a selection of 11 states but lived throughout the United States during follow-up. Since the start of the study, participants completed a biennial questionnaire with questions related to demographics, lifestyle characteristics, health outcomes, and residential address. All residential address locations have been geocoded.[14] Response rates have been consistently over 90% in each questionnaire cycle.

The study protocol was approved by the Institutional Review Boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health, and those of participating registries as required.

Outcome definition

Deaths were ascertained from reports from the US Postal Service and next of kin, and by National Death Index searches.[15] Death certificates and medical records were reviewed by trained study staff blind to exposure status to detect the primary cause of death. We looked at deaths from all nonaccidental causes (International Classification of Diseases, Eight Revision [ICD-8] codes 001–796), all cancers (ICD-8 codes 140–209), CVDs (ICD-8 codes 390–458), and respiratory diseases (ICD-8 codes 460–519).

Exposure assessment

$PM_{2.5}$ concentrations were estimated by three different spatiotemporal models (Table 1): from University of Washington (hereafter referred to as UW $PM_{2.5}$), from Pennsylvania State University (hereafter referred to as PSU $PM_{2.5}$), and from Harvard TH Chan School of Public Health (hereafter referred to as HSPH $PM_{2.5}$). For all three $PM_{2.5}$ predictions, we calculated monthly average $PM_{2.5}$ concentrations over follow-up by averaging concentrations in each month. Next, we calculated time-varying 12-month moving averages based on the current and previous 11 months. The 12-month moving average incorporated changes in concentrations due to residential mobility. The models are briefly described in the following sections; additional information about the models can be found elsewhere.[11–13]

University of Washington fine particulate matter

Two-week average residential UW $PM_{2.5}$ concentrations were predicted by a multiregion land use regression model within a universal kriging framework.[13] To develop this model, $PM_{2.5}$ concentration data were obtained from the US Environmental Protection Agency (EPA) Air Quality System (including the Interagency Monitoring of Protected Visual Environments [IMPROVE] network), and residential and fixed-site monitoring data from cohort-specific campaigns.[13] For each modeling region, a land use regression model in a kriging framework was built. The models included geographic covariates (e.g., road networks, industrial emissions, population density), annual averages of specific emission sources for NO_x, SO_2, CO, $PM_{2.5}$, and PM_{10} from the US EPA Emission Inventory Groups, and annual average satellite-measured ground-level NO_2.[13] The model performance was good with a spatiotemporal cross-validated (CV)

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R^2 of 0.87 and a spatial CV R^2 of 0.93. UW $PM_{2.5}$ concentrations were estimated at the time-matched exact geocoded residential address of each participant.

Pennsylvania State University fine particulate matter

Daily average residential PSU $PM_{2.5}$ concentrations were predicted using generalized additive mixed models.[11,16] For the development of these models, $PM_{2.5}$ concentration data were obtained from the US EPA Air Quality System (including the IMPROVE network) and the Southern Aerosol Research and Characterization Study network. The models included spatial covariates (e.g., county-level population density, urban land use, elevation) and spatiotemporal covariates, such as traffic-related primary PM concentration estimates from a line-source Gaussian plume dispersion model, chemical transport model $PM_{2.5}$ predictions, and meteorological covariates.[11,16] Spatiotemporal models of daily $PM_{2.5}$ levels across 1999–2019 had moderate predictive accuracy (CV R^2=0.69). PSU $PM_{2.5}$ concentrations were estimated at the exact geocoded residential address of each participant.

Harvard TH Chan School of Public Health fine particulate matter

Daily average HSPH $PM_{2.5}$ concentrations on a 1 km spatial resolution for the contiguous United States were estimated by an ensemble model.[12] For the development of this model, $PM_{2.5}$ concentration data were obtained from the EPA Air Quality System (including the IMPROVE network and the Clean Air Status and Trends network) and other regional or local monitoring data sets. The ensemble model combined $PM_{2.5}$ predictions from gradient boosting, random forest, and neural network algorithms in a geographically weighted regression.[12] Multiple predictors were included in the models, including chemical transport model $PM_{2.5}$ predictions, meteorological variables, satellite-derived aerosol optical depth, and land use variables. The model performance was good with a spatiotemporal CV R^2 of 0.86 and a spatial CV R^2 of 0.89. HSPH $PM_{2.5}$ concentrations were linked to the residential address of each participant based on the 1 km grid cell the address was located within.

Covariates

We considered time-varying information on age, living alone, marital status, physical activity, diet (Alternate Healthy Eating Index[17]), body mass index (kg/m^2), and alcohol intake obtained from the biennial follow-up questionnaires. Pack-years of smoking and current smoking status were calculated for each time period from information on lifetime smoking history. Missing covariate information was assigned using values from the last available questionnaire. We also included time-fixed information on race, educational attainment of spouse/partner, if appropriate, and occupation of both of the nurses' parents when she was 16.

We linked neighborhood-level (census tract) socioeconomic status (SES) to each participant. We obtained census tract-level variables from the Neighborhood Change Database, which provides US census data every 10 years from 1970 to 2010 in a harmonized spatial extent. To create a time-varying neighborhood SES score, we *z*-standardized and summed the following variables: percent non-Hispanic White, percent non-Hispanic Black, percent of foreign-born residents, percent with a college degree, percent unemployed, percent of families receiving interest or dividends, median household income, median home value, and percent of occupied housing units.[18] US Census region (Northeast, South, Midwest, West) of residence was also derived based on the census tract of each address.

We also linked NO_2 data predicted at the exact residential address of each participant. Daily NO_2 concentrations over follow-up were predicted by a spatiotemporal model.[4,19] More information about the NO_2 model can be found elsewhere.[4,19] Daily NO_2 estimates were averaged to get monthly concentrations. For each participant and follow-up month, we calculated the time-varying 12-month (current + previous 11 months) moving average NO_2 concentrations.

Statistical analyses

We followed each participant, based on the availability of $PM_{2.5}$ exposure, from January 2001 until they died, were censored, or reached the end of follow-up (December 2016). We converted the dataset to an Anderson–Gill counting structure with the appropriate person-time, covariates, exposures, and censoring data. Calendar month was used as the underlying timescale. We specified single-exposure Cox proportional hazard models with different sets of potential confounders to estimate hazard ratios (HRs) and 95% confidence intervals (95% CI). The Basic model was stratified by age in months and calendar years. The Main model was additionally adjusted for individual SES indicators (race, marital status, living alone, parental occupation status, and partner's education), lifestyle indicators (smoking status, pack-years, diet, physical activity, alcohol intake, body mass index), neighborhood SES, and region. Cubic regression splines were used to assess exposure–response curves.

To determine if there were associations below current and proposed regulatory limits, we performed additional analyses in a subset restricted to participants who were always exposed to $PM_{2.5}$ below 12 μg/m^3 (US National Ambient Air Quality Standard since 2013) and below 10 μg/m^3 for all three $PM_{2.5}$ estimates (US EPA proposed standard in 2023).[20] To assess if associations were robust to adjustment for co-exposures, we additionally adjusted for 12-month moving average NO_2. To determine if a harmonized prediction would lead to different conclusions, we also used the average $PM_{2.5}$ exposure ([UW $PM_{2.5}$ + PSU $PM_{2.5}$ + HSPH $PM_{2.5}$]/3) in our models. Finally, to assess if associations varied by the variability in predictions, we tested whether associations were modified by the variability (standard deviation) of UW, PSU, and HSPH $PM_{2.5}$. For each person-month of follow-up, we calculated the standard deviation of the three 12-month moving average $PM_{2.5}$ predictions. If the three models predicted very similar $PM_{2.5}$ concentrations the variability would be low; if the models predicted very different $PM_{2.5}$ concentrations the variability would be high and this may indicate locations with more exposure error in the predictions. Analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC).

Results

Our cohort included 107,906 participants of the NHS. We observed 30,242 nonaccidental deaths in 1.4 million person-years; about 26% (7,932) were cancer deaths, 24% (7,255) were CVD deaths, and 10% (2,902) were respiratory disease deaths. Most participants were White, did not live alone, and lived in the Northeast. The mean age over the follow-up period was 73.3 years (Table 2). All three models showed that $PM_{2.5}$ concentrations decreased over time (Figure 1). In general, the median, 25th, and 75th percentile were highest for HSPH $PM_{2.5}$ and lowest for PSU $PM_{2.5}$, but differences were small. Monthly UW, PSU, and HSPH $PM_{2.5}$ concentrations were generally highest in the summer and lowest in the spring and fall (Figure S1; http://links.lww.com/EE/A317). The mean variability of UW, PSU, and HSPH $PM_{2.5}$ was 0.89 μg/m^3 and slightly attenuated over time (Figure S2; http://links.lww.com/EE/A317). Scatterplots showed strong agreements between the predictions and correlations were high (0.88–0.91, Figure 2 and

Table 2.

Age-standardized characteristics of female participants of the Nurses' Health Study over follow-up (2001–2016)[a,b]

Variable	Full (N = 107,906) Mean (SD) or %	<12 µg/m³ $PM_{2.5}$ (n = 18,882) Mean (SD) or %
UW $PM_{2.5}$ (µg/m³)	9.8 (2.8)	7.2 (1.7)
PSU $PM_{2.5}$ (µg/m³)	10.2 (2.8)	7.6 (1.7)
HSPH $PM_{2.5}$ (µg/m³)	10.7 (3.0)	7.7 (1.9)
$PM_{2.5}$ average (µg/m³)	10.2 (2.8)	7.5 (1.6)
$PM_{2.5}$ variability (µg/m³)	0.89 (0.54)	0.81 (0.48)
Age (years)[c]	73.3 (8.0)	73.5 (8.0)
White	94	95
Married, %	54	57
Living alone, %	21	22
Husbands education		
Less than high school, %	4	4
High school graduate, %	26	25
More than high school, %	36	39
Missing, %	34	32
Occupation mother		
Housewife mom, %	64	62
Outside job mom, %	36	38
Occupation father		
Professional or manager dad, %	26	28
Other job dad, %	74	72
Diet (alternative health eating index)	53.4 (10.3)	54.0 (10.4)
Alcohol		
0 g/day, %	30	28
0.1–4.9 g/day, %	16	16
5.0–14.9 g/day, %	11	13
15.0+ g/day, %	8	11
Missing, %	35	32
Weight status		
Normal/underweight, %	39	42
Overweight, %	29	29
Obese, %	19	18
Missing, %	13	10
Physical activity		
<3 MET hour/week, %	17	16
3 to <9 MET hour/week, %	16	16
9 to <18 MET hour/week, %	14	15
≥18 MET hour/week, %	18	20
Missing, %	35	34
Smoking status		
Past smoker, %	46	50
Current, %	6	6
Never smoker, %	45	41
Missing, %	4	3
Pack-years	12.0 (19.4)	13.1 (19.8)
Neighborhood SES	−0.06 (3.60)	−0.77 (3.60)
Region		
Northeast, %	49	48
Midwest, %	17	6
South, %	20	27
West, %	14	19
NO_2 (ppb)	8.6 (5.1)	6.2 (2.9)

[a]Values are standardized to the age distribution of the study population, except for age.

[b]$PM_{2.5}$ average is the average prediction of the UW, PSU, and HSPH $PM_{2.5}$ model predictions. $PM_{2.5}$ variability is the standard deviation of the 12-month moving average UW, PSU, and HSPH $PM_{2.5}$ predictions.

[c]Value is not age adjusted.

Table S1; http://links.lww.com/EE/A317). We observed that correlations between the $PM_{2.5}$ predictions attenuated during follow-up (Table S2; http://links.lww.com/EE/A317).

In general, exposure–response curves showed linear associations for all $PM_{2.5}$ models with all outcomes (Figure S3; http://links.lww.com/EE/A317). For UW, PSU, and HSPH $PM_{2.5}$, we observed positive associations with nonaccidental, cancer, CVD, and respiratory disease mortality in the Basic model (Table 3 and Figure S4; http://links.lww.com/EE/A317). Associations were generally slightly stronger for UW and PSU than for HSPH. In the Main model, UW, PSU, and HSPH $PM_{2.5}$ were not associated with nonaccidental mortality, were positively associated with cancer mortality, and were suggestively positively associated with CVD and respiratory disease mortality. Associations with cancer and CVD mortality were slightly weaker for HSPH $PM_{2.5}$ than for UW and PSU $PM_{2.5}$, but the 95% CIs overlapped. For cancer mortality, HRs (95% CI, expressed per 5 µg/m³ increase) were 1.06 (1.01, 1.12) for UW $PM_{2.5}$, 1.08 (1.03, 1.13) for PSU $PM_{2.5}$ and 1.05 (1.00, 1.10) for HSPH $PM_{2.5}$. Associations with average $PM_{2.5}$ of all three models showed similar patterns; no association with nonaccidental mortality, positive associations with cancer mortality, and suggestive positive associations with CVD and respiratory disease mortality.

For those always exposed to <12 µg/m³ $PM_{2.5}$ (n = 18,882), we found positive associations for $PM_{2.5}$ with nonaccidental mortality in all models (Table 3). We also observed stronger positive associations with cancer, CVD, and respiratory disease mortality in this population compared with the full population. Associations of UW, PSU, and HSPH $PM_{2.5}$ were similar in strength for nonaccidental mortality, while associations of UW, PSU, and HSPH $PM_{2.5}$ for cause-specific mortality outcomes differed in strength with no clear pattern. In the population always exposed to <10 µg/m³ $PM_{2.5}$, the associations with nonaccidental mortality were similar to the associations in the population always exposed to <12 µg/m³ $PM_{2.5}$ (Table S3; http://links.lww.com/EE/A317).

Effect modification by the variability of $PM_{2.5}$ showed indications that associations of UW, PSU, and HSPH $PM_{2.5}$ with respiratory disease mortality were stronger when the variability was lower (Figure S5; http://links.lww.com/EE/A317). No clear pattern of effect modification by $PM_{2.5}$ variability was observed for nonaccidental, cancer, and CVD mortality. Adjustment for NO_2 did not affect associations with nonaccidental, cancer, and CVD mortality; however, the suggestive associations with respiratory disease mortality disappeared (Table S3; http://links.lww.com/EE/A317).

Discussion

In this nationwide US-based study, we found high correlations and similar temporal trends between $PM_{2.5}$ concentrations from three different spatiotemporal models developed at UW, PSU, and HSPH. In the full population, we observed indications of positive associations of $PM_{2.5}$ with cancer, CVD, and respiratory disease mortality, as well as with nonaccidental mortality in the low-level population. All three $PM_{2.5}$ estimates showed the strongest associations with cancer mortality and weaker suggestive associations with respiratory disease mortality. There were small differences in HRs using the three models of $PM_{2.5}$, indicating that differences in $PM_{2.5}$ exposure assessment methods could lead to minor differences in strengths of associations.

Descriptive statistics showed similarities between predictions from the UW, PSU, and HSPH $PM_{2.5}$ models. All three $PM_{2.5}$ predictions showed that concentrations decreased between 2001 and 2016, likely due to successful implementation of national air quality policies. Predicted means, medians, and ranges were slightly larger for HSPH $PM_{2.5}$ than for UW and PSU $PM_{2.5}$. The slightly higher concentrations could be due to the inclusion of $PM_{2.5}$ data from different monitoring stations, the inclusion and importance of potential predictors, such as the satellite-derived aerosol optical depth in the HSPH model, or because HSPH $PM_{2.5}$ is predicted at a 1 km spatial resolution. Correlations between $PM_{2.5}$ estimates were very strong, however, they attenuated over time. A declining trend was also reported for the UW and HSPH model performances.[12,13] The declining correlations could be due to lower model performances in more recent years; however, declining correlations and model performances

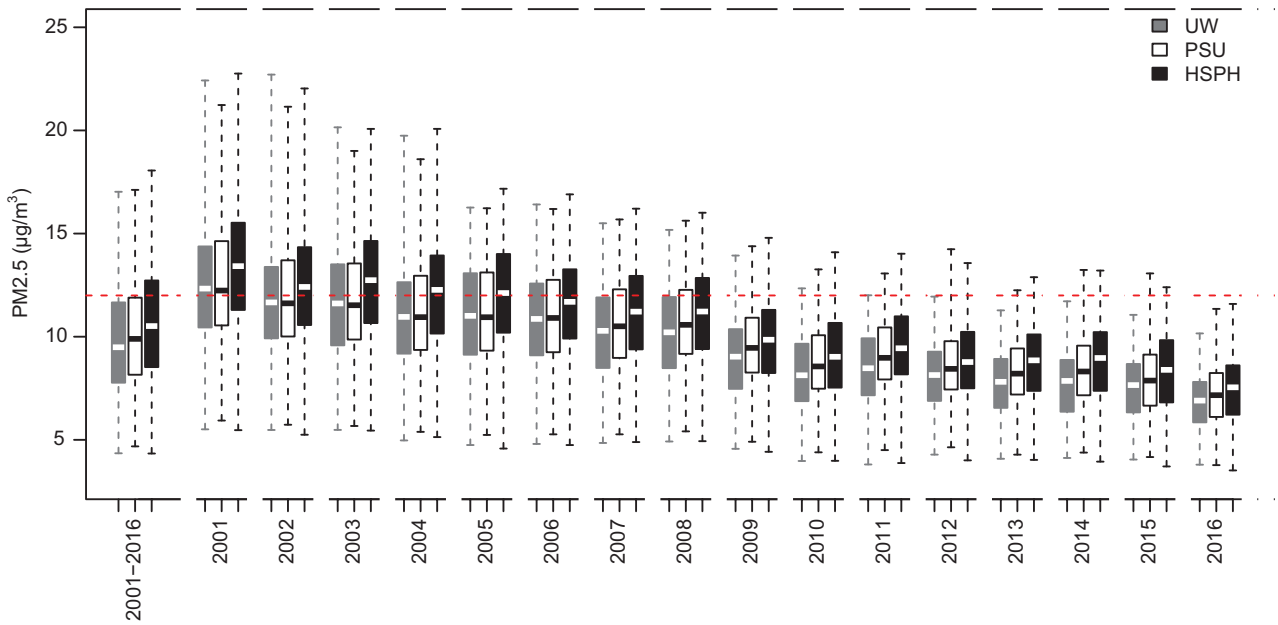

Figure 1. Boxplots of 12-month moving average UW, PSU, and HSPH $PM_{2.5}$ for the entire follow-up period (2001–2016) and by calendar year among 107,906 participants of the Nurses' Health Study. $PM_{2.5}$ predictions estimated by a model developed by researchers at the University of Washington (UW), the Pennsylvania State University (PSU), or the Harvard TH Chan School of Public Health (HSPH).

may also be due to decreasing $PM_{2.5}$ variability over time. When $PM_{2.5}$ variability is low, the impact of minor $PM_{2.5}$ differences on correlation coefficients and model performances becomes larger. Other explanations could be the inclusion of different $PM_{2.5}$ monitoring data over time and differences in emission and traffic density covariates in the models that may better reflect historical concentrations than those from more recent years, especially after the economic crisis in 2008.

We observed minor differences in HRs for cancer and CVD mortality using the different models. The minor differences in HRs observed in the fully adjusted (Main) model were also observed in the minimally adjusted (Basic) model, indicating that differences in HRs are unlikely to be caused by differences in sensitivity to adjustment for potential confounders. Performance of the UW, PSU, and HSPH $PM_{2.5}$ models was moderate to good with CV R^2 of around 0.90 for UW and HSPH $PM_{2.5}$ and 0.69 for PSU $PM_{2.5}$. We note that the CV R^2s were based on daily or annual $PM_{2.5}$ predictions, while in our models 12-month moving average $PM_{2.5}$ was used. The models did not use the exact same monitoring sites, which makes it difficult to compare CV R^2. In addition, as performances of the different $PM_{2.5}$ models differ by region,[11–13] differences between the $PM_{2.5}$–mortality associations may differ in study populations with different geographical representation than the NHS. The minor differences in HRs could be because the UW and PSU $PM_{2.5}$ models predicted concentrations at the exact residential address, while the HSPH model predicted concentrations at a 1 km spatial resolution, possibly increasing exposure measurement error. However, we acknowledge that the small-scale spatial variability of predicted $PM_{2.5}$ depends on the availability and importance of small-scale spatial resolution predictors in the models. As $PM_{2.5}$ has a longer atmospheric lifetime than some other pollutants (e.g., NO_2 or Black Carbon), it can be transported further, and predicted $PM_{2.5}$ concentrations at the exact residential address and at 1 km spatial resolution may barely differ. UW and PSU $PM_{2.5}$ were slightly more correlated

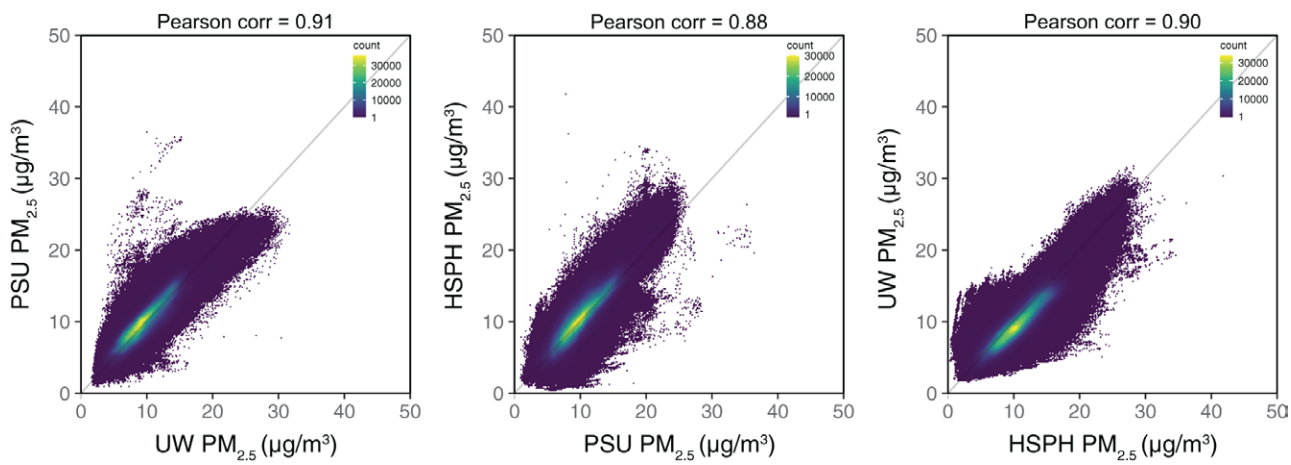

Figure 2. Scatterplots of UW, PSU, and HSPH $PM_{2.5}$ among 107,906 participants of the Nurses' Health Study (2001–2016). $PM_{2.5}$ predictions estimated by a model developed by researchers at the University of Washington (UW), the Pennsylvania State University (PSU), or the Harvard TH Chan School of Public Health (HSPH).

Table 3.

Associations between UW, PSU, and HSPH $PM_{2.5}$ and mortality expressed per 5 μg/m³ increase among participants in the Nurses' Health Study (2001–2016)[a,b]

Mortality outcome	Model	Participants	Cases (person-years)	UW PM2.5 HR (95%CI)	PSU PM2.5 HR (95%CI)	HSPH PM2.5 HR (95%CI)	PM2.5 avg. HR (95%CI)
Nonaccidental	Basic	107,906	30,242 (1,435,097.5)	1.07 (1.04, 1.10)	1.06 (1.03, 1.09)	1.05 (1.02, 1.07)	1.07 (1.04, 1.10)
	Main	107,906	30,242 (1,435,097.5)	1.00 (0.97, 1.03)	1.01 (0.98, 1.03)	1.00 (0.98, 1.03)	1.00 (0.97, 1.03)
	<12 μg/m³	18,882	5,563 (248,500.9)	1.31 (1.17, 1.47)	1.31 (1.18, 1.46)	1.25 (1.15, 1.37)	1.42 (1.26, 1.60)
Cancer	Basic	107,906	7,932 (1,435,097.5)	1.06 (1.01, 1.11)	1.08 (1.03, 1.13)	1.04 (0.99, 1.08)	1.06 (1.01, 1.12)
	Main	107,906	7,932 (1,435,097.5)	1.06 (1.01, 1.12)	1.08 (1.03, 1.13)	1.05 (1.00, 1.10)	1.07 (1.02, 1.13)
	<12 μg/m³	18,882	1,548 (248,500.9)	1.24 (1.01, 1.53)	1.36 (1.12, 1.65)	1.19 (1.00, 1.41)	1.37 (1.10, 1.71)
CVD	Basic	107,906	7,255 (1,435,097.5)	1.14 (1.08, 1.20)	1.11 (1.05, 1.17)	1.09 (1.04, 1.15)	1.13 (1.07, 1.19)
	Main	107,906	7,255 (1,435,097.5)	1.05 (1.00, 1.12)	1.05 (1.00, 1.11)	1.03 (0.98, 1.09)	1.05 (0.99, 1.11)
	<12 μg/m³	18,882	1,276 (248,500.9)	1.59 (1.26, 2.01)	1.46 (1.18, 1.82)	1.30 (1.08, 1.57)	1.63 (1.27, 2.08)
Respiratory	Basic	107,906	2,902 (1,435,097.5)	1.10 (1.01, 1.20)	1.08 (0.99, 1.17)	1.06 (0.98, 1.14)	1.09 (1.00, 1.18)
	Main	107,906	2,902 (1,435,097.5)	1.05 (0.96, 1.14)	1.02 (0.94, 1.11)	1.03 (0.95, 1.12)	1.04 (0.95, 1.13)
	<12 μg/m³	18,882	507 (248,500.9)	1.31 (0.90, 1.90)	1.11 (0.78, 1.57)	1.45 (1.07, 1.95)	1.42 (0.96, 2.11)

[a]$PM_{2.5}$ predictions estimated by a model developed by researchers at the University of Washington (UW), the Pennsylvania State University (PSU), or the Harvard TH Chan School of Public Health (HSPH). $PM_{2.5}$ average is the average prediction of the UW, PSU, and HSPH $PM_{2.5}$ model predictions.

[b]Basic: Model included strata for age in months and calendar year; Main: Basic model additionally adjusted for race, marital status, husband's education, mother's occupation, father's occupation, diet, alcohol, weight status, physical activity, smoking status, pack-years, neighborhood SES, and region; <12 μg/m³: Main model that included participants that were always exposed to $PM_{2.5}$ concentrations below 12 μg/m³ during the follow-up period.

with NO_2 than HSPH $PM_{2.5}$, suggesting that the UW and PSU $PM_{2.5}$ models may rely more on traffic-related predictors than HSPH $PM_{2.5}$ and may represent more traffic-related particles. However, adjustments for NO_2 did not affect associations with cancer and CVD mortality. It is hard to compare the importance of different predictors due to differences in modeling structure and included covariates between the models. The minor difference in HRs could also be due to differences in predicted concentration ranges. The interquartile range for HSPH $PM_{2.5}$ is slightly larger than for UW and PSU $PM_{2.5}$ and may translate into slightly weaker HRs expressed per 5 μg/m³.

A recent meta-analyses of associations of $PM_{2.5}$ with mortality reported pooled HRs (95% CI) of 1.08 (1.06, 1.09) for nonaccidental mortality, 1.11 (1.09, 1.14) for circulatory disease mortality, and 1.10 (1.03, 1.18) for respiratory disease mortality per 10 μg/m³ increase.[1] No pooled HRs for cancer mortality were reported, but the HR for lung cancer mortality was 1.12 (1.07, 1.16).[1] These HRs are in line with some of the associations that we observed, except for nonaccidental mortality. The null associations with nonaccidental mortality in our study could be due to a combination of a relatively old study population and higher competing risks for the elderly that may translate into weaker associations. Previous studies in the NHS reported strong positive associations of $PM_{2.5}$ with all-cause mortality in follow-up periods from 1992 to 2002 (HR = 1.26 per 10 μg/m³ increase, 95% CI: 1.02, 1.54)[21] and from 2000 to 2006 (HR = 1.13 per 10 μg/m³ increase, 95% CI: 1.05, 1.22).[22] In general, associations with cause-specific mortality were stronger in the population restricted to those always exposed to low levels of $PM_{2.5}$ (<12 and <10 μg/m³), consistent with other studies that evaluated associations of low-level $PM_{2.5}$ with mortality.[23–25] However, 95% CI was wide in the low-level population, because the number of cases was small, especially for cause-specific mortality outcomes.

This study has multiple strengths and some limitations. We were able to study the heterogeneity of $PM_{2.5}$–mortality associations by linking $PM_{2.5}$ predictions from three different models to the NHS cohort and using the same potential confounders and follow-up in our models. We assessed 12-month moving average $PM_{2.5}$ concentrations from 2001 through 2016 from three different spatiotemporal models. We included 107,906 participants of the nationwide NHS and had information on individual-level SES and time-varying lifestyle factors, neighborhood SES, and residential mobility during follow-up. However, we acknowledge that the potential for residual confounding remains. HSPH $PM_{2.5}$ was only available at 1 km spatial resolution, while UW and PSU $PM_{2.5}$ were only available at the residential addresses. Hence, we could not test whether differences in HRs were due to differences in the spatial resolution of the models. We emphasize that our findings do not indicate which model predicts $PM_{2.5}$ most accurately. We compared $PM_{2.5}$ predictions and evaluated whether associations with mortality differed. Stronger associations may indicate less measurement error but could also be due to other factors as discussed above. We were not able to test whether differences in $PM_{2.5}$–mortality associations were due to differences in the (number of) included monitoring sites, included predictors, importance of predictors, modeling techniques, or a combination of these factors, as these factors differed to some extent between the models. The majority of participants were of similar occupation and lived in the Northeastern United States, which may limit the generalizability of our findings. In addition, no information about daily mobility patterns was available, which may have biased associations.

In general, we found high correlations and similar temporal trends between $PM_{2.5}$ concentrations predicted from three different models developed at UW, PSU, and HSPH. We found that differences between $PM_{2.5}$ exposure assessment methods could lead to minor differences in strengths of associations between $PM_{2.5}$ and cause-specific mortality in a population of US female nurses.

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Conflicts of interest statement

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

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