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Multilevel Modeling of PM2.5 and Risk of Cardiovascular Disease and Diabetes Mellitus in Adults Aged 65 and Older

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Abstract

We aimed to test a hypothesis that elevated ambient particulate matter (PM) 2.5 concentrations are significantly associated with risk of coronary heart disease (CHD), stroke, and diabetes mellitus (DM) in adults aged 65 and older. We analyzed data (2010-2013) from U.S. 1118 counties to examine the association between PM2.5 concentrations and risk of prevalent CHD, stroke, and DM, and mortality from cardiovascular disease (CVD), CHD, stroke, and DM in adults aged ≥ 65. Multilevel regression analysis technique was applied to test these associations. The results show that the annual mean of PM2.5 concentration was 8.7 μg/m^3 in the total study sample. Significant differences in mean PM2.5 concentrations were observed across counties and states in the U.S. Multilevel regression analysis indicates that an average annual concentration of 1 μg/m^3 increase in PM2.5 concentration was significantly associated with an increased prevalence of CHD, stroke, and DM by 4.9‰ (95% CI: 3.1‰ - 6.7‰), 0.8‰ (0.5‰ - 1.1‰), and 3.3‰ (2.9‰ - 4.4‰), respectively. State-level correlation analyses indicate that increased PM2.5 concentrations were significantly associated with increased age-adjusted mortality from CVD (r = 0.76, $p < 0.001$), CHD (r = 0.0.40, $p = 0.004$), stroke (r = 0.60, $p < 0.001$), and diabetes (r = 0.34, $p = 0.02$). In conclusion, Elevated PM2.5 concentrations were significantly associated with an increased risk of the prevalence and mortality from CVD, CHD, stroke, and DM. Continued effort to control ambient PM2.5 concentrations could play an important role in risk reduction of cardiovascular disease and diabetes in the elderly.

Keywords

PM2.5, Cardiovascular Disease, Coronary Heart Disease, Stroke, Diabetes Mellitus

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in the United States (U.S), with an estimate of 665,000 Americans dying from heart disease every year (CDC, 2019; Virani et al., 2020). It is estimated that CVD costs about $219 billion yearly in the U.S (Fryar, Chen, & Li, 2012). Coronary heart disease (CHD) and stroke are the two major forms of CVD. CHD, caused by plaque buildup in the wall of the arteries that supply blood to the heart, accounts for almost 50% of CVD. An estimate of 360,900 death occurred due to CHD in 2019 (CDC, 2019). Stroke occurs when the blood supply to part of a person's brain is interrupted or reduced, ether by a blood clot or bleeding, preventing brain tissue from getting oxygen and nutrients. In 2018, 1 in every 6 deaths from CVD was due to stroke. Stroke costs the U.S. nearly $46 billion between 2014 and 2015 (CDC, 2019; Virani et al., 2020). Diabetes mellitus (DM) is the sixth leading cause of death in the U.S. DM itself is also a risk factor for CVD. An estimate of 34.2 million Americans (10.5% of the U.S. total population) had been diagnosed with having DM (CDC, 2014). The risk of CVD and DM significantly increases with age. Although several studies observed an association of PM2.5 with the risk of CVD and DM, few studies tested the risk in the elderly (Bateson & Schwartz, 2004; Hayes et al., 2020; Liu et al., 2016; Zanobetti, Dominici, Wang, & Schwartz, 2014). In this study, we aimed to address the burden of air pollution attributable to ambient PM2.5 across the U.S. counties, regions, and states, and to examine the association between ambient PM2.5 concentrations and risk of CHD, stroke, and DM in adults aged 65 and older in the U.S.

2. Methods

2.1. Study Design and Population

We analyzed daily measures of ambient PM2.5 data for 2010-2013 from a total sample of 1118 counties in 50 states of the U.S., in which the data were available from the Environmental Protection Agency air quality report files (EPA, 2018, 2022). We applied a multilevel regression analysis approach to examine the association of average PM2.5 concentrations with the risk of prevalent CHD, stroke, and DM. We collected the county-level prevalent CHD, stroke, and DM among adults aged ≥ 65 from the U.S. 2011 Medicare Fee-For-Service (FFS) Beneficiaries data of the Center for Medicare and Medicaid Services (CMS, 2018).

In the prevalence analysis, data for the three chronic conditions were not available from the state of Louisiana. Therefore, we included 49 states of the U.S. Regional differences in ambient PM2.5 concentrations and prevalent CHD, stroke and DM were compared across four Census regions of the U.S. The four regions include: 1) Northeast (includes 9 states, Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont); 2) Midwest (n = 12, Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin); 3) South (n = 15, Alabama, Arkansas, Delaware, Florida, Georgia, Kentucky, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia); and 4) West (n = 13, Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming). In state-level mortality analysis, we collected 2010-2013 age-adjusted mortality data from the U.S. CDC Wide-ranging Online Data for Epidemiologic Research (CDC WONDER, 1999-2015 Data).

2.2. Exposures

The U.S. Environmental Protection Agency (EPA) utilizes air quality monitors at State and Local Air Monitoring Stations (SLAMS), to monitor and measure six major pollutants across the nation (EPA, 2018, 2020a, 2022). PM2.5, an important air pollutant, are fine inhalable particles with a diameter of 2.5 micrometers (μm) or smaller, approximately 30 times smaller than the diameter of human hair or one 400th of a millimeter. Of the six regulated and measured air pollutants (particulate matters, carbon monoxide, lead, nitrogen dioxide, ozone, and sulfur dioxide) by the EPA, PM2.5 is one of the most important indicators. As much of the PM2.5 pollutant is from the emissions of combustion of gasoline, oil, diesel fuel or wood. Elevated PM2.5 concentrations may cause serious short and long-term adverse effects on human health. In this study, we focused on the study of PM2.5 concentrations across multiple counties and regions, and data extracted from the EPA surveillance system in years 2010-2013 (EPA, 2018).

2.3. Health Outcomes Data

In the study, we had two groups of outcomes: 1) to examine the association between county-level PM2.5 concentrations and three major health conditions in the elderly, we collected data of the prevalent CHD, stroke, and DM from the U.S Medicare Fee-for-Service (FFS) Beneficiaries among adults aged ≥ 65 (CMS, 2018). We focused on the three conditions, because they are the leading morbidities and leading causes of death in the elderly. 2) State-level age-adjusted mortality data (death rate per 100,000 population) from CVD (ICD-10: I00 - I78), CHD (ICD-10: I20 - I25), stroke (cerebrovascular disease, ICD-10: I60 - I69), and DM (ICD-10: E10 - E14) among adults aged ≥ 65 were collected from the US CDC Wide-ranging Online Data for Epidemiologic Research (CDC WONDER, 1999-2015 Data).

2.4. Covariates

To control potential confounders in multivariate regression analysis, we adjusted demographic and socioeconomic covariates, collected from the U.S. 2010 Census. These adjusted covariates were county-levels of percentage of adults aged 65 and older, percentage of Non-Hispanic Black (NHB), and percentage of poverty (Census, 2010).

2.5. Statistical Analysis

First, we described the characteristics of exposure, covariates, and outcomes by four regions of the U.S. (Northeast, Midwest, South, and West). Differences in county-level annual means of ambient PM2.5 concentrations, % of adults aged ≥ 65, % of Non-Hispanic Black (NHB), % of people with poverty, the prevalence of CHD, stroke, and DM by regions were tested using analysis of variance (ANOVA). Second, we tested regional means of ambient PM2.5 concentrations by months using ANOVA as well. Third, we applied multilevel hierarchical linear regression modeling technique to examine the association of ambient PM2.5 concentrations with the prevalent CHD, stroke, and diabetes at county level (level 1) and state levels (level 2) (Li et al., 2010; Liu et al., 2013). In the analysis, Model 1 is the base model that included no predictor (i.e., PM2.5), only the random intercept was included to evaluate the crude variability in the study outcomes (prevalent CHD, stroke and DM) across county and state levels. In Models 2 to 4, the same random intercepts were included as those in Model 1, along with the following additional predictors entered into the regression models in a step-by-step manner: level 1 fixed effect of ambient PM2.5 on the study outcomes (Model 2), plus random slope for level 1 predictor (Model 3) and control for covariates (% of adults aged ≥ 65, % of NHB, and % of poverty, Model 4). Last, we tested the correlation between state-level PM2.5 concentration and age-adjusted mortality of CVD, CHD, stroke and DM among adults aged ≥ 65. All statistical analyses were conducted using SAS software version 9.3. The level of significance was set at $p \leq 0.05$ for a two-sided test.

3. Results

3.1. Characteristics of Participants

Table 1 shows the characteristics of the study sample of 1118 counties across the U.S. four regions (Northeast, Midwest, South, and the West). Of the total 1118 study counties, the annual average (standard error, SE) of ambient PM2.5 concentration was 8.7 (0.1) $\mu g/m^3$. The prevalence of CHD, stroke and DM were 28.9%, 3.8%, and 26.0%, respectively. There were significant differences in the means of ambient PM2.5 concentrations and the prevalence of CHD, stroke, and DM across the four regions (compared to the West, $p < 0.001$).

Table 1. Characteristics of study sample by regions (counties) in the United States.

	Total		Northeast		Midwest		South		West		*p*-value (Ref to West)		
			By regions (no. of the county in the study)										
	(1118)		(137)		(297)		(428)		(256)				
	Mean	(SE)	Mean	(SE)	Mean	(SE)	Mean	(SE)	Mean	(SE)	NE	MW	South
Particulate matter													
PM2.5, μg/m³	8.7	(0.1)	8.5	(0.2)	9.6	(0.1)	9.5	(0.1)	6.1	(0.2)	<0.001	<0.001	<0.001
Population Characteristics													
Poverty level, %	15.5	(0.2)	12.4	(0.4)	13.9	(0.2)	17.6	(0.3)	15.6	(0.3)	<0.001	<0.001	<0.001
Age, % of people ≥ 65 yrs	14.8	(0.1)	15.3	(0.2)	15.0	(0.2)	14.4	(0.2)	14.7	(0.3)	0.13	0.32	0.36
Race, % of NHB	8.6	(0.4)	6.3	(0.6)	4.5	(0.4)	16.7	(0.8)	1.6	(0.1)	<0.001	<0.001	0.021
Prevalence of disease, %													
CHD	28.9	(0.3)	31.6	(0.5)	29.5	(0.3)	31.3	(0.3)	23.1	(0.3)	<0.001	<0.001	<0.001
Stroke	3.8	(0.0)	4.2	(0.1)	3.6	(0.1)	4.2	(0.0)	3.0	(0.0)	<0.001	<0.001	<0.001
Diabetes	26.0	(0.3)	27.4	(0.4)	26.0	(0.2)	28.5	(0.2)	22.0	(0.3)	<0.001	<0.001	<0.001

SE: Standard error. *p*-values were from ANOVA. NE: Northeast. MW: Midwest. NHB: Non-Hispanic Black. PM2.5: Measured using non-Federal Reference Method (as federal equivalent methods), 2010-2013. Prevalence of coronary heart disease (CHD), stroke and diabetes were calculated from Medicare fee-for-service (FFS) Beneficiaries aged 65 and older in 2011.

3.2. Variation in PM2.5 across the US Regions

Table 2 shows that in the U.S. West it had the lowest monthly mean (SE) ambient PM2.5 concentrations compared to the other regions ($p < 0.001$), except for the differences between South and West in January (8.61 vs. 8.4 μg/m³, $p = 0.53$), and between Northeast and West in September (6.98 vs. 6.74 μg/m³, $p = 0.35$). In the South region it had higher mean ambient PM2.5 concentrations between May and September, followed by Midwest, Northeast, and West (Figure 1). Overall, the highest mean (SE) ambient PM2.5 was observed in July, 10.21 (0.10) μg/m³ in the total study counties. Higher mean (SE) ambient PM2.5 concentrations were observed in winter (November to January) as well.

3.3. Association between PM2.5 and Prevent CHD, Stroke and Diabetes

Table 3 shows the results from two-level hierarchical linear modeling of the association between ambient PM2.5 concentrations and the prevalent CHD, stroke, and diabetes. Model 1 indicates that 56% of the variations in the prevalence of CHD could be accounted by the random effect in states (56% = 20.9/[16.5 + 20.9] * 100, $p < 0.001$). Model 2 shows that there was a positive and significant association between ambient PM2.5 concentrations and prevalence of CHD (i.e., the fixed effect, β = 0.36, $p < 0.001$) with control of the random effects of the variations in counties and states. Model 3 shows that the association between ambient PM2.5 concentrations and the prevalence of CHD (i.e., the fixed

Table 2. Monthly mean (SE) PM2.5 concentrations by geographic regions in the United States, 2010-2013.

Month	Total		Northeast		Midwest		South		West		*p* values(ref to West)		
	Mean	(SE)	Mean	(SE)	Mean	(SE)	Mean	(SE)	Mean	(SE)	Northeast	Midwest	South
Jan	9.30	(0.13)	10.06	(0.26)	10.73	(0.19)	8.61	(0.10)	8.40	(0.46)	0.001	<0.001	0.53
Feb	8.58	(0.10)	8.65	(0.20)	10.72	(0.18)	8.53	(0.08)	6.14	(0.28)	<0.001	<0.001	<0.001
Mar	8.04	(0.09)	7.07	(0.17)	9.85	(0.14)	8.92	(0.08)	4.99	(0.17)	<0.001	<0.001	<0.001
Apr	7.72	(0.08)	6.83	(0.17)	8.35	(0.12)	9.34	(0.08)	4.74	(0.13)	<0.001	<0.001	<0.001
May	8.16	(0.08)	7.83	(0.20)	8.59	(0.14)	9.91	(0.07)	4.94	(0.14)	<0.001	<0.001	<0.001
Jun	9.20	(0.10)	9.19	(0.23)	9.61	(0.15)	11.31	(0.08)	5.22	(0.18)	<0.001	<0.001	<0.001
Jul	10.21	(0.10)	10.97	(0.22)	11.23	(0.17)	11.75	(0.09)	6.05	(0.17)	<0.001	<0.001	<0.001
Aug	9.84	(0.09)	9.79	(0.24)	10.57	(0.18)	11.31	(0.10)	6.59	(0.17)	<0.001	<0.001	<0.001
Sep	8.10	(0.08)	6.98	(0.15)	8.06	(0.13)	9.31	(0.09)	6.74	(0.22)	0.35	<0.001	<0.001
Oct	7.63	(0.07)	6.91	(0.18)	8.09	(0.12)	8.48	(0.07)	6.08	(0.19)	0.000	<0.001	<0.001
Nov	8.20	(0.09)	8.60	(0.20)	9.47	(0.15)	8.21	(0.08)	6.52	(0.28)	<0.0001	<0.001	<0.001
Dec	8.96	(0.12)	9.08	(0.24)	10.43	(0.18)	8.62	(0.09)	7.76	(0.41)	0.001	<0.001	0.005

Table 3. Estimates from two-level hierarchical linear models of the association between PM2.5 and prevalence of CHD, stroke, and diabetes.

	Model 1			Model 2			Model 3			Model 4		
	β	(SE)	*p* value	β	(SE)	*p* value	β	(SE)	*p* value	β	(SE)	*p* value
CHD, %												
Fixed Effects												
Intercept	28.21	(0.67)	<0.001	25.23	(0.84)	<0.001	24.95	(0.81)	<0.001	21.34	(1.13)	<0.001
PM2.5 μg/m^3				0.36	(0.07)	<0.001	0.38	(0.09)	<0.001	0.49	(0.09)	<0.001
Random Effects												
Level 1	16.52	(0.73)	<0.001	16.28	(0.73)	<0.001	15.95	(0.72)	<0.001	15.61	(0.71)	<0.001
Intercept(State)	20.89	(4.51)	<0.001	16.82	(3.75)	<0.001	11.85	(3.99)	0.002	10.74	(3.89)	0.003
Slope (PM2.5)							0.09	(0.05)	0.022	0.10	(0.05)	0.015
Model Fit Statistics												
AIC	6227.30			6102.70			6097.10			6088.50		
BIC	6231.20			6106.50			6102.80			6094.20		
Stroke, %												
Fixed Effects												
Intercept	3.66	(0.10)	<0.001	2.83	(0.13)	<0.001	2.70	(0.12)	<0.001	3.07	(0.16)	<0.001
PM2.5 μg/m^3				0.10	(0.01)	<0.001	0.11	(0.01)	<0.001	0.08	(0.01)	<0.001

Continued

Random Effects												
Level 1	0.42	(0.02)	<0.001	0.39	(0.02)	<0.001	0.37	(0.02)	<0.001	0.34	(0.02)	<0.001
Intercept (State)	0.49	(0.11)	<0.001	0.35	(0.08)	<0.001	0.19	(0.08)	0.011	0.18	(0.07)	0.007
Slope (PM2.5)							0.00	(0.00)	0.001	0.00	(0.00)	0.003
Model Fit Statistics												
AIC	2246.40			2126.70			2103.50			2039.00		
BIC	2250.20			2130.50			2109.20			2044.80		
Diabetes, %												
Fixed Effects												
Intercept	25.58	(0.50)	<0.001	21.68	(0.63)	<.0001	21.87	(0.64)	<0.001	20.86	(0.85)	<0.001
PM2.5 μg/m^3				0.47	(0.06)	<.0001	0.44	(0.07)	<0.001	0.33	(0.06)	<0.001
Random Effects												
Level 1	11.71	(0.52)	<0.001	11.02	(0.49)	<.0001	10.79	(0.49)	<0.001	8.46	(0.39)	<0.001
Intercept (State)	11.28	(2.47)	<0.001	7.75	(1.80)	<.0001	7.48	(2.10)	0.000	7.82	(2.03)	<0.001
Slope (PM2.5)							0.03	(0.02)	0.053	0.02	(0.02)	0.101
Model Fit Statistics												
AIC	5845.20			5673.90			5670.60			5437.30		
BIC	5849.00			5677.70			5676.30			5443.00		

Multilevel regression modeling (two levels: county and state), Model 1: Base model, fit random effects only. Model 2: Model 1 + key level 1 fixed effects, Model 3: Model 2 + random slope for key level 1 predictor. Model 4: Model 3 + other level 1 covariates, including county-level % of NHB, % of poverty, % of people aged 65 and older. AIC and BIC indicators: The lower he AIC and BIC values, the better fit a model.

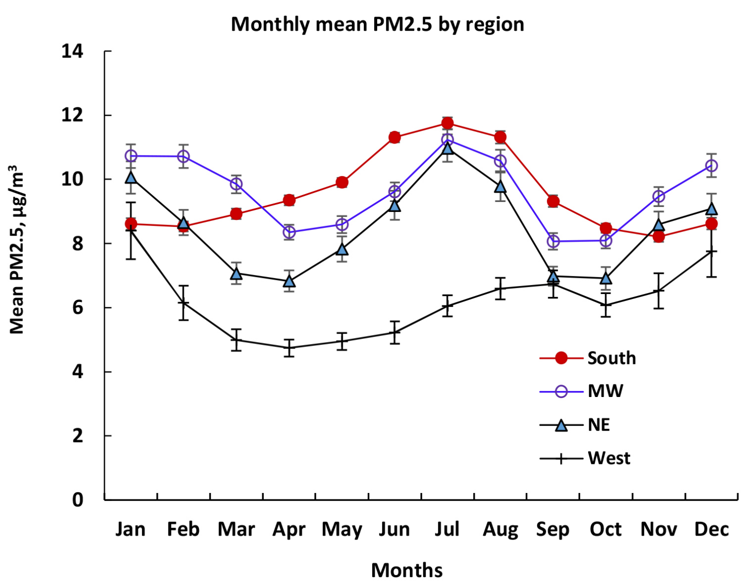

Figure 1. Monthly mean PM2.5 concentrations by regions.

effect) remained significant (β = 0.38, $p < 0.001$) after taking account of the random effects of ambient PM2.5 concentrations. Model 4, the full-adjusted model, shows that the association between ambient PM2.5 concentrations and the prevalence of CHD remained significant after further adjusting for age, race/ethnicity and poverty. These results suggest that the prevalence of CHD significantly increased by 4.9‰ (95% CI: 3.1‰ - 6.7‰) for every 1 μg/m³ increase in ambient PM2.5 concentrations. Similar to CHD, Model 4 indicate that elevated ambient PM2.5 concentrations were significantly associated with risk of prevalent stroke (β = 0.08, $p < 0.001$), and DM (β = 0.33, $p < 0.001$). These results suggest that for every 1 μg/m³ increase in PM2.5 concentrations, the prevalence of stroke and DM increased by 0.8‰ (95% CI: 0.5‰ - 1.1‰), and 3.3‰ (95% CI: 2.1‰ - 4.4‰).

3.4. Association between PM2.5 and Mortality from CVD, CHD, Stroke and Diabetes

Figure 2 depicts the overall distributions of annual average PM2.5 concentrations across the states, with a clear higher level in the east of the US South-Central, Middle-South, and Southeastern states (Figure 2(a)). Increased PM2.5 concentrations were significantly and positively correlated with age-adjusted mortality rates from CVD (r = 0.76, $R^2 = 0.58$, $p < 0.001$, Figure 2(b)) and CHD (r = 0.40, $R^2 = 0.16$, $p < 0.004$, Figure 2(b)), and stroke (r = 0.60, $R^2 = 0.36$, $p = 0.001$, Figure 2(c)), and DM (r = 0.34, $R^2 = 0.12$, $p = 0.02$, Figure 2(c)).

4. Discussion

The main findings of the study indicate that 1) the overall mean of ambient PM2.5 concentration (8.7 μg/m³) met the standard of the US EPA and the WHO criteria among the study 1118 counties. 2) Significant differences in mean ambient

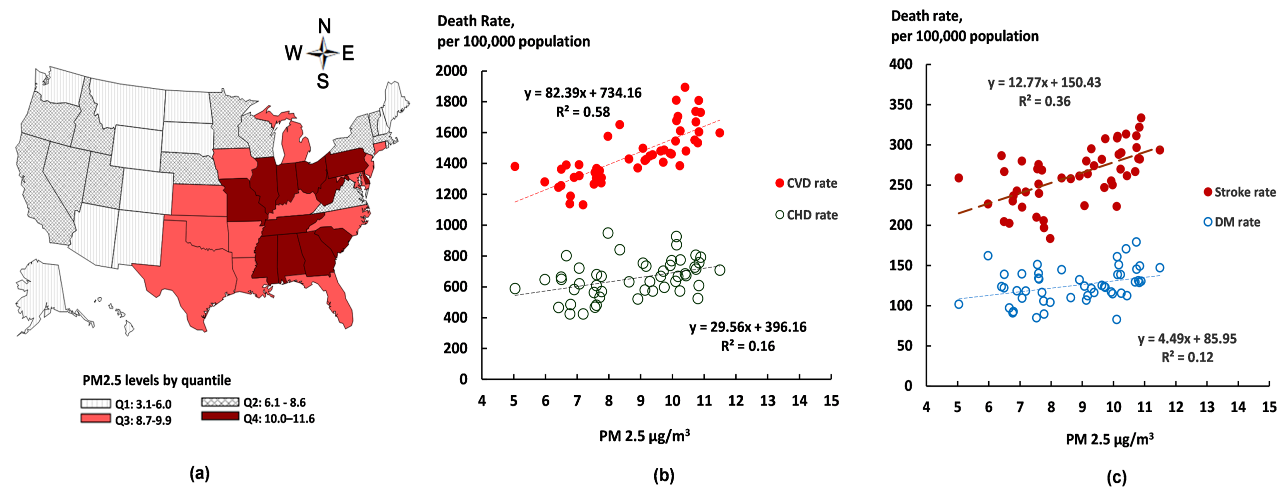

Figure 2. Annual average PM2.5 concentration across the states of the US (in (a)), and its correlation with mortality from cardiovascular disease (CVD, in (b)) and coronary heart disease (CHD, in (b)), and stroke (in (c)), and diabetes (in (c)) among adults aged 65 and older.

PM2.5 concentrations by months were observed, with higher means of ambient PM2.5 concentrations in summer and winter. 3) Elevated ambient PM2.5 concentrations were significantly associated with an increased risk of prevalent CHD, stroke, and DM in adults aged 65 or older. An estimated every 1 μg/m³ increase in PM2.5 was significantly associated with an increase in the prevalence of CHD, stroke, and DM by 4.9‰ (95% CI: 3.1‰ - 6.7‰), 0.8‰ (95% CI: 0.5‰ - 1.1‰), and 3.3‰ (95% CI: 2.1‰ - 4.4‰), respectively ($p < 0.001$). 4) Elevated ambient PM2.5 concentrations were significantly associated with an increased risk of CVD, CHD, stroke, and DM mortality in adults aged 65 or older.

4.1. PM2.5 in the U.S.

The World Health Organization (WHO) Air quality guideline for the standard of annual mean ambient PM2.5 concentration is 10 or less than micrograms per cubic meter (μg/m³) (WHO, 2018). The U.S. EPA for PM2.5 standard is set at ≤12 μg/m³ annual mean. Results of our study indicate that the average of ambient PM2.5 concentration (8.7 μg/m³) across the nation was lower than the standard averages. However, our study indicates that even meeting the standard of PM2.5 concentration, elevated PM2.5 concentrations remained significantly associated with increased prevalence of CHD, stroke, and DM in the elderly. This finding may suggests that the current set-up safety thresholds of annual ambient PM2.5 concentrations by the WHO (≤10 μg/m³) or by the U.S. EPA (≤12 μg/m³) may underestimate the risk effect of exposure to ambient PM2.5 concentrations on the study heath conditions. The study further addresses significant variations in ambient PM2.5 concentrations across counties and states. The Midwest and South had higher ambient PM2.5 concentrations than the other regions (the Northeast and West). Higher ambient PM2.5 concentrations were observed during the summer and winter. This seasonal difference may be partly attributable to higher traffic-associated pollutions during summer and winter, and air conditioner and heater use due to the seasonal higher in summer or lower temperature in winter, as well as changes in humidity by seasons. In the U.S., approximately 37.2% of occupied housing units have two vehicles available (Census, 2019). It has been estimated that air pollution from transportation significantly contributes to poor air quality, accounting for more than 10% of all pollution in the nation (EPA, 2020b). Studies have observed that air pollution from vehicles has contributed to a large portion of deaths in the U.S., specifically those tied to the prevalence and mortality of CHD (Ghosh et al., 2016; Kheirbek, Haney, Douglas, Ito, & Matte, 2016). Meanwhile, the significant variations in PM2.5 concentrations by counties and states address the possibilities of control ambient PM2.5 concentrations at county and state levels, which could subsequently contribute to risk reduction of CHD, stroke and DM at population levels in the nation.

4.2. CHD, Stroke, and DM in the U.S.

CHD and stroke have continued to be the top causes of death, as well as DM be the sixth leading cause of death in the U.S. Multiple risk factors are associated with the risk of CHD, stroke and DM. However, not much is known regarding the impact of ambient PM2.5 concentrations on the diseases among the elderly. Most previous studies examined the association between air pollution and health outcomes using traditional one-level analysis approaches, which does not take account of multilevel random effects on the study association between exposures and outcomes. This one-level analysis approach may lead to an overestimate of the exposure-outcomes associations. In our study, employing multilevel regression modeling technique is able to control random effects attributable to the variation across the counties and states. Findings from this analysis address the significant and fixed association between ambient PM2.5 concentrations and the study outcomes. The effect of elevated ambient PM2.5 concentrations may be more sensitive to the elderly. Because of an increase in aging populations, findings of our study add to new evidence to the body of research, and are informative to the other countries around the world, where both air pollution and chronic conditions of CHD, stroke and DM have significant impact on public health, such as China and India.

4.3. Limitations and Strengths

It should be noted that several limitations should be kept in mind while interpreting the results of the study.

- We applied cross-sectional and ecological analysis approaches. Therefore, it is not necessary to interpret any causal association between the study exposure and outcomes, although several experimental studies have reported a potential causal effect of elevated ambient PM2.5 concentrations on risk of CVD and DM (Haberzettl, O'Toole, Bhatnagar, & Conklin, 2016; Wagner et al., 2014).
- Potential ecological bias may occur in our analysis. We assumed that ambient PM2.5 concentrations were equally distributed within a county in county-level analysis, and within a state in state-level analysis. However, this assumption may lead to underestimate the effect of PM2.5 for communities that had much higher ambient PM2.5 levels than the average in a county.
- Findings of the study have limitations to its generalizability for young populations because the study outcomes were classified for those aged 65 and older.
- This study did not test gender difference due to lack of the detail data.

Meanwhile, the study has several strengths:

- The study sample size included more than 1000 counties, which is about one-third of the total 3006 counties in the U.S.
- The measures of ambient PM2.5 concentrations were standardized by the U.S. EPA and applied to all counties. This approach ensured comparability from multiple counties and across states.
- The application of multilevel regression analysis, a novel analysis approach,

controls confounding effects due to random impact by counties and states.

5. Conclusion

Findings of the study indicate that there are significant variations in PM2.5 concentrations across counties and states in the nation. Although the annual average PM2.5 levels met the safety standard of annual PM2.5 emission in the U.S., elevated PM2.5 concentrations remain significantly associated with increased risk of prevalent CHD, stroke, and DM, and mortality from CVD, CHD, stroke and DM. Continued effort to control ambient PM2.5 concentration may play a pivotal role in risk reduction of CVD, CHD, stroke and DM at population levels.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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