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# The effect of atmospheric particulate matter on survival of breast cancer among US females

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**Abstract** Short-term effects of ambient particulate matter (PM) on cardiopulmonary morbidity and mortality have been consistently documented. However, no study has investigated its long-term effects on breast cancer survival. We selected all female breast cancer cases ($n = 255{,}128$) available in the California Surveillance Epidemiology and End Results cancer data. These cases were linked to 1999–2009 California county-level PM daily monitoring data. We examined the effect of PM on breast cancer survival. Results from Kaplan–Meier survival analysis show that female breast cancer cases living in areas with higher levels of $PM_{10}$ and $PM_{2.5}$ had a significant shorter survival than those living in areas with lower exposures ($p < 0.0001$). The results from marginal cox proportional hazards models suggest that exposure to higher $PM_{10}$ (HR 1.13, 95 % CI 1.02–1.25, per 10 μg/m$^3$) or $PM_{2.5}$ (HR 1.86, 95 % CI 1.12–3.10, per 5 μg/m$^3$) was significantly associated with early mortality among female breast cancer cases after adjusting for individual-level covariates such as demographic factors, cancer stage and year diagnosed, and county-level covariates such as socioeconomic status and accessibility to medical resources. Interactions between cancer stage and PM were also observed; the effect of PM on survival was more pronounced among individuals diagnosed with early stage cancers. This study suggests that exposure to high levels of PM may have deleterious effects on the length of survival from breast cancer, particularly among women diagnosed with early stage cancers. The findings from this study warrant further investigation.

**Keywords** Air pollution · Breast cancer · Cancer survival · Particulate matter

**Abbreviations**

| | |
|---|---|
| CI | Confidence interval |
| EPA | U.S. environmental protection agency |
| HR | Hazard ratio |
| ICD-O-3 | International classification of disease for oncology, third edition |
| PM | Particulate matter |
| $PM_{10}$ | Particles less than 10 μm in diameter |
| $PM_{2.5}$ | Particles less than 2.5 μm in diameter |
| SEER | Surveillance Epidemiology and End Results |

## Introduction

Breast cancer is the most commonly diagnosed cancer, as well as the second leading cause of cancer death, among females in the United States. An estimated 226,870 new cases of invasive breast cancer are expected to occur among females in the US during 2012, and the age-adjusted death rate from female breast cancer was 23.5 per 100,000 based on data from 2004 to 2008 [1]. Breast cancer has large variations in survival [2]. Some research suggests that survival after diagnosis with breast cancer is associated with modifiable factors including environmental exposures [3].

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Ambient outdoor air pollution has been associated with increased morbidity and mortality from a variety of cancers [4–7]. Some epidemiological studies have reported associations between air pollution and breast cancer incidence [8, 9]. However, to our knowledge, no studies have been conducted to examine the long-term effects of air pollution on survival of breast cancer. With the advancement of urbanization and industrialization, releases of toxic pollutants into the air continue to increase [10]. Because of the high prevalence of both air pollution and breast cancer, and the observed linkage of air pollution with breast cancer incidence, it is necessary to understand whether exposure to air pollution also has adverse effects on female breast cancer survival.

Since air pollution is a complex mixture of different gaseous and particulate components, it is difficult to define, given that the biological mechanisms of air pollution's effects on human health are largely unknown [11]. Particulate matter (PM) includes a variety of pollutants made up of extremely small particles and liquid droplets containing acids, organic chemicals, metals, and soil or dust particles, which can remain suspended in the atmosphere [12]. Inhalable particles, which have an aerodynamic diameter less than 10 μm ($PM_{10}$), can reach the upper airways, while fine particles (less than 2.5 μm, $PM_{2.5}$) can even reach more deeply and be retained in the pulmonary alveoli [13]. PM's effect on human morbidity and mortality has been suggested by many studies, and it is continued to be the most reliable component of air pollution that is associated with human health [14].

In this study, we examined adverse effects of PM on female breast cancer survival using the 1999–2009 Surveillance Epidemiology and End Results (SEER) cancer data in the U.S. to be linked with PM data which were obtained from the U.S. Environmental Protection Agency (EPA). In addition, this study further investigated whether there were interactions between PM and different stages of cancer at diagnosis on female breast cancer survival.

## Materials and methods

### Study population

The SEER cancer registry is the premier source for cancer statistics in the United States, which collects information on incidence, prevalence and survival from specific geographic areas representing 28 % of the US population. We selected all incident breast cancer cases in 1999–2009 from all counties in California, United States available from SEER cancer data ($n = 287{,}623$). All male cases were excluded ($n = 1{,}801$). Cases from three counties (Alpine, Sierra, and Yuba) were further excluded because of lacking of PM data in those counties during the study period ($n = 716$). A total of 285,106 cases were then linked to ambient PM monitoring data in this study. Female breast cancers were identified based on primary site using International Classification of Disease for Oncology, Third Edition (ICD-O-3). Cancers included were nipple (including areola, C500), central portion of breast (C501), upper-inner quadrant of breast (C502), lower-inner quadrant of breast (C503), upper-outer quadrant of breast (C504), lower-outer quadrant of breast (C505), axillary tail of breast (C506), overlapping lesion of breast (C508), and breast, NOS (C509).

### Outcome assessment

Death from breast cancer among females was the main outcome of interest. All deaths caused by other diseases and survival cancer patients at the end of the study period were considered as censored cases. Survival time (unit: months) was calculated as the interval from the time of diagnosis to the time of death or to the end of the study.

### Exposure assessment

We obtained daily monitoring data of $PM_{10}$ and $PM_{2.5}$ from the U.S. EPA's monitors located in different areas in each county. Since the monitoring data of $PM_{2.5}$ were only available from 1999, we selected the incident breast cancer cases of 1999–2009 from SEER. If there were more than one monitor in a county, the mean concentrations of these different monitors were used as daily concentrations of $PM_{10}$ and $PM_{2.5}$ in that county. A monthly mean concentration was then calculated based on daily mean concentration for each county. Finally, we linked the monthly mean concentration of $PM_{10}$ and $PM_{2.5}$ to the cases to be obtained from SEER by county identifiers, and the mean concentrations of $PM_{10}$ and $PM_{2.5}$ during survival time were calculated for each case. For the accuracy of the estimation of exposure to PM, we further excluded cases with any missing PM data during any month of the survival period ($n = 17{,}446$). Both $PM_{10}$ and $PM_{2.5}$ were then categorized into three groups (low, medium and high exposures) using tertiles.

### Covariates

SEER contains individual-level information for each cancer case, including demographics (age at diagnosis, race/ethnicity, and marital status at diagnosis) and cancer characteristics (date of diagnosis, site, and stages of cancer). These factors available from SEER were included as potential confounders in the statistical models. In addition, the year diagnosed was also considered as a potential

confounder due to the improvement of treatments and care over time.

Data of county-level covariates were obtained from the 2000 Census and the 2006 Behavioral Risk Factor Surveillance System (BRFSS). We extracted county-level median household income, cumulative educational attainment for female population 25 years and over, population size of female 25 years and over, population inside urbanized areas, and total population of all the counties in California. Percentages of those who had at least neither a high school diploma nor GED among the female population 25 years and over, and percentages of those who live inside urbanized areas were calculated for each county. In addition, the count of hospital beds at general hospitals per 100,000 population in 2004 was obtained from the 2006 BRFSS supplement county-level data. The median household income and calculated percentages were then linked to the cancer cases and categorized into three groups (low, medium, and high) by tertiles as indicators of county-level income, education level, and accessibility to medical resources, respectively. The count of hospital beds was categorized into two groups (low, high) by the median as an indicator of the overall medical resources level in each county, which was taken into account with percentages of population inside urbanized areas.

Additional 12,532 cases were excluded from the analysis because of missing data of covariates such as age, race, marital status, and cancer stages. A total of 255,128 female breast cancer cases were finally analyzed in this study.

### Statistical analysis

Descriptive statistics (e.g., $\chi^2$ tests) were performed for comparing the distributions of categorical variables among different exposure levels of both $PM_{10}$ and $PM_{2.5}$. Survival curves were created using Kaplan–Meier life table analyses, and log-rank tests were applied to test the significance of the difference of survival among three groups for both $PM_{10}$ and $PM_{2.5}$. Marginal Cox proportional hazard models to be implemented in PROC PHREG in SAS (SAS Institute Inc., Cary, NC) were used to estimate the hazard of mortality due to different exposure levels of $PM_{10}$ and $PM_{2.5}$ among breast cancer cases [15]. Marginal approach was used for the county-level analysis that included multiple subjects and was carried out using maximum partial likelihood estimates of regression parameters and a robust sandwich covariance matrix estimate to account for the dependence among subjects within counties [15, 16]. $PM_{10}$ and $PM_{2.5}$ were modeled as both categorical variables and continuous variables. We also considered the interactions between cancer stage and PM. All statistical analyses were conducted using SAS 9.3 software (SAS Institute Inc., Cary, NC).

## Results

Table 1 presents the characteristics of all female breast cancer cases by PM concentration level. Exposure levels of $PM_{10}$ and $PM_{2.5}$ significantly differed by age at diagnosis, race/ethnicity, marital status at diagnosis, cancer stage at diagnosis, and year diagnosed as well as the education, income level, medical resources, and urbanization on county-level.

Figure 1 shows the results of Kaplan–Meier survival curves of all female breast cancer cases by $PM_{10}$ and $PM_{2.5}$ levels. These figures suggest that female breast cancer cases that lived in counties with higher exposures to $PM_{10}$ and $PM_{2.5}$ experienced significantly shorter survival than those living in counties with lower exposures ($p < 0.0001$).

Tables 2 and 3 show the unadjusted and adjusted hazard ratios (HR) and 95 % confidence intervals (CI) for death due to breast cancer among females. Cases who lived in counties with high $PM_{10}$ or high $PM_{2.5}$ level during survival period had a statistically significant increase of 33 and 40 %, respectively, in mortality compared to those living in counties with low $PM_{10}$ or low $PM_{2.5}$ level (for $PM_{10}$, HR = 1.33, 95 % CI: 1.01–1.76; for $PM_{2.5}$, HR = 1.40, 95 % CI: 1.14–1.73). After adjusting for both individual-level covariates such as age, race/ethnicity, marital status, cancer stage and year diagnosed, and county-level covariates such as education level, income level, and accessibility to medical resources, the rates of mortality among subjects living in counties with high $PM_{10}$ levels and high $PM_{2.5}$ levels remained statistically significantly higher (HR = 1.44 and HR = 1.76, respectively). In the models which $PM_{10}$ and $PM_{2.5}$ were analyzed as continuous variables, cases had HRs of 1.14 and 1.13 with per 10 $\mu g/m^3$ increase in $PM_{10}$ concentration and 1.61 and 1.86 with per 5 $\mu g/m^3$ increase in $PM_{2.5}$ concentration for unadjusted and adjusted models, respectively.

Table 4 presents the results of the models in which cancer stage at diagnosis was considered as an effect modifier. The HRs of cases living in areas with high PM exposure levels decrease when the cancer stage at diagnosis is advanced. Similar results were observed in the continuous models.

## Discussion

In this study, we found that female breast cancer patients who live in high PM level areas had significantly shorter survival time compared to those living in a low PM level area. Our study also suggests that female breast cancer patients with earlier cancer stages are likely to be more sensitive to the adverse effects on survival time caused by air pollution. Our findings raised great concerns that air

**Table 1** Characteristics of breast cancer cases among females in California, U.S. from 1999 to 2009 by pollution levels ($n = 255,128$)

| Characteristics | $PM_{10}$ | | | | $PM_{2.5}$ | | | |
|---|---|---|---|---|---|---|---|---|
| | <23.09 μg/m$^3$ ($n$ = 84,741) | 23.09–28.82 μg/m$^3$ ($n$ = 85,293) | ≥28.82 μg/m$^3$ ($n$ = 85,094) | $P$ value* | <11.64 μg/m$^3$ ($n$ = 85,043) | 11.64–15.04 μg/m$^3$ ($n$ = 85,0047) | ≥15.04 μg/m$^3$ ($n$ = 85,081) | $P$ value* |
| Individual-level covariates | | | | | | | | |
| Age at diagnoses | | | | | | | | |
| ≤54 | 29,495 (32.22) | 32,068 (35.05) | 29,968 (32.74) | <0.0001 | 29,998 (32.77) | 31,077 (33.95) | 30,456 (33.27) | <0.0001 |
| 55–69 | 30,441 (33.67) | 29,848 (33.01) | 30,130 (33.32) | | 30,727 (33.98) | 30,213 (33.41) | 29,479 (32.60) | |
| 70–84 | 20,882 (33.62) | 20,126 (32.40) | 21,112 (33.99) | | 20,504 (33.01) | 20,213 (32.54) | 21,403 (34.45) | |
| 85+ | 3,923 (35.48) | 3,251 (29.40) | 3,884 (35.12) | | 3,814 (34.49) | 3,501 (31.66) | 3,743 (33.85) | |
| Race | | | | | | | | |
| White | 68,626 (32.72) | 69,228 (33.00) | 71,905 (34.28) | <0.0001 | 70,158 (33.45) | 70,122 (33.43) | 69,479 (33.12) | <0.0001 |
| Black | 5,129 (30.85) | 6,248 (37.58) | 5,251 (31.58) | | 4,448 (26.75) | 5,212 (31.34) | 6,968 (41.91) | |
| Others | 10,986 (38.22) | 9,817 (34.16) | 7,938 (27.62) | | 10,437 (36.31) | 9,670 (33.65) | 8,634 (30.04) | |
| Marital status at diagnoses | | | | | | | | |
| Single | 12,469 (33.89) | 12,570 (34.16) | 11,757 (31.95) | <0.0001 | 12,219 (33.21) | 12,011 (32.64) | 12,566 (34.15) | <0.0001 |
| Married | 48,191 (32.97) | 49,183 (33.65) | 48,780 (33.38) | | 49,483 (33.86) | 48,830 (33.41) | 47,841 (32.73) | |
| Separated | 920 (29.66) | 1,132 (36.49) | 1,050 (33.85) | | 934 (30.11) | 1,057 (34.07) | 1,111 (35.82) | |
| Divorced | 9,396 (33.56) | 8,984 (32.09) | 9,620 (34.36) | | 9,131 (32.61) | 9,707 (34.67) | 9,162 (32.72) | |
| Windowed | 13,765 (33.51) | 13,424 (32.68) | 13,887 (33.81) | | 13,276 (32.32) | 13,399 (32.62) | 14,401 (35.06) | |
| Cancer stage at diagnoses | | | | | | | | |
| In situ | 16,016 (34.47) | 15,390 (33.13) | 15052 (32.40) | <0.0001 | 16,311 (35.11) | 15,783 (33.97) | 14,364 (30.92) | <0.0001 |
| Localized | 44,270 (33.83) | 43,575 (33.30) | 43,001 (32.86) | | 44,387 (33.92) | 43,382 (33.16) | 43,077 (32.92) | |
| Regional | 20,519 (31.40) | 22,453 (34.36) | 22,380 (34.25) | | 20,563 (31.46) | 21,912 (33.53) | 22,877 (35.01) | |
| Distant | 3,936 (31.56) | 3,875 (31.07) | 4,661 (37.37) | | 3,782 (30.32) | 3,927 (31.49) | 4,763 (38.19) | |
| Year diagnosed | | | | | | | | |
| 1999–2003 | 39,642 (31.01) | 57,114 (44.68) | 31,085 (24.32) | <0.0001 | 37,116 (29.03) | 32,304 (25.27) | 58,421 (45.70) | <0.0001 |
| 2004–2009 | 45,099 (35.43) | 28,179 (22.14) | 54,009 (42.43) | | 47,927 (37.65) | 52,700 (41.40) | 26,660 (20.94) | |
| County-level covariates | | | | | | | | |
| Education | | | | | | | | |
| Low | 37,246 (57.37) | 20,327 (31.31) | 7,352 (11.32) | <0.0001 | 36,825 (56.72) | 20,393 (31.41) | 7,707 (11.87) | <0.0001 |
| Medium | 18,490 (16.31) | 47,210 (41.65) | 47,641 (42.03) | | 23,881 (21.07) | 37,821 (33.37) | 51,639 (45.56) | |
| High | 29,005 (37.74) | 17,756 (23.10) | 30,101 (39.16) | | 24,337 (31.66) | 26,790 (34.85) | 25,735 (33.48) | |
| Income | | | | | | | | |
| Low | 8,661 (21.91) | 12,595 (31.86) | 18,279 (46.23) | <0.0001 | 8,852 (22.39) | 16,393 (41.46) | 14,290 (36.15) | <0.0001 |
| Medium | 20,111 (15.88) | 46,319 (36.57) | 60,229 (47.55) | | 17,008 (13.43) | 46,781 (36.93) | 62,870 (49.64) | |
| High | 55,969 (62.93) | 26,379 (29.66) | 6,586 (7.41) | | 59,183 (66.55) | 21,830 (24.55) | 7,921 (8.91) | |

**Table 1** continued

| Characteristics | $PM_{10}$ | | | | $PM_{2.5}$ | | | |
|---|---|---|---|---|---|---|---|---|
| | <23.09 μg/m$^3$ ($n$ = 84,741) | 23.09–28.82 μg/m$^3$ ($n$ = 85,293) | ≥28.82 μg/m$^3$ ($n$ = 85,094) | $P$ value* | <11.64 μg/m$^3$ ($n$ = 85,043) | 11.64–15.04 μg/m$^3$ ($n$ = 85,0047) | ≥15.04 μg/m$^3$ ($n$ = 85,081) | $P$ value* |
| Medical resources | | | | | | | | |
| Low | 38,662 (30.94) | 34,256 (27.41) | 52,056 (41.65) | <0.0001 | 50,077 (40.07) | 49,060 (39.26) | 25,837 (20.67) | <0.0001 |
| High | 46,079 (35.40) | 51,037 (39.21) | 33,038 (25.38) | | 34,996 (26.87) | 35,944 (27.62) | 59,244 (45.52) | |
| Urbanization | | | | | | | | |
| Low | 33,528 (40.23) | 18,887 (22.66) | 30,936 (37.12) | <0.0001 | 38,425 (46.10) | 19,377 (23.25) | 25,549 (30.65) | <0.0001 |
| Medium | 31,361 (53.10) | 4,795 (8.12) | 22902 (38.78) | | 29,303 (49.62) | 28,509 (48.27) | 1,246 (2.11) | |
| High | 19,852 (17.61) | 61,611 (54.66) | 31,256 (27.73) | | 17,315 (15.36) | 37,118 (32.93) | 58,286 (51.71) | |

*$P$ value from $\chi^2$ test

pollution exposure may have a great impact on the length of survival of female breast cancer patients. More importantly, this study also calls attention to preventive efforts to protect female breast cancer patients from air pollution, especially those with less advanced cancer stages. Clinicians may assume those with advanced cancer are more vulnerable to environmental exposures, yet our data suggest that we need to be concerned about preventing exposure among early stage cancer patients in particular.

The adverse effect of ambient PM exposures on the survival of female breast cancer patients is biologically plausible. Both short-term and long-term exposures to PM have been linked with cancer-specific mortality [17–21]. A recent ecological study suggests that high levels of $PM_{2.5}$ may be associated with an increased risk of death from breast cancer among 61 municipalities [22]. Results from these studies are all consistent with our findings.

The biological mechanisms by which exposures to high levels of PM can impact the length of survival of female breast cancer patients are not clear. But, several previous studies may suggest some potential pathways underlying it. Air pollution is a prevalent environmental oxidative stressor, which can trigger redox-sensitive pathways that lead to different biological processes such as inflammation and cell death [23]. Through the potential biological mechanisms of oxidative stress and inflammation, air pollution can compromise the function of cardiovascular system and/or respiratory system and increase the risk of morbidity and mortality, which has been consistently reported and may also play a role in this observed association [24]. In addition, another plausible mechanism is through DNA methylation induced by high air pollution in breast cancer patients. A study found that exposure to higher air pollution was associated with changes in p16, a gene involved in tumor suppression among breast cancer patients, which may aggregate the progression of breast cancer [25]. Moreover, DNA damage such as polycyclic aromatic hydrocarbons (PAH)–DNA adducts may be another critical underlying mechanism to explain the shorter survival time we observed. PM in urban air is comprised of a complex mixture of organic and inorganic chemicals. PAH, is an important group of chemicals with adverse health effects associated with air PM. Several animal and epidemiologic studies reported an association between PAH and DNA adducts and breast cancer [26–31]. The accumulation of PAH–DNA adducts might increase mutations and genomic instability, further contributing to the cancerous phenotype of the cells, thus playing an important role in the further progression of the malignant cells. Moreover, a recent study found the links between airborne particle-induced oxidative stress and the subsequent induction of DNA damage as well as repair in human breast cancer cells, leading to more rapid progressions of breast cancer,

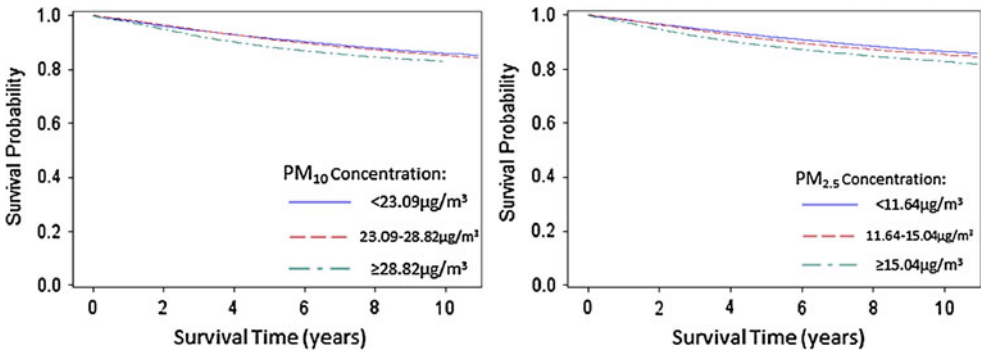


**Fig. 1** Survival plot for female breast cancer cases in California, U.S. from 1999 to 2009 by $PM_{10}$ and $PM_{2.5}$ levels

which further confirms the potential pathways as we suggested above [32].

In addition, a recent study suggests that patients in early stages (i.e., ductal carcinoma in situ, DCIS) were most common to take radiation therapy and hormone therapy were more frequently adopted by those in advanced stages [33]. It has also been found that patients received radiation therapy had a twofold to sixfold higher adduct associations with breast cancer mortality, while those received hormone therapy had relatively lower associations and treatment is a stronger effect modifier between environmental exposures and breast cancer mortality [34]. This finding may help us explain the mechanism underlying the observed elevated risks among patients in early cancer stages in the present study.

Our study offered several strengths. First, using the SEER cancer data linked with county-level PM data, we have a unique opportunity to study the relationships between exposure to PM and survival of female breast cancer in a large multiethnic sample. What is the most novelty about our study is that we were able to link daily PM exposure data for each case's county of residence, providing individual measurements of $PM_{10}$ and $PM_{2.5}$ levels post-diagnosis. Therefore, using these existing data, it provided an extremely cost-effective way of studying this topic. Furthermore, the SEER data included patient's demographic information and information on cancer characteristics and treatment, whose potential confounding effects we were able to control for when the associations between PM exposures and breast cancer survival were investigated.

Several limitations of this study also needed to be noted. First, although we were able to choose cases from one state, which may have minimized the effects of some potential confounders, we were unable to control for differences in types of healthcare, culture, dietary habits, individual-level socio economic status, smoking, and alcohol consumption. However, confounding effects of substance abuse may be limited, as current tobacco use and alcohol consumption among cancer patients after diagnosis is not common [35, 36]. In addition, in order to minimize the potential impacts of social economic status and types of healthcare access, we used the data from the 2000 Census and the 2006 Behavioral Risk Factor Surveillance System (BRFSS) to get information on median family income, educational level and medical resources at county-level in our analysis. After controlling for these county-level predictors, the results remain consistent. Second, we used the county-level monitored air pollution data to estimate individual air pollution exposure, which may cause misclassification of exposure. The closest air monitor to individual address may provide a better estimation of individual exposure than the county average of air pollution data. However, the SEER data which we obtained only include county-level identifiers instead of residential address. We cannot link the cases with the nearest monitors by their residential addresses. Furthermore, since breast cancer patients may spend significant time indoors and individual exposure to PM for all cases may be different from ambient air monitored levels, the misclassification of exposure may still exist. However, this misclassification of exposure is more likely to be a non-differential bias, which would cause our estimation biased toward null. Third, we excluded the cases in three counties because of no availability of PM monitored data, which may introduce another source of bias. However, these counties only had a total of 716 cases (i.e., 0.25 % of all cases). Given such a small proportion of cases in these counties, it would not dramatically affect the result even if extreme scenario occurs. In addition, we compared our selected cases with all cases regarding demographical distribution. It shows that two groups of cases were no significant differences regarding demographical distribution. Finally, the status of migrant worker in some counties where have agriculture based pollution may also cause another potential sources of bias because these worker are unlikely to have health care coverage. While we were controlling for race/ethnicity in our analysis, this may not be subtle enough given the large population of Hispanic residents who are not engaged in agribusiness. As individual status of migrant worker is not available in the data, we are unable to control for the impacts of this variable in our analysis. However, we conducted sensitive analysis among only white cases and

**Table 2** Adjusted and unadjusted hazard ratios (HR) and 95 % confidence intervals (CI) for breast cancer death from 1999 to 2009 among females in California, U.S. ($n$ = 255,128)

| Characteristics | Categorical model | | Continuous model (per 10 μg/m$^3$) | |
|---|---|---|---|---|
| | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) |
| $PM_{10}$ | | | | |
| <23.09 (μg/m$^3$) | 1.00 | 1.00 | 1.14 (1.05–1.22)* | 1.13 (1.02–1.25)* |
| 23.09–28.82 (μg/m$^3$) | 1.03 (0.76–1.39) | 0.96 (0.64–1.44) | | |
| ≥28.82 (μg/m$^3$) | 1.33 (1.01–1.76)* | 1.44 (1.18–1.76)* | | |
| Individual-level covariates | | | | |
| Age at diagnoses | | | | |
| ≤54 | 1.00 | 1.00 | 1.00 | 1.00 |
| 55–69 | 0.90 (0.86–0.94)* | 1.01 (0.95–1.08) | 0.90 (0.86–0.94)* | 1.01 (0.96–1.07) |
| 70–84 | 1.22 (1.13–1.30)* | 1.45 (1.33–1.57)* | 1.22 (1.13–1.30)* | 1.45 (1.34–1.57)* |
| 85+ | 3.00 (2.68–3.37)* | 2.96 (2.64–3.31)* | 3.00 (2.68–3.37)* | 2.98 (2.70–3.29)* |
| Race | | | | |
| White | 1.00 | 1.00 | 1.00 | 1.00 |
| Black | 1.90 (1.80–2.01)* | 1.61 (1.52–1.69)* | 1.90 (1.80–2.01)* | 1.61 (1.52–1.70)* |
| Others | 0.78 (0.74–0.83)* | 0.92 (0.88–0.97)* | 0.78 (0.74–0.83)* | 0.92 (0.87–0.97)* |
| Marital status | | | | |
| Single | 1.00 | 1.00 | 1.00 | 1.00 |
| Married | 0.62 (0.59–0.65)* | 0.77 (0.73–0.82)* | 0.62 (0.59–0.65)* | 0.77 (0.73–0.81)* |
| Separated | 0.98 (0.87–1.11) | 1.02 (0.94–1.11) | 0.98 (0.87–1.11) | 1.01 (0.93–1.11) |
| Divorced | 0.84 (0.78–0.90)* | 0.91 (0.87–0.96)* | 0.84 (0.78–0.90)* | 0.91 (0.87–0.96)* |
| Widowed | 1.13 (1.03–1.24)* | 1.00 (0.95–1.04) | 1.13 (1.03–1.24)* | 0.99 (0.95–1.04) |
| Cancer stage | | | | |
| In situ | 1.00 | 1.00 | 1.00 | 1.00 |
| Localized | 4.91 (4.29–5.63)* | 4.60 (4.00–5.31)* | 4.91 (4.29–5.63)* | 4.61 (3.99–5.32)* |
| Regional | 17.69 (15.47–20.23)* | 17.36 (15.22–19.80)* | 17.69 (15.47–20.23)* | 17.41 (15.23–19.90)* |
| Distant | 143.36 (125.66–163.56)* | 133.10 (117.04–151.35)* | 143.36 (125.66–163.56)* | 134.24 (117.69–153.13)* |
| Year diagnosed | | | | |
| 1999–2003 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2004–2009 | 0.91 (0.86–0.95)* | 0.85 (0.75–0.98)* | 0.91 (0.86–0.95)* | 0.91 (0.88–0.94)* |
| County-level covariates | | | | |
| Education | | | | |
| Low | 1.00 | 1.00 | 1.00 | 1.00 |
| Medium | 1.11 (0.90–1.38) | 1.15 (0.89–1.51) | 1.11 (0.90–1.38) | 1.04 (0.92–1.18) |
| High | 1.18 (0.95–1.47) | 1.05 (0.84–1.32) | 1.18 (0.95–1.47) | 0.98 (0.79–1.22) |
| Income | | | | |
| Low | 1.00 | 1.00 | 1.00 | 1.00 |
| Medium | 0.89 (0.79–1.00) | 0.76 (0.58–0.99)* | 0.89 (0.79–1.00) | 0.80 (0.69–0.93)* |
| High | 0.77 (0.65–0.91)* | 0.87 (0.69–1.11) | 0.77 (0.65–0.91)* | 0.86 (0.75–0.97)* |
| Accessibility to medical resources (medical recourses/urbanization) | | | | |
| Low/low | 1.00 | 1.00 | 1.00 | 1.00 |
| Low/medium | 0.87 (0.77–0.98)* | 0.79 (0.61–1.03) | 0.87 (0.77–0.98)* | 0.94 (0.81–1.10) |
| Low/high | 0.73 (0.65–0.83)* | 0.80 (0.60–1.08) | 0.73 (0.65–0.83)* | 0.79 (0.65–0.97)* |
| High/low | 0.93 (0.82–1.05) | 0.72 (0.53–0.99)* | 0.93 (0.82–1.05) | 0.83 (0.69–1.01) |
| High/medium | 0.96 (0.63–1.48) | 1.25 (0.91–1.72) | 0.96 (0.63–1.48) | 1.16 (0.85–1.58) |

**Table 2** continued

| Characteristics | Categorical model | | Continuous model (per 10 μg/m$^3$) | |
|---|---|---|---|---|
| | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) |
| High/high | 0.99 (0.87–1.13) | 1.09 (0.91–1.31) | 0.99 (0.87–1.13) | 1.03 (0.89–1.19) |

* Statistically significant at alpha = 0.05

[a] Adjusted hazard ratios are adjusted for individual-level covariates (i.e., age at diagnoses, race, marital status at diagnoses, cancer stage, and year diagnosed) and county-level covariates (i.e., education, income, and accessibility to medical resources)

**Table 3** Adjusted and unadjusted hazard ratios (HR) and 95 % confidence intervals (CI) for breast cancer death from 1999 to 2009 among females in California, U.S. ($n$ = 255,128)

| Characteristics | Categorical model | | Continuous model (per 5 μg/m$^3$) | |
|---|---|---|---|---|
| | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) |
| $PM_{2.5}$ | | | | |
| <11.64 μg/m$^3$ | 1.00 | 1.00 | 1.61 (1.22–2.12)* | 1.86 (1.12–3.10)* |
| 11.64–15.04 μg/m$^3$ | 1.10 (0.80–1.50) | 1.24 (0.79–1.94) | | |
| ≥15.04 μg/m$^3$ | 1.40 (1.14–1.73)* | 1.76 (1.24–2.49)* | | |
| Individual-level covariates | | | | |
| Age at diagnoses | | | | |
| ≤54 | 1.00 | 1.00 | 1.00 | 1.00 |
| 55–69 | 0.90 (0.86–0.94)* | 1.02 (0.96–1.08) | 0.90 (0.86–0.94)* | 1.02 (0.96–1.08) |
| 70–84 | 1.22 (1.13–1.30)* | 1.46 (1.34–1.58)* | 1.22 (1.13–1.30)* | 1.44 (1.31–1.58)* |
| 85+ | 3.00 (2.68–3.37)* | 2.97 (2.69–3.29)* | 3.00 (2.68–3.37)* | 2.88 (2.50–3.33)* |
| Race | | | | |
| White | 1.00 | 1.00 | 1.00 | 1.00 |
| Black | 1.90 (1.80–2.01)* | 1.60 (1.51–1.70)* | 1.90 (1.80–2.01)* | 1.59 (1.50–1.68)* |
| Others | 0.78 (0.74–0.83)* | 0.92 (0.88–0.98)* | 0.78 (0.74–0.83)* | 0.92 (0.87–0.97) |
| Marital status | | | | |
| Single | 1.00 | 1.00 | 1.00 | 1.00 |
| Married | 0.62 (0.59–0.65)* | 0.77 (0.73–0.81)* | 0.62 (0.59–0.65)* | 0.77 (0.73–0.81)* |
| Separated | 0.98 (0.87–1.11) | 1.02 (0.93–1.11) | 0.98 (0.87–1.11) | 1.00 (0.92–1.09) |
| Divorced | 0.84 (0.78–0.90)* | 0.91 (0.87–0.95)* | 0.84 (0.78–0.90)* | 0.91 (0.87–0.96)* |
| Widowed | 1.13 (1.03–1.24)* | 0.99 (0.95–1.03) | 1.13 (1.03–1.24)* | 0.98 (0.94–1.03) |
| Cancer stage | | | | |
| In situ | 1.00 | 1.00 | 1.00 | 1.00 |
| Localized | 4.91 (4.29–5.63)* | 4.60 (3.98–5.31)* | 4.91 (4.29–5.63)* | 4.56 (3.97–5.24)* |
| Regional | 17.69 (15.47–20.23)* | 17.34 (15.16–19.83)* | 17.69 (15.47–20.23)* | 17.05 (15.05–19.31)* |
| Distant | 143.36 (125.66–163.56)* | 132.73 (116.38–151.37)* | 143.36 (125.66–163.56)* | 125.68 (110.16–143.38)* |
| Year diagnosed | | | | |
| 1999–2003 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2004–2009 | 0.91 (0.86–0.95)* | 1.00 (0.92–1.09) | 0.91 (0.86–0.95)* | 1.11 (0.85–1.44) |
| County-level covariates | | | | |
| Education | | | | |
| Low | 1.00 | 1.00 | 1.00 | 1.00 |
| Medium | 1.11 (0.90–1.38) | 0.83 (0.72–0.95)* | 1.11 (0.90–1.38) | 0.81 (0.60–1.10) |
| High | 1.18 (0.95–1.47) | 0.83 (0.65–1.08) | 1.18 (0.95–1.47) | 0.63 (0.33–1.18) |
| Income | | | | |
| Low | 1.00 | 1.00 | 1.00 | 1.00 |
| Medium | 0.89 (0.79–1.00) | 0.79 (0.62–1.00)* | 0.89 (0.79–1.00) | 0.76 (0.45–1.28) |

**Table 3** continued

| Characteristics | Categorical model | | Continuous model (per 5 μg/m$^3$) | |
|---|---|---|---|---|
| | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) | Unadjusted HR (95 % CI) | Adjusted HR[a] (95 % CI) |
| High | 0.77 (0.65–0.91)* | 0.94 (0.66–1.32) | 0.77 (0.65–0.91)* | 1.07 (0.72–1.58) |
| Accessibility to medical resources (medical recourses/urbanization) | | | | |
| Low/low | 1.00 | 1.00 | 1.00 | 1.00 |
| Low/medium | 0.87 (0.77–0.98)* | 1.08 (0.82–1.43) | 0.87 (0.77–0.98)* | 0.99 (0.68–1.45) |
| Low/high | 0.73 (0.65–0.83)* | 0.53 (0.33–0.86)* | 0.73 (0.65–0.83)* | 0.36 (0.15–0.82)* |
| High/low | 0.93 (0.82–1.05) | 0.71 (0.53–0.97)* | 0.93 (0.82–1.05) | 0.73 (0.44–1.22) |
| High/medium | 0.96 (0.63–1.48) | 1.06 (0.69–1.61) | 0.96 (0.63–1.48) | 0.95 (0.50–1.81) |
| High/high | 0.99 (0.87–1.13) | 0.86 (0.71–1.05) | 0.99 (0.87–1.13) | 0.66 (0.41–1.10) |

* Statistically significant at alpha = 0.05

[a] Adjusted hazard ratios are adjusted for individual-level covariates (i.e., age at diagnoses, race, marital status at diagnoses, cancer stage, and year diagnosed) and county-level covariates (i.e., education, income, and accessibility to medical resources)

**Table 4** Adjusted hazard ratios (HR) and 95 % confidence intervals (CI) for breast cancer death from 1999 to 2009 among females in California, U.S. by cancer stage ($n$ = 255,128)

| Characteristics | $PM_{10}$ | | | | $PM_{2.5}$ | | | |
|---|---|---|---|---|---|---|---|---|
| | Categorical model adjusted HR (95 % CI) | | | Continuous model | Categorical model adjusted HR (95 % CI) | | | Continuous model |
| Cancer stage (μg/m$^3$) | <23.09 | 23.09–28.82 | ≥28.82 | Per 10 | <11.64 | 11.64–15.04 | ≥15.04 | Per 5 |
| In situ | 1.000 | 0.88 (0.56–1.38) | 1.59* (1.08–2.34) | 1.26[a] (0.99–1.60) | 1.000 | 1.31 (0.84–2.05) | 2.03* (1.35–3.06) | 2.36* (1.37–4.04) |
| Localized | 1.000 | 1.08 (0.73–1.59) | 1.54* (1.21–1.95) | 1.13* (1.01–1.26) | 1.000 | 1.29 (0.84–1.98) | 1.92* (1.39–2.66) | 2.13* (1.15–3.95) |
| Regional | 1.000 | 1.01 (0.69–1.49) | 1.48* (1.21–1.82) | 1.13* (1.01–1.26) | 1.000 | 1.35 (0.84–2.16) | 1.87* (1.31–2.66) | 2.07* (1.11–3.84) |
| Distant | 1.000 | 0.82 (0.80–1.34) | 1.32* (1.04–1.68) | 1.13* (1.03–1.23) | 1.000 | 1.09 (0.70–1.71) | 1.53* (1.04–2.24) | 1.62* (1.05–2.51) |

* Statistically significant at alpha = 0.05

[a] Marginally significant at alpha = 0.10

Adjusted hazard ratios are adjusted for individual-level covariates (i.e., age at diagnoses, race, marital status at diagnoses, cancer stage, and year diagnosed) and county-level covariates (i.e., education, income, and accessibility to medical resources). Cancer stage is also considered as an effect modifier

found consistent results. Moreover, we further checked our data and found that there were about 11 % of cases who were other than white and black included in this study. Given the migrant workers who are only a small proportion of this group, the results may not be largely impacted by this potential confounder.

## Conclusion

Although these limitations were noted in the study, our results suggested that exposure to high PM levels may have deleterious effects on the length of survival from breast cancer among females. Besides, compared to patients with advanced cancer stages, those with earlier cancer stages were more likely to be impacted by such exposures. Although further studies are necessary to confirm our findings, our study provides preliminary evidence that air pollution may contribute to decreased length of survival among female breast cancer patients.

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