



Associations between long-term exposure to PM_{2.5} and site-specific cancer mortality: A nationwide study in Brazil between 2010 and 2018[☆]

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ABSTRACT

Long-term exposure to PM_{2.5} has been linked to lung cancer incidence and mortality, but limited evidence existed for other cancers. This study aimed to assess the association between PM_{2.5} on cancer specific mortality. An ecological study based on the cancer mortality data collected from 5,565 Brazilian cities during 2010–2018 using a difference-in-differences approach with quasi-Poisson regression, was applied to examine PM_{2.5}-cancer mortality associations. Globally gridded annual average surface PM_{2.5} concentration was extracted and linked with the residential municipality of participants in this study. Sex, age stratified and exposure-response estimations were also conducted. Totaling 1,768,668 adult cancer deaths records of about 208 million population living across 5,565 municipalities were included in this study. The average PM_{2.5} concentration was 7.63 µg/m³ (standard deviation 3.32) with range from 2.95 µg/m³ to 28.5 µg/m³. With each 10 µg/m³ increase in three-year-average (current year and previous two years) concentrations of PM_{2.5}, the relative risks (RR) of cancer mortality were 1.16 (95% confidence interval [CI]: 1.11–1.20) for all-site cancers. The PM_{2.5} exposure was significantly associated with several cancer-specific mortalities including oral, nasopharynx, oesophagus, and stomach, colon rectum, liver, gallbladder, larynx, lung, bone, skin, female breast, cervix, prostate, brain and leukaemia. No safe level of PM_{2.5} exposure was observed in the exposure-response curve for all types of cancer. In conclusion, with nationwide cancer death records in Brazil, we found that long-term exposure to ambient PM_{2.5} increased risks of mortality for many cancer types. Even low level PM_{2.5} concentrations had significant impacts on cancer mortality.

1. Introduction

Despite great progress in diagnosis and treatment, cancer is still a major public health problem with poor survival rates (Siegel et al., 2021). According to the present trends, cancer may become the leading cause of premature death in most countries this century (Bray et al., 2021). The increasing burden due to cancer poses a barrier to sustainable human development and translate into a significant decrease in gross domestic product (GDP) (Wild, 2019). Though cancer prevention has never stopped, including mainly ongoing smoking bans and cancer screening programs, the cancer mortality keeps increasing in Brazil (Silva et al., 2020). The direct healthcare costs of cancer also showed an increasing trend in Brazil (Zhao et al., 2020). The number of deaths from cancer in Brazil are projected to increase 80.9% from 2020 to 2040

(Ferlay et al., 2020). The fight against cancer is still underway, and controlling preventable risk factors is an indispensable part of this fight to decrease cancer mortality.

Environmental pollution is the largest environmental cause of premature death, causing estimated 16% of all deaths in 2015 worldwide, 15 times more than from violence (Landrigan et al., 2018). Long-term exposure to ambient air pollution has been associated with mortality from various non-communicable diseases, including lung cancer (Bowe et al., 2019; Katanoda et al., 2011; Pun et al., 2017). The hazardous effect of fine particles less than 2.5 µm in diameter (PM_{2.5}) on lung cancer has been well established, but limited evidence supports a causal link for mortality from other types of cancer (Turner et al., 2020). The current epidemiological studies provided evidence on the potential associations between PM_{2.5} exposure and mortality from other cancers,

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like breast or bladder cancer, but only part of them showed significant positive association and further studies should be conducted to accumulate the evidence for PM_{2.5} on site-specific cancer mortality risk (Yu et al., 2021a, 2021b). Studies from the US suggested that the exposure to PM_{2.5} may shorten cancer survival (Coleman et al., 2021; Deng et al., 2017; Eckel et al., 2016). Assessment for the impacts of long-term exposure to PM_{2.5} on mortality from all types of cancer would inform public health measures to improve cancer survival, particularly among patients.

The primary objective of this study was to estimate the association between ambient PM_{2.5} exposure and adult site-specific cancer risk in Brazil based on national data using a difference in difference design. The secondary objectives were to evaluate whether the PM_{2.5}-cancer mortality associations varied by sex and age and examine the dose response relationship for PM_{2.5} on cancer mortality.

2. Materials and methods

2.1. Data collection

Individual level death records from 2010 to 2018 were collected from the Brazil Mortality Information System (Sistema de Informação sobre Mortalidade, SIM) (Morais and Costa, 2017). Each death record included information on municipality, age, sex, death date and primary cause of death coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Cancer death records were totalled for every city-year and grouped as follows: oral (C00–C10, C12–C14), nasopharynx (C11), oesophagus (C15), stomach (C16), colon-rectum (C18–C21), liver (C22), gallbladder (C23–C24), pancreas (C25), larynx (C32), lung (C33–C34), bone (C40–C41), skin (C43), breast (C50), cervix (C53), uterine (C54–C55), ovary (C56), prostate (C61), testis (C62), kidney (C64–C66), bladder (C67), brain (C70–C72), lymphoma (C81–C85), and leukaemia (C91–C95). The death counts were also divided by sex and age groups (i.e., male vs. female, aged 20–59 vs. 60+ years). Child and adolescent cancers are not the same as adult cancers with different types, treatment and survival (Kaatsch, 2010; Stiller, 2002), thus only cancer deaths aged ≥20 were included in the analyses. Brazil has 5,570 municipalities in total, the present study included cancer death records from 5,565 municipalities with complete records for each year between 2010 and 2018. In 2018, about 99.98% of Brazilian population lived in the selected 5,565 municipalities.

We used globally gridded annual average surface PM_{2.5} concentration estimates during 2001–2018 at 0.05° × 0.05° resolution (Hammer et al., 2020). The PM_{2.5} concentration was estimated using the GEOS-Chem chemical transport model by combining information from aerosol optical depth (AOD) retrievals from the National Aeronautics and Space Administration's Moderate-Resolution Imaging Spectro-Radiometer (MODIS), Multiangle Imaging Spectro Radiometer (MISR), and Sea-Viewing Wide Field-of-View Sensor satellite instruments and then calibrated to the ground-based monitor stations using geographically weighted regression. These estimates were highly consistent with global ground-based observation (cross-validation R²: 0.90–0.92) (Hammer et al., 2020). Each municipality's annual average PM_{2.5} level was calculated as the average of PM_{2.5} estimates for all grids in its geographical boundary. The official geographical boundary of municipalities was downloaded from the website of the Brazilian Institute of Geography and Statistics (IBGE, <https://www.ibge.gov.br/pt/inicio.html>).

Daily mean temperatures were calculated from hourly temperature records from ERA5 reanalysis dataset with a 0.25° × 0.25° spatial resolution ($\approx 6 \text{ km} \times 6 \text{ km}$) and then calculated to annual mean temperature in summer and winter. This dataset has global coverage and is comparable to weather station observations in evaluating temperature-mortality associations. The city-level temperature was represented by the temperature of the grid at the geographical centre of each city (P. Yu et al., 2021; Zhao et al., 2019).

Municipality-level population sizes were also collected from the SIM. City-level GDP per capita for every year during the study period were downloaded from the IBGS. We adjusted all GDP per capita statistics to United States dollars (USD) at current price, according to the consumer price index during 2008–2020 and the average exchange rate in 2020 (R. Xu et al., 2020; Xu et al., 2020a, 2020b).

2.2. Statistical analysis

A difference-in-difference (DID) approach with quasi-Poisson regression was applied to examine the associations between PM_{2.5} exposure and cancer, cancer-specific mortality. The essence of the DID design is that the difference in temporal concentrations are related to the difference in mortality rates in each location during the study period. Thus the factors that keep stable during the study time and time trends in confounders that changed similarly across locations are controlled. Confounders correlated with the temporal concentrations (PM_{2.5} concentration in this study) and changed differently across regions by time should be adjusted in the model. Temperature has been demonstrated to be associated with cancer mortality (Lehrer and Rosenzweig, 2014; Sharma et al., 2017). Thus, we fitted change of temperature in the main model. In this model, we assumed that temperature, GDP per capita and population size that changed differentially across space and over time confounded the association between PM_{2.5} exposure and the risk of cancer-specific mortality. We use the conditional Poisson model parameters conditioning on spatial units and eliminating the estimates of the variables that did not contribute to the likelihood. Cancer-specific mortality associations were evaluated using the following model:

$$\ln[E(Y_{s,t})] = \beta_0 + \beta_1 I_s + \beta_2 I_t + \beta_3 PM_{2.5s,t} + \ln(Pop_{s,t}) + \beta_4 Temp_{sum\ s,t} \\ + \beta_5 Temp_{win\ s,t} + \beta_6 SD(Temp_{sum\ s,t}) + \beta_7 SD(Temp_{win\ s,t}) + \beta_8 GDP_per.capita_{s,t}$$

where:

$Y_{s,t}$ represents the number of cases in city s , year t ;

I_s is a dummy variable for municipality s ;

I_t is a dummy variable for year t ;

$PM_{2.5s,t}$ is the average population-weighted PM_{2.5} concentration in city s , year t ;

β_0 is the intercept term;

β_1, β_2 are regression coefficients adjusting for confounding induced by factors varying across regions and over time;

$\beta_3 - \beta_8$ are the regression coefficients for the effects of PM_{2.5}, mean summer and winter temperatures and their standard deviations, respectively;

$\ln(Pop_{s,t})$: an offset term representing the natural log of the population in city s , year t .

$Temp$: the means of summer and winter temperatures and their standard deviations (SD) respectively.

In order to better account for the lagged effect of PM_{2.5} on cancer mortality, PM_{2.5} concentrations 0–5 years prior the death were also extracted and linked by city code. Our initial analyses showed that the effect of PM_{2.5} exposure on cancer mortality was only statistically significant from lag 0 to lag 2 years (Figure S1). Thus, we used the 3-year average PM_{2.5} concentration as the exposure. In summary, I_s in the model represents the indicators for each municipality which is to control the geographical differences (i.e., factors that were stable during the time). I_t represents the indicators for each year which is to control the country-wide time trend (i.e., factors that changed parallel across municipalities). Other temporal factors which were not stable or changing parallel were also controlled including seasonal temperatures (mean temperature in summer and winter and their standard deviation) that were correlated with PM_{2.5}, socioeconomic factors (GDP per capita) and population size of each municipality in each year. These non-parallel factors were defined based on previous studies (Renzi et al., 2019;

Schwartz et al., 2020; Yu et al., 2020). The potential non-linear relationship between PM_{2.5} and mortality was evaluated by applying a natural cubic spline with best degrees of freedom (df), i.e. lowest Quasi-Bayesian Information Criteria (QBIC), to the PM_{2.5}.

We also performed subgroup analyses by age groups (20–59 years vs. 60 years or above) and sex. We used random-effect meta-analyses to compare the effect estimates between sex and age groups considering the potential differences. All results were expressed as relative risks (RR) and 95% confidence intervals (95% CI) per 10 µg/m³ increase in annual average PM_{2.5} concentration.

We performed several sensitivity analyses to check the robustness of the main findings. We modelled the summer and winter temperatures using natural cubic splines with 2 and 3 df; removed GDP per capita from the main model; and applying NO₂, SO₂, O₃, CO, Normalized Difference Vegetation Index (NDVI) to the main model.

R software (V3.4.3, www.R-project.org) was used to perform all data analyses. The “gnm” package was used to perform conditional Poisson regression model. The “mvmeta” package was used to compare the subgroup differences. Statistical significance was defined as a two-side *P*-value < 0.05 unless otherwise indicated. In addition, we used a Bonferroni correction for each of the subgroups and end points. The cut-points for statistically significant *P* values after Bonferroni correction are described with each table.

This study was approved by the Monash University Human Research Ethics Committee. The Brazilian Ministry of Health did not require ethics approval or informed consent for secondary analysis of aggregated anonymized data from the SIM.

3. Results

A total of 1,768,668 adult cancer deaths records (830,468 females) of about 208 million population living across 5,565 cities were included in this study. The national average PM_{2.5} concentration was 7.60 (standard deviation 3.20) µg/m³ during the study period. PM_{2.5} concentrations ranged from 3.40 µg/m³ to 21.0 µg/m³ (Table 1). Fig. 1 shows the average PM_{2.5} concentrations and average cancer mortality rates for municipalities included in the analyses from 2010 to 2018. The annual cancer mortality rate was 72.4/100,000 ranging from 0 to 1,499/100,000. The number of deaths for each cancer site by sex and age was presented in Table S1. Cancer distribution was different between males and females. Lung cancer was the leading cause of cancer death in males and elderly people (≥ 60 years) while breast cancer was in females and younger people (20–59 years).

Estimated PM_{2.5}-cancer specific mortality associations using the current year and lag 1–5 year (1–5 year before the death year) are shown in Figure S1. The consistent significant effect is observed from the current year to 2-years before for most cancer sites. Therefore we estimated the PM_{2.5}-cancer mortality associations using the 3-year-average PM_{2.5} concentrations. Every 10 µg/m³ increase in 3-year-average PM_{2.5} exposure was associated with a 15.8% higher risk for total cancer mortality (RR = 1.16; 95%CI: 1.11, 1.20) (Fig. 2). The associations were robust to changing the df of temperature or covariates in the model. Effect estimates from models without adjusting for GDP per capital, adding NO₂, SO₂, O₃, CO, NDVI had no statistically significant difference from the primary model. We also took drowning and misadventure as the negative control which were less association with PM_{2.5} exposure (Table S2).

Statistically significant positive associations were found for cancers of all sites, oral, nasopharynx, oesophagus, stomach, colon rectum, liver, gallbladder, larynx, lung, bone, skin, female breast, cervix, prostate, brain and leukaemia. The associations were still significant for total cancer and cancers of nasopharynx, stomach, colon rectum, larynx, lung, bone, skin, female breast, cervix and leukaemia after allowing for multiple comparisons (Fig. 2).

Fig. 3 compares the differences of the associations for cancers affected by PM_{2.5} potentially by sex and age. For all cancers combined,

Table 1

Descriptive Characteristics of Study Participants and summary statistics for the 5,565 municipalities in Brazil during 2010–2018.

Characteristic	All Participants, No.	Mean	SD	Median	Range
Health data					
Cancer death number (in person)	1,768,668	317	3,083	38	0–161,937
Demographic data					
Population size (in person)	208,447,903	36,242	213,959	11,378	808–11,859,359,
Adult population size (in person)	147,514,042	24,896	154,064	7,589	587–8,551,316
Age					
20–59	548,148	99	987	9	0–50,468
≥ 60	1,220,520	219	2,101	29	0–111,469
Sex					
Male	938,075	169	1,518	23	0–80,357
Female	830,468	149	1,567	16	0–81,580
Environmental data					
PM _{2.5} (µg/m ³)	–	7.63	3.16	6.91	3.37–21.02
lag1 (µg/m ³)	–	7.66	3.16	6.89	3.36–21.36
lag2 (µg/m ³)	–	7.52	3.10	6.79	3.33–20.29
lag0–2 (µg/m ³)	–	7.60	3.14	6.86	3.35–20.89
Mean winter temperature (°C)	–	25.25	4.44	25.44	18.2–29.7
Mean summer temperature (°C)	–	21.34	1.86	21.65	10.6–30.3
SD of winter temperature (°C)	–	1.95	1.18	1.57	0.37–4.85
SD of summer temperature (°C)	–	1.44	0.44	1.48	0.43–2.58
Socioeconomic data					
GDP per capita (USD)	–	4,362	4,502	3,272	809–133,088

Note: SD: standard deviation. Lag1 and lag2 refer to 1 and 2 years prior to the current year, respectively.

the RRs did not vary by sex and age, with 1.17 (95%CI: 1.11–1.23) for males, 1.15 (1.09–1.21) for females, 1.21 (1.14–1.28) for younger people (20–59 years) and 1.22 (1.17–1.28) for older without statistically differences ($P = 0.656$ by sex and $P = 0.859$ by age). RRs appear higher in males than females for cancers of oral, nasopharynx, gallbladder, kidney than females, while females had higher RR in skin cancers than males. People ≥ 60 years old had higher RRs than those < 60 for cancers of nasopharynx, bone, cervix, lymphoma and leukaemia. People < 60 years had higher RRs for oral and testicular cancer than those ≥ 60 years.

The relationships between PM_{2.5} and total cancer mortality modelled by natural cubic spline with 1–4 degrees of freedom were similar (Figure S2), indicating linear association between PM_{2.5} and total cancer mortality. Similar linear associations were observed for site specific cancer risks (Fig. 4, and Table S3).

4. Discussion

This study observed that there are positive associations between long-term PM_{2.5} exposure and adult mortality from most types of cancer which is the first study to examine the impacts of long-term exposure to ambient PM_{2.5} on mortality from all common types of adult cancer based on national records. Overall, the RR of cancer mortality with each 10 µg/m³ increase in three-year-average concentrations of PM_{2.5} was 1.16 (1.11–1.20) for all-site cancers. The estimation was statistically robust after applying other covariates into the model. Additionally, age and sex differences were observed on the PM_{2.5}-cancer-specific mortality risk.

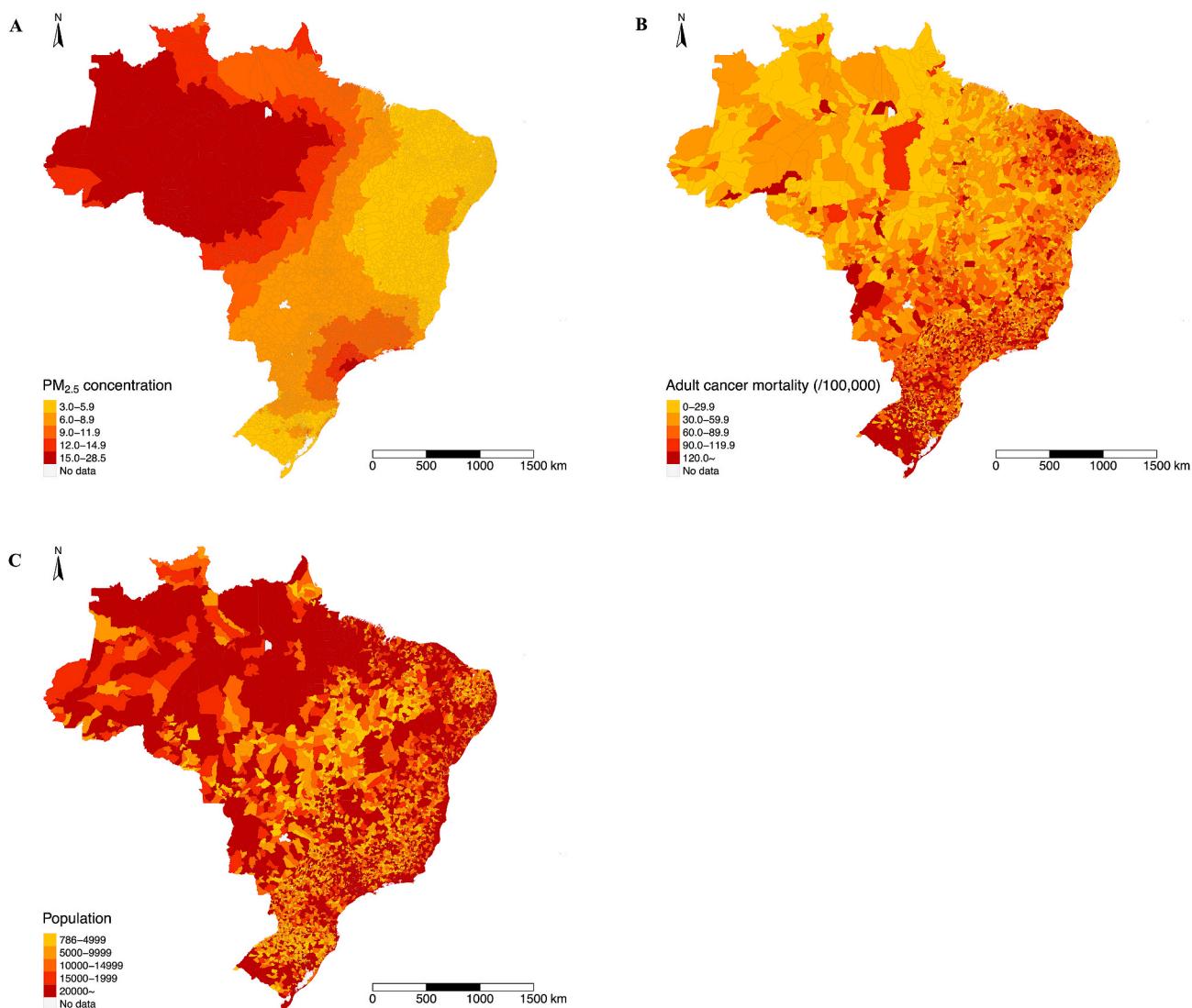


Fig. 1. Estimated (A) average PM_{2.5} concentration, (B) average adult cancer mortality rate and (C) average population (age ≥ 20) for municipalities in Brazil from 2010 to 2018. Note: areas in grey were not included in our analyses, thus data were not presented.

Finally, we did not observe a threshold of ambient PM_{2.5} concentration for cancer mortality, even at low levels below the current WHO air quality guideline values (i.e., 5 $\mu\text{g}/\text{m}^3$) (WHO, 2020).

The PM_{2.5}-cancer-specific mortality associations were significant for total cancer and cancers of nasopharynx, stomach, colon rectum, larynx, lung, bone, skin, female breast, cervix and leukaemia even after allowing for multiple comparisons. This indicated that the adverse effect of PM_{2.5} exposure on cancer mortality may not be limited to lung cancer. There are two potential reasons to explain how PM_{2.5} exposure may increase cancer mortality. One is that higher exposure to PM_{2.5} may accelerate cancer progression. Oxidative stress, genotoxicity and inflammation were demonstrated to be closely related to the progression of cancer (Coussens and Werb, 2002; Gill et al., 2016; Klaunig, 2018; Reuter et al., 2010; Roos et al., 2016). PM_{2.5} can move into interstitial spaces between alveoli and towards other organs after breath through the air way (Guarnieri and Balmes, 2014) and promote the process of these pathways, such as molecular changes (i.e. DNA adducts, gene mutations, apoptosis inhibition) and inflammation (i.e. promote the inflammation of cytotoxicity of T cells) (Ma et al., 2017; Turner et al., 2020). Population studies from the US also found that exposed to high levels of PM_{2.5} may have deleterious effects on the survival from breast cancer and liver cancer (Deng et al., 2017; Hu et al., 2013) which could

support the potential explanation. Another is that people diagnosed with cancer have weakened immune systems and cancer treatments also weaken the immune system and may increase vulnerability to PM_{2.5} (Rolston, 2017). PM_{2.5} exposure also weakens the immune system (Glencross et al., 2020).

For total cancer, we found a 15.8% higher risk associated with each 10 $\mu\text{g}/\text{m}^3$ increase based on the national cancer death records using the DID design. Similarly, the results from a representative cohort of the US adults showed 15% higher risk (Pope et al., 2019). Cohort study from Hong Kong of people older than 65 years reported an estimated 22% higher risk which was higher than our study (Wong et al., 2016). Considering the genetic background, socioeconomic status, climate, component and study design differed in these studies, the evidence is not enough to find a possible adaptive response leading to a smaller change in cancer mortality rates. Further global studies should be conducted to examine the association between PM_{2.5} and cancer mortality.

Stratification results suggested that different age or sex groups may have different vulnerability at various cancer sites. Significant differences were observed that male had greater risks than females for cancers of oral, nasopharynx, gallbladder, while greater risk for female skin cancers than male in this study. Previous studies showed inconsistent sex difference on PM_{2.5}-cancer mortality association (Pope et al., 2019;

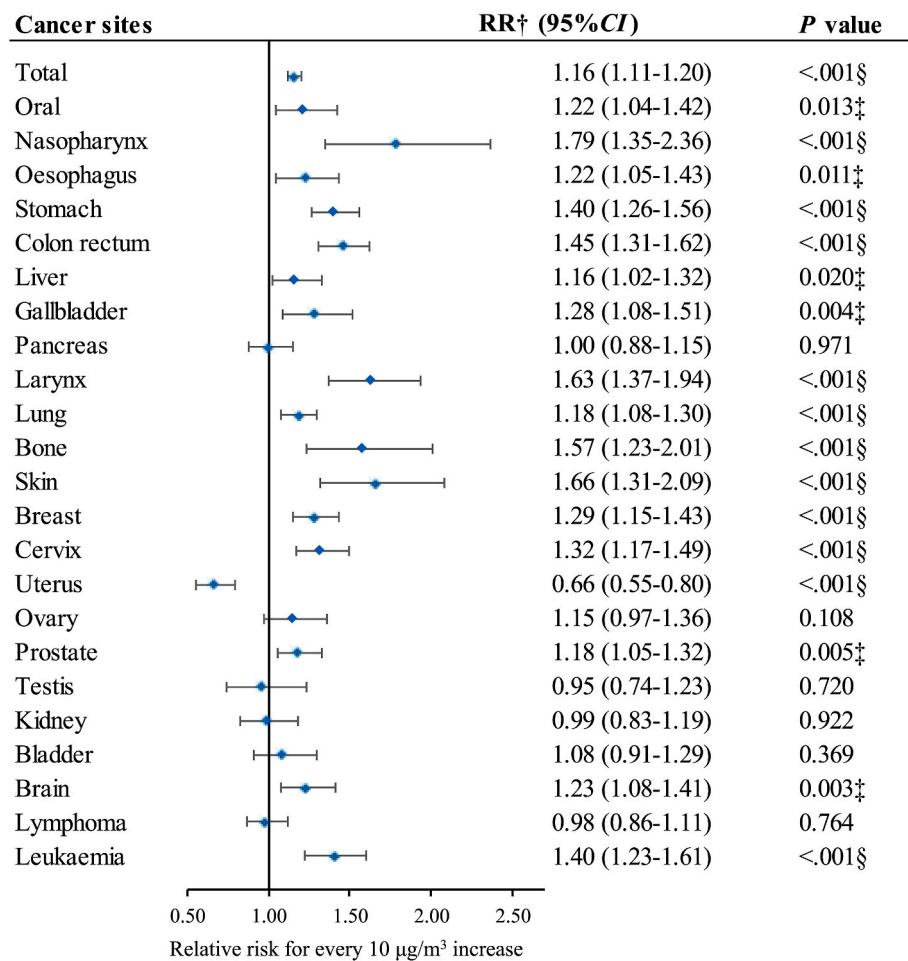


Fig. 2. Estimated RR and 95% confidence interval [RR (95%CI)] for the association between a 10 µg/m³ increase in 3-year-average (lag0-2 year) PM_{2.5} and cancer, cancer-specific mortality in Brazil during 2010–2018. Note: †The Bonferroni-corrected critical P = 0.05/24 = 0.0021. ‡Uncorrected P value was less than 0.05. §Uncorrected P value was less than the Bonferroni-corrected critical P value.

Wang et al., 2019). The study from the US reported similar associations between PM_{2.5} and lung cancer mortality in males and females (Pope et al., 2019), while the study from China showed significantly higher risk in females for lung cancer and leukaemia than males (Wang et al., 2019). The animal experiment demonstrated that sex-associated differences in the effect of PM_{2.5} exposure on insulin resistance and disorder of hepatic lipid metabolism which were closely associated with cancer (Li et al., 2020). Estrogen receptor β was also suggested to be involved in the PM_{2.5} organic extract induced inflammation and lung cancer (Luo et al., 2021). Evidence of a differential effect of PM_{2.5} on cancer mortality across age are limited as well (Coleman et al., 2020; Coleman et al., 2021; Guo et al., 2020). The current study showed that people older than 60 years had higher risks for death from cancers of nasopharynx, bone, cervix, lymphoma and leukaemia as expected. But younger people were more likely to suffer higher risk for oral cancers. The potential reason for the similar effect between PM_{2.5} and cancer mortality by age groups can be explained by that 1) some types of cancer mortality were more sensitive to PM_{2.5} for younger people than elderly (oral cancer), vice versa (cancers of nasopharynx, bone, cervix, lymphoma and leukaemia); 2) So, for all cancers combined, the RRs did not vary by age. The mechanisms underlying the sex and age difference in PM_{2.5}-cancer mortality associations are unclear and warrant further investigation.

Unexpected statistically significant protective associations were observed between PM_{2.5} and cancers of uterus, oral cavity, kidney in female and testis in older people. One of the potential explanations that could be proposed is that higher PM_{2.5} exposure may increase the hospital visits by other diseases at the same site and occasionally lead to

early detection and early treatment of cancer. Another potential reason is the most vulnerable population may die from other severe comorbidities. Study from Taiwan suggested that patients with endometrial hyperplasia in poor air quality areas had more severe comorbidities, such as diabetes or hypertension (Chang et al., 2019).

The exposure-response relationships for most cancer sites were linear, except for cervix and brain. For the cancer sites with significant associations with PM_{2.5} exposure, the exposure-response curve showed no threshold in the current study. This means there may be no safe level of PM_{2.5} exposure for deaths from most cancers. The current study is the first to estimate the exposure-response curves for mortality for almost all types of cancers, to the best of our knowledge. Some studies estimated the lung cancer mortality related to PM_{2.5} exposure, but the conclusions were inconsistent (Guo et al., 2017; Pinault et al., 2017). The PM_{2.5}-lung cancer mortality associations were non-linear with thresholds of 40–48 µg/m³ for various subgroups in China (Guo et al., 2017). A pattern with a low HR estimate in the lowest range, a high effect in the middle range, and a moderate effect in the highest range was observed in Canadian Census Health and Environment Cohort (Pinault et al., 2017).

A major strength of our study is that we are the first to evaluate the association between ambient PM_{2.5} exposure and cancer-specific mortality risk based on the nationwide death records covering 99.98% of Brazilian population with only 7 cities lost without death records during study period. Secondly, exposure-response relationships were also estimated in a non-linear model to find whether there was safe level of PM_{2.5} exposure on cancer mortality. Furthermore, the design of the difference in differences method was able to eliminate most unmeasured

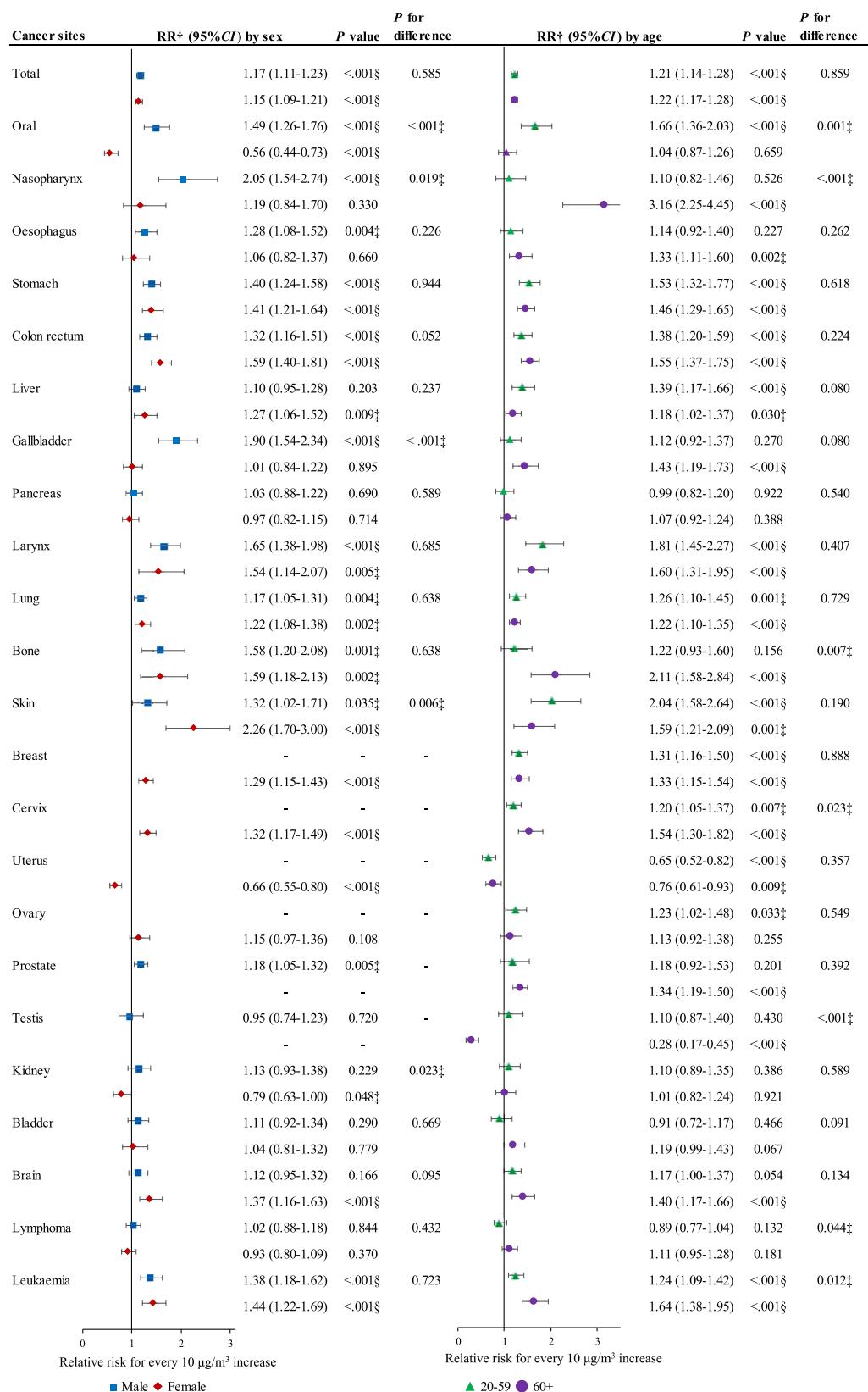


Fig. 3. Estimated RR and 95% confidence interval [RR (95%CI)] for the association between a 10 µg/m³ increase in 3-year-average (lag0-2 year) PM_{2.5} and cancer, cancer-specific mortality in Brazil during 2010–2018 by sex and age. P-value for difference were between sexes difference estimated by random effect meta-analysis with no statistical adjustment. † Uncorrected P value was less than 0.05. § Uncorrected P value was less than the Bonferroni-corrected critical P value. The Bonferroni-corrected critical P = 0.05/90 = 0.00056.

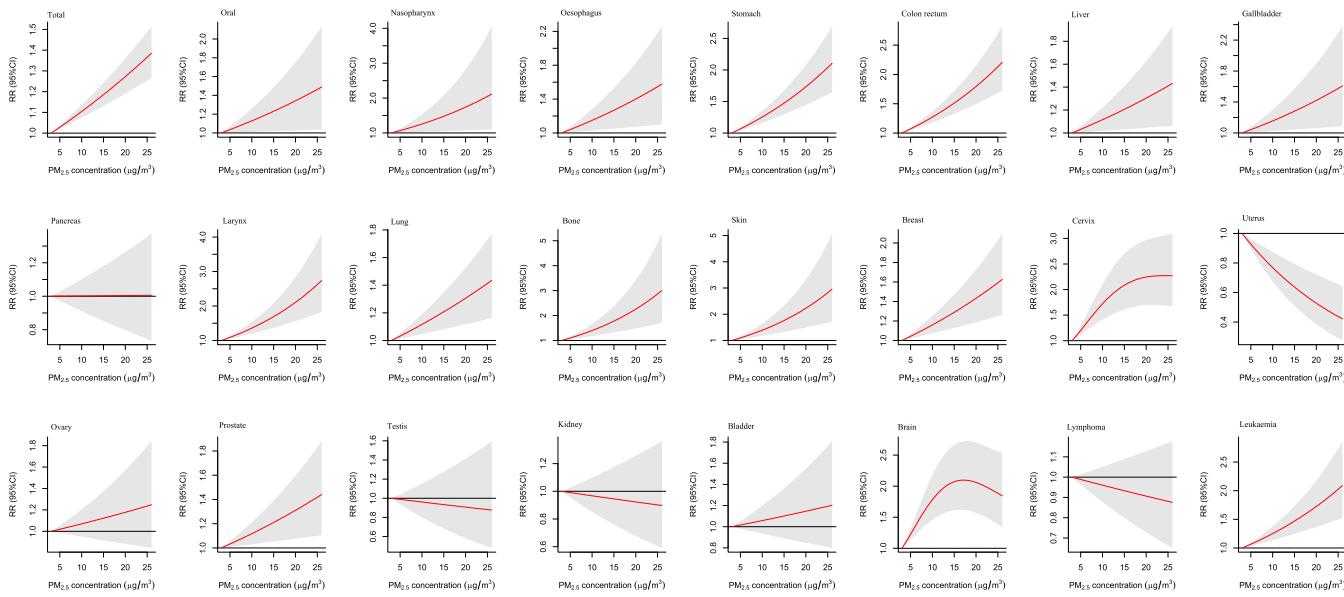


Fig. 4. Estimated response relationship between PM_{2.5} and cancer, cancer-specific mortality, modelled by natural cubic spline with two degree of freedom for cancers of cervix and brain and one degree of freedom for other cancer sites in Brazil during 2010–2018 (quasi-BIC see Table S2).

confounders, especially the changes in the ability of cancer diagnosis and registry, which was not adjusted by other cohort studies.

This study has several limitations. The PM_{2.5} exposure was estimated at global scale and the regional validation result was not available due to limited grounded monitors in Brazil. We could only get the access to the municipality-level PM_{2.5} exposure data, but not individual level data. Municipality-level exposure may introduce exposure bias which might make the PM_{2.5}-cancer mortality association under-estimated (Hutchesson et al. 2010). The PM_{2.5} and cancer mortality association was based on the PM_{2.5} exposure by the residential city and the migration of residents could not be captured. According to the census results in 2010 in Brazil published in BIGS, nearly 90% adults had uninterrupted time of residence in the municipality at least three years, ranged from 81.4% (aged 20–30 year) to 94.9% (age >80 year). The migration may not affect the estimation of this study. We used the city-level GDP per capita data to represent the socioeconomic status. Some potential trends of health behaviours, such as smoking, were not able to be analysed due to the limited data. Although smoking was not able to be added in the model, the potential changing trend was adjusted by the year in the mode, so it should not change the results much. Another study found that PM_{2.5}-cancer mortality associations were similar in the full cohort compared with the never-smoking population (Coleman et al., 2020). Some other potential confounding factors may be ignored in the analyses. Besides, the effect of PM_{2.5} on cancer mortality may be underestimated due to cancer patients dying from other diseases (i.e., cardiopulmonary diseases (Coleman et al., 2021; Strongman et al., 2019)) affected by PM_{2.5}.

5. Conclusions

With nationwide death records in Brazil, this study provides evidence about the cancer mortality risk associated with long-term PM_{2.5} exposure, with no safe threshold observed. These results are of substantial clinical and public health importance. The exposure-response curves also give evidence that further reduction in PM_{2.5} concentrations should yield additional public health benefits.

CRediT authorship contribution statement

Pei Yu: Conceptualization, Formal analysis, Data curation, Investigation, Methodology, Software, Visualization, Writing – original draft. **Rongbin Xu:** Data curation, Methodology, Supervision, Validation, Writing – review & editing. **Shanshan Li:** Data curation, Methodology, Supervision, Writing – review & editing. **Micheline S.Z.S. Coelho:** Data curation, Resources, Funding acquisition, Writing – review & editing. **Paulo H.N. Saldiva:** Data curation, Investigation, Resources, Funding acquisition, Supervision, Writing – review & editing. **Malcolm R. Sim:** Supervision, Writing – review & editing. **Michael J. Abramson:** Supervision, Writing – review & editing. **Yuming Guo:** Conceptualization, Data curation, Investigation, Project administration, Resources, Funding acquisition, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envpol.2022.119070>.

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