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Chronic exposure to fine particles ($PM_{2.5}$) and mortality: Evidence from Chile

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Background: Many Chilean cities suffer from high air pollution from industrial, mobile, and residential wood-burning sources. Several studies have linked $PM_{2.5}$ air pollution exposure to higher mortality risk from cardiovascular, pulmonary, and lung cancer causes. In recent years, Chile has developed an extensive air pollution monitoring network to enforce air quality standards for $PM_{2.5}$, allowing the study of the medium-term association between $PM_{2.5}$ and mortality.

Methods: A negative binomial regression model was used to study the association between 3-year average $PM_{2.5}$ concentrations and age-adjusted mortality rates for 105 of the 345 municipalities in Chile. Models were fitted for all (ICD10 A to Q codes), cardiopulmonary (I and J), cardiovascular (I), pulmonary (J), cancer (C), and lung cancer (C33-C34) causes; controlling for meteorological, socioeconomic, and demographic characteristics.

Results: A significant association of $PM_{2.5}$ exposure with cardiopulmonary (relative risk for 10 μg/m^3 $PM_{2.5}$: 1.06; 95% confidence interval = 1.00, 1.13) and pulmonary (1.11; 1.02, 1.20) age-adjusted mortality rates was found. Cardiovascular (1.06; 0.99, 1.13) and all causes (1.02; 0.98, 1.07) were positive, but not significant. No significant association was found between cancer and lung cancer. The positive associations remained even when controlling for multiple confounding factors, model specifications, and when considering different methods for exposure characterization. These estimates are in line with results from cohort studies from the United States and European studies.

Conclusion: Three-year average $PM_{2.5}$ exposure is positively associated with the age-adjusted mortality rate for cardiopulmonary and cardiovascular causes in Chile. This provides evidence of the medium-term exposure effect of fine particles on long-term mortality rates.

Keywords: Air pollution; Ecological study; Middle-income countries; Mortality rates; $PM_{2.5}$

Introduction

Background

Though classified as a high-income country by the World Bank, Chile still faces many challenges of a developing country, especially concerning environmental problems. Most cities in Chile have annual average $PM_{2.5}$ concentrations that exceed 20 μg/m^3, the Chilean national standard.[1,2] The unique geography of Chile, and its varied climatic conditions, impact the pollution sources. Although cities in the northern and central regions suffer from mining, industrial and mobile sources, cities in the southern regions suffer mainly from residential wood burning pollution.

Fine particles cause an inflammatory response in the cardiovascular system, with long-term exposure having a greater risk for mortality and morbidity effects than short-term exposures.[3] Studies have linked the physiology of damage to small particles, noting that these affect human health by penetrating the bloodstream via the respiratory system.[4–9] Multiple studies have found strong evidence of the relation between air pollution and cause-specific mortality rates.[10–14] The impact of short and long-term exposure to fine particle air pollution on a wide variety of health endpoints has been studied throughout the world, and findings are consistent regarding their significant effect.[15–19] The majority of the studies have been conducted in the developed world, which has lower fine particle concentrations, so there remains a need to study the association in highly polluted areas.

What this study adds

This study provides the first evidence of a significant association between medium-term $PM_{2.5}$ exposure and mortality rates in a middle-income country. These results are in line with those of developed countries and may provide stronger support for more aggressive pollution abatement regulation in Chile and in other Latin American countries.

This article along with the processed data has been not published anywhere else. The authors declared that there is no conflict of interest and that there is no closely related article published by the authors.

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All the processes required to replicate the analysis, along with all the data collected and code can be found at: https://github.com/pmbusch/MortalityRR-PM2.5.

SDC *Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.environepidem.com).*

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Pope et al[19] reviewed over 70 cohort studies on air pollution and human mortality, with China being the only developing country for which results were available. Relative risks (per an increase of 10 µg/m^3 in the annual average of $PM_{2.5}$) obtained from a meta-analysis were: 3% for the age group 30+, 16% for the age group 25+, and 4% increase for the age group 30+.[10–13] Positive associations have been found for other mortality causes: 6% for cardiopulmonary (CPM), and 8% for lung cancer (LCA).[10,11,13]

The association between long-term exposure to $PM_{2.5}$ and premature mortality rates has not been extensively studied outside of developed countries. In Chile, the relation of long-term mortality has been reported by at least 2 studies: 1 has reported increased rates of LCA, cardiovascular, and pulmonary disease mortality associated with the proximity to industrial facilities,[20] and in the mining city of Andacollo.[21] Many more have studied the relation of daily air pollution levels with short-term mortality and morbidity effects. A recent study analyzed the relation between short-term exposure to $PM_{2.5}$ and cardiorespiratory mortality and morbidity in several zones of Santiago, controlling for age and socioeconomic variables.[22] Significant statistical associations using a Poisson regression model have been found in Santiago for daily mortality cases (all causes) and ambient air pollution, $PM_{2.5}$, CO, and NO_2, linked with combustion sources.[23] The association of particulate matter and mortality and morbidity for cardiovascular and respiratory diseases has been studied with Poisson regression in Temuco, a highly polluted city in Chile.[24] Short-term association between medical consultations for respiratory diseases and particulate matter concentration has been established in Chile for the winter season.[25] Further studies have been conducted to assess the relative risk on subgroups that could be heavily affected, such as the elderly. A time series study with Poisson count in Santiago finds evidence that elderly populations are increasingly susceptible to mortality from air pollution, specifically from PM_{10}, O_3, SO_2, and CO.[26]

In Chile, the quantitative results from these studies are important, because, by law, the authority is required to conduct an analysis of the social and economic impact of any new environmental regulation. This requires the quantification of the reduction in health effects resulting from the reduction in ambient concentrations. Currently, the Ministry of the Environment recommends the use of the coefficient derived by Pope et al for CPM mortality for adults 30+ years old.[10,11,27,28] Efforts have been made to extrapolate the relative risk function of $PM_{2.5}$ to specific conditions, such as demographic differences or higher air pollution observed in several places in the world, and for considering mortality causes for ischemic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, and LCA,[29] but these extrapolations have limitations and are look with suspicion by interested parties. A study conducted in Chile, besides providing a local risk estimate, could contribute to improving the acceptability of the health effects of $PM_{2.5}$ air pollution, and the benefits of its reduction.

Objective

The objective of this work is to assess the association of medium-term exposure to $PM_{2.5}$ ambient concentrations and mortality rates from several causes in Chile, through a cross-sectional ecological study of data at the municipality level.

Period and study area

The study included all municipalities in Chile for which population exposure to $PM_{2.5}$ could be computed (Figure 1). Municipalities are the smallest administrative division in Chile, and depending on their size and location can contain several cities, towns, and rural areas, or can be part of a bigger urban area, such as those that compose the Santiago Metropolitan area. The temporal period was determined by data availability. We chose the 3-year period from 2017 to 2019, which provided a good balance of length and availability of $PM_{2.5}$ data.

Data

Data on death certificates were obtained from the Ministry of Health. Each record includes the date, diagnostic (ICD10), birthday, sex, and municipality of residence. $PM_{2.5}$ and Meteorological data were obtained from the National System of Air Quality System managed by the Ministry of the Environment. The network has been growing steadily since 1988, gradually covering smaller towns and sparsely populated areas. As of 2019, it includes 90 monitors that measure $PM_{2.5}$.[30] Demographic data at the census district level were obtained from the 2017 Census from the National Institute of Statistics.[31] Data includes age, sex, urban-rural residence, and ethnic origin. Socioeconomic data, including housing characteristics, were obtained from the 2017 National Socioeconomic Characterization Survey (CASEN).[32] It includes data for each municipality on many social and economic dimensions. We chose to use income, educational level attained, household occupancy rates, health care provider, and the fuel used for heating, cooking, or hot water.

Study design

Causes of death

We studied mortality rates from several causes: all deaths excluding external causes (ICD10 codes A00-Q99), of cardiovascular (I), respiratory (J), CPM (I and J), cancer (C), and LCA (C33-C34 codes).[33] The focus was on CPM causes, as $PM_{2.5}$ has been extensively documented to affect the cardiovascular and respiratory systems.[11,13]

Age-adjusted mortality rates

To avoid the effect of age distribution on mortality rates, we adjusted the rates to the national age profile using 5-year age groups: from 0–4 to 75–79 and 80+. The supplementary material; http://links.lww.com/EE/A224 presents details on the method and a comparison of crude and age-adjusted rates.

Pollution

We used the average for $PM_{2.5}$ concentrations for the period 2017–2019. $PM_{2.5}$ is measured hourly with the beta-attenuation method.[34] Only monitors with data for at least 80% of the days with more than 18 hours each were considered.

Population exposure

The concentration for each census district was computed as the inverse distance weighted average of all monitors within 20 km from the centroid of the district. The municipality's average concentration was obtained as the population-weighted average of all the districts within it. A detailed explanation of the exposure calculation method is provided in the supplementary material; http://links.lww.com/EE/A224.

Meteorological data

Temperature and relative humidity for each municipality were computed using the same method as pollution but using a 50 km cutoff distance. We used a bigger cutoff distance than for $PM_{2.5}$ for 2 reasons. First, temperature and humidity have less geographic variation than air pollution and secondly, because not all monitoring stations record meteorological data, we avoided excluding 15 municipalities. Heating degree days for 15°C were used as a proxy for heating requirements.

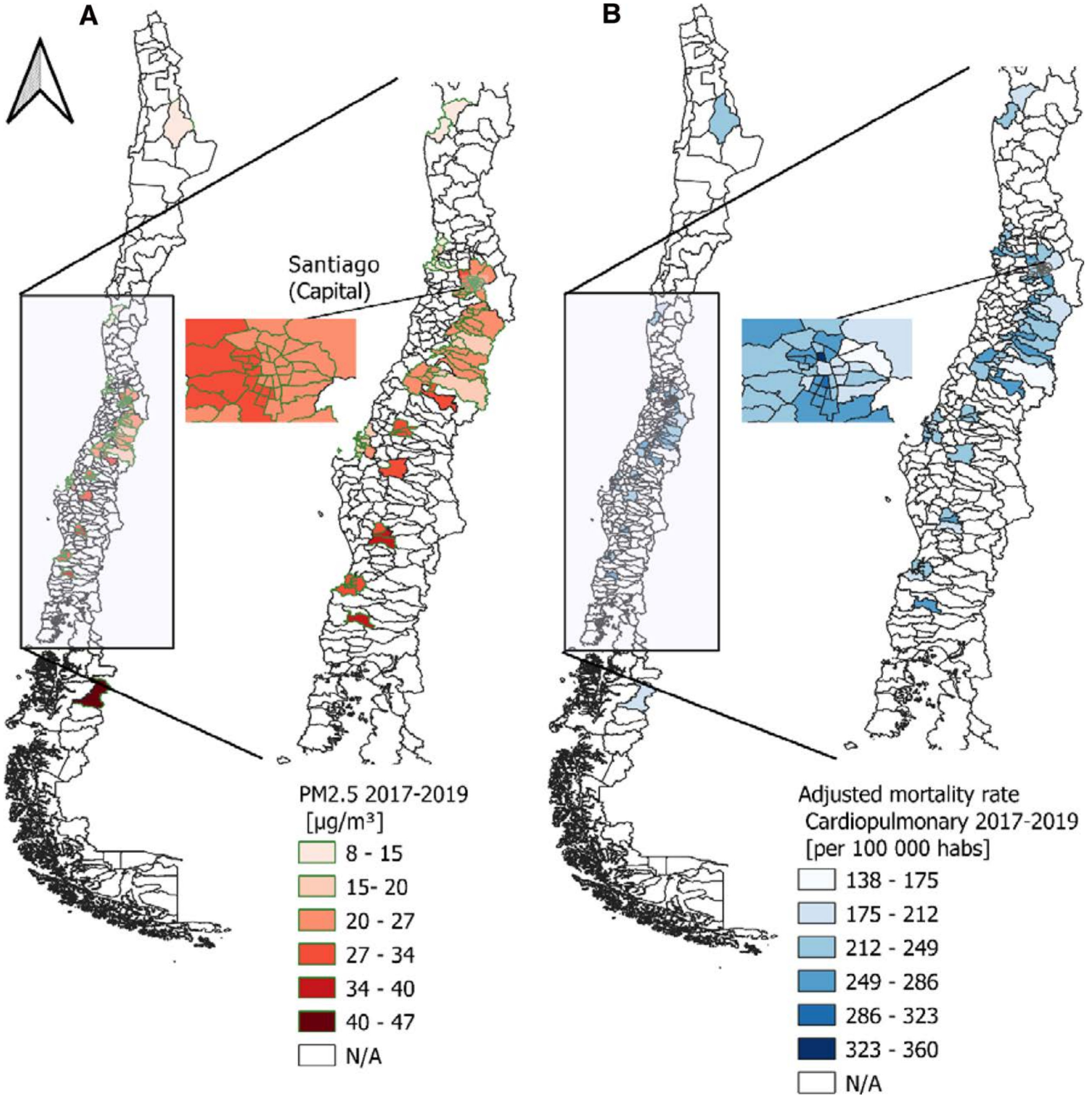

Figure 1. A, Location of municipalities with $PM_{2.5}$ data. B, Age-adjusted mortality rate for CPM (all I and J) causes. n = 105 municipalities.

Methods

Negative binomial regression has been used extensively in ecological studies to assess the association between long-term pollution exposure and health effects.[35–38] It is more appropriate than the Poisson distribution in cases with over-dispersion, as it allows the variance to be different from the mean. The equation of the generalized linear model is

$$\ln(MR_i) = \beta_0 + \beta_{pm}PM_i + \beta_m M_i + \beta_d D_i + \beta_s S_i + \varepsilon_i,$$

where i stands for municipality, MR_i for age-adjusted mortality rate, PM_i for the 3-year average $PM_{2.5}$ concentration, M_i for meteorological variables, D_i for demographics, S_i for socioeconomic characteristics, and ε_i for the residual error. We performed all the statistical analysis using the R software version 4.0.3,[39] with the "mass" package.[40] Results are presented as mortality risk ratios (MRR) for an increase of 10 µg/m^3 of $PM_{2.5}$. Coefficients for the other variables were centered and standardized to facilitate comparisons.

Model specification and sensitivity analysis

We fitted several models testing different socioeconomic, demographic, and meteorological variables. We settled on a unique model for all the groups of causes, selected based on the Akaike Information Criterion[41] and our own judgment. We call this the "full model." To test for model specification and to allow difference among cause groups, we used the stepwise method with a Poisson model for selecting covariables, and then adjusting a negative binomial model for comparing the coefficients with the full model (more detail is presented in the supplementary material; http://links.lww.com/EE/A224).

To test if the method for computing $PM_{2.5}$ exposure has an effect on the association, we used 2 additional cutoff distances of 50 and 100 km. Increasing this distance increased the sample to 191 municipalities with air pollution data in both cases. We tested a model using all municipalities (n = 324) to check whether there is a difference in the age-adjusted mortality rates between municipalities with exposure estimation (n = 105) and the others. We tested the full model in a sample that included only municipalities with more than 50,000 people, and another excluding those with less than 13,000 people. We also split the data into 2 sets, 1 with all municipalities from the Santiago Metropolitan area and the other with the rest. Finally, we tested a sample that excluded municipalities with extreme $PM_{2.5}$ concentrations: below 16 μg/m^3 (10th percentile) and above 31 μg/m^3 (90th percentile).

Results

Descriptive statistics

During the 3-year period, there were 299,209 deaths from all disease causes, of which 28% were from cardiovascular causes, 12% from pulmonary causes, 27% from cancer (CAN) causes, and 3% from LCA causes.

Using a 20 km cutoff distance with data from 59 monitor sites we were able to estimate $PM_{2.5}$ exposure for 105 of the 345 municipalities that represent 68% of the population. Table 1 presents descriptive statistics for the 105 municipalities (see Figure 1 for spatial extent). The population-weighted average $PM_{2.5}$ concentration is 24.4 μg/m^3, well above the Chilean national standard.

The 105 municipalities included in the analysis have an average population of over 100,000, with important differences in urban density, percentage of rural population, and percentage of ethnicity origin. Regarding health care providers, there are important differences: some municipalities have more than 80% of their population insured by the private health care system, whereas most have populations that have access to the public health system.

Mortality risk ratios for $PM_{2.5}$

Table 2 presents the $PM_{2.5}$ MRR estimated under different model specifications for all-cause groups. For the full model (last row of the table) the association is positive for all the cause groups considered, though it is significant and robust against model specifications for CPM and respiratory RSP causes only. The MRR for cardiovascular CVD causes is significant in the model with socioeconomic variables only. The MRR for ALL causes is not significant for any model specification. CAN and LCA do not have any meaningful association.

Mortality risk ratios for covariables

Table 3 presents the MRR for all the variables included in the full model. In general, mortality rates are associated with socioeconomic conditions. Though median income has an effect, it is not significant. Overcrowded housing conditions and the percentage of people with lower than high school education are significant for all groups except CAN and LCA and have a simple average MRR over ALL, CPM, CVD, and RSP groups of 1.10 and 0.91, respectively. Though they are correlated with income, their effect is independent of it. The percentage of people affiliated with the public health system (Fonasa) is also important. The

Table 1.

Descriptive statistics for the 105 municipalities included in the main analysis.

Variable	Mean	SD	Min	Median	Max
Adjusted mortality rate 2017–2019 (per 100,000)					
All causes (A00–Q99)	560.4	62.8	357.4	564.8	788.3
CPM (all I and J)	232	32.0	138	229	360
Cardiovascular (all I)	162.0	23.5	91.3	161.9	254.0
Pulmonary (all J)	69.5	16.2	28.2	67.3	111.5
CAN (all C)	148.5	16.0	100.6	150.9	182.3
LCA (C33–C34)	19	5.3	5	19	33
Air pollution concentration					
$PM_{2.5}$ 2017–2019 (μg/m^3)	24.2	6.0	8.0	25.1	46.2
Residential wood consumption					
% Wood usage as main fuel in cooking	4.4	9.1	0.0	1.0	56.4
% Wood usage as main fuel in heating	36.8	32.8	0.0	35.4	93.6
% Wood usage as main fuel in warm water	2	4.6	0	1	39
Demography					
Population 2017 (thousands)	113.8	106.7	5.3	91.8	568.1
Population municipality density (urban area) (hab/km^2)	5 717.6	3 492.5	542.1	4 551.0	17 464.2
% Age 15–44	43.6	3.4	36.8	43.2	62.9
% Age 45–64	25	2.0	17	25	29
% Age 65–74	12	2.4	5	12	18
% Female	51.1	1.3	48.1	51.1	55.0
% Rural	16.5	21.2	0.0	6.8	72.8
% Native origin	9.1	7.8	1.0	7.2	52.9
% Medium overcrowding in housing (2.5–5 persons per room)	6.6	2.0	0.7	6.9	11.9
% High overcrowding in housing (more than 5 persons per room)	0.7	0.6	0.1	0.5	3.0
Socioeconomic data					
Median monthly income per capita (USD)	480.3	240.5	221.9	430.6	1 800.7
% Less than high school education	40.6	10.4	15.3	39.9	66.6
% Occupancy rate	52.6	5.9	41.2	52.4	75.1
% Private health care provider (Isapre)	13	14.4	0	10	83
% Public health care provider—high income (Fonasa C-D)	23	7.2	4	23	45
% Public health care provider—low income (Fonasa A-B)	53.6	15.8	4.1	53.4	83.7
Meteorology					
Summer relative humidity (%)	54.3	9.8	40.7	48.1	74.4
Winter relative humidity (%)	73.1	8.0	17.6	71.3	84.8
Summer temperature (°C)	20.4	2.1	12.9	21.5	22.6
Winter temperature (°C)	9.9	1.2	4.1	9.9	13.3
HDD 15°C summer (°C)	0.5	0.5	0.0	0.3	3.2
HDD 15°C winter (°C)	5.6	1.0	2.8	5.6	10.9

Table 2.

$PM_{2.5}$ mortality rate ratio (MRR) estimated under different model specifications

Model	n	ALL	CPM	CVD	RSP	CAN	LCA
$PM_{2.5}$ only	120	0.99 (0.96–1.02)	1.02 (0.98–1.06)	1.00 (0.96–1.04)	**1.06 (1.01–1.12)**	**0.96 (0.94–0.99)**	**0.86 (0.8–0.93)**
$PM_{2.5}$ + meteorological[a]	105	1.01 (0.96–1.07)	**1.06 (1.00–1.14)**	1.06 (0.99–1.14)	**1.09 (1.00–1.20)**	0.97 (0.92–1.01)	1.09 (0.98–1.22)
$PM_{2.5}$ + demographic[b]	120	0.99 (0.96–1.02)	**1.01 (0.97–1.05)**	0.99 (0.95–1.03)	**1.05 (1.00–1.11)**	0.98 (0.95–1.01)	**0.90 (0.83–0.98)**
$PM_{2.5}$ + socioeconomic[c]	120	1.02 (0.99–1.05)	**1.05 (1.02–1.09)**	**1.03 (1.00–1.07)**	**1.11 (1.06–1.16)**	**0.97 (0.94–1.00)**	**0.91 (0.85–0.98)**
Full model[d]	**105**	1.02 (0.98–1.07)	**1.06 (1.00–1.13)**	1.06 (0.99–1.13)	**1.11 (1.02–1.20)**	1.02 (0.97–1.08)	1.06 (0.91–1.24)

MRR represents the increase in risk per 10 μg/m³.

ALL: ICD10 A to Q codes; CVD: ICD10 I codes; RSP: ICD10 J codes; CPM: ICD10 I and J codes; CAN: ICD10 C codes; LCA:ICD10 C33-C34 codes.

Significant coefficients ($P \leq 0.05$) are in bold.

[a]Meteorological variables: relative humidity + HDD 15° winter.

[b]Demographic variables: urban population density + % female + % native origin + % rural + % high overcrowding in housing (more than 5 persons per room).

[c]Socioeconomic variables: log(median of monthly income) + % less than high school education + % public health care provider—low income (Fonasa A-B) + % public health care provider—high income (Fonasa C-D).

[d]Full: $PM_{2.5}$ + meteorological + demographic + socioeconomic variables.

Table 3.

Mortality rate ratios (MRR) for $PM_{2.5}$ and covariables for all-cause groups, full model.

Variable	ALL	CPM	CVD	RSP	CAN	LCA
$PM_{2.5}$ 2017–2019 (10 μg/m³)[a]	1.02 (0.98–1.07)	**1.06 (1.00–1.13)***	1.06 (0.99–1.13).	**1.11 (1.02–1.20)***	1.02 (0.97–1.08)	1.06 (0.91–1.24)
Municipality density (urban area) (inhabitants/km²)[b]	0.99 (0.97–1.01)	0.98 (0.95–1.00).	0.99 (0.96–1.01)	**0.95 (0.92–0.99)****	**0.97 (0.95–0.99)****	0.96 (0.91–1.01)
% Female	1.03 (0.91–1.17)	1.11 (0.94–1.31)	1.01 (0.84–1.21)	**1.40 (1.12–1.74)****	1.08 (0.95–1.23)	0.82 (0.59–1.16)
% Ethnicity origin	1.00 (0.96–1.05)	0.97 (0.92–1.03)	0.96 (0.90–1.02)	1.01 (0.93–1.09)	0.99 (0.94–1.04)	0.92 (0.78–1.08)
% Rural	0.99 (0.93–1.05)	1.06 (0.98–1.15)	1.02 (0.93–1.12)	**1.17 (1.04–1.31)****	0.97 (0.90–1.04)	0.96 (0.77–1.20)
% Wood as main fuel in heating	1.00 (0.95–1.06)	0.96 (0.89–1.02)	0.97 (0.90–1.05)	0.92 (0.84–1.02)	1.02 (0.97–1.08)	0.87 (0.73–1.02).
Median monthly income per capita	0.98 (0.94–1.02)	0.95 (0.90–1.01).	**0.93 (0.87–0.99)***	0.98 (0.91–1.06)	1.00 (0.96–1.05)	1.02 (0.91–1.16)
% Less than high school education	**0.92 (0.88–0.96)*****	**0.90 (0.84–0.95)*****	**0.89 (0.83–0.95)*****	**0.91 (0.84–0.99)***	**0.93 (0.88–0.98)****	1.01 (0.87–1.17)
% Health care provider Fonasa A-B	**1.06 (1.02–1.11)****	**1.06 (1.00–1.12)***	1.05 (0.99–1.12)	1.06 (0.98–1.15)	**1.07 (1.02–1.12)****	0.95 (0.84–1.08)
% Health care provider Fonasa C-D	**1.04 (1.02–1.06)****	**1.03 (1.00–1.07)***	1.02 (0.99–1.06)	**1.06 (1.01–1.10)***	**1.04 (1.01–1.07)****	1.01 (0.95–1.08)
Medium overcrowding in housing (2.5–5 persons per room)	**1.07 (1.03–1.10)*****	**1.10 (1.06–1.15)*****	**1.08 (1.03–1.14)*****	**1.14 (1.07–1.20)*****	1.03 (1.00–1.07).	1.02 (0.93–1.12)
Average relative humidity (%)	0.98 (0.96–1.01)	0.98 (0.95–1.02)	1.00 (0.96–1.04)	**0.94 (0.89–0.98)****	0.99 (0.96–1.02)	0.98 (0.91–1.07)
HDD 15°C winter	1.00 (0.96–1.03)	0.99 (0.94–1.05)	0.99 (0.93–1.05)	1.01 (0.93–1.08)	0.99 (0.95–1.03)	0.96 (0.84–1.10)

MRR is the increase in relative risk per 1 SD.

ALL: ICD10 A to Q codes; CVD: ICD10 I codes; RSP: ICD10 J codes; CPM: ICD10 I and J codes; CAN: ICD10 C codes; LCA:ICD10 C33-C34 codes.

Significant codes: 0 "***" 0.001 "**" 0.01 "*" 0.05 "." 0.1 " " 1.

Significant coefficients ($P \leq 0.05$) are in bold.

[a]For $PM_{2.5}$ MRR is computed for an increase of 10 μg/m³.

[b]For every other variable MRR is presented for an increase in 1 SD from the mean.

simple average MRR for the lower income group (Fonasa A-B) is 1.06, whereas it is 1.06 for the higher income group (Fonasa C-D). Regarding meteorological conditions, we found that relative humidity has a negative association with mortality rate.

To test for possible different effects by sex and age groups, we adjusted models for 4 different age groups, and for crude mortality rates. MRR for $PM_{2.5}$ are presented in supplementary materials, Figure 14; http://links.lww.com/EE/A224. In general, we do not see major differences in the coefficients, only a larger confidence interval associated with the loss of explanatory power owing to the smaller population.

Discussion

Sensitivity analysis and limitations

Several sensitivity analyses were conducted to test the results under different conditions (Figure 2). Overall, there are no major differences, except for the analysis constrained to the Metropolitan Region of Santiago. The cutoff distance to estimate exposure has no important effect. Restricting the sample to municipalities with higher populations increased the MRR slightly. Eliminating the municipalities with extreme concentrations also increased the MRR, but CPM became not significant. The results are consistent across all scenarios, with CPM and RSP MRRs almost always significant, whereas less so for ALL and CVD causes.

Regarding the omitted variable bias, all potential confounder variables that we could get data on were included. One important missing variable that could potentially bias the results is the percentage of people with a smoking habit, though there is no reason to believe it is correlated to $PM_{2.5}$. Other potential omitted variables are alcohol consumption and physical activity. Unfortunately, there is no data available for including them. Finally, we did not control for spatial autocorrelation.

Another source of concern is selection bias, as our main analysis includes municipalities closer than 20 km to a $PM_{2.5}$ monitor. However, extending the cutoff distance up to 100 km did not change the results, most likely because the monitoring network covers all municipalities with higher $PM_{2.5}$ concentrations. The models with a cutoff distance of 50 and 100 km were consistent with the 20 km base level, estimating an MRR for CPM mortality causes of 1.07 (1.02–1.12; n = 191) for the 50 km model, and of 1.09 (1.03–1.15; n = 191) for the 100 km model (Figure 2). There was no indication that the age-adjusted mortality rate was different between municipalities with or without $PM_{2.5}$ measurement [MRR for the dummy: 1.00, 95% confidence interval (CI) = 0.95, 1.04]. This implies that there is no evidence to reject the null hypothesis that there is no difference between mortality rates in municipalities with or without $PM_{2.5}$ exposure estimation.

Another possible source of bias is measurement errors. Mortality rates are of high precision, as death certificates are quite important legal documents. Still, there is a possibility of

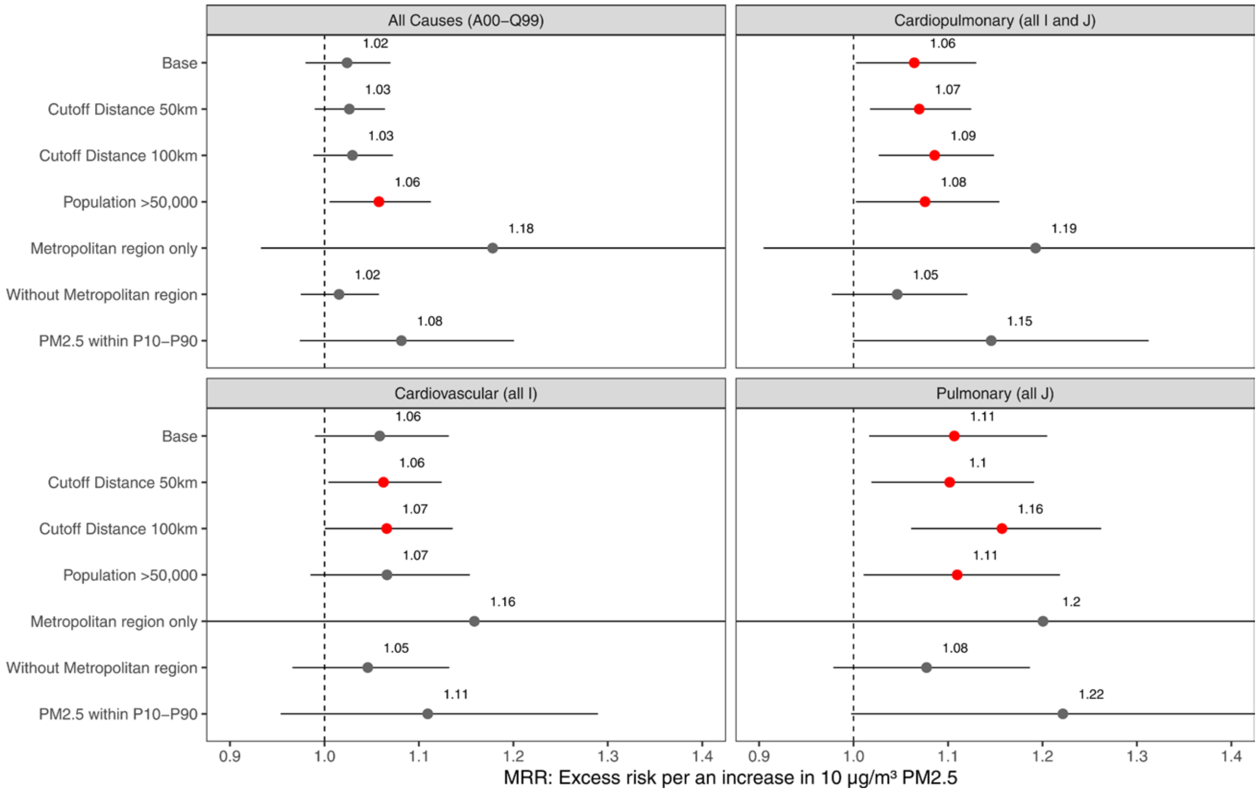

Figure 2. $PM_{2.5}$ sensitivity of the $PM_{2.5}$ MRR when considering different groups of municipalities. Bars indicate a 95% confidence interval; the red dot indicates a significant effect (*P*-value ≤ 0.05).

misclassification of the cause of death and of the municipality of residence. Though the municipality registered is the one at the time of death, residence mobility in Chile is low. Regarding population data, it was gathered as recently as 2017 by the census bureau. Its finer geographical resolution was useful to compute population-weighted pollutant concentrations, which might be more precise than a simple average for each municipality. Socioeconomic variables, which can have an important effect on mortality, were obtained from the CASEN survey, and are subjected to all the limitations of a sample survey. However, CASEN information is used in many social programs, so it has rigorous quality control. Nonetheless, their estimates are more uncertain than those of the other variables. Last, but not least important, the air pollution monitoring network is managed by the Ministry of the Environment, and its precision is regularly verified.

One important source of variability in mortality rates is the sample size, that relates to the number of deaths and population in each age and sex group analyzed. Municipalities with smaller populations have greater variability in their mortality rates which could potentially introduce bias into the model. Nevertheless, the negative binomial regression weights data by population, so it should reduce the potential bias. MRRs for municipalities with more than 50,000 inhabitants (shown in Figure 2) did not change much, as were the 1 for the model excluding the 10% municipalities with fewer people.

The only notable difference occurred for the group of municipalities belonging to the Santiago Metropolitan Region. Although the model without the Metropolitan Region of Santiago had similar results for CPM mortality (1.05; 95% CI = 0.98, 1.10; n = 62), the model municipalities from the Santiago region had a much higher MRR for CPM (1.19; 95% CI = 0.90, 1.60; n = 43), as well as for other causes of death (Figure 2). This might be owing to the temporal evolution of pollution. In fact, $PM_{2.5}$ concentrations in the Santiago Metropolitan area had continuously decreased since 1988, when monitoring started, up to 2005, so 2017–2019 average misrepresents the long-term exposure of the population. Unfortunately, the temporal pattern cannot be verified for other municipalities since systematic monitoring outside Santiago is available only after 2007.

Comparison to the results from cohort studies

Many cohort studies conducted in the United States and Europe have found a positive association between long-term exposure to $PM_{2.5}$ and mortality rate for all causes, CPM and LCA. Pope III et al[13] found an increase in mortality associated with 10 μg/m³ of $PM_{2.5}$ of 4% (1%–8%), 6% (2%–10%), and 8% (1%–16%) for all causes, CPM and LCA, respectively. The updated assessment of the Harvard 6 cities study found an increase in mortality rate per 10 μg/m³ increase in $PM_{2.5}$ of 14% (7%–22%) for all-cause mortality, 26% (14%–40%) for cardiovascular mortality and 37% (7%–75%) for LCA mortality.[11] Krewski et al. found a change in risk of 3% (1%–4%), 6% (4%–8%), 12% (9%–16%), and −2% (−4% to 0%) for all causes, CPM, IHD, LCA, and all other causes, respectively.[10]

Though ours is an ecological study, the results are generally comparable to those obtained by Pope III et al[13] and Krewski et al[10] for CPM causes. However, 2 issues should be considered: the decreasing slope of the concentration-response function,[42] and the differences in socioeconomic and education levels. Both affect the MRR in opposing directions, so their effects may cancel out, but that needs more research. Also, although the association of $PM_{2.5}$ with LCA mortality has been profusely documented, we did not find any statistically significant association in our study.

In terms of future directions to study, we plan to improve the model by including additional confounders, such as smoking habits, drinking water quality, and dietary habits, and using satellite-based data to include more municipalities. Also, the analysis could be extended to consider other endpoints such as hospital admissions. This will improve the assessment of the full impact of air pollution on the health of the Chilean population.

Conclusion

We found evidence of an association between age-adjusted mortality rates for CPM and respiratory causes and the 3-year annual average $PM_{2.5}$ in a sample of 105 municipalities in Chile. The associations are robust, and their magnitude is in line with results from studies in the United States and Europe. These results may contribute to stress the need to reduce air pollution in Chile and in other middle-income countries.

Conflicts of interest statement

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

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