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Source: Environmental Health Insights, 16(1)

Published By: SAGE Publishing

URL: <https://doi.org/10.1177/11786302221107136>

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Air Pollution and Cardiorespiratory Changes in Older Adults Living in a Polluted Area in Central Chile

Environmental Health Insights
Volume 16: 1–12
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DOI: 10.1177/11786302221107136



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ABSTRACT: One recognized cause of cardiorespiratory diseases is air pollution. Older adults (OA) are one of the most vulnerable groups that suffer from its adverse effects. The objective of the study was to analyze the association between exposure to air pollution and changes in cardiorespiratory variables in OA. Observational prospective cohort study. Health questionnaires, blood pressure (BP) measurements, lung functions, respiratory symptoms, physical activity levels, and physical fitness in high and low exposure to air pollution were all methods used in evaluating OAs in communes with high contamination rates. Linear and logistic models were created to adjust for variables of interest. A total of 92 OA participated in this study. 73.9% of the subjects were women with 72.3 ± 5.6 years. 46.7% were obese, while 12.1% consumed tobacco. The most prevalent diseases found were hypertension, diabetes, and cardiovascular disease. Adjusted linear models maintained an increase for systolic BP of 6.77 mmHg (95% CI: 1.04–12.51), and diastolic of 3.51 mmHg (95% CI: 0.72–6.29), during the period of high exposure to air pollution. The adjusted logistic regression model indicated that, during the period of high exposure to air pollution increase the respiratory symptoms 4 times more (OR: 4.43, 95% CI: 2.07–10.04) in the OA. The results are consistent with an adverse effect on cardiorespiratory variables in periods of high exposure to air pollution in the OA population.

KEYWORDS: Air pollution, older adults, physical activity, blood pressure, respiratory diseases

RECEIVED: October 2, 2021. **ACCEPTED:** May 12, 2022.

TYPE: Original Research

FUNDING: The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was conducted thanks to internal funding from the Pontificia Universidad Católica de Chile.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Air pollution is a public health problem that occurs in the main cities of Chile, including Santiago. Progress in business development, dense population, and geography favors increased emissions and accumulation of pollutants such as particulate matter (PM) and nitrogen dioxide (NO₂) in this city.

Massive amounts of PM in the atmosphere are associated with chronic health problems. Inhaled particles between 2.5 and 10 µm in diameter travel to the respiratory system and, depending on their diameter; they can be deposited in the upper respiratory tract or even reach the alveoli, causing inflammation, irritation, and remodeling.¹ Systemic inflammatory effects can then take place causing cardiovascular, respiratory, and pulmonary diseases in the exposed population.² The World Health Organization (WHO)³ reported that in 2016 chronic exposure to air pollution contributed to more than 4 million deaths worldwide. The recent update for the air quality guidelines from the WHO suggest that even a higher amount of people are exposed to prejudicial levels,³ meaning that

attributable risk it would be greater in larger population exposed at even lower levels.⁴ In Chile, statistics indicate that environmental pollution causes more than 3500 premature deaths per year due to cardiopulmonary diseases.⁵ The primary air quality standard for particulate matter with an aerodynamic of less than 2.5 µm (PM_{2.5}) is 20 µg/m³ as the annual concentration, and 50 µg/m³, as a concentration of 24 hours; while for particulate matter with an aerodynamic of less than 10 µm (PM₁₀) it is 50 and 150 µg/m³ respectively,^{5,6} values that exceed the recommendations of the WHO.³

The Metropolitan Region has more than 7 million inhabitants. Santiago, specifically, is one of the most polluted cities in the Metropolitan Region in South America.^{6–8} PM levels vary dramatically according to seasonality. During the winter months that occur from March until August, there are days in which PM concentrations exceed the national limits. Decreases in air currents make it difficult for PM contaminants to spread in the Metropolitan basin (communes of the province of Santiago), affecting the health of the entire population, especially children and older people.^{8,9}



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Currently, Chile has the second highest life expectancy rate in Latin America, having one of the highest rates in the world. Consequently, this poses a significant challenge at the public health in an aging population. Developing a social system that supports the health of the aging of the population is paramount.¹⁰ Older people typically have several comorbidities, making them more susceptible to the harmful effects that high levels of environmental pollution can bring.¹¹ Addressing this problem involves evaluating strategies and promoting factors that protect the environment and lifestyle in one of the most polluted cities in South America.

Within lifestyle variables, physical activity is a protective factor. Maintaining adequate levels assists in the prevention of cardiovascular disease, as well as 34 chronic non-communicable diseases (NCD) and premature mortality.¹² In older people, the WHO recommended dose of physical activity is 150 minutes of moderate-vigorous activity per week, with the dose-response linked to health benefits.¹³ On the other hand, prolonged exposure to pollutants such as PM_{2.5}, PM₁₀, NO₂, and sulfur dioxide (SO₂) is associated with an increased risk of dying or becoming ill due to cardiovascular and respiratory causes.^{9,14} Furthermore, PM_{2.5}, PM₁₀, and NO have been associated with increased systolic blood pressure and hospitalizations due to exacerbation of symptoms of pulmonary disease symptoms.^{1,15} There is limited evidence on the role of physical activity in people chronically exposed to air pollution in Chile. In the central zone of the country, where the urban population is concentrated, an exposure scenario with high levels of air pollution, high rates of social inequity, and high prevalence of cardiovascular diseases.¹⁶

In 2018, the Metropolitan Region had 35 days of high air pollution episodes.⁵ Applying the precautionary principle measures against the possible adverse health effects of exposure during these episodes, all vulnerable populations were recommended to avoid physical activities. However, the elderly population is characterized by low levels of physical activity and poor physical condition, contributing to an environment conducive to other adverse health-related consequences during aging.^{17,18}

Both self-reported physical activity and physical fitness based on performance are highly predictive measures of morbidity, hospitalization, institutionalization, and mortality.¹⁹⁻²² Regular physical activity improves insulin sensitivity, increases muscle mass, basal metabolic rate, decreases fat deposits, favors bone mineral density, improves autoimmune function, increases musculoskeletal, cardiac, and cerebral vascularization, among other adaptations.²³ On the other hand, not meeting the recommended dose of physical activity is one of the main risk factors for NCDs such as cardiovascular disease, cancer, and diabetes, which are attributed to approximately 1.6 million deaths worldwide.^{3,24} People who are not physically active are considered to have a 20% to 30% higher risk of mortality than

those who meet the minimum recommended levels of moderate physical activity.²⁵

There is little scientific evidence to explore the association between exposure to ambient air pollution, considering the level of activity and physical fitness in the elderly population.

The objective of this study was to analyze the association between air pollution and cardiorespiratory variables, considering as covariables the level of physical activity and physical fitness, in OA that live in communes with high levels of air pollution in the Metropolitan Region of Chile.

We hypothesize that exposure to high levels of air pollution increases blood pressure, decreases lung function, and exacerbates respiratory symptoms in the elderly population.

Material and Method

Study design and participants

The selected study design was an observational prospective cohort study. Individuals over 60 years of age, residents of Cerro Navia and Pudahuel communes registered in the Family Health Centers of the respective communes in the Metropolitan Region of Santiago, were invited to participate. The communes are the minor and basic unit of administrative division in Chile in a specified territory (Figure 1).²⁶ Cerro Navia and Pudahuel communes were selected due to the high density of inhabitants, levels of air pollution, and the high rates of poverty.²⁷

The evaluation of the selected participants occurred during 2 different periods of exposure to air pollutants; a period of high exposure that occurred during the winter season of 2017 and a period of low exposure corresponding to the summer season of 2018.

Data were collected using a self-report health survey, respiratory symptoms, a physical activity questionnaire, and a battery of physical health exams to measure the physical condition of the participants. Evaluations were carried out in the facilities of the corresponding public health center of each participant. The health professionals trained for this study administered these evaluations. The inclusion criteria used were voluntary participation, stay in health control in public family health center, ability to walk on their own or stand without assistance, understanding the instructions, and agreement that they would not change places of residence during the development of the study. The exclusion criteria were: having undergone surgery or having suffered a myocardial infarction in the last 3 months, having terminal disease, neuromuscular disease, or severe dementia.

Each participant received detailed information on the scope of the investigation. All questions and concerns were addressed before the signed informed consent forms were taken and admission into the study was granted.

The Institutional Ethics Committee of the University (No. 160914001) and the Metropolitan Health Service approved this study according to the Declaration of Helsinki.

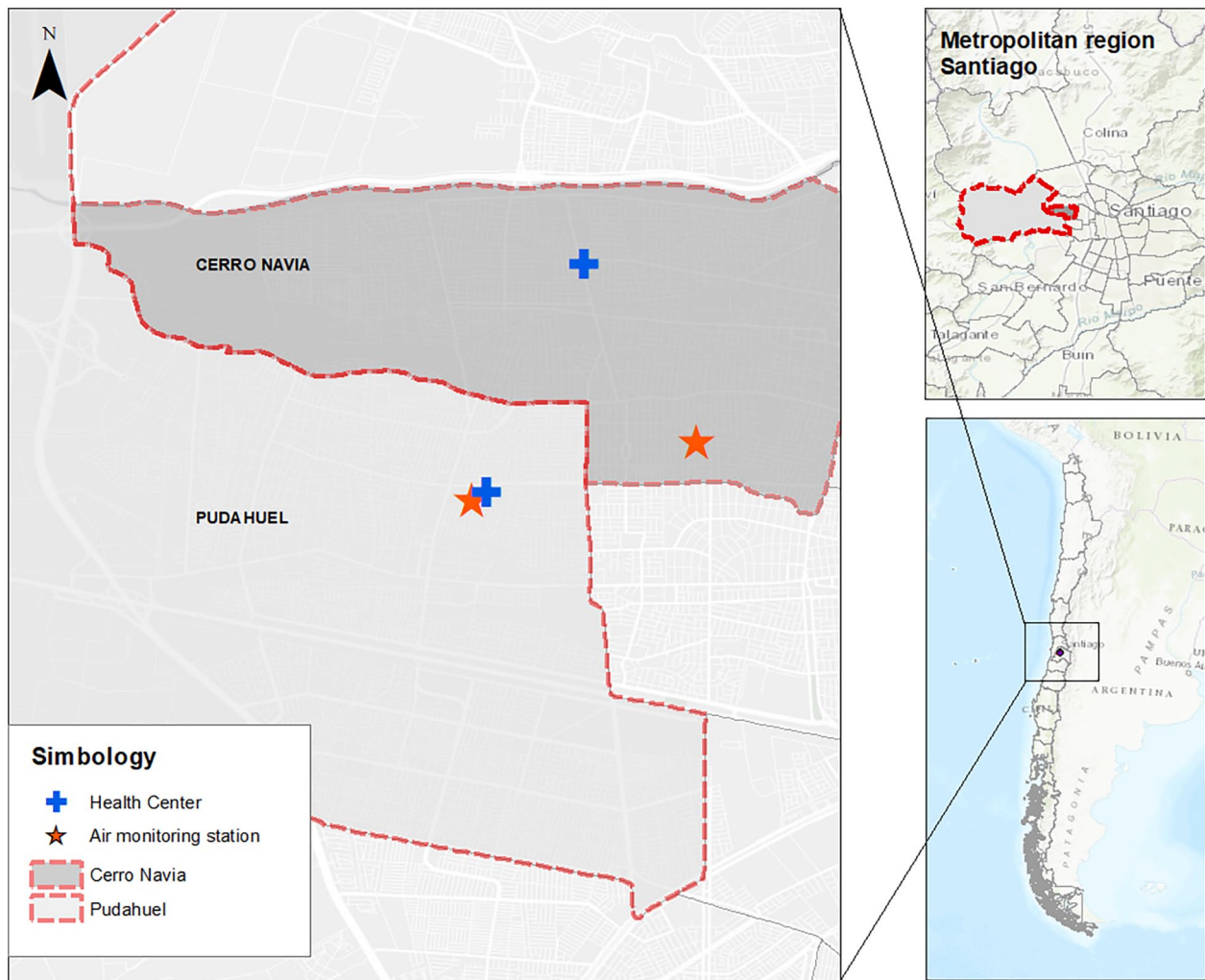


Figure 1. Characterization of the study area.

Characterization of the study site

The communes of Cerro Navia and Pudahuel lie in the northwest of Santiago, Metropolitan Region, approximately 5 km from each other. When observing their levels of $PM_{2.5}$, PM_{10} , NO_2 , humidity, temperature, and wind speed, during the last 5 years of registration, both communes reported high levels of air pollution compared to other communes located east of the region. The geomorphological characteristics of the basin of the Metropolitan Region favor the confinement of air masses, the presence of morning mist, and an increase in the concentration of atmospheric pollutants in these communes. Also, socioeconomic indicators such as multidimensional poverty level (29% vs 16%) and schooling (6.4 years vs 7.0 years) in these communes are above or below the national value respectively.²⁸

Cerro Navia and Pudahuel have a shortage of green areas in accordance with the sustainability indicator. Pudahuel's potable water consumption is higher than the reference. This is also the case for electricity use where both communes exceed the reference value. Overcrowding and child poverty are also high in both communes (Table 1).

Variables

Cardiorespiratory health. The cardiorespiratory health indicators used were blood pressure (BP), peak expiratory flow and respiratory symptoms.

The diastolic and systolic BP measured with the Omro digital sphygmomanometer model HEM 7200 was recorded 3 times in the right arm of the participant and distributed at different times during the development of the health survey.²⁹

Before physical evaluation, peak expiratory flow using a flowmeter, the Adult Mini-Wright model CE-0120. After recording 3 different measurements, the analysis of the maximum registered value began, according to other national studies.^{30,31}

A validated self-reported respiratory health questionnaire was used to assess respiratory symptoms.^{32,33} The questionnaire focused on the presence of 3 specific symptoms: cough without having a cold, phlegm without having a cold, and wheezing (Supplemental Material, questionnaire). From these parameters, the variable "respiratory symptoms" constructed with the favorable report of one of the 3 defined symptoms was generated.

Table 1. Sociodemographic characteristics in Cerro Navia and Pudahuel.

DIMENSION	INDICATOR	UNIT	CERRO NAVIA	PUDAHUEL	SUSTAINABILITY REFERENCE
Green areas	Supply of green areas in relation to the size of the population.	m ² /room	4.1	2.3	>11
Drinking water consumption	Volume of drinking water that each inhabitant uses for direct consumption, food preparation, household cleaning, personal care, irrigation of gardens inside their home.	L/day	136	162.5	100-150
Electrical consumption	Energy consumed per dwelling/month.	kWh/month/living	196	207	<150
Generation of household solid waste	Kilograms of household solid waste generated per person per day.	kg/day/inhab	1.41	1	<0.5
Overcrowding	Population inhabited by 2.5 or more people per bedroom in the dwelling.	Percentage (%)	14.8	9	<1
Child poverty	Children <14 years of age, living in poverty.	Percentage (%)	13	15.8	<2.5
Access to green areas	Population residing within a 5-min walk of a green area with a surface area $\geq 5000\text{m}^2$ or up to 10 min away from a green area $\geq 20000\text{m}^2$	Percentage (%)	60	44	>75.0

Source: Observatory CEDEUS.

All measurements were performed in both high and low exposure periods. Also, the team that performed the tests was the same in both periods.

Physical activity and physical fitness. The Global Physical Activity Questionnaire-GPAQ, which was prepared by the WHO for the monitoring of physical activity, was a tool used to evaluate the physical activity of the participant. The level of compliance with the physical activity were also noted.³⁴

The physical fitness evaluation occurred by analyzing the following 5 physical performance capacities linked to physical health:

- Manual grip strength, evaluated with dynamometry (TKK 5401, Japan). Three measurements were made in the dominant hand, using the average of the 3 for analysis.³⁵
- Balance, participants were evaluated while standing in 3 following positions and conditions maintained for 10 seconds each (support of feet side by side, semi-tandem, and tandem).
- Running speed, the number of seconds recorded that each participant took to walk 4 m.³⁶ Each participant began standing in a standing position behind a line; at the signal, they began to walk as fast as possible to the indicated 4 m line. Time stopped after crossing the line. Two meters were used more as deceleration area.
- Agility, evaluated by the "Up and Go" test, counted the time an individual took to get up from a designated chair, walk in a straight line 3 m, and sit down again. It was done twice, leaving the best evaluation to be included in the analysis.^{37,38}

- Cardiovascular health was evaluated using the 6-minute walk test (6MWT) according to the protocol established by the American Thoracic Society.^{38,39}

The category of results obtained in each of the physical health tests was evaluated either not (0 points), average (1 point), good (2 points), and optimal (3 points) according to the reference values available in the scientific literature. Definition of the general physical condition of each participant occurred by calculating the sum of the scores obtained in the 5 tests. The placement of the result was in 1 of the 3 levels of physical condition: low (1-7 points), regular (8-14 points), and optimal (15 points).

Environmental conditions. The categorization of air quality and meteorological conditions was carried out according to the records of the monitoring stations of each commune and the data was collected from the National Air Quality Information System (SINCA).⁴⁰ For air quality, PM levels were considered 2.5 and 10 and nitrogen dioxide. For exposure assessment, considering timing of occurrence of respiratory symptoms, an average of the 3 before the day of evaluation was assigned for each participant as dose of exposure to PM_{2.5}, PM₁₀, and NO₂. Prior studies using air quality data from SINCA indicate representative concentration of areas with largest potential impact on human health within the Metropolitan Region of Santiago.⁴¹ According to the environmental authority of Chile, a monitoring station with population representation, considers a representative area of the exposed population around of a circle with a radius of 2 km, counted from the location of the station. In the study area (Figure 1), we collected public databases for Pudahuel and Cerro Navia.

For meteorological conditions, humidity, temperature, and wind speed were included using the same criterion of dose assignment for each participant, corresponding to the average of the last 3 previous days.

The high exposure period was correlated with the period between July and September 2017 and PM₁₀ levels ranged from 14.3 to 294.6 µg/m³ while PM_{2.5} varied between 9.9 and 111.1 µg/m³. Temperatures ranged from 4.4°C to 23.1°C. Low exposure period correlated the period between January and March 2018. This season presented PM₁₀ levels that ranged from 11.8 to 109.8 µg/m³ and PM_{2.5} levels between 4.7 and 31.6 µg/m³. The temperatures ranged from 15.2°C in winter to 33.1°C in summer.

Statistical analyses

The characteristics of the general sample were described using means and percentages for the variables of the health

$$\begin{aligned} \text{SBP}_i &= \beta_0 + \beta_1 \text{Period}_i + \beta_2 \text{Age}_i + \beta_3 \text{Sex}_i + \beta_4 \text{Smok}_i + \beta_5 \text{Obes}_i + \beta_6 \text{HTA}_i + \beta_7 \text{PCond}_i + \varepsilon_i \\ \text{DBP}_i &= \beta_0 + \beta_1 \text{Period}_i + \beta_2 \text{Age}_i + \beta_3 \text{Sex}_i + \beta_4 \text{Smok}_i + \beta_5 \text{Obes}_i + \beta_6 \text{HTA}_i + \beta_7 \text{PCond}_i + \varepsilon_i \\ \text{logit}(\text{Resp}) &= \beta_0 + \beta_1 \text{Period} + \beta_2 \text{Age} + \beta_3 \text{Sex} + \beta_4 \text{PCond} + \beta_5 \text{Comorb} + \beta_6 \text{Smok} + \beta_7 \text{Obesi} \end{aligned}$$

Where SBP is systolic blood pressure (mmHg), DBP is diastolic blood pressure (mmHg), Resp is the presence of adverse respiratory symptoms, Period is the exposure period (High exposure and Low exposure), Smok is smoking habits (Never, Former smoker, current), Obes is obesity (BMI > 30, kg/m²), HTA is self-reported hypertension, Comorb is the presence of comorbidities (by medical diagnosis, as obesity, hypertension), and PCond is the level of physical fitness (Low, regular, optimal). The β's in the equation correspond to unknown parameters that must be estimated and are different for each of the 3 equations.

Supplemental Figures S1 and S2 presents the distribution of variables of Systolic blood pressure, Diastolic blood pressure and maximum concentration air pollutants. A correlation matrix is presented for the air pollutants variables (Supplemental Figure S3).

Participants not evaluated in the second exposure period, as well as those with the presence of respiratory disease for the lung function model, were excluded from the analysis. The significance value was $P < .05$, using SPSS v20 and Rstudio v1.4.1717 software.

Results

Sociodemographic and health characteristics

Ninety-two older adults living in communes with high levels of air pollution were evaluated. 73.9% were women (this is a pilot study, where generally female participation is always higher than male participation.), averaging 72.3 ± 5.6 years of age.

Of all the people evaluated, 46.7% had obesity and 12.1% were current smokers. The most prevalent chronic diseases

questionnaire differentiated according to sex. We compared the indicators of cardiorespiratory health, physical activity level, physical fitness, and the variables of environmental conditions between the periods. According to each type of variable, Chi-square tests or t tests were the statistical measures used for the analysis.

We analyze the change in cardiorespiratory variables in both periods of exposure. The analysis considered the level of physical condition as a covariable when performing logistic (for respiratory symptoms) and linear regression models (for blood pressure). For the logistic and linear regression models, odds ratio (OR) and beta coefficient (β) were obtained respectively, 95% confidence interval were calculated for each of them. We adjusted for the respective variables of interest, including physical condition. The proposed multivariate models are the following:

were hypertension (71.7%), followed by diabetes (32.6%), and then cardiovascular disease (23.9%). Women had two-thirds more prevalence of respiratory disease than men; however, there was no significant difference between the sexes. Only 20.7% of the participants did not present any of the indicated chronic diseases (Table 2).

Table 3 shows the characterization of the sample according to the cardiorespiratory variables, condition, and physical activity evaluated, comparing both periods of exposure. The results indicate that cardiovascular health assessed by BP between the period of high and low exposure to air pollution had a decrease of 6 mmHg ($P = .034$) for systolic BP and 4 mmHg for diastolic BP between the evaluated periods ($P = .013$).

Regarding PEF, there was a tendency to increase slightly by 13 L/min during the period of low exposure to air pollution ($P = .421$), when performing the analysis excluding participants with respiratory disease, there were no differences in the results for this variable.

For the adverse respiratory symptoms evaluated (cough and cough without having a cold and presence of wheezing), a significant decrease of 32% occurred during the low exposure period with respect to the high exposure period ($P < .001$).

Regarding the amount of physical activity performed, there were no differences between the 2 periods evaluated. Fifty nine percent of older adults met the WHO's recommendation for physical activity. Men and women showed no difference in this regard. During periods of low exposure to air pollution, low physical fitness increased by 3%. However, optimal physical fitness showed an increase of 14% during that period (Table 3).

Table 2. Demographic and health characteristics of older adults, Metropolitan Region of Santiago, Chile.

	TOTAL N=92	WOMEN N=68	MEN N=24	P-VALUE
Sex, %		73.9	26.0	
Age, years, mean, SD	72.3 ± 5.6	72.1 ± 5.7	72.9 ± 5.2	.530
Weight, kg, mean, SD	72.1 ± 13.1	70.3 ± 12.8	77.2 ± 13.0	.029*
Height, cm, mean, SD	153.8 ± 7.8	150.5 ± 5.7	162.9 ± 5.3	≤.001*
Obesity, ≥30 BMI (kg/m ²), %	46.7	51.5	33.3	.126
Waist, cm, mean, SD	102.6 ± 12.6	103.0 ± 13.6	105.4 ± 11.0	.399
Smoking				
Never, %	51.6	55.2	41.7	.259
Former smoker, %	36.3	31.3	50.0	
Current, %	12.1	13.4	8.3	
Diabetes, %	32.6	33.8	29.2	.676
Hypertension, %	71.7	70.6	75.0	.680
Respiratory diseases, %	10.9	13.2	4.2	.220
Cardiovascular diseases, %	23.9	21.9	29.2	.475
Multi-morbidity				
0 chronic disease, %	20.7	22.1	16.7	.487
1 chronic disease, %	47.8	44.1	58.3	
≥2 chronic diseases, %	31.5	33.8	25.0	
Respiratory query last months, %	5.4	5.9	4.2	.750
Cardiovascular query last months, %	6.6	7.5	4.2	.576
Hospitalization, least 3 months, %	3.3	2.9	4.2	.771

Abbreviations: BMI, Body mass index; SD, standard deviation.

*Statistically significant values, $P < .05$.

Environmental conditions

When comparing air pollution during periods of high exposure with that of low exposure, the recordings show that the values of PM₁₀, PM_{2.5}, and NO₂ decreased by 46.1, 30.5, and 20 µg/m³ respectively. Wind speed and temperature were lower during the period of high exposure (Table 4).

Multivariate analysis

We excluded 14% (n=13) participants who did not attend the second evaluation during the low exposure period (Supplemental Table S7). Linear regression models were performed to analyze changes in systolic BP and diastolic BP considering exposure to periods of high and low contamination. Different combinations of adjustment variables were

evaluated for each outcome (Supplemental Figures S4-S6). Moreover, physical activity levels were included in the analysis as a categorical variable through the variable level of physical fitness (Low, regular, optimal). Age, sex, smoking, obesity, hypertension, and were adjusted, respectively. Assumptions of normality, homoscedasticity, and independence were validated. During the high-exposure period to air pollution, the data showed an increase of 6.77 mmHg (95% CI: 1.04-12.51) for systolic BP and 3.51 mmHg (95% CI: 0.72-6.29) for diastolic BP (Figure 2).

The results of the model assessed the presence of adverse respiratory symptoms considering the high and low exposure to pollutants. We adjusted for age, sex, level of physical activity, comorbidity, smoking habit, and obesity. During the period of high exposure, the prevalence of respiratory symptoms was 4

Table 3. Cardiorespiratory and health characteristic variables by high and low exposure, Metropolitan Region of Santiago, Chile.

	HIGH EXPOSURE (N=92)	LOW EXPOSURE (N=79)	P-VALUE
Blood pressure			
Systolic blood pressure, mmHg, mean, SD	132.4 ± 18.6	126.2 ± 18.9	.034*
Diastolic blood pressure, mmHg, mean, SD	69.5 ± 10.2	65.8 ± 8	.011*
Respiratory function			
PEF. L/min. mean, SD	334.2 ± 104.8	392.5 ± 409.3	.233
Respiratory symptoms, %	48.9	17.0	<0.001*
Cough without cold, %	23.9	10.2	.015*
Phlegm without cold, %	26.1	6.8	.001*
Wheezing, %	16.3	2.3	.001*
Physical activity. GPAQ			
Moderate intensity, minutes, mean, SD	367.4 ± 754.9	203.3 ± 229.4	.054
≥150 min of moderate intensity, %	59.6	58.7	.909
Level physical fitness .028*			
Low, %	13.0	19.3	
Regular, %	63.0	43.2	
Optimal, %	23.9	37.5	

Abbreviations: PEF, peak expiratory flow; SD, standard deviation.

*Statistically significant values, $P < .05$.**Table 4.** Air pollution and environmental variables by high and low exposure, Metropolitan Region of Santiago, Chile.

	HIGH EXPOSURE		LOW EXPOSURE		P-VALUE		
	MEDIAN ± SD	95% CI	MEDIAN ± SD	95% CI			
Pollutants ($\mu\text{g}/\text{m}^3$)		Lower	Upper	Lower	Upper		
PM ₁₀	98.7 ± 30.7	92.4	105.0	52.6 ± 5.8	51.4	53.8	≤.001
PM _{2.5}	46.4 ± 13.4	43.7	49.0	15.9 ± 2.2	15.4	16.3	≤.001
NO ₂	35.4 ± 6.8	34.0	37.0	15.4 ± 2.4	15.0	15.9	≤.001
Air velocity							
Max	3.5 ± 0.5	3.4	3.6	5.0 ± 0.6	4.9	5.2	≤.001
Min	0.1 ± 0	0.1	0.1	0.2 ± 0.1	0.2	0.2	≤.001
Temperature (°C)							
Max	23.1 ± 2.2	22.6	24.0	33.1 ± 2.4	32.6	33.6	≤.001
Min	4.4 ± 2.4	3.9	5.0	15.2 ± 2.8	14.6	15.8	≤.001
Humidity (%)							
Max	96.1 ± 3.2	95.5	97.0	86.2 ± 4.7	85.2	87.2	≤.001
Min	29.1 ± 6.6	27.8	31.0	21.9 ± 7.3	20.4	23.4	≤.001

Abbreviations: CI, confidence interval; SD, standard deviation.

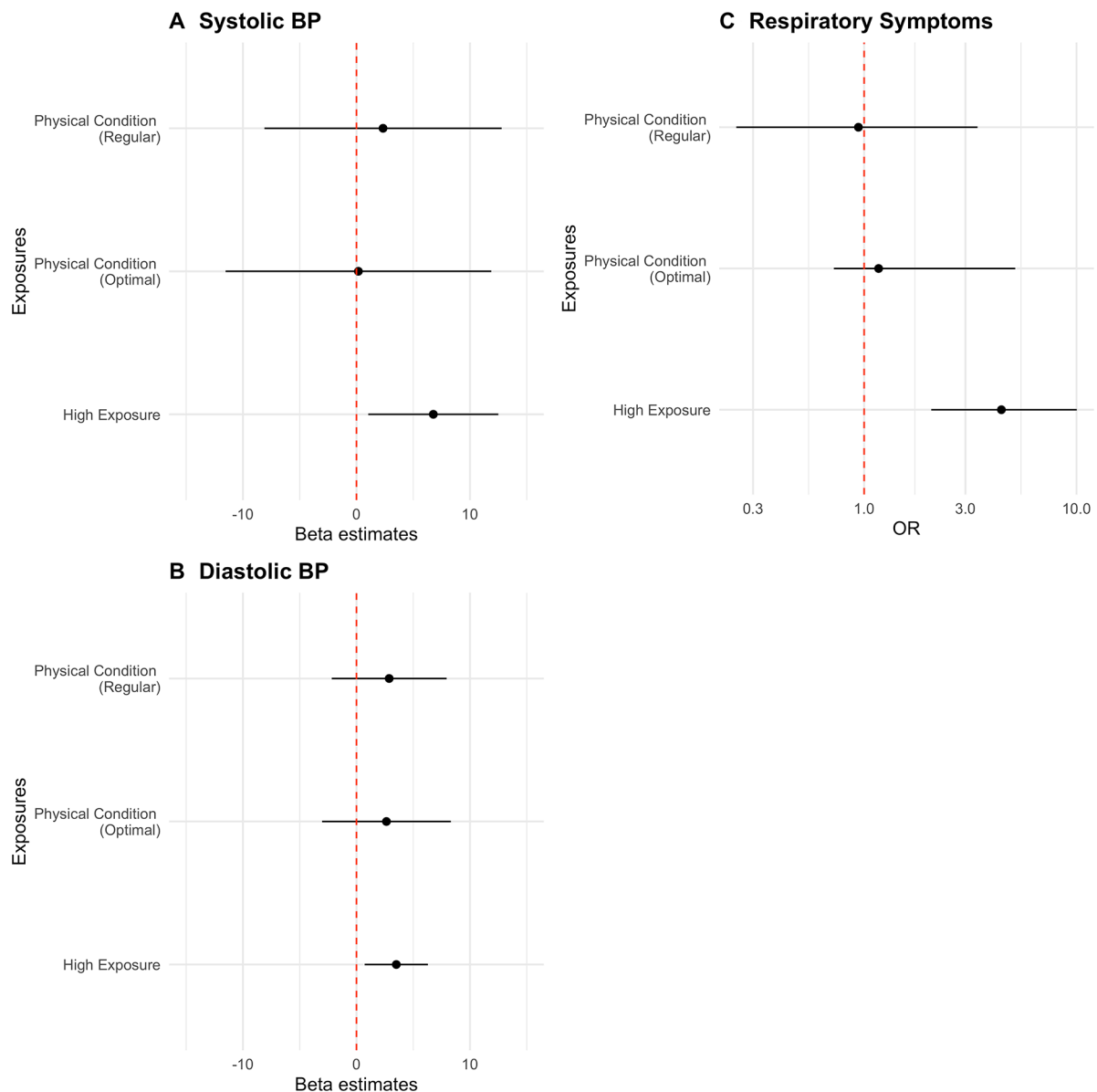


Figure 2. Associations between exposures, cardiovascular, and respiratory outcomes in multivariate models. Beta estimates for change in DBP and SBP, and self-reported respiratory symptoms are compared with the reference category low exposure (summer) and physical condition (low) for categorical variables. Multivariate models for blood pressure were adjusted for age, sex, smoking habits, obesity, and hypertension, for respiratory symptoms we add comorbidities on the adjusted model.

times higher (OR: 4.43, 95% CI: 2.07-10.04) than during the period of low air pollution. Eleven percent of the participants ($n=10$) were excluded from the analysis for declaring having any of the respiratory diseases evaluated.

We found no differences in lung function measured by the PEF between both periods and considering adjustment variables.

For more details of the adjusted models, see Supplemental Tables S1-S6.

Discussion

The findings of our study indicate that older people had an increase in BP, together with a higher prevalence of adverse

respiratory symptoms during the period of high exposure to $PM_{2.5}$ and NO_2 . Our results agree with extensive scientific evidence that points to air pollution as a factor that negatively affects cardiorespiratory variables, even at low exposure levels and that negatively affects health in the most vulnerable population such as the elderly.⁴²⁻⁴⁴

This is the first study conducted in Chile that collects information on the change in cardiorespiratory variables with respect to air pollution levels evaluated in 2 exposure periods (a period of high exposure that occurred during the winter season and a period of low exposure corresponding to the summer season), including OA. The Metropolitan Region is characterized by high levels of air pollution, and specifically

Cerro Navia and Pudahuel are 2 of the communes that reach the highest concentrations in the region, during the months of the year when the problem becomes more evident, it also has an impact on the demand for health care services.²⁷

The records obtained from the air quality and meteorology monitoring stations showed that the period of high exposure had higher levels of air pollutants, higher humidity, and lower wind speed and temperatures than in the period of low exposure. The environmental conditions together with the geographical characteristics, the abundant vehicular traffic and the economic activity favor the accumulation of particles and gases in the air of both communes, chronically exposing their inhabitants. In addition, scientific studies provide evidence about ambient PM_{2.5} concentration as a proxy of population personal exposure on air pollution, evidence show highly correlated outdoor concentrations with personal exposure, indicating that PM is an appropriate surrogate for air pollution exposure.⁴⁵⁻⁴⁷

According to CENSO 2017, more than 12% of the population of both communes are people older than 60 or more.²⁹ In Chile, 87.9% of the population over 60 years of age is in the National Health Fund, corresponding to 95.2% of the lowest-income population.⁴⁸

The III National Health Survey indicates that in the elderly population 14% have <5 comorbidities, 37% obesity, and 94% perform physical activity less than 3 times a week,⁴⁹ a combination of factors that, added to a low socioeconomic level, significantly increase health risks due to chronic exposure to pollutants such as PM and NO₂.

The data analyzed showed that a combination of high exposure given by high levels of air pollutants, humidity, and low temperatures were associated with increases in blood pressure. Such results have also been found in research conducted in the United States, Germany, Taiwan, and Canada.⁵⁰⁻⁵³ A longitudinal study that analyzed chronic exposure to PM_{2.5} in 12665 participants over 50 years of age indicates an increase of 1.04 mmHg (95% CI: 0.31-1.78) for diastolic BP and 1.30 mmHg (95% CI), 0.04 to 3.56 for systolic BP for each increase of 10 µg/m³ in PM_{2.5}. Even, the risk attributable to the increase in the prevalence of hypertension by PM_{2.5} over 25 µg/m³ has been reported in 11.6% (95% CI: 5.82%-18.53%).³⁴ Our preliminary results show an association between cardiorespiratory variables and exposure to air pollution that occurs throughout the year in the metropolitan region. Air pollution is a modifiable factor that similarly affects respiratory symptoms and BP, the latter being a risk factor for chronic diseases such as hypertension, which represents a high burden for the health system, especially in deranged communities.

Our results regarding the role of physical activity and physical condition is not conclusive. The lower the exposure, the better the physical condition and the lower the occurrence of respiratory symptoms; the same occurs with systolic blood pressure but for systolic blood pressure no clear association is observed. It is striking that the recommendation of the national authority during

periods of high contamination is usually no physical activity.⁵⁴ The objective is to avoid an excessive increase in pulmonary ventilation when performing physical exercise, which causes a greater inhalation of harmful substances and consequently more significant damage in some systems. However, some studies indicate that the practice does not harm the long-term benefits of regular physical activity in the population.¹⁹

This recommendation does not discriminate between outdoor or indoor sessions, such as family health centers, which entails a barrier to the practice of physical activity, at the risk of reaching the recommended levels as a protective factor for the health of the population. In this context, this recommendation favors sedentary activities in the elderly by reducing the opportunity to practice physical activity and increasing the risk of suffering a cardiovascular event.

In the sample analyzed, we found moderate compliance with the recommendation for physical activity (59%) despite being participants in physical activity programs within the Family Health Center and showed a slightly positive direction to be a protective effect for OA. However, the cardiorespiratory variables of interest were not significant, possibly because although they stimulate the participation of the elderly during a period of 8 to 9 months of the year, this type of activity is not offered during the months of better air quality, producing an effect contrary to the expected behavior of the variable. Based on these results, recommendations were provided to review the public programs of physical activity in older people, throughout the year. A better geographic characterization and access to urban infrastructure is needed that encourages physical activity in areas with high levels of air pollution and poverty, through international collaboration and incentives for better public funds to investigate these problems in other similar cities in Latin America.

It is not yet clear what level of exposure to particulate matter is safe for health during physical activity. It is also unclear at which intensity and duration the practice of physical activity can become harmful to health. Physical activity did not appear to be a significant variable in the model. However, we maintained that the trend was in the expected direction. It is essential to establish the optimal threshold for physical activity and its effect on exposure to particulate material regarding the risks or benefits to the health of the population.^{55,56} According to the results presented, looking for mechanisms to improve the levels of air pollution through necessary control actions, the short- and long-term cardiorespiratory health of the most vulnerable population will be better. Moreover, improvement in the exposure assignment to air pollution concentrations, will need to consider approaches that take advantage of geographic information system and geocoding study participants.⁵⁷

In this study, public air pollution data were used, routinely collected by the environmental authority. It is estimated that there could be an error in the assignment of the exposure since these data could not always capture the local variability in the

proximity of the residence of the elderly. In addition, the lack of information on daily patterns of activities of the elderly and the potential exposure due to proximity to streets and avenues with high vehicular traffic; According to the health teams, the people cared for in these health centers tend to have limited movement. Land use regression models (LUR), has been prove that can accomplish a more refined assignment of the exposure, decreasing the measurement error and improving underestimation and attenuation effect in the assessment of long-term exposure to air pollutants, and. LUR models.^{57,58} In addition, despite that elderly have a more restricted movement, air pollution can vary across time and space,^{47,59} built environment and environmental factors can play a role in the air basin of Santiago creating microenvironments of exposures, this needs to take into account in future research,^{60,61} and the quantification of the impact of the daily mobility activity patterns in air pollution exposure estimation.⁶²

Regarding the statistical analysis and lower sample size, complete case analysis utilizes only cases in the study population which no missing values on any variable, this result in a significant amount of loss information that reduce statistical power and in consequence reduces the chance of detecting of the true effect size.⁶³ A multiple imputation approach will be consider to future analysis, this methods has proven an increase in statistical power, where sample size is reduce due to missing observations on the study participants.^{64,65}

The strengths of this study are the longitudinal design and the possibility of continuing to advance the subject of study. Evaluating how the health of a vulnerable population responds to different levels of exposure to contamination during 2 different periods of the year allows one to observe significant health patterns in a region characterized as one of the most contaminated in Chile.

The weaknesses are the selection bias in the participants, low sample size, and reduced study time to perform more complex analyzes with the assignment of exposure doses to evaluate the impact on cardiorespiratory variables. Given the preliminary nature of these results, a potential bias due to sex is evident, given the predominance of people of the female sex. In addition the mixture between different exposure could contribute to the observed differences in the outcomes evaluated, however due to the limitations on the design and the lack of a more refined assessment of the exposure in this study, it is not possible to evaluate the individual impact of each of these exposure factors. Studies in development will allow us to improve these limitations.

Conclusions

Our study expands on existing scientific evidence that air pollutant is a risk factor for the health of older adults, affecting negative blood pressure and increasing adverse respiratory symptoms. These results were obtained from 2 highly polluted

communities, in a deprived social context, which could affect, the life expectancy and quality of life of OA. Future studies could apply complementary exposure assessment methods to better capture the spatial heterogeneity of PM_{2.5} and PM₁₀ in small units and increase the number of people evaluated. Furthermore, environmental health authorities could work to mitigate exposures in residential neighborhoods to reduce the negative impact on health and stimulate physical activity in the aged population. More efforts should also be made to reduce the current national air quality standards to protect the health of the elderly population in this community. Additionally, it is necessary to review public programs of physical activity in older people and promote actions that allow evaluating and improving access to healthy urban infrastructure

Acknowledgements

The research team appreciates the valuable collaboration of the Director of Health, Dr. Patricio Troncoso and Natalia Aliaga, for facilitating the dependencies of the health centers, belonging to the communes of Cerro Navia and Pudahuel, respectively, to develop the present research study. We also appreciate the collaboration of the professionals of each health center for the help given during the development of this study. We also thank each of the participants for their collaboration.

Author Contributions

Sandra Cortes: conception, funding, design, writing original draft, review, and editing. Cinthya Leiva: curation, validation, resources, and projects administration. María José Ojeda: curation and validation. Natalia Bustamante-Ara: formal analysis. Wanjiku Wambaa: writing the original draft and editing the paper. Alan Domínguez: editing paper, formal analysis, validation. Carlos Pasten Salvo, Bárbara Rojas Arenas, Camila Rodríguez Peralta, Diego. Vargas Mesa: investigation and resources. Ericka Ahumada-Padilla: investigation, curation, resource and project administration.

Data Availability Statement

Data supporting the findings of this study are available upon request from the corresponding author.

Ethics Approval

The Institutional Ethics Committee of Pontificia Universidad Católica de Chile No. 160914001 and the Metropolitan Health Service approved this study in accordance with the Declaration of Helsinki.

Consent to Participate

Study participants signed an informed consent approved by the ethics committee of Pontificia Universidad Católica de Chile and the Metropolitan Health Service, where they were authorized to carry out the study and publish the results in a scientific journal, maintaining anonymity.

Consent for Publication

All authors have read and approved the article for submission to the publication.

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Supplemental Material

Supplemental material for this article is available online.

REFERENCES

- Guarnieri M, Balmes JR. Outdoor air pollution and asthma. *Lancet*. 2014;383:1581-1592.
- Hamanaka RB, Mutlu GM. Particulate matter air pollution: effects on the cardiovascular system. *Front Endocrinol*. 2018;9:680.
- World Health Organization. *WHO Global Air Quality Guidelines: Particulate Matter (PM_{2.5} and PM₁₀), Ozone, Nitrogen Dioxide, Sulfur Dioxide and Carbon Monoxide*. World Health Organization; 2021.
- Lanphear BP. Low-level toxicity of chemicals: no acceptable levels? *PLoS Biol*. 2017;15:e2003066.
- MDMAC. Cuarto Reporte del Estado del Medio Ambiente 2018 [Environment]. Accessed de octubre 2, 2021. <https://sinia.mma.gob.cl/wp-content/uploads/2017/08/IEMA2016.pdf>
- Riojas-Rodríguez H, da Silva AS, Texcalac-Sangrador JL, Moreno-Banda GL. Air pollution management and control in Latin America and the Caribbean: implications for climate change. *Rev Panam Salud Publica*. 2016;40:150-159.
- Koutrakis P, Sax SN, Sarnat JA, et al. Analysis of PM₁₀, PM_{2.5}, and PM_{2.5-10} concentrations in Santiago, Chile, from 1989 to 2001. *J Air Waste Manag Assoc*. 2005;55:342-351.
- Gouveia N, Washington Leite Junger, ESCALA Investigators. Effects of air pollution on infant and children respiratory mortality in four large Latin-American cities. *Environ Pollut*. 2018;232:385-391.
- Romieu I, Gouveia N, Cifuentes LA, et al. Multicity study of air pollution and mortality in Latin America (the Escala study). *Res Rep Health Eff Inst*. 2012;171:5-86.
- Simoni M, Baldacci S, Maio S, Cerrai S, Sarno G, Viegi G. Adverse effects of outdoor pollution in the elderly. *J Thorac Dis*. 2015;7:34-45.
- Huang Y-CT, Al-Hegelan M. Adverse effects of outdoor air pollution. *Clin Pulm Med*. 2012;19:14-20.
- Reiner M, Niermann C, Jekauc D, Woll A. Long-term health benefits of physical activity—a systematic review of longitudinal studies. *BMC Public Health*. 2013;13:813.
- World Health Organization. *Global Action Plan on Physical Activity 2018–2030: More Active People for a Healthier World*. World Health Organization; 2018.
- Achilleos S, Kioumourtzoglou MA, Wu CD, Schwartz JD, Koutrakis P, Papatheodorou SI. Acute effects of fine particulate matter constituents on mortality: a systematic review and meta-regression analysis. *Environ Int*. 2017;109:89-100.
- Wells EM, Dearborn DG, Jackson LW. Activity change in response to bad air quality, National Health and Nutrition Examination Survey, 2007-2010. *PLoS One*. 2012;7:e50526.
- Romero H, Irrázaval F, Opazo D, Salgado M, Smith P. Climas urbanos y contaminación atmosférica en Santiago de Chile. *EURE*. 2010;36:35-62.
- Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc*. 2009;41:1510-1530.
- Tainio M, Jovanovic Andersen Z, Nieuwenhuijsen MJ, et al. Air pollution, physical activity and health: a mapping review of the evidence. *Environ Int*. 2021;147:105954.
- Andersen ZJ, de Nazelle A, Mendez MA, et al. A study of the combined effects of physical activity and air pollution on mortality in elderly urban residents: the Danish diet, cancer, and health cohort. *Environ Health Perspect*. 2015;123:557-563.
- Mutambudzi M, Chen NW, Howrey B, Garcia MA, Markides KS. Physical performance trajectories and mortality among older Mexican Americans. *J Gerontol A Biol Sci Med Sci*. 2019;74:233-239.
- Roshanravan B, Robinson-Cohen C, Patel KV, et al. Association between physical performance and all-cause mortality in CKD. *J Am Soc Nephrol*. 2013;24:822-830.
- Pavasini R, Guralnik J, Brown JC, et al. Short physical performance battery and all-cause mortality: systematic review and meta-analysis. *BMC Med*. 2016;14:215.
- Oliver TD, Ferguson BS, Laughlin MH. Molecular mechanisms for exercise training-induced changes in vascular structure and function: skeletal muscle, cardiac muscle, and the Brain. *Prog Mol Biol Transl Sci*. 2015;135:227-257.
- Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet*. 2012;380:219-229.
- Ding D, Lawson KD, Kolbe-Alexander TL, et al. The economic burden of physical inactivity: a global analysis of major non-communicable diseases. *Lancet*. 2016;388:1311-1324.
- Development SoRaa. *Territorial Structuring Methodology of Urban Communes*. 2011.
- Clements A, Herrera R, Hurn S. Network analysis: a novel approach to identify PM_{2.5} hotspots and their spatio-temporal impact on air quality in Santiago de Chile. *Air Qual Atmos Health*. 2020;13:1075-1082.
- BdCNdCLotNCo. *Reportes Estadísticos Comunes [Chile]*. 2019.
- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens*. 2018;36:1953-2041.
- Moscato G, Godnic-Cvar J, Maestrelli P, Malo JL, Sherwood Burge P, Coifman R. Statement on self-monitoring of peak expiratory flow in the investigation of occupational asthma. Subcommittee on Occupational Allergy of the European Academy of Allergology and Clinical Immunology. *Allergy*. 1995;50:711-717.
- Quanjer PH, Lebowitz MD, Gregg I, Miller MR, Pedersen OF. Peak expiratory flow: conclusions and recommendations of a working party of the European Respiratory Society. *Eur Respir J Suppl*. 1997;24:2s-8s.
- Ferreccio C, Roa JC, Bambs C, et al. Study protocol for the Maule Cohort (MAUCO) of chronic diseases, Chile 2014-2024. *BMC Public Health*. 2016;16:122.
- INDEC. *Manual del Encuestador*. Instituto Nacional de Estadística y Censos; 2009.
- World Health Organization. *Global Physical Activity Questionnaire (GPAQ) Analysis Guide*. World Health Organization; 2018.
- Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing*. 2011;40:423-429.
- Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *New Engl J Med*. 1995;332:556-561.
- Kalaphotharakos VI, Diamantopoulos K, Tokmakidis SP. Effects of resistance training and detraining on muscle strength and functional performance of older adults aged 80 to 88 years. *Aging Clin Exp Res*. 2010;22:134-140.
- Brooks D, Solway S, Gibbons WJ. AT'S statement on six-minute walk test. *Am J Respir Crit Care Med*. 2003;167:1287.
- Celedón JC, Roman J, Schraufnagel DE, Thomas A, Samet J. Respiratory health equality in the United States. The American thoracic society perspective. *Ann Am Thorac Soc*. 2014;11:473-479.
- MdMAC. Sistema Nacional de Calidad del Aire (SINCA) 2021 [Environment]. <https://sinca.mma.gob.cl> (accessed June 2018).
- González P, Domínguez A, Moraga AM. The effect of outdoor PM_{2.5} on labor absenteeism due to chronic obstructive pulmonary disease. *Int J Environ Sci Technol*. 2019;16:4775-4782.
- Strak M, Weinmayr G, Rodopoulou S, et al. Long term exposure to low level air pollution and mortality in eight European cohorts within the ELAPSE project: pooled analysis. *BMJ*. 2021;374:n1904.
- Dominici F, Schwartz J, Di Q, Braun D, Choirat C, Zanobetti A. Assessing adverse health effects of long-term exposure to low levels of ambient air pollution: phase 1. *Research Reports: Health Effects Institute*. 2019;2019:1-51.
- Thurston GD, Kipen H, Annesi-Maesano I, et al. A joint ERS/ATS policy statement: what constitutes an adverse health effect of air pollution? An analytical framework. *Eur Respir J*. 2017;49:1600419.
- Rojas-Bracho L, Suh HH, Koutrakis P. Relationships among personal, indoor, and outdoor fine and coarse particle concentrations for individuals with COPD. *J Expo Anal Environ Epidemiol*. 2000;10:294-306.
- Janssen NA, Hoek G, Harssema H, Brunekreef B. Childhood exposure to PM₁₀: relation between personal, classroom, and outdoor concentrations. *Occup Environ Med*. 1997;54:888-894.
- Nieuwenhuijsen MJ. *Exposure Assessment in Environmental Epidemiology*. Oxford University Press; 2015.
- MdDS. CASEN. Módulo Salud Gobierno de Chile [Chile]. 2011.
- MdSdC. Resultados III Encuesta de Salud (ENS) [Chile]. 2016.
- Yang BY, Qian Z, Howard SW, et al. Global association between ambient air pollution and blood pressure: a systematic review and meta-analysis. *Environ Pollut*. 2018;235:576-588.

51. Liang R, Zhang B, Zhao X, Ruan Y, Lian H, Fan Z. Effect of exposure to PM_{2.5} on blood pressure: a systematic review and meta-analysis. *J Hypertens*. 2014;32:2130–2140; discussion 2141.
52. Khosravi A, Rajabi HR, Vakhshoori M, et al. Association between ambient fine particulate matter with blood pressure levels among Iranian individuals admitted for cardiac and respiratory diseases: data from CAPACITY study. *ARYA Atheroscler*. 2020;16:178–184.
53. Lin H, Guo Y, Zheng Y, et al. Long-term effects of ambient pm_{2.5} on hypertension and blood pressure and attributable Chinese risk among older Chinese adults. *Hypertension*. 2017;69:806–812.
54. Chile. MdSd. Resolucion 9294. Prohibe funcionamiento de fuentes estacionarios durante los estados de preemergencia y emergencia ambiental. 2017.
55. Lü J, Liang L, Feng Y, Li R, Liu Y. Air pollution exposure and physical activity in China: current knowledge, public health implications, and future research needs. *Int J Environ Res Public Health*. 2015;12:14887–14897.
56. Lu F, Xu D, Cheng Y, et al. Systematic review and meta-analysis of the adverse health effects of ambient PM_{2.5} and PM₁₀ pollution in the Chinese population. *Environ Res*. 2015;136:196–204.
57. Kinnee EJ, Tripathy S, Schinasi L, et al. Geocoding error, spatial uncertainty, and implications for exposure assessment and environmental epidemiology. *Int J Environ Res Public Health*. 2020;17:5845.
58. M QC, C B, F R, et al. Development of Land-Use regression models for particulate matter due to residential wood burning in Temuco, Chile. *Environ Epidemiol*. 2019;3:320–321.
59. Medgyesi DN, Fisher JA, Cervi MM, et al. Impact of residential mobility on estimated environmental exposures in a prospective cohort of older women. *Environ Epidemiol*. 2020;4:e110.
60. Rosso AL, Auchincloss AH, Michael YL. The urban built environment and mobility in older adults: a comprehensive review. *J Aging Res*. 2011;2011: 816106.
61. Yen IH, Anderson LA. Built environment and mobility of older adults: important policy and practice efforts. *J Am Geriatr Soc*. 2012;60:951–956.
62. Yu X, Ivey C, Huang Z, et al. Quantifying the impact of daily mobility on errors in air pollution exposure estimation using mobile phone location data. *Environ Int*. 2020;141:105772.
63. Jamshidian M, Mata M. 2 - Advances in analysis of mean and covariance structure when data are incomplete. This research was supported in part by the National Science Foundation Grant DMS-0437258. In: Lee S-Y, ed. *Handbook of Latent Variable and Related Models*. North-Holland; 2007;21–44.
64. McCleary L. Using multiple imputation for analysis of incomplete data in clinical research. *Nurs Res*. 2002;51:339–343.
65. Van Buuren S. *Flexible Imputation of Missing Data*. CRC Press; 2018.