

# PM2.5 exposure on daily cardio-respiratory mortality in Lima, Peru, from 2010 to 2016.

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## Research

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# Abstract

**Background:** There have been no studies of air pollution and mortality in Lima, Peru. We evaluate whether daily environmental PM 2.5 exposure is associated to respiratory and cardiovascular mortality in Lima during 2010 to 2016. **Methods:** We analyzed 86,970 deaths from respiratory and cardiovascular diseases in Lima from 2010-2016. Estimated daily PM 2.5 was assigned based on district of residence. Poisson regression was used to estimate associations between daily district-level PM 2.5 exposures and daily counts of deaths. **Results:** An increase in 10  $\mu\text{g}/\text{m}^3$  PM 2.5 on the day before was significantly associated with daily all-cause (respiratory and circulatory) mortality (RR 1.029; CI 95% CI: 1.01 – 1.05) across all ages and in the age group over 65 (RR 1.04; 95% CI: 1.005 – 1.09) which included 74% of all deaths. We also observed associations with circulatory deaths for all age groups (RR 1.06; 95% CI: 1.01 – 1.11), and those over 65 (RR 1.06; 95% CI 1.00 - 1.12). A borderline significant trend was seen (RR 1.05; 95% CI 0.99 – 1.06;  $p = 0.10$ ) for respiratory deaths in persons aged over 65. Trends were driven by the highest quintile of exposure. **Conclusions:** PM 2.5 exposure is associated with daily all-cause, cardiovascular and respiratory mortality in Lima, especially for older people. Our data suggest that the existing limits on air pollution exposure are too high.

## Introduction

Approximately 4.2 million people are estimated to die annually from exposure to fine particles contained in polluted air [1]. Fine particulate matter (PM<sub>2.5</sub>) is considered the most harmful pollutant to human health, because it penetrates deep into the lungs [1]. Epidemiological studies conducted mainly in developing countries have associated PM<sub>2.5</sub> with all cause and cause-specific mortality [2, 3, 4, 5, 6, 7]. These studies have evaluated short-term and long-term PM<sub>2.5</sub> exposure on mortality, primarily cardiovascular and respiratory deaths [3, 4, 8], but also some kinds of cancer [9, 10, 11]. Based on epidemiological evidence, the World Health Organization (WHO) estimated that air pollution is associated with premature deaths related to ischemic heart disease, strokes, chronic obstructive pulmonary disease, acute lower respiratory infections and lung cancer [9, 2, 3, 4, 6, 7].

Lima, the capital of Peru, is one of the most polluted cities in the Latin American region [12], with annual concentrations of PM<sub>2.5</sub> ranging from 35  $\mu\text{g}/\text{m}^3$  in the east side of Lima to 16  $\mu\text{g}/\text{m}^3$  in the districts within the center of Lima. The mean value for 2015 was 26  $\mu\text{g}/\text{m}^3$  [13]. The air pollution mainly comes from vehicular emissions, although there is some contribution from industrial activity [14]. The government has implemented some regulations to reduce pollution and established safety thresholds for environmental concentrations [15]. Since then, PM<sub>2.5</sub> levels have decreased markedly in the last 20 years, but high levels of pollutant are still observed in some areas of Lima [16, 17].

Gonzales and Steenland [18], analyzed PM<sub>2.5</sub> data available from 2001 to 2010, and estimated that air pollution was responsible for 2,300 premature deaths related to cardiorespiratory disease in adults, based on relative risk data from other parts of the world. Tapia et al. [19] have shown short-term effects of PM<sub>2.5</sub>

on emergency room visits in 9 Lima hospitals from 2010-2016. However, to date there is no specific epidemiological evidence that show the effects of air pollution on mortality in Peru. In this study, we have conducted daily time-series analysis using district-specific PM<sub>2.5</sub> estimates in Lima [20] to evaluate whether daily environmental PM<sub>2.5</sub> exposure is associated to respiratory and cardiovascular mortality in Lima during 2010 to 2016.

## Methods

### *Study area:*

Lima is located on the central coast of Peru, at an average of 150 meters above sea level, covers a geographical area of 2819 Km<sup>2</sup> and a population density of 3392 inhabitants/km<sup>2</sup>. Lima has a population of 9,562,000 representing about 30% of the national population. [21]. Lima is comprised of 43 districts and divided into four zones: North Lima, Central Lima, East Lima, and South Lima. We excluded 4 districts at high altitude (all above 570 meters average altitude) due to uncertainty about the PM<sub>2.5</sub> model predictions in these districts. The uncertainty was largely driven by the fact that ground monitoring stations providing inputs to the PM<sub>2.5</sub> model were all located below 375 meters, requiring a large extrapolation to these four high districts, using the model's prediction of the altitude effect. These districts (district numbers 150106, 150107, 150109, and 150118) represented only 4% of the total population of Lima.

### *Mortality Data*

Data on daily mortality were obtained from the Ministry of Health (MoH). Variables included in this data were age, gender, district of residence, district of occurrence of death, cause of death with respective International Classification of Disease 10<sup>th</sup> revision (ICD-10). Deaths from respiratory (J00-J99) and circulatory (I00-I99) disease were considered for the study. The database included 109,951 recorded deaths from respiratory and circulatory disease, between January 2010 and December 2016. We excluded four districts (10,228 deaths) because the model may be inaccurate above 375 meters (as noted above), and also excluded some other observations because pollution on some days could not be estimated due to lack of satellite coverage (12,753 deaths) (see below); the remaining sample was 86,970.

### *Meteorological and Ambient PM<sub>2.5</sub> Data*

Ground-monitoring PM<sub>2.5</sub> data in Lima were available from March 2010 through December 2016, from ten stations from the Servicio Nacional de Meteorología e Hidrología del Perú (SENAMHI, Ministry of the Environment), and 6 stations operated from 2011-2012 by Johns Hopkins University [22]. However, these

data were not available on a daily basis during our study period, covering only about 10% of days. Hence, the ground-monitoring network was considered too sparse to adequately capture the spatiotemporal variability in PM<sub>2.5</sub> levels that occurs in Lima. Thus, we based our PM<sub>2.5</sub> exposure data from a model developed by Vu et al. [20]. Briefly, daily PM<sub>2.5</sub> concentrations at a 1 km<sup>2</sup> spatial resolution for 2010-2016 were estimated using a combination of the available ground measurements plus aerosol optical depth (AOD) data from satellites, and meteorological and land use data chemical transport models. AOD was obtained from NASA, using the MAIAC (Multi-Angle Implementation of Atmospheric Correction) algorithm. Meteorological fields (temperature, wind, and barometric pressure) were obtained from the European Centre for Medium-Range Weather Forecasts (ECMWF) and the Weather Research and Forecasting model coupled with Chemistry (WRF-Chem). A random forest model was used to regress the available ground measurements with 14 variables, including MAIAC AOD, meteorological variables from WRF-Chem and ECMWF, and land use variables. The overall cross-validation R<sup>2</sup> value (and root mean square prediction error) was 0.70 (5.97 µg/m<sup>3</sup>), comparing predicted to observed ground level data. The mean difference between ground and predicted measurements was -0.09 µg/m<sup>3</sup>. This regression model was then used to predict daily PM<sub>2.5</sub> levels for each km<sup>2</sup> grid across Lima. These estimates were then used in epidemiologic analyses, in which daily deaths were aggregated by district, and daily population-weighted average PM<sub>2.5</sub> levels were calculated for each district from the 1 km<sup>2</sup> data.

On every 16<sup>th</sup> day throughout the study period, we were unable to estimate PM<sub>2.5</sub> due to lack of satellite coverage. Furthermore, PM<sub>2.5</sub> estimates for October 15 to December 31, 2015 could not be made because the WRF-Chem model failed to estimate data within reasonable bounds for that period. Hence, we had PM<sub>2.5</sub> estimates for 2236 days (91%) out of the 2465 days during the study period. The daily weather data (temperature and relative humidity) also was provided by SENAMHI.

The protocol was approved by Ethics Review Committee of Cayetano Heredia University (SIDISI code 104102)

### *Statistical analysis:*

For each death we had the district of residence, which we used to assign PM<sub>2.5</sub> daily exposure (or a lagged exposure) to that death. Using our daily estimates of PM<sub>2.5</sub> at a 1 square km resolution, as well as estimated population in that same area, we created daily population-weighted PM<sub>2.5</sub> averages by district, which were in turn assigned to all daily deaths in that district. Daily deaths in each district were grouped for a Poisson regression analysis.

We used generalized linear models with Poisson regression to estimate associations between daily district-level PM<sub>2.5</sub> levels and daily counts of deaths for the outcomes of interest. PM<sub>2.5</sub> effects were assessed using same day (lag 0), previous day (lag 1), two day (lag 2), three days (lag 3) average PM<sub>2.5</sub>

for two (0-2), three days (0-3) as well as the prior 30 days average; lag 1 was eventually chosen based on superior fit to the data using Akaike's Information Criteria (AIC). To control for spatially varying factors and allow the analysis to be based on temporal contrasts only, the models included indicator variables for district to represent the geographical area over which deaths counts were spatially aggregated; this also controlled for spatial autocorrelation in the baseline deaths across the districts [23]. The models also included variables included for day of week, daily relative humidity, and maximum daily temperature. We compared two methods for controlling for long-term trends, either via parametric cubic splines with monthly knots, or with variables for month, year and an interaction between these variables (month\*year). The latter fit appreciably better via the AIC and was used. The continuous PM<sub>2.5</sub> variable was also categorized into quintiles: Q1st: 11.27 – 17.07 µg/m<sup>3</sup>; Q2nd: 17.08 – 18.60 µg/m<sup>3</sup>; Q3rd: µg/m<sup>3</sup> 18.61 – 20.58), Q4th: 20.59 – 25.23 µg/m<sup>3</sup>; and Q5th: 25.24 - 60.18 µg/m<sup>3</sup>. Mortality was analyzed as a whole, and also stratified by three age groups (<18, 18-64, 65 years or more). We analyzed combined respiratory and circulatory deaths, and separately, respiratory deaths (ICD10 codes J00-J45), and circulatory mortality deaths (ICD10 codes I00-I99), as well as infectious respiratory disease (IRD)(ICD10 codes 00-J06, J09-J22) and cardiovascular disease (CVD)(ICD10 codes ICD10: I20-I22, I24, I25, I46-I50, I63-I67, I70, I73-I75, I77, I79, G45). Models for several other sub-categories with fewer daily deaths did not converge. Standard errors of coefficients were adjusted for over-dispersion, which generally was very modest. Analyses were conducted using SAS v9.4 PROC GENMOD (SAS Institute Inc., Cary, NC, USA).

## Results

The final analysis included 86,970 deaths; 59 % were from respiratory causes, and 41% were from circulatory disease. The daily average was 22 deaths from respiratory disease and 15 from circulatory disease. On average, 74% of respiratory and circulatory deaths occurred in people over 65 years (Table 1).

Table 1. Descriptive characteristic of deaths, pollutant and meteorology data in Lima-Peru, during 2010 to 2016.

| Variable                               | Mean | SD   | Median | 25%  | 75%  |
|--|------|------|--------|------|------|
| Respiratory and circulatory deaths     | 37.2 | 7.29 | 37     | 32   | 42   |
| Respiratory deaths                     | 21.8 | 5.40 | 21     | 18   | 25   |
| Circulatory disease                    | 15.4 | 4.58 | 15     | 12   | 18   |
| PM <sub>2.5</sub> (µg/m <sup>3</sup> ) | 21.0 | 4.96 | 19.4   | 17.4 | 23.6 |
| Temperature max (°C)                   | 23.9 | 3.77 | 23.7   | 20.8 | 27.1 |
| Relative humidity (%)                  | 72.7 | 14.0 | 73.5   | 60.6 | 85.8 |

The daily variation of estimated PM<sub>2.5</sub> across Lima throughout the period is shown in Figure 1. An increase in PM<sub>2.5</sub> concentrations can be observed during the cold months (June-Sept). These values often exceeded the WHO air quality standards (24-hour: 25 µg/m<sup>3</sup>), but were below the national Peruvian standard (24-hour: 50 µg/m<sup>3</sup>).

The population-weighted average of PM<sub>2.5</sub> estimated for Lima, across all districts during the study period, was 21.0 µg/m<sup>3</sup>. The highest average PM<sub>2.5</sub> concentrations (29.3 ± 4.21 µg/m<sup>3</sup>) were observed in East Lima and the lowest average concentrations were found in Centre Lima (18.0 ± 1.95 µg/m<sup>3</sup>) (Table 2).

Table 2. Mean PM<sub>2.5</sub> levels by district in Lima during 2010-2016

| No.                | District        | X (µg/m <sup>3</sup> ) | SD   | No. | District                | X (µg/m <sup>3</sup> ) | SD   |
|--------------------|-----------------|------------------------|------|-----|-------------------------|------------------------|------|
| <b>North Lima</b>  |                 | 22.7                   |      |     |                         |                        |      |
| 1                  | Ancon           | 22.3                   | 2.43 | 5   | Puente Piedra           | 27.2                   | 2.93 |
| 2                  | Comas           | 27.3                   | 3.31 | 6   | San Martin de Porras    | 18.3                   | 2.19 |
| 3                  | Independencia   | 23.3                   | 2.43 | 7   | Santa Rosa              | 21.1                   | 1.98 |
| 4                  | Los Olivos      | 19.3                   | 2.30 |     |                         |                        |      |
| <b>Centre Lima</b> |                 | 18.0                   |      |     |                         |                        |      |
| 1                  | Cercado de Lima | 18.4                   | 2.13 | 9   | Miraflores              | 16.9                   | 1.58 |
| 2                  | Barranco        | 16.8                   | 1.47 | 10  | Rimac                   | 20.4                   | 2.35 |
| 3                  | Breña           | 17.6                   | 2.21 | 11  | San Borja               | 19.7                   | 2.27 |
| 4                  | Jesus María     | 16.5                   | 2.31 | 12  | San Isidro              | 17.0                   | 1.97 |
| 5                  | La Victoria     | 19.2                   | 2.25 | 13  | San Luis                | 20.3                   | 2.22 |
| 6                  | Lince           | 17.3                   | 2.25 | 14  | San Miguel              | 17.1                   | 1.31 |
| 7                  | Magdalena       | 16.4                   | 1.51 | 15  | Santiago de Surco       | 20.3                   | 1.79 |
| 8                  | Pueblo Libre    | 16.8                   | 1.68 | 16  | Surquillo               | 17.4                   | 1.93 |
| <b>South Lima</b>  |                 | 20.5                   |      |     |                         |                        |      |
| 1                  | Chorrillos      | 17.9                   | 1.25 | 7   | San Bartolo             | 21.4                   | 2.79 |
| 2                  | Lurin           | 18.6                   | 1.39 | 8   | San Juan de Miraflores  | 20.3                   | 1.88 |
| 3                  | Pachacamac      | 27.7                   | 1.55 | 9   | Santa Maria             | 18.1                   | 1.11 |
| 4                  | Pucusana        | 17.9                   | 1.03 | 10  | Villa El Salvador       | 19.4                   | 1.95 |
| 5                  | Punta Hermosa   | 19.6                   | 1.83 | 11  | Villa Maria del Triunfo | 24.7                   | 2.14 |
| 6                  | Punta Negra     | 19.8                   | 2.10 |     |                         |                        |      |
| <b>East Lima</b>   |                 | 29.3                   |      |     |                         |                        |      |
| 1                  | Ate             | 29.1                   | 4.12 | 4   | San Juan de Lurigancho  | 32.1                   | 4.92 |
| 2                  | El Agustino     | 27.4                   | 3.77 | 5   | Santa Anita             | 28.8                   | 4.87 |
| 3                  | La Molina       | 29.1                   | 3.38 |     |                         |                        |      |

Air quality guidelines PM<sub>2.5</sub>: WHO: 10 µg/m<sup>3</sup> annual mean; MINAM-Peru: 25 µg/m<sup>3</sup> annual mean.

Lag 1 PM<sub>2.5</sub> levels generally produced the best fit models, and are presented here. Tables 3-5 show the associations of daily PM<sub>2.5</sub> with combined respiratory and circulatory deaths, and separate respiratory, and circulatory disease mortality; results are presented as rate ratios (RRs) and 95% confidence intervals (CIs) calculated for 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> across all districts and years.

PM<sub>2.5</sub> was significantly positively associated with combined respiratory and circulatory deaths (RR 1.029; CI 95%: 1.005 – 1.052) and in the age group over 65 (74% of all deaths) (RR 1.048; CI 95%: 1.005 –

1.093) per 10  $\mu\text{g}/\text{m}^3$  increase of  $\text{PM}_{2.5}$  (Table 3). Other age groups did not show positive trends. Positive trends were driven by the association in the top quintile, especially for deaths over 65 (RR 1.081, CI 95% 1.014 – 1.153).

A borderline significant RR (1.048; IC 95% 0.999 – 1.098;  $p= 0.06$ ) for respiratory deaths in persons aged over 65 also observed (Table 4). We found significant positive RRs per 10  $\mu\text{g}/\text{m}^3$  of increase in  $\text{PM}_{2.5}$  for circulatory deaths for all age groups (RR 1.06; CI 95%: 1.008 – 1.011), and for the group over 65 years (RR 1.06; IC 95% 1.001 - 1.127) (Table 5). Trends were driven by the top quintile with highest concentrations. Positive associations for CVD, a subset of circulatory disease, was seen in the group over 65 years (RR: 1.10; CI 95% 1.01 – 1.22) (Table 5). We could not do detailed analyses of other specific causes as deaths were too few and models did not converge.

Table 3. Risk estimates and 95% confidence intervals (CI) for daily mortality for all cause (respiratory and circulatory deaths) for lag 1, 2010 – 2016.

| Age Group  | <i>B coefficient</i> | RR             |             | <i>p</i> |
|--|----------------------|----------------|-------------|----------|
|  |                      | <i>Exp(B)*</i> | 95% CI      |          |
| <b>Respiratory and circulatory deaths (n= 86970)</b> | 0.0029               | <b>1.029*</b>  | 1.005 1.052 | 0.012    |
| Q1st (11.27 – 17.07) <sup>a</sup>                    | 1.0                  |                |             |          |
| Q2nd (17.08 – 18.60)                                 | 0.0254               | 1.025          | 1.006 1.044 | 0.007    |
| Q3rd (18.61 – 20.58)                                 | -0.0014              | 0.998          | 0.977 1.019 | 0.90     |
| Q4th (20.59 – 25.23)                                 | 0.0129               | 1.012          | 0.987 1.038 | 0.31     |
| Q5th (25.24 – 60.18)                                 | 0.0359               | <b>1.036</b>   | 1.001 1.073 | 0.04     |
| <b>Age: 65 or more (n= 64792)</b>                    | 0.0048               | <b>1.048*</b>  | 1.005 1.093 | 0.028    |
| Q1st (11.27 – 17.07) <sup>a</sup>                    | 1.0                  | 1.0            |             |          |
| Q2nd (17.08 – 18.60)                                 | 0.0303               | 1.030          | 0.997 1.065 | 0.07     |
| Q3rd (18.61 – 20.58)                                 | 0.0228               | 1.023          | 0.985 1.061 | 0.25     |
| Q4th (20.59 – 25.23)                                 | 0.0270               | 1.027          | 0.982 1.074 | 0.24     |
| Q5th (25.24 – 60.18)                                 | 0.0788               | <b>1.081</b>   | 1.014 1.153 | 0.016    |

<sup>a</sup>Referent category. Per unit of  $\text{PM}_{2.5}$ . \*Per 10  $\mu\text{g}/\text{m}^3$   $\text{PM}_{2.5}$ . Model adjusted by day of week (dow), month, year, humidity and temperature.

Table 4. Risk estimates and 95% confidence intervals (CI) for daily respiratory mortality for lag 1, 2010 – 2016.

| Age Group                               | <i>B coefficient</i> | RR             |             | <i>P</i> |
|---|----------------------|----------------|-------------|----------|
|   |                      | <i>Exp(B)*</i> | 95% CI      |          |
| <b>All deaths respiratory (n=51306)</b> | 0.003                | 1.030*         | 0.990 1.073 | 0.15     |
| Q1st (11.27 - 17.07) <sup>a</sup>       | 1.0                  | 1.0            |             |          |
| Q2nd (17.08 - 18.60)                    | 0.0271               | 1.027          | 0.993 1.062 | 0.12     |
| Q3rd (18.61 - 20.58)                    | -0.0069              | 0.993          | 0.956 1.031 | 0.72     |
| Q4th (20.59 - 25.23)                    | -0.0012              | 0.998          | 0.954 1.044 | 0.96     |
| Q5th (25.24 - 60.18)                    | 0.0256               | 1.025          | 0.963 1.091 | 0.42     |
| <b>Age: 65 or more (38,293)</b>         |                      |                |             |          |
| Q1st (11.27 - 17.07) <sup>a</sup>       | 1.0                  | 1.0            |             |          |
| Q2nd (17.08 - 18.60)                    | 0.0246               | 1.024          | 0.986 1.064 | 0.22     |
| Q3rd (18.61 - 20.58)                    | 0.0042               | 1.004          | 0.961 1.048 | 0.85     |
| Q4th (20.59 - 25.23)                    | 0.0212               | 1.021          | 0.970 1.075 | 0.42     |
| Q5th (25.24 - 60.18)                    | 0.0515               | 1.052          | 0.979 1.131 | 0.16     |

<sup>a</sup>Referent category. Per unit of PM<sub>2.5</sub>. \*Per 10 µg/m<sup>3</sup> of PM<sub>2.5</sub>. Model adjusted by day of week (dow), month, year, humidity and temperature.

Table 5. Risk estimates and 95% confidence intervals (CI) for daily circulatory mortality for lag 1, 2010 - 2016.

| Age Group                                | <i>B</i> coefficient | RR              |             | <i>p</i> |
|--|----------------------|-----------------|-------------|----------|
|  |                      | <i>Exp(B)</i> * | 95% CI      |          |
| <b>All deaths circulatory (n= 35664)</b> | 0.0059               | <b>1.060*</b>   | 1.008 1.113 | 0.02     |
| Q1st (11.27 - 17.07) <sup>a</sup>        | 1.0                  | 1.0             |             |          |
| Q2nd (17.08 - 18.60)                     | 0.0386               | 1.039           | 0.999 1.081 | 0.054    |
| Q3rd (18.61 - 20.58)                     | 0.0074               | 1.007           | 0.963 1.053 | 0.74     |
| Q4th (20.59 - 25.23)                     | 0.0107               | 1.010           | 0.958 1.066 | 0.69     |
| Q5th (25.24 - 60.18)                     | 0.0849               | <b>1.088</b>    | 1.009 1.174 | 0.03     |
| <b>Age: 65 or more (n=26499)</b>         |                      |                 |             |          |
| Q1st (11.27 - 17.07) <sup>a</sup>        | 1.0                  | 1.0             |             |          |
| Q2nd (17.08 - 18.60)                     | 0.0414               | 1.042           | 0.996 1.089 | 0.7      |
| Q3rd (18.61 - 20.58)                     | 0.0368               | 1.037           | 0.986 1.091 | 0.15     |
| Q4th (20.59 - 25.23)                     | 0.0352               | 1.035           | 0.974 1.101 | 0.26     |
| Q5th (25.24 - 60.18)                     | <b>0.1055</b>        | <b>1.111</b>    | 1.017 1.214 | 0.02     |
| <b>CVD: all-age (32,937)</b>             |                      |                 |             |          |
| Q1st (11.27 - 17.07) <sup>a</sup>        | 1.0                  | 1.0             |             |          |
| Q2nd (17.08 - 18.60)                     | 0.0351               | 1.035           | 0.993 1.079 | 0.10     |
| Q3rd (18.61 - 20.58)                     | 0.0066               | 1.006           | 0.960 1.055 | 0.78     |
| Q4th (20.59 - 25.23)                     | 0.0194               | 1.019           | 0.963 1.079 | 0.50     |
| Q5th (25.24 - 60.18)                     | 0.0871               | <b>1.091</b>    | 1.006 1.182 | 0.03     |
| <b>CVD: age 65 or more (24,890)</b>      |                      |                 |             |          |
| Q1st (11.27 - 17.07) <sup>a</sup>        | 1.0                  | 1.0             |             |          |
| Q2nd (17.08 - 18.60)                     | 0.0376               | 1.038           | 0.990 1.088 | 0.12     |
| Q3rd (18.61 - 20.58)                     | 0.0379               | 1.039           | 0.984 1.095 | 0.16     |
| Q4th (20.59 - 25.23)                     | 0.0401               | 1.041           | 0.975 1.110 | 0.22     |
| Q5th (25.24 - 60.18)                     | 0.1015               | <b>1.106</b>    | 1.008 1.215 | 0.03     |

<sup>a</sup>Referent category. Per unit of PM<sub>2.5</sub>. \*Per 10 µg/m<sup>3</sup> of PM<sub>2.5</sub>. Model adjusted by day of week (dow), month, year, humidity and temperature.

## Discussion

In this study, we estimated PM<sub>2.5</sub> data using a satellite-driven PM<sub>2.5</sub> exposure model [20] which provided daily population-weighted average PM<sub>2.5</sub> concentrations for all districts of Lima, from 2010 to 2016. We then examined PM<sub>2.5</sub> short-term exposure in relation to all cause and cause-specific mortality in Lima, one of the most polluted cities in Latin America [12]. We observed positive associations of daily PM<sub>2.5</sub> exposure with all-cause mortality, with an increase of 1.8% per 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration, driven largely by those over 65 years of age. Our results are congruent with previous findings of statistically associations of PM<sub>2.5</sub> with combined respiratory and circulatory deaths [1, 3, 24]. In a systematic review of seven time series studies of all-cause deaths, the researchers found an increase of 1.4% per 10 µg/m<sup>3</sup> increment in PM<sub>2.5</sub> [24]. In another systematic review of 37 studies, the researchers reported a 0.9% increase in all-cause mortality per 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> [2].

For circulatory mortality, our results show an increase of 3.7% per 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  for both mortality for all ages, and 3.8% those over 65 years. We also found increased risk with CVD, a large subset of circulatory disease. Newell, in a systematic review of 91 published studies, found a 0.47% increase in cardiovascular mortality per 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  [25]. Likewise, Zhao et al observed an increased CVD mortality risk (0.68%) associated with a 10  $\mu\text{g}/\text{m}^3$  increase in  $\text{PM}_{2.5}$  [7].

For respiratory mortality, we found an association only for the elderly group, which was borderline significant. Our results showed a slight increased risk of 3% per 10  $\mu\text{g}/\text{m}^3$  increase of  $\text{PM}_{2.5}$ . One systematic review reported positive effects, with a 10  $\mu\text{g}/\text{m}^3$  increment in  $\text{PM}_{2.5}$  being associated with 1.51% (95% IC 1.01 to 2.01) in all cause respiratory mortality [24].

In our data adverse health effects were driven by high rate ratios in the 5<sup>th</sup> quintile. The exposure contrast between the 5<sup>th</sup> and 4<sup>th</sup> quintile (mean 29.2  $\mu\text{g}/\text{m}^3$  vs 22.6  $\mu\text{g}/\text{m}^3$ ) was 6.6  $\mu\text{g}/\text{m}^3$ , larger than the inter-quartile range (IQR) of 6.2  $\mu\text{g}/\text{m}^3$  for the entire population. Important exposure effects would have been lost with the use of broader categories in our categorical analyses.

Our study showed that  $\text{PM}_{2.5}$  exposure has a significant impact on the health of people in Lima, in particular among elderly people. The population structure is changing [21]; the number of individuals over 65 years is increasing.  $\text{PM}_{2.5}$  exposure along with a pre-existing condition, such as cardiometabolic disorders [26] or diabetes [27], has been shown to increase the risk of CVD deaths. Elderly people are more likely to have more of these conditions and be more vulnerable to the effects of air pollution.

Our study has several strengths. Firstly, we used a predictive model that estimated daily  $\text{PM}_{2.5}$  concentrations for 39 districts of Lima and for the entire study period, which replaced the relative scarce data from ground monitoring. Second, the allocation of  $\text{PM}_{2.5}$  concentrations to each death according to the district of residence allowed us to reduce possible exposure measurement by using district-specific  $\text{PM}_{2.5}$  estimates than using city-wide average data, thereby avoiding bias in our RR estimates. Third, we used the data of people who had habitual residence in Lima and died there. Limitations in our study included missing some exposure data (9% of days), some inaccuracy in our 1  $\text{km}^2$  exposure estimates, and our inability to assign exposure estimates at a spatial resolution smaller than the district, due to lack of exact addresses. Another limitation is our lack of data regarding occupation, which will have led to some mismeasurement of estimated air pollution exposure for person who worked outside of their district.

Our study provides evidence regarding the effects of  $\text{PM}_{2.5}$  on cardio-respiratory deaths in moderate concentrations. The local recommendations for daily  $\text{PM}_{2.5}$  established by the Peruvian Ministry of Environment, are currently 25  $\mu\text{g}/\text{m}^3$ , compared to the recommendations given by WHO, which are 10  $\mu\text{g}/\text{m}^3$ . We believe that these recommendations for air quality in Peru are likely to be too high, and probably needs to be reviewed.

## Conclusions

The results of our study show that the short-term PM<sub>2.5</sub> exposure is associated with all cause, respiratory and circulatory disease mortality, especially in the elder population. This result was observed at PM<sub>2.5</sub> concentration, which is well below the daily limit established by the Ministry of Environment (MINAM in Spanish) in Lima.

## Abbreviations

AOD: aerosol optical depth

CI: Confidence interval

CVD: cardiovascular disease

ECMWF: European Centre for Medium-Range Weather Forecasts

ICD: International Classification of Disease

IRD: infectious respiratory disease

MAIAC: Multi-Angle Implementation of Atmospheric Correction

MINAM: Ministry of the Environment

MoH: Ministry of Health

PM<sub>2.5</sub>: Fine particulate matter

SENAMHI: Servicio Nacional de Meteorología e Hidrología del Perú

WHO: World Health Organization.

WRF-Chem: Weather Research and Forecasting model coupled with Chemistry

## Declarations

**Ethics approval:** This study was approved by the ethics review board of Universidad Peruana Cayetano Heredia. SIDISI 104102

**Consent for publication:** All authors agree in the publication of the final version of this manuscript.

**Availability of supporting data:** data of this study is available upon request

**Competing interests:** The authors have no competing interests.

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**Authors' contributions:** All authors have reviewed the manuscript and consent to publication. Authors Liu and Vu were responsible for developing the exposure model; authors Tapia and Steenland were primarily responsible for data analysis and manuscript preparation; author Vasquez helped gather the mortality data; author Gonzales oversaw the overall project and helped with interpretation.

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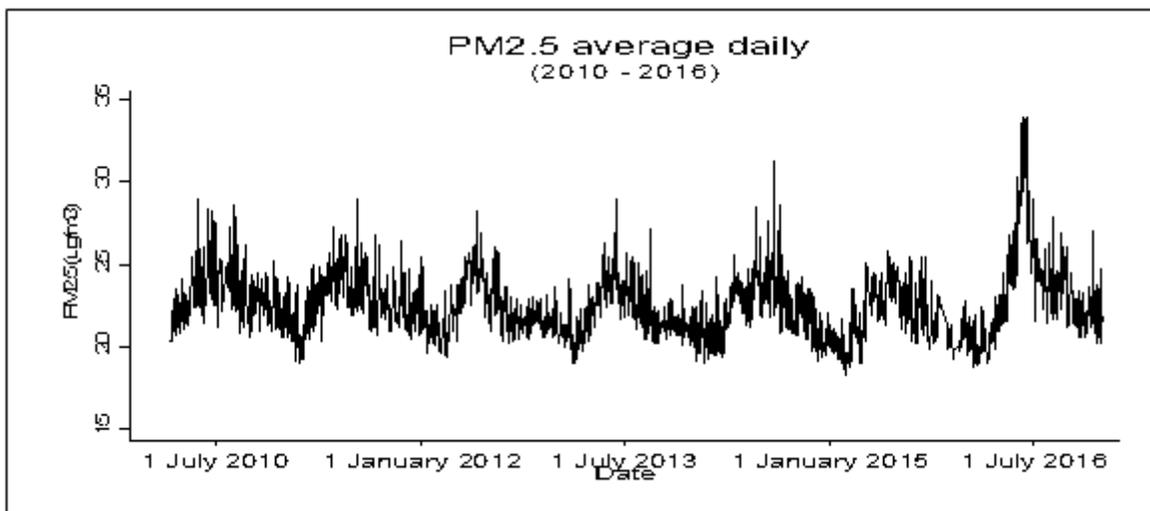
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## Figures



**Figure 1**

Daily average estimated PM2.5 in Lima, 2010 – 2016.