# Air pollutants and hospital admissions due to cardiovascular diseases in São José do Rio Preto, Brazil

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> Abstract This study aimed to estimate the effects of environmental pollutants on the increase of hospitalizations due to cardiovascular diseases. This was an ecological study conducted in the city of São José do Rio Preto, São Paulo, Brazil, with data from hospital admissions with diagnoses in the categories of I-00 to I-99, from October, 1, 2011, to September 30, 2012. Fineparticulate matter (PM, s), ozone, carbon monoxide, nitrogen oxide and nitrogen dioxide were the pollutants studied; they were estimated by CATT-BRAMs model. The use of an additive Poisson regression model showed association between exposure to PM<sub>2,5</sub> and hospital admission due to cardiovascular diseases. In the fifth day after exposure to this pollutant (lag 5), the relative risk for hospitalization due to cardiovascular diseases increased 15 percent in according to 10 µg/m³ increase on PM, 5 concentrations. There were 650 avoidable hospital admissions and an excess of R\$ 1.9 million in hospital expenses. Thus, it was possible to identify the association between exposure to PM<sub>25</sub> and hospital admission due cardiovascular diseases in medium-sized cities, like São José do Rio Preto.

> **Key words** Air pollutants, Particulate matter, Cardiovascular diseases, Hospital costs, Mathematical models

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## Introduction

In 2012, there was about 1.1 million hospitalization due to cardiovascular disease (CVD) in Brazil, which represented an expense of R\$ 2.3 billion (USD 1  $\approx$  RS \$ 2.20), being about 260,000 hospitalizations in the State of São Paulo at a cost of about R \$ 625 million¹. There are several factors associated to cardiovascular disease such as smoking, high cholesterol levels, diabetes mellitus, hypertension, family history, obesity, physical inactivity, central obesity, metabolic syndrome and alcohol ingestion. However, there are also studies that identify associations between exposure to air pollutants and such diseases²-6.

Among the air pollutants, stand out: primary pollutants, such as carbon monoxide (CO), nitrogen oxides (NOx),  $PM_{10}$  (particles with diameter of less than 10) and fractions as  $PM_{2.5}$  (particles with diameter of less than or equal to 2.5  $\mu$ M), which comprise between 60% and 70% of the particulate  $PM_{10}^{7.8}$ .

Nitrogen oxides (NOx), among they nitric oxide (NO), that under the action of sunlight becomes NO<sub>2</sub>, and nitrogen dioxide (NO<sub>2</sub>) are formed during combustion processes and vehicles usually are the main emission contributors.

The main sources of emissions of particulate matter into the atmosphere are: motor vehicles, industrial processes, biomass burning, and other<sup>9</sup>.

Secondary pollutants, which are those resulting from chemical reactions in the atmosphere, such as tropospheric ozone (O<sub>3</sub>) are the main product released in the reactions between nitrogen oxides and volatile organic compounds in the presence of sunlight.

Most published studies use data from state environmental agencies that measure air pollutants concentrations; nevertheless, there are no such agencies in all cities and in all states of Brazil and, for this, an alternative is to use estimated data by mathematical models, as Coupled Chemistry Aerosol-Tracer Transport model to the Brazilian developments on the Regional Atmospheric Modeling System (CCATT BRAMS)<sup>10-12</sup>.

This is a mathematical model that allows to perform numerical simulations of weather solving spatial phenomena of large scales and parameterizing the processes that occur at scales smaller than the spatial resolution of the model (subgrid processes). Center for Weather Forecasting and Climate Research of National Institute of Spatial Research (CPTEC/INPE) run this model in an operational way, producing daily diagnoses and forecasts for up to three days, with coverage for

all the South America. It considers the transport and the emission of several gases and aerosol particles, which is estimated from the number and location of outbreaks of fires observed by remote sensing, generating daily estimates of various air pollutants. The horizontal resolution of this operation is 25 km by 25 km, seven soil levels and 38 atmospheric levels, with the first level at 38.8 meters above the ground. Freitas et al.<sup>10</sup> validated this model and Ignotti et al.<sup>13</sup>.

This study aimed to estimate the effects of exposure to fine particles ( $PM_{2.5}$ ) in hospital admissions due to cardiovascular disease in São Jose do Rio Preto, Brazil.

#### Methods

## Place of study

São Jose do Rio Preto is a medium-sized city in southeastern Brazil, with estimated population of 450,000 inhabitants, located in the northwest of São Paulo State (about 450 km from the capital). This city is located at 49° 22' W and 20° 49' S and its area is 431.3 square kilometers. According to the Brazilian Institute of Geography and Statistics (IBGE), this city has a car fleet of 320,000 vehicles, an average annual temperature of 23.6 ° C and is an important industrial and sugar cane production center, with an output of about 500 tons in 2012<sup>14</sup>.

## Type of study

This is an ecological time series study with daily records of hospitalization due to cardiovascular disease in all age groups in hospitals under the Unified Health System (SUS) of São José do Rio Preto between 01.10.2011 and 30.09.2012.

Data on hospital admissions were according to the International Classification of Diseases (ICD-10), I-00 up to I-99 diagnostics, and the places of residence were obtained from the Ministry of Health database using the hospitalization authorizations from Unified Health System for 2011 and 2012<sup>15</sup>.

Daily concentrations of PM<sub>2.5</sub>, CO, NO, NO<sub>2</sub> and O<sub>3</sub> and climate variables such as temperature and humidity were obtained through CCATT-BRAMS model, provided by the National Institute for Space Research (CPTEC/INPE), with data every three hours<sup>12</sup>. Means values with the respective standard deviations, minimum and maximum values were calculated for each vari-

able and identified how many days the PM<sub>2.5</sub> concentrations exceeded the limits adopted by Environmental Company of São Paulo State (CETESB)<sup>16</sup>.

We used the technique of generalized additive models of Poisson regression to data analysis. The analysis of the strategy was to model the trend and seasonality of the series through splines functions of time by means of indicator variables; weather conditions by means of splines functions of temperature and relative humidity. The study period was from 10/01/2011 to 09/30/2012. Lags were adopted from zero to five days, because the effects can manifest days after of exposure, and there is no consensus on the extent of this window.

The relative risks (RR) for admissions correspond to the increase of 10 µg/m³ in the levels of PM<sub>2,5</sub>, an internationally accepted parameter.

This analysis provided the relative risk for hospitalization due to CVD, adjusted for concentrations of CO, NOx,  $O_3$ , temperature and humidity besides the seasonality and day of the week. Percentage increases in RR were obtained in according to a increase of  $10 \, \mu g/m^3$  of  $PM_{2.5}$ . Analyses were performed using Statistica version 7, and alpha = 5% was the significance level adopted in the analysis.

The impacts on the number of hospitalizations and total cost of exposure to fine particulate matter were calculated using the population attributable fraction.

## Results

There were 4,505 cases of hospitalization due to cardiovascular disease during the study period. The number of admissions per day ranged 2-27, with a mean of 12.3 hospitalizations/day (SD = 4.7). During the analyzed period, there was one day with fault on information for concentrations of O3, PM<sub>2.5</sub>, NO2, NO, CO and there was fault on information for temperature and humidity variables in 18 days.

Descriptive analyzes of the variables are presented in Table 1.

Air quality was considered good most days (PM<sub>2.5</sub> concentration of 0 to 25 $\mu$  g/m<sup>3</sup>), in 115 days the quality was moderate (concentration of PM<sub>2.5</sub>, from 25 to 50 $\mu$  g/m<sup>3</sup>) and in 1 day the air quality was considered bad (concentration of PM<sub>2.5</sub>, 50-75  $\mu$ g/m<sup>3</sup>) according to standards from CETESB<sup>16</sup>.

Table 2 presents the coefficients and standard error provided by the additive model in different lags of  $PM_{2.5}$  in São Jose do Rio Preto; it is possible to identify that exposure to this pollutant was significantly associated in lag 5, and a increase of  $10~\mu g/m^3$  in  $PM_{2.5}$  concentration implied an increased risk of hospitalization due to cardiovascular disease in 15 %.

Figure 1 shows the result of  $10 \mu g/m^3$  increase in PM<sub>25</sub> concentrations in the relative risk.

An excess of 650 admissions and an expense excess of R\$ 1.9 milion were possible to identify with this information.

## Discussion

This study used pollutant concentrations estimated by CCATT-BRAMS model and found association between exposure to PM<sub>2.5</sub> and hospitalizations due to cardiovascular diseases 5 days after this exposure.

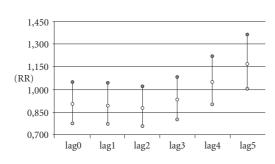
**Table 1.** Descriptive analysis of environmental pollutants and climatic variables, Sao Jose do Rio Preto, from 2011 to 2012.

Variables	Mean Value (dp)	Minimum- Maximum
O <sub>3</sub> (ppb)	36,5 (11,2)	7,5-89,8
$PM_{2.5}(\mu g/m^3)$	23,8(4,6)	13,6-57,2
NO2 (ppb)	7,1(7,2)	1,2-45,0
NO(ppb)	1,3(2,4)	0,0-27,4
CO (ppb)	226,8 (62,9)	118,7-583,6
Temperature (°C)	19,1(3,21)	7,71-26,0
Humidity (%)	71,7(15,7)	23,8-99,0

**Table 2.** Coefficients (Coef) and their standard errors (SE) obtained by Poisson regression lags 0-5 in hospitalizations for pollutant PM <sub>2.5</sub>, Sao Jose do Rio Preto from 2011 to 2012.

Lag	Coef (SE)		
Lag0	-0,0102 (0,0076)		
Lag1	-0,0111 (0,0076)		
Lag2	-0,0130 (0,0076)		
Lag3	-0,0072 (0,0077)		
Lag4	0,0046 (0,0077)		
$Lag5^*$	0,0156 (0,0077)		

<sup>\*</sup> p < 0,05



**Figure 1.** Relative risks (RR) for hospitalization due cardiovascular disease, according an increase of  $10 \mu g$  / m3 in PM<sub>2.5</sub> concentrations, São José do Rio Preto, SP, from 2011 to 2012.

In São José do Rio Preto (SP), the burning of sugarcane happens in addition to the pollutants released by vehicle fleet, which are responsible for the release of particles and gases in the environment. And, to the best of our knowledge, there are no studies on exposure to pollutants and hospitalizations in this city so far.

Studies on the subject of air pollutants produced by the burning of sugarcane straw and by the automotive fleet resulting in hospitalizations due to respiratory and cardiovascular diseases are discussed in Brazil, such as the one carried out in Araraquara<sup>3</sup>, city in the interior of São Paulo State, where an association between the weight of the sediment and the number of patients who needed inhalation therapy was found. An 10 µg increase in sediment weight was associated with a relative risk of inhalation therapy of 1.09 (1.00 to 1.19). In the most polluted days the relative risk of inhalation therapy was 1.20 (1.03-1.39). These results indicated that the burning of sugarcane plantations can cause harmful effects to the health of the exposed population.

Significant associations between exposure to particulate matter and hospitalizations due to cardiovascular diseases such as hypertension and stroke<sup>4,6</sup> were found in São José dos Campos, a city which has a considerable automobile fleet and many industrial plants located around. Another study on the same issue, carried out in Cubatão (SP), shown significant association between hospitalizations due to respiratory and cardiovascular diseases, for each increment of 10μg/m³ of PM<sub>10</sub>, with an excess of 2.29% in admissions with heart disease in person 39 years older<sup>17</sup>.

In Itabira, MG, the open pit mining of iron ore is apparently the more relevant emission source of inhalable particulate matter being that 10μg/m<sup>3</sup> increases in the concentration of this pollutant resulted, for cardiovascular disease, an acute effect that can lead to increases of over 4% (95% CI: 0.8 to 8.5) in emergency room visits on the same day of exposure to the pollutant. The effect appears to be greater for patients aged between 45 and 64 years. Compared to this study in São José do Rio Preto, it was found that for five-day lag and considering an increase of 10 µg/ m3 in the concentration of PM<sub>25</sub>, a percentage increase of 15 %, possibly by different composition of the adsorbed material in this particulate as well as the size of the particles; moreover, this pollutant is released by the vehicle fleet and the burning of the sugar cane straw, contributing differently in people.

In Finland<sup>18</sup> and in Taiwan<sup>19</sup>, particulate matter, both PM<sub>10</sub> and PM<sub>25</sub>, was associated with the occurrence of stroke. In Finland, the PM<sub>2.5</sub> was associated with death due to stroke on the same day and on the previous day (lag 0 and lag 1) of exposure, with risk between 6.5% and 8.5%18. Mean concentrations of this pollutant were around 8µg/m³, values lower than those found in San Jose do Rio Preto, but reaching maximum values of the order of 70µg/m3, higher than those found in our study. In Taiwan, the odds of hospitalization for stroke were 54% when PM<sub>10</sub> concentrations increased about 60 µg/m<sup>3</sup>. In this study, the mean values of PM<sub>10</sub> were 77.6  $\mu$ g/m<sup>3</sup>, which may equate to values between 46 g/m3 and 53 μg/m³ of PM<sub>2.5</sub>, considering that this fraction corresponds to values between 60 and 70% of PM<sub>10</sub>, being the estimated mean values of PM<sub>25</sub> well above those found in our study19.

Effects of exposure to this pollutant are also pointed out in mortality due to cardiovascular diseases such as myocardial infarction and stroke in elderly people living in the Amazon<sup>20</sup>. A study carried out in 51 metropolitan areas of the United States showed that decrease of 10 µg/m³ in PM<sub>2.5</sub> concentration was associated with an increase in average life expectancy of approximately 0.64 years, and the reduction of air pollution was responsible for up to 15% of the overall increase in life expectancy in these studied areas21. Ostro and Chestnut estimated that a reduction in PM<sub>2.5</sub> concentrations to 15 μg/m<sup>3</sup> would imply health benefits of US\$ 32 billion a year and, if concentrations fall to 12  $\mu g/m^3$ , the benefits would be in the order of US\$ 70 billion<sup>22</sup>. From the estimation of mortality attributable to particulate matter concentrations (PM<sub>10</sub>) the costs associated with this premature mortality in Brazil resulted US\$ 1.7 billion annually<sup>23</sup>.

In this study of São José do Rio Preto, hospitalization excess was approximately 650 cases representing an expense excess of R\$ 1.9 million (≈ US\$ 870,000).

Exposure to PM<sub>2.5</sub> is extremely harmful to the circulatory system and its action appears to be associated with platelet aggregation that could promote increased risk to acute thrombosis formation after exposure to the particles. The mechanisms responsible for the activation of platelets and fibrinogen levels are not yet fully elucidated, but appear to be related to the release of cytokines such as interleukins24. Another possibly associated inflammatory mediator would be C-reactive protein (CRP), a major acute phase protein with inflammatory action<sup>24</sup>. Exposure to fine particulate and ozone causes an increase in plasma endothelin that is an important vasoconstrictor associated with vascular endothelial dysfunction and adverse cardiovascular prognosis<sup>25</sup>.

This study emphasized the fine particulate material (below 2.5 µm aerodinamic diameter), which is between 60% and 70% of the particulate PM<sub>10</sub><sup>9</sup>. Although the study of air pollutants using the CCATT-BRAMS data, there may be some limitations to this study, since it was carried out using data estimated by numerical model, and not by data obtained through equipment such as Cetesb. There may also be some limitations in data collection of hospitalizations provided by Datasus, which are secondary sources for accounting purposes and misdiagnosis may occur, besides the lack of comorbidities information, but this source (Datasus) is widely used in national studies. Another possible limitation would be no discrimination based on gender because the variation in response to air pollution may be a function of both the vital stage of the exposed person or the simultaneous exposure to several factors, whether the person's hormonal status in question or other factors that could alter the response to exposure to pollutants<sup>26</sup>.

The strength of this study lies in the use of PM<sub>2.5</sub> estimated data by mathematical modelling. It is clear, therefore, that many researchers have done this study on air pollution and cardiovascular disease and, although studies show different rates of relative risk, they always conclude the association between increased relative risk and one specific pollutant.

The advantages of this study permeate about using CCATT-BRAMS model allows the study of

municipalities that do not have an environmental agency to measure air pollutants concentration, and there are few studies with this focus in medium-sized cities. However, despite the importance of this study to general health, and the results shown on the deleterious effects of exposure to pollutants, it is necessary that public authorities can create projects in healthcare that are to benefit of the population and that will reduce spending on hospital admissions for cardiovascular diseases.

Another issue is that there are few studies on the association of exposure to PM<sub>2.5</sub> pollution and some kind of disease, but most of them focused on the respiratory tract, such as studies of Ignotti et al.<sup>13</sup>, Silva et al.<sup>27</sup> and Cesar et al.<sup>28</sup>.

The study of Ignotti et al. <sup>13</sup> evaluated the effect of the daily variation in PM<sub>2.5</sub> concentrations estimated by CCATT-BRAMS model by biomass burning on the daily number of hospitalizations of children and the elderly people due to respiratory diseases in Alta Floresta and Tangará da Serra, located in Brazilian Amazon, in 2005 and they found that emissions of this pollutant increased hospitalizations due to respiratory diseases in children and the elderly.

Silva et al.<sup>27</sup> analyzed the effects of exposure to fine particles (PM<sub>2.5</sub>) from burnings on admissions for respiratory diseases in children and the elderly in Cuiaba (MT) in 2005 and evidenced the influence of this pollutant on the occurrence of hospitalizations due respiratory diseases in children under five years in the study area.

César et al.<sup>28</sup> estimated the association between exposure to fine particulate matter (PM<sub>2.5</sub>) and hospitalizations for respiratory diseases in children living in Piracicaba (SP) checking that exposure to PM<sub>2.5</sub> was associated with hospitalizations for respiratory diseases.

Therefore, this research shown the importance of study on the association to PM<sub>2.5</sub> exposure and cardiovascular disease, since there are several studies of effects on respiratory tract.

The lack of Datasus information on related diseases is a problem that researches with the same focus face, thus someone who has been hospitalized for a certain cardiovascular disease may also have other kind that led to hospitalization. The possible inaccuracy of the data is another difficulty found in studies using a mathematical model to estimate its variables; however, the concentrations calculated by the fixed stations considered in the vicinity there of, which may also present a certain inaccuracy in the data quantized by these environmental agencies measuring stations.

This study showed the concern about exposure to air pollutants, as shown in other studies, and identified the association between exposure to air pollutants and cardiovascular disease contributing to the literature in this sense, since there are few studies on the fine particulate matter in Brazil.

Given the importance of the data presented in this paper, it is necessary that managers be able to propose measures to reduce the emission of pollutants to minimize the recurrence of admissions for cardiovascular disease, as well as the best quality of life for the population, the financial cost involved in these admissions reaches considerable values.

## **Collaborations**

KCC Mantovani, LFC Nascimento, DS Moreira, LCPFS Vieira and NP Vargas participated equally of all stages of the article preparation.

#### References

- Brasil. Ministério da Saúde. DATASUS. Informações de Saúde. Epidemiológicas e morbidade. [acessado 2014 abr 08]. Disponível em: http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/nruf.def.
- Almeida IT. A poluição atmosférica por material particulado na mineração a céu aberto [dissertação]. São Paulo: Universidade de São Paulo; 1999.
- Arbex MA, Saldiva PHN, Pereira LAA, Braga ALF. Impact of outdoor biomass air pollution on hypertension hospital admissions. *J Epidemiol Community Health* 2010; 64(7):573-579.
- NascimentoLFC, Francisco, JB. Particulate matter and hospital admission due to arterial hypertension in a medium-sized Brazilian city Cad Saude Publica 2013; 29(8):1565-1571.
- Braga ALF, Pereira LAA, Procópio M, André PA, Saldiva PHN. Associação entre poluição atmosférica e doenças respiratórias e cardiovasculares na cidade de Itabira, Minas Gerais, Brasil. Cad Saude Publica 2007; 23(Supl. 4):S570-S578.
- Nascimento LFC. Air pollution and cardiovascular hospital admissions in a medium-sized city in São Paulo State, Brazil. Braz J Med Biol Res 2011; 44(7):720-724.
- Gomiscek B, Frank A, Puxbaum H, Stopper S, Preining O, Hauck H. Spatial and temporal variations of PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub> and particle number concentration during the AUPHEP—project. *Atmos Environ* 2004; 38(24):3917-3934.
- Perez P. Hemoglobina Proteína Transportadora de oxigênio. [acessado 2014 jul 22]. Disponível em: http:// www.biocristalografia.df.ibilce.unesp.br/xtal/texto\_ hb.php
- São Paulo. Companhia Ambiental do Estado de São Paulo (CESTEB). Qualidade do ar. [acessado 2014 jul 22]. Disponível em: http://www.cetesb.sp.gov.br/ar/Informa??es-B?sicas/21-Poluentes#co
- Freitas SR, Longo KM, Dias MAFS, Chatfield R, Dias PLS, Artaxo P, Andreae MO, Grell G, Rodrigues LF, Fazenda A, Panetta J. The Coupled Aerosol and Tracer Transport model to the Brazilian developments on the Regional Atmospheric Modeling System (CATT-BRAMS). Part 1: Model description and evaluation. Atmos Chem Phys Discuss 2009; 9(8):2843-2861.
- Longo KM, Freitas SR, Setzer A, Prins E, Artaxo P, Andreae M. The Coupled Aerosol and Tracer Transport model to the Brazilian developments on the Regional Atmospheric Modeling System (CATT-BRAMS). Part 2: Model sensitivity to the biomass burning inventories. Atmos. Chem. Phys. Discuss. 2010; 10(13):5785-5795.
- 12. Longo KM, Freitas SR, Pirre M, Marécal V, Rodrigues LF, Panetta J, Alonso MF, Rosário NE, Moreira DS, Gácita MS, Arteta J, Fonseca R, Stockler R, Katsurayama DM, Fazenda A, Bela M. The Chemistry CATT-BRAMS model (CCATT-BRAMS 4.5): a regional atmospheric model system for integrated air quality and weather forecasting and research. Geosci. Model Dev. 2013; 6(5):1389-1405.
- 13. Ignotti E, Valente JG, Longo KM, Freitas SR, Hacon SDS, Netto PA. Impact on human health of particulate matter emitted from burning in the Brazilian Amazon
- 14. region. Rev Saude Publica 2010; 44(1):121-130. São Paulo. Decreto Nº 59.113, de 23 de abril de 2013. Estabelece novos padrões de qualidade do ar e dá providências correlatas. Diário Oficial do Estado de São Paulo 2013; 24 abr.

- Brasil. Ministério da Saúde. DATASUS. Informações em Saúde. Brasília; 2014. [acessado 2014 abr 22]. Disponível em: http://w3.datasus.gov.br/datasus/datasus. php
- Instituto Brasileiro de Geografia e Estatística (IBGE). [acessado 2014 abr 10]. Disponível em: http://www.ibge.gov.br/home/
- NardocciAC, Freitas CU, Ponce de Leon ACM, Junger WL, Gouveia NC. Poluição do ar e doenças respiratórias e cardiovasculares: estudo de séries temporais em Cubatão, São Paulo, Brasil. Cad Saude Publica 2013; 29(9):1867-1876.
- Kettunen J, Lanki T, Tiittanen P, Pasi PA, Koskentalo T, Kulmala M, Salomaa V, Pekkanen J. Associations of fine and ultrafine particulate air pollution with stroke mortality in an area of low air pollution levels. *Stroke* 2007; 38(3):918-922.
- Tsai SS, Goggins WB, Chiu HF, Yang CY. Evidence for an Association Between Air Pollution and Daily Stroke Admissions in Kaohsiung, Taiwan. Stroke 2003; 34(11):2612-2616.
- Nunes KVR, Ignotti E, Hacon SS. Circulatory disease mortality rates in the elderly and exposure to PM2.5 generated by biomass burning in the Brazilian Amazon in 2005. Cad Saude Publica 2013; 29(3):589-598.
- Pope CA III, Ezzati M, Dockery DW. Fine-particulate air pollution and life expectancy in the United State. N Engl J Med 2009; 360(4):376-386.
- Ostro B, Chestnut L. Assessing the Health Benefits of Reducing Particulate Matter Air Pollution in the United States. *Environ Res* 1998; 76(2):94-106.
- 23. Brook RD, Barry F, Chair WC, Hong Y, Howard G, Lipsett M, Luepker R, Mittleman M, Samet J, Smith SC Jr, Tager I; Expert Panel on Population and Prevention Science of the American Heart Association. Air Pollution and Cardiovascular Disease. A Statement for Healthcare Professionals From the Expert Panel on Population and Prevention Science of the American Heart Association. Circulation 2004; 109(21):2655-2671.
- Miraglia SGK, Gouveia N. Custos da poluição atmosférica nas regiões metropolitanas brasileiras. Cien Saude Colet 2014; 19(10):4141-4147.
- Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F. Inhalation of Fine Particulate Air Pollution and Ozone Causes Acute Arterial Vasoconstriction in Healthy Adults. Circulation 2002; 105(13):1534-1536.
- Clougherty JE. A growing role for gender analysis in air pollution epidemiology. Cien Saude Colet 2011; 16(4):2221-2238.
- Silva AMC, Mattos IE, Ignotti E, Hacon SS. Material particulado originário de queimadas e doenças respiratórias. Rev Saude Publica 2013; 47(2):345-352.
- Cesar ACG, Nascimento LFC, Carvalho Júnior JA. Associação entre exposição ao material particulado e internações por doenças respiratórias em crianças. Rev Saude Publica 2013; 47(6):1209-1212.