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ORIGINAL RESEARCH PAPER

The effect of short-term of fine particles on daily respiratory emergency in cities contaminated with wood smoke

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BACKGROUND AND OBJECTIVES: The goal of this study is to evaluate in a time-series
study the short-term effects of particulate matter-2.5 exposure on respiratory emergency
visits in six central-southern Chilean cities highly contaminated by wood smoke.
METHODS: Association was assessed using both distributed lag linear and non-linear
Delegan models constrained to a 7 day lag pariad adjusting for temporal trands and

Poisson models constrained to a 7-day lag period, adjusting for temporal trends and meteorological variables and stratifying seasonally into cold and warm periods.

FINDINGS: The results showed that the daily average concentrations of particulate matter-2.5 in the cold period were 3 to 6 times those recorded in the warm period, exceeding the daily norm of $50 \ \mu g/m^3$ the 93.3% of the time *versus* 6.7%, respectively. The average daily number of respiratory emergency visits were between 30% and 64% higher in the cold period compared to the warm one. From linear models, cumulative relative risk ratios over 0-7 day lags per $10 \ \mu g/m^3$ of fine particle increase were between 1.004 (95% confidence Interval: 0.998 - 1.010) and 1.061 (95% confidence Interval: 1.049 - 1.074); these annual effects are attributable to the cold period impact where the cumulative risk ratios were between 1.008 (95% confidence Interval: 1.026 - 1.047), since significant effects of fine particles on the studied risk were not found for the warm period.

CONCLUSION: With non-linear models we observed strong increasing associations with the level of particles for the overall period. High levels of fine particles from firewood are associated with respiratory effects observable several days after exposure. Health effects found in this study suggest that current policies tending to mitigate woodsmoke-related emissions should continue and reinforce.

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INTRODUCTION

Ambient air pollution is a global health crisis. More than 9 out of 10 (91%) of the world's population is exposed to fine particulate matter at levels that exceed the health-based World Health Organization (WHO) recommended limits (Osseiran and Lindmeier, 2018). Over 100 million people in Latin America and the Caribbean (LAC) are also exposed to or live in areas with high levels of air pollution (Cifuentes et al., 2005; Green and Sánchez, 2013). The population in cities, particularly large cities, may generate intensive human social and economic activities that result in urban environmental pollution. The urbanization process is increasing in LAC, with increased motorization of the urban population and increased household combustion of solid fuels (Orellano et al., 2018). Urban air pollution is highly attributable to fossil fuel consumption; however, energy consumption efficiency and per capita emission differ among continents and countries (Lamsal et al., 2013; Mayer., 1999). The evidence shows that people with scarce resources are more exposed to environmental problems, generating problems of equity. The pollution generated in the home is also worrisome, according to the WHO, since the smoke coming from solid fuels burned in the home is one of the main risks for people living in developing countries. The use of these fuels contributes to high rates of acute and chronic respiratory diseases (Cerda and Garcia, 2010). These emissions also generate environmental impacts to surrounding populations, both for users and non-users of solid fuels, who are even willing to pay for environmental control measures or firewood certification. The combustion of biomass, especially firewood, as a source of energy for heating and cooking has occurred since records have been kept in the history of man; the book "Fire in the World" by Stephen Pyne (2014) relates "wherever human beings have lived in the vicinity of forests, the rate of combustion of firewood has increased". This occurs through forest fires, use of fire in agricultural-forest lands and the use of firewood as fuel. According to global estimates, approximately 40% of households use firewood and other biofuels for cooking and/ or heating (GEA, 2012). Several studies carried out in developed countries indicate that wood smoke is the main source of exposure to particulate matter (PM) during the colder months, from the use of residential stoves (Fairley. 1999; Maykut et al., 2003;

Naeher et al., 2007). According to FAO estimates (2010), in developing countries between 50 to 90% of the fuel used by the population for cooking or heating is firewood. In decreasing order worldwide, the continents that use firewood the most are Asia (42%), Africa (32%), America (18%) especially Latin America (FAO, 2010). It is known that, depending on the quality of the combustion, the type and characteristics of the wood used, fires can emit a series of compounds in the smoke including metals, gases (carbon monoxide, nitrogen oxides), polycyclic aromatic hydrocarbons (many carcinogenic), volatile organic compounds (aldehydes, alcohols, phenols), chlorinated compounds, free radicals, particulate matter, sulfates, endotoxins and organic constituents, many of which are very harmful to health (Naeher et al., 2007). The highest percentage of particles present (> 90%) in wood smoke are less than 2.5 microns particulate matter-2.5 (PM_{2,5}), considered together with the ultrafine particles as the most dangerous, as they penetrate deeply into the respiratory system where they can remain for months, causing damage and chemical structural changes. These are particularly dangerous because a series of highly toxic and carcinogenic compounds can be adsorbed, which would be involved in the process of cell damage and the subsequent inflammatory response in pulmonary and cardiovascular diseases, which occur in response to the exposure to air pollutants (Bergamaschi et al., 2001; Diociaiuti et al., 2001; Ghio and Cohen, 2005; Hong et al., 2010; Roemer et al., 2000; Ward and Ayres, 2004). The air pollution by particulate matter in cities of centralsouthern Chile associated largely with residential use of firewood is recognized as one of the main environmental problems (Molina et al. 2017; MMA. 2014). Several cities in the central and southern zones of Chile have been declared saturated due to particulate matter pollution $(PM_{10/25})$ in the air, since national standards are repeatedly exceeded during the year (Molina et al., 2017). The main source of air pollution in these cities is the use of firewood as heating and/or cooking fuel. The objective of this study was to estimate the short-term lag structure effect of exposure to PM2.5 on the daily number of respiratory emergency visits (REVs) in six different cities in central-southern Chile. This study has been carried out in the cities of Rancagua, Talca, Temuco, Valdivia, Osorno and Coyhaique during 2014-2017.

MATERIAL AND METHODS

Study areas

The study areas comprised six urban centers located between the central and southern zones of Chile (Fig. 1) affected by air pollution mainly from burning wood for heating homes, corresponding

to the cities of Rancagua, Talca, Osorno, Valdivia, Coyhaique and Temuco. Table 1 presents the geographic and climatic characteristics of these cities and percentage of use of firewood as source of primary energy for heating and cooking (Molina *et al.*, 2017).

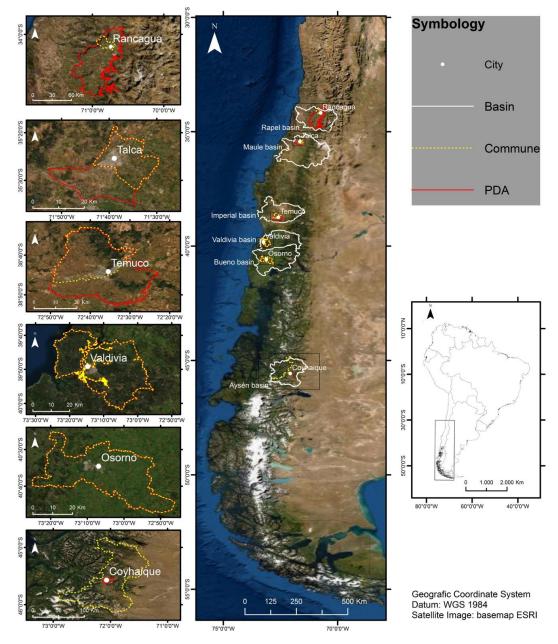


Fig. 1: Geographic location of the study areas in cities of Rancagua, Talca, Osorno, Valdivia, Coyhaique and Temuco of Chile

Respiratory emergency visit data

The daily numbers of REVs recorded between 2014 and 2017 were obtained from statistical records of the Ministry of Health of Chile (DEIS, 2019). The specific causes according to the International Classification of Diseases, ICD-10, corresponded to upper respiratory disease (J00-J06), Influenza (J09-J11), Pneumonia (J12-J18), Bronchitis/Acute bronchiolitis (J20-J21), Bronchial Obstructive Crisis (J40-J46) and other respiratory causes (J22, J30-J39, J47, J60-J98).

Air pollution and meteorological data

Air quality (PM_{2.5}) and meteorological (temperature and relative humidity) data were obtained with hourly frequency from automated monitoring stations located inside the study areas from the Chilean Ministry of Environment via the web site (Sistema Nacional de Calidad de Aire (SINCA, 2019). The daily average value of a variable was generated only if at least 16 hourly measurements were available. Otherwise, for the cities that have two stations (Rancagua, Temuco, and Coyhaique) data from the other station were used.

Statistical analyses

Descriptive position and dispersion statistics were used to summarize the data. Pearson correlation was used to explore the relationship between PM₂₅ concentrations and meteorological factors. Two time series approaches were used to estimate the effects of PM₂₅ on REVs, evaluating exposure-response relationships in both overall and seasonal terms, considering a "cold season" for the autumn-winter period (March 21 - September 21) and a "warm season" for the rest of the year. For each city and season both traditional distributed lag linear models (DLMs) and distributed lag non-linear models (DLNMs) were used to evaluate exposure-response association (Almon, 1965; Armstrong, 2006; Gasparrini et al., 2010; Peng and Dominici, 2008; Wyzga, 1978), specifying a lag lapse of 7 days in both types of analysis. In order to model the daily counts of the REVs attentions as a function of the predictive variables considering an eventual over-dispersion of data, semi-parametric generalized additive model (GAM) Poisson regressions were used. To remove seasonal and non-seasonal cyclic effects on the health variable, functions of cubic natural splines on the calendar time variable were added to all models, in addition to a term for day of the week (Peng and Dominici, 2008). The models were initially specified using a smoother for the calendar time of 7 degrees of freedom in order to remove longterm trends and seasonal effects (Dominici et al., 2004; Goldberg et al., 2011) and then explore the sensitivity of the results obtained using 6, 8 and 9 degrees of

Locations	Population	Area (Km²)	Altitude (meters)	Basin	Climate (Geiger, 1954)	Predominant wind direction	% use firewood (Molina <i>et al.,</i> 2017)
Rancagua	241,774	260	572	Middle Rapel River basin	Csb: Mediterranean warm/cool summer climate	South	57.8
Talca	220,357	232	102	Middle Maule River basin	Csb: Mediterranean warm/cool summer climate	South	64.1
Temuco	282,415	464	122	Middle basin of the Imperial River	Csb: Mediterranean warm/cool summer climate	Southwest	91.2
Valdivia	166,080	1016	14	Lower basin of the Valdivia River	Cfb (s) (i): Temperate rain with mild summer dryness and coastal influence	North - Northeast	94.6
Osorno	161,460	951	39	Middle basin of the Bueno river	Cfb (s): Temperate rain with mild summer dryness	North-northwest (NNW) and south-southeast (SSE)	96,3
Coyhaique	57,818	7,290.2	302	Middle basin of the Aysén River	Cfb: Temperate rain	WNW (West- northwest)	99.3

Table 1: Geographic characteristics of the cities studied

freedom. The potentially non-linear confounding effects of the meteorological variables were controlled in all cases using functions analogous to those used with calendar time for temperature and humidity but employing 6 and 3 degrees of freedom, respectively (Dominici *et al.*, 2000; Peng and Dominici, 2008), and then analyze the sensitivity of the effects for 5, 7 and 8 degrees of freedom in the case of temperature and 2, 4 and 5 degrees of freedom for humidity. Specifically, let Y_t^c be the total number of REVs on day *t* in the city *c*, the DLMs and DLNMs city-specific models have the general form shown in Eqs.1 and 2.

$$Y_t^c \sim Poisson(\mu_t^c) \tag{1}$$

$$\operatorname{Var}\left(Y_{t}^{c}\right) = \phi^{c} \mu_{t}^{c} \tag{2}$$

Where μ_t^c and ϕ^c are the expectation and overdispersion of Y_t^c , respectively. The DLMs and the DLNMs specific models are shown in Eqs. 3 and 4, respectively

$$\log(\mu_{t}^{c}) = \alpha + \sum_{l=0}^{7} \beta_{l}^{c} P M_{t-l}^{c} + s^{c}(t, 7x4) +$$

$$s^{c}(temp_{t}, 6) + s^{c}(hum_{t}, 3) + \eta^{c} I_{dow}$$
(3)

$$\log\left(\mu_{t}^{c}\right) = \alpha + \mathbf{B}^{cT} P M_{t,l}^{c} + s^{c} \left(t, 7x4\right) + s^{c} \left(temp_{t}, 6\right) + s^{c} \left(hum_{t}, 3\right) + \eta^{c} I_{dow}$$

$$\tag{4}$$

Eq.3 and Eq.4 approaches have a common structure sharing the use of natural cubic splines s^c (.) of the calendar time (t), temperature ($temp_t$) and humidity (hum_t) levels on day t and the term I_{dow} as an indicator function of the day of week, being η^c a vector of coefficients. In Eq.1 the terms β_l^c (l = 0, 1, 2, ..., 7) represent the lag l distributed log-relative risks of REVs for the city c, PM_{t-l}^c the lag l PM_{2.5} level on day t. In Eq.4 the object $PM_{t,l}^c$ represent a city-specific matrix obtained by the application of DLNM methodology to the observed exposures of fine particles in order to estimate the unknown parameters represented by B^cdefining the bi-dimensional shape of the relationship between the lagged and current levels of exposure and health response.

The effects of other possible confounders such as epidemics of influenza, other infectious disease epidemics, ozone pollution or other air contaminants were not controlled in this study, since this information is not available for all the areas studied and the data available is incomplete. Nevertheless, the smooth function of time is included in the models precisely to remove most of these unmeasured confounding effects (Goldberg et al., 2011; Peng and Dominici, 2008). The cumulative effect was determined up to a lag of 7 days for the linear models. DLNM-based analyses represent the relationship between the exposure and its effects in a non-linear way, accounting simultaneously for the lagged effects, generalizing the linear models of distributed lags and thus increasing significantly the flexibility in the description of the exposure-response relationship. This approach forces us to adopt a twodimensional perspective to represent non-linear associations that may change both along the level of contamination and along the temporal lags. The DLNM methodology is based on the concept of a "cross-basis" function, consisting of a two-dimensional space of available functions which allow the already mentioned specification of the potentially non-linear exposure response. Once the functions of the crossbasis are chosen, they are combined for the two dimensions chosen (PM₂₅ and its delayed effects, in our case) (Goldberg et al., 2011). For the analysis the dlnm package written by A. Gasparrini in the R Project was used for statistical computing (version 3.5.3). Cubic natural splines were used both for the exposure and the temporal lags (Ma et al., 2019), the degrees of freedom were determined for each adjustment based on the modified Akaike information criterion for models with over-dispersed response, adjusted through quasi-likelihood (Gasparrini et al., 2010). We used GraphPad Prism software to make some graphs.

RESULTS AND DISCUSSION

Descriptive analysis

Table 2 shows descriptive statistics by city for REVs, PM_{2.5}, temperature and humidity for the entire period, and stratified by cold and warm seasons. As can be seen, the daily averages of REVs were between 30% and 64% higher in the cold period compared to the warm one. The ranges of the daily count of REVs oscillated from 19 (Coyhaique) to 688 (Talca) in the cold season, versus 0 (Coyhaique) to 533 (Talca) in the warm period. Greater variability -measured by the coefficient of variation (CV)- of the daily REVs was also observed in the warm period compared to the cold for all cities. Daily average concentrations of PM_{2.5} in the cold season-warm season ratios were between 3.04 and 6.0; the four southernmost cities

			Ó	Overall period	iod					CO	Cold season (CS)	(CS)					Warm se	Warm season (WS)	(
Variables	Mean	Min	P25	Median	P75	Max	CV(%)	Mean	Min	P25	Median	P75	Max	CV(%)	Mean	Min	P25	Media n	P75	Max	CV(%)	cs/ws
REVs																						
	166,2	41	112	158	205	522	42.28	206.0	72	158.	195	236.2	522	32.31	125.8	41	06	114	155	325	37.41	1.64
Talca	276.5	72	203	268	336	688	37.19	337.7	136	274	322	385	688	25.90	214.4	72	157	205	214.	533	35.82	1.57
Temuco	135.9	31	103	135	169	329	37.32	163.1	73	133	157.5	187	329	26.29	108.2	31	70	108	138	241	39.24	1.51
Valdivia	149.8	30	101	145	189	414	41.50	179.7	56	139	172.5	212	414	31.80	119.4	30	77	110	154	286	43.08	1.50
Osorno	201.8	44	145	200	253	472	39.66	239.4	111	186	228	283	472	28.65	163.5	44	98	156	221	366	44.24	1.46
	65.49	0	43	62	83	228	49.19	74.01	19	54	68	87	221	40.02	56.90	0	30	53	76	228	57.08	1.30
PM _{2.5} (µg/m ³)	3)																					
	29.93	1.37	12.3	19.54	40.8	191.3	84.89	45.02	1.90	24.4	39.21	59.54	191.	61.26	14.66	1.37	9.69	13.00	17.4	70.15	55.46	3.07
Talca	19.09	1.00	6.00	11.60	25.7	161.2	104.1	28.64	1.42	13.2	23.63	37.83	144.	73.57	9.41	1.00	4.76	6.52	10.1	161.2	134.9	3.04
Temuco	53.21	5.00	20.9	36.00	70.3	300.3	85.46	52.02	5.00	22.6	41.52	69.52	230.	77.05	8.67	1.00	4.15	6.18	9.63	60.30	89.85	6.00
Valdivia	35.24	1.16	8.51	21.92	51.1	203.1	98.23	56.69	4.29	28.0	49.00	78.77	203.	63.70	12.97	1.64	6.06	8.71	16.0	63.67	83.19	4.37
Osorno	36.64	1.28	8.33	19.28	45.8	359	126	62.30	5.28	23.5	43.00	79.94	359.	89.28	11.93	1.28	5.23	8.23	13.8	103.7	96.98	5.22
	58.38	1.73	15.0	33.29	77.1	510.5	112.2	95.53	8.31	43.2	73.00	123.8	510.	77.10	20.66	1.73	10.1	15.11	24.0	166.6	88.04	4.62
Temperature (°C) *	* (C) *																					
	15.44	3.46	10.7	15.20	20.3	27.07	1.94	11.26	3.46	8.63	10.92	13.54	21.7	1.24	19.71	8.25	17.2	20.31	22.4	27.08	1.30	0,97
Talca	14.18	1.75	9.92	13.70	18.9	27.37	1.92	10.08	1.75	7.56	10.04	12.44	20.3	1.28	18.37	9.13	15.7	18.98	21.0	27.37	1.27	0,97
Temuco	11.60	3.00	9.70	11.53	13.6	22.00	1.00	9.85	3.00	8.32	9.91	11.30	16.6	0.79	13.08	7.20	11.7	13.17	14.4	18.31	0.68	0,99
Valdivia	12.04	0.45	9.17	11.85	15.1	24.75	1.45	9.46	0.45	7.26	9.53	11.52	19.8	1.12	14.70	5.33	12.4	14.83	16.9	24.75	1.13	0,98
Osorno	11.33	-1.15	8.33	11.26	14.2	23.04	1.42	8.76	-1.15	6.66	8.71	10.64		1.08	13.96	5.02	11.7	13.93	16.0	23.05	1.10	0,98
	8.81	-6.00	5.24	8.53	12.1	23.26	1.72	5.81	-6.00	3.40	5.65	7.92	18.6	1.31	11.93	2.17	9.18	11.70	14.4	23.26	1.35	0,98
Humidity (%	()																					
	62.86	29.2	51.9	63.00	74.6	93.25	22.78	71.95	39.7	65.0	73.44	79.85	93.2	15.07	53.60	29.2	45.1	52.96	60.4	85.42	20.84	1.34
Talca	74.16	39.4	60.6	75,08	88.2	100.0	21.16	85.77	41.7	79.8	87.75	93.00	100.	11.40	62.32	39.5	54.5	61.04	68.2	98.33	17.78	1.38
Temuco	81.50	26.6	74.2	81.66	89.5	105.0	13.33	87.74	26.6	82.9	88.33	94.17	105.	10.53	76.33	40.3	71.3	76.04	81.1	98.67	10.31	1.15
Valdivia	79.44	44.0	70.7	81.00	89.0	104.1	15.23	85.80	50.2	81.8	86.27	90.37	104.	9.37	69.63	50.6	62.5	69.42	75.9	91.69	12.25	1.23
Osorno	72.04	45.1	64.3	72.65	79.9	93.55	13.68	78.67	45.3	75.0	79.31	83.53	93.5	8.85	65.26	45.1	59.9	64.96	70.1	88.25	11.48	1.21
Oyhaique	66.98	31.48	58.78	67.02	75.50	95.75	18.00	73.90	38.70	67.18	74.38	81.08	95.75	13.19	59.63	31.49	53.00	60.12	66.50	86.00	16.62	1.24

R. Torres et al.

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(Temuco, Valdivia, Osorno and Coyhaique) were quite remarkable in this aspect. The average daily concentrations per period varied from 1.42 to 510.57 $\mu g/m^3$ in the cold season, and 1.0 to 166.64 $\mu g/m^3$ in the warm season. The average concentrations in decreasing order were Coyhaique > Osorno > Valdivia > Temuco > Rancagua > Talca, and Coyhaique > Rancagua > Valdivia > Osorno > Talca > Temuco, in the cold and warm period, respectively. The daily mean concentration of PM25 showed higher variability (CV) during the warm season (55.46% to 134.96%) compared to the cold season (61.26% to 89.28%) in all cities, with Osorno > Coyhaigue > Temuco > Talca > Valdivia > Rancagua and Talca > Osorno > Temuco > Coyhaique > Valdivia > Rancagua, for cold and warm seasons, respectively. The cold season-warm season ratio for mean temperature (°K) varied from 0.97 (Rancagua, Talca) to 0.99 (Temuco). During the cold period, the average daily temperatures were between 5.81 °C and 11.26 °C, with a range of -6.0 °C (Coyhaique) to 21.7 °C (Rancagua). The order of the urban centers latitudinally is Coyhaique < Osorno < Valdivia < Temuco < Talca < Rancagua. The temperature variability in the cold season measured by CV was Temuco < Rancagua < Valdivia < Osorno < Talca < Coyhaique. During the warm period, daily

average temperatures varied from 11.93 °C to 19.71 °C, with Coyhaique > Temuco > Osorno > Valdivia > Talca > Rancagua. The CV of temperature for this season was between 0.68% (Temuco) and 1.35% (Coyhaique). Finally, average relative humidity was in all cities higher in the cold period compared to the warm one. Valdivia, Osorno and Coyhaique recorded similar values. The average daily values in the cold period varied between 71.95% and 87.74%, in the following order Temuco > Talca > Valdivia > Osorno > Coyhaique > Rancagua. During the warm period the average daily values varied between 53.60% and 76.33%; the order was Temuco > Valdivia > Osorno > Talca > Coyhaique > Rancagua.

Fig. 2 shows the annual distribution patterns for $PM_{2.5'}$ REVs and temperature, which are for all cases markedly seasonal but more homogeneous for the cities of southern Chile, that is, Temuco, Valdivia, Osorno and Coyhaique, compared to Rancagua and Talca, where a greater dispersion is observed. The daily norm of 50 µg/m³ PM_{2.5} was exceeded in all cities especially during the cold periods; extreme values were recorded in Osorno and Coyhaique--the latter had days with daily averages greater than 400 µg/m³. During the whole study period the daily norm was exceeded in the studied cities a total of 2128 days,

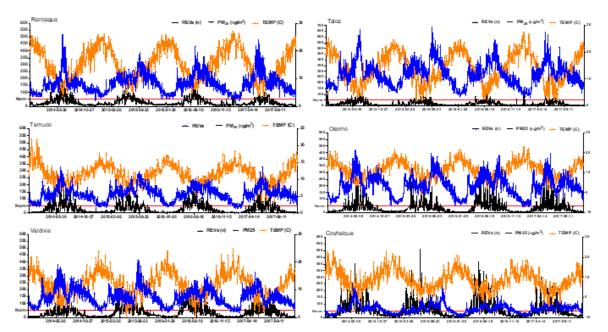


Fig. 2: Time series of PM_{2.5} (Black line), REVs (Blue line) and temperature (Orange line) by cities. Red line shows the daily norm of PM_{2.5} (50 μ g/m³)

93.3% in the cold months and 6.7% in the warm ones, 25.7% (585 days) in Coyhaique, 24.8% (528 days) in Temuco, 17.0% (362 days) in Valdivia, 14.7% (313 days) in Osorno, 12.7% (270 days) in Rancagua and 5.1% (108 days) Talca. The daily average consultations by REVs in all cities clearly present a seasonal distribution pattern similar to the behavior of PM₂. The distribution of the daily average temperatures presents an inverse pattern compared to the average daily concentrations of PM₂₅ and REVs, respectively. Table 3 shows the Pearson correlation coefficients between the REVs, the meteorological variables and the concentrations of $PM_{2.5}$ for each city. In the warm season the correlations between REVs and PM₂ and humidity were weak to moderate (-0.08 to 0.56) and (0.01 to 0.45), respectively. REVs and temperature show a clear inverse relationship with moderate correlation values (-0.46 to -0.66). The correlation between PM₂₅ and temperature was direct but almost null for Rancagua and weak for Talca. However, this relationship was moderate and inverse for the cities of Temuco, Valdivia, Osorno and Coyhaique. PM₂₅ and humidity, generally showed weak to moderate positive correlations (-0.15 to 0.42). Temperature and humidity have a clear inverse relationship with moderate to high correlations (-0.39 to -0.72).

The correlations between REVs with $PM_{2.5}$ and humidity in the cold period were positive but weak (0.07 to 0.31) and almost null (0.04 to 0.07), respectively. The correlations of REVs with temperature were inverse and weak (-0.15 to -0.31). The temperature correlations with $PM_{2.5}$ (-0.36) to -0.60) and humidity (-0.31 to -0.58) in all cities were inverse and moderate. The correlations were positive and weak (0.04 to 0.07) for humidity versus respiratory events.

Distributed lag linear model

Based on the DLM approach, for each city is shown the current day and delayed effects of the PM₂ on the risk ratios (RR) of REVs for an increase of $10 \,\mu g/m^3$ of pollutant, for the whole year and seasonstratified (the values are given in supplementary data) are presented in Fig. 3. There was a marked and positive acute effect in the entire annual cycle for each city (overall) and each lag studied in the cities of Rancagua, Talca and Valdivia; although in Osorno, Temuco and Coyhaique this positive relationship is maintained, it is less marked and the 95% confidence intervals of the cumulative lags of 0-7 day effect include the null value. Although the lag structure in the overall period has effects below 1 in some cities, most of the fitted effects are greater; cumulative effects showed a fluctuating RR between 1.004 (95% confidence Interval as CI: 0.998 -1.010) and 1.061 (95% CI: 1.049 -1.074), with Osorno being the lowest and Rancagua the highest, respectively. Stratifying the period, it can be seen that during the warm months the current and lagged effects of PM₂₅ on REVs were quite variable around the null value, with cumulative effects RR between 0.954 (95% CI: 0.910 -1.001) and 1.034 (95% CI: 1.002-1.067) with Temuco being the lowest and Osorno the highest, respectively. In contrast, for the cold period most of

Table 3: Correlations of the meteorological variables, daily average of PM_{2.5} and respiratory emergency visits for six cities in centralsouthern Chile. 2014-2017.

Climate periods	REVs-PM _{2.5}	REVs- ⁰T	REVs- RH%	PM _{2.5} -≌T	PM _{2.5} -RH%	ºT- RH%
			Warm period			
Rancagua	0.12 *	-0.57 ‡	0.32 ‡	0.01	0.09 *	-0.72 ‡
Talca	-0.08 +	-0.65 ‡	0.45 ‡	0.19 ‡	-0.15 +	-0.68 ‡
Temuco	0.38 ‡	-0.55 ‡	0.28 ‡	-0.53 ‡	0.18 ‡	-0.44 ‡
Valdivia	0.56 ‡	-0.59 ‡	0.33 ‡	-0.69 ‡	0.42 ‡	-0.51 ‡
Osorno	0.49 ‡	-0.66 ‡	0.31 ‡	-0.59 ‡	0.27 ‡	-0.46 ‡
Coyhaique	0.38 ‡	-0.46 ‡	0.01	-0.46 ‡	0.12 *	-0.39 ‡
			Cold period			
Rancagua	0.31 ‡	-0.31 ‡	0.07 +	-0.48 ‡	0.16 ‡	-0.56 ‡
Talca	0.21 ‡	-0.24 ‡	0.06	-0.50 ‡	0.29 ‡	-0.58 ‡
Temuco	0.17 ‡	-0.27 ‡	0.07	-0.60 ‡	0.27 ‡	-0.41 ‡
Valdivia	0.07	-0.15 ‡	0.06	-0.50 ‡	0.19 ‡	-0.31 ‡
Osorno	0.16 ‡	-0.24 ‡	0.04	-0.36 ‡	0.19 ‡	-0.35 ‡
Coyhaique	0.10 +	-0.17 ‡	0.06	-0.41 ‡	0.39 ‡	-0.37 ‡

REVs: Respiratory Emergency Visits; RH: Relative Humidity; PT: Temperature.; *: P<0.01; †: p<0.05; ‡: p<0.0001

Global J. Environ. Sci. Manage., 7(1): *-*, Winter 2021

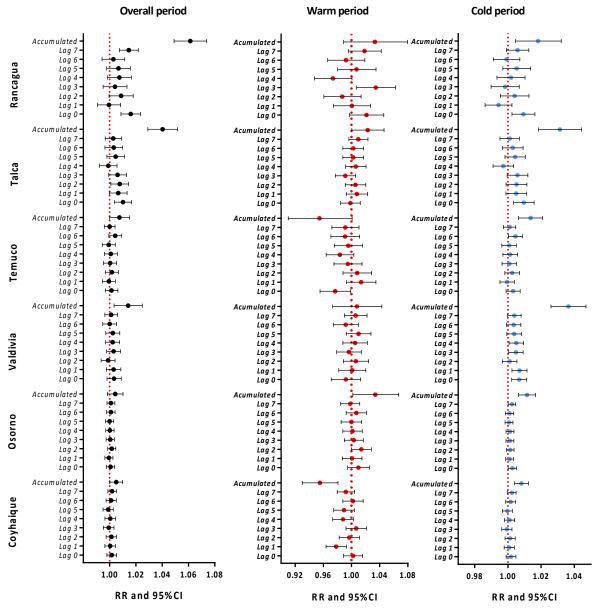


Fig. 3: Increase in the relative risk (RR) of REVs for each increase of 10 μ g/m³ of PM_{2.5}, for the overall period and stratified by cold and warm periods in each city

the lag effect structure was positive and significant, especially for Rancagua, Talca, Valdivia, and Osorno. It was not well defined for Temuco and Coyhaique, with ranges fluctuating RR between 1.008 (95% CI: 1.004 -1.012) and 1.036 (95% CI: 1.026 -1.047) with Coyhaique being the lowest and Valdivia the highest, respectively.

Distributed lag non-linear model

The following results are based on the DLNM approach, depicting associations which may vary nonlinearly with the magnitude of the pollutant in their delayed effects. Figs. 4 and 5 correspond to 3-D and contour plots, respectively, offering complementary visual summaries of the bi-dimensional association

R. Torres et al.

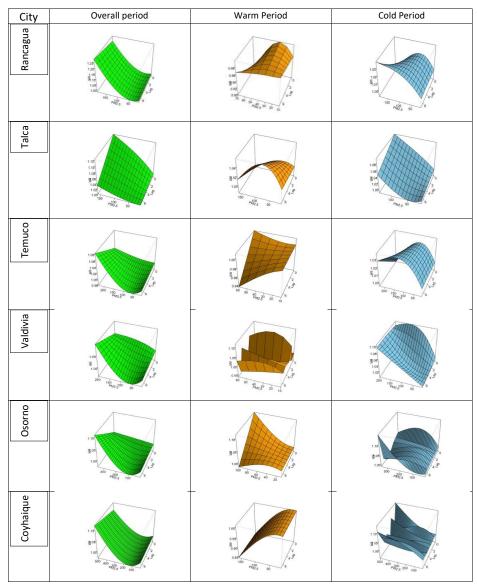


Fig. 4: Three dimensional plots of the association between PM_{2.5} concentrations and RR of REVs for overall, warm and cold periods along the 7-day lag

of the contaminant with the health outcome up to a lag period of 7 days, considering 0 μ g/m³ level as reference the. It is observed that for the overall period, the southern non-coastal cities (Temuco, Osorno and Coyhaique) present a similar risk pattern, that is, the RR increases appreciably as the PM_{2.5} concentrations rise over levels of 100, 150 and 300 μ g/m³, respectively, and their effects are maintained during the 7 days of lag studied. Talca and Valdivia showed something similar, but the health effects appear at lower levels of $PM_{2.5}$ concentration, increasing until day 4 and 5 of exposure to subsequently decrease, especially in Valdivia. In Rancagua there is a marked and growing effect (similar in structure to Coyhaique) above 100 µg/m³ during the exposure period studied. The fitted RR were more dissimilar among cities during the warm period, with clear effects observed in Talca and Osorno. For Rancagua, Temuco, Valdivia and Coyhaique, the increment in concentrations was not plainly related to an increase in the risk. However, for

Warm Period Overall period **Cold Period** City Rancagua Talca 1.02 100 60 80 100 120 200 220 500 Temuco 0.99 89.0 0.97 Valdivia Osorno 1.08 1.05 1.04 1.02 Coyhaique 2 100 120 140

Global J. Environ. Sci. Manage., 7(1): *-*, Winter 2021

Fig. 5: Contour of cumulative effects (RR) of the association between PM_{2.5} concentrations and REVs for overall, warm and cold period respectively, along 7 lags

the cold period, higher levels in PM_{2.5} concentration showed a clear association with the increment in REVs in all cities. In Rancagua, Talca and Valdivia, the RR increased significantly as the concentration of PM_{2.5} was higher in the first 3 to 4 days, remained constant for Rancagua and decreased for Talca and Valdivia. Temuco, Osorno and Coyhaique presented a similar pattern, increasing the RR as concentrations of pollutant increased, effects appearing at about 50 $\mu g/m^3$ in Temuco and Osorno, and over 100 $\mu g/m^3$ in Coyhaique.

Based on the same DLNM models, Fig. 6 shows "slices" of the effects surface accounting for associations along the pollutant extent at fixed lags of 1 day and 7 days, as well as through lags at 10 μ g/m³ and a high concentration level specific to the city and period, including 95% confidence intervals. The lag-fixed graphs for the overall period show that PM_{2.5} level is not linearly associated with REV risk, exhibiting in some cities an apparent "protective"

effect for lower pollutant levels, especially at lag 7. No evident effect in any city is observed at the 10 $\mu g/m^3$ fixed level of fine particles, except for a slight but significant effect until lag 4 days in Talca. A clear effect is observed for the city-specific high levels of pollutant, increasing along the temporal lag, except in Talca where there is a decreasing relationship. Significant effects were not observed for lag 1 and 7 in the warm season in the cities of Rancagua, Temuco, Valdivia and Osorno, but in Talca some effect is suggested at lag 7 for levels of PM₂₅ less than 100 $\mu g/m^3$ and in Coyhaique a seeming protective effect is observed, which would be reinforced along the concentration level of pollutants. The warm season graphs with low and high fixed levels of PM₂ do not indicate clear evidence of health effects of the pollutant with the exception of Talca, which showed a small effect from lag 3. However, for the cold season there is evidence of a significant and monotonically increasing effect along all the pollutant level range in Talca at lag 1 day, Valdivia at both lag 1 and 7 days and Osorno at lag 7 days from about the 220 µg/m³ level. Significant effects were observed In Temuco at lag 1 as well as lag 7 days, with maximum impacts around the 100 and 120 μ g/m³ levels, respectively. Although not-significant statistically, fixed lag plots suggest the existence of effects in Rancagua at both lag 1 day and lag 7 days, Talca at lag 7 days for high levels of exposure and Coyhaique especially at lag 7 days. Weak non-significant Although not-significant statistically effects appear for the cities of Osorno and Coyhaique at lag 1 day. The 10 μ g/m³-fixed graphs do not show clear evidence of effect for the cold season, however they suggest the existence of relatively slight effects along all the studied lag dimension at this lower level of pollutant in Rancagua and Temuco, and for lags 0-2 days in Talca and Valdivia. These graphs do not show evidence of effect at 10 μ g/m³ in Osorno and Coyhaique. For the city-specific high level of fine particles analyzed, the graphs show significant effects in Talca and Valdivia through all the lag period, and near lag 7 days for Osorno. Nevertheless, nonsignificant effects were observed in Rancagua and Temuco from lag 2 days and in Coyhaique for most of the studied period. In general, the DLNM analysis show that the lag structure of the different cities showed a positive non-linear association between PM₂₅ daily mean concentrations and the risk of REVs, which is explained mostly by the conditions

12

associated with the colder months. The lagging of the effects of $PM_{2.5}$ on the REVs in the different cities showed that there were excess risks in the first days, which for most cases remained during all the period evaluated. The concentration levels were relevant, observing effects from levels below 50 µg/m³ of $PM_{2.5}$. The most intense risks for cities were observed in most of the analyses at the highest concentrations recorded of $PM_{2.5}$. However, the risks tended to decrease from north to south, being much more marked for the cities that presented less variation in the concentration levels of $PM_{2.5}$, as was the case of Rancagua and Talca during cold months.

Sensitivity analysis

We found that the effects of fine particles on REVs were mostly quite insensitive to the smoothers for time, temperature and humidity used, for all types of analyses performed. However, Osorno and Temuco showed a slight decrease in effects for the cold season when 9 degrees of freedom were used in the time smoother, which is compatible with a possible over-adjustment of data when smoothers with higher degrees of freedom are used (Goldberg *et al.*, 2011).

Results in context

There are few studies describing the impact of wood smoke on the change in the number of respiratoryrelated emergency visits using time series analysis in the literature reviewed. Most of these have focused on children and adults in cities with air pollution problems related to the use of firewood for residential heating. The most studied respiratory diseases have been asthmatic problems and chronic respiratory diseases, among others, with relative risks ranging between RR (1.01 to 1.12) for every 3 to 12 μ g/m³ of PM₂₅ increase (Koenig et al., 1993; Schreuder et al., 2006; Norris et al., 1999; Sheppard et al., 1999; Yu et al., 2000). These RR values are in accordance with those reported in the present study. In line with our results, Yañez et al., (2017) studied in the cold season between 2014 and 2016 the impact of the meteorological conditions on the concentration of fine and coarse (PM₁₀ -PM₂₅) particles in cities of central-southern Chile, finding great variation among cities with a marked latitudinal pattern, where the northern cities have lower levels of PM₂₅ and higher levels of coarse particles; relative humidity is one of the variables that would explain this difference. The lag period considered varies widely in studies similar to

Global J. Environ. Sci. Manage., 7(1): *-*, Winter 2021

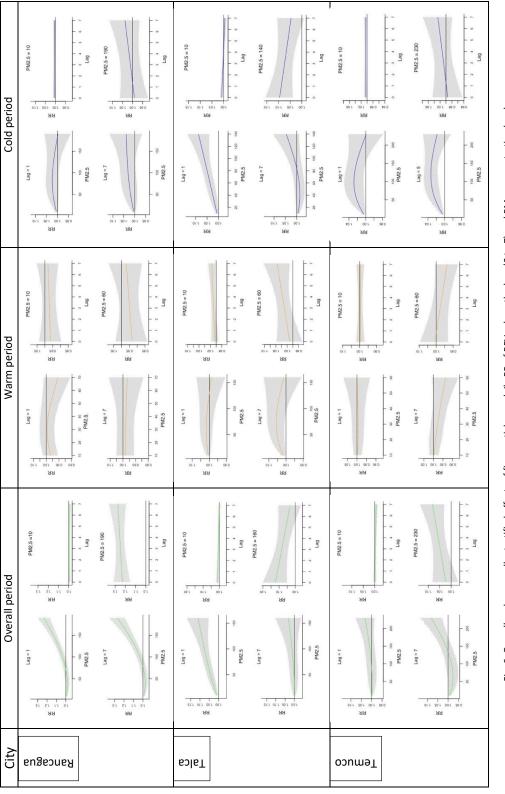
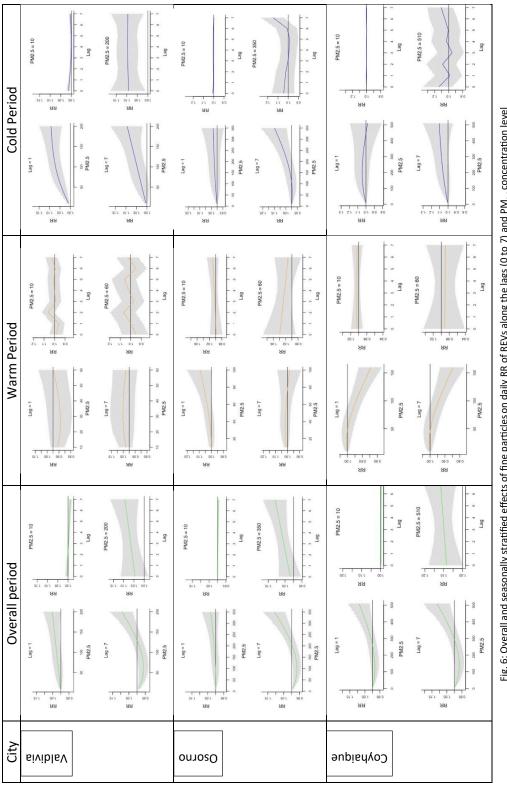


Fig. 6: Overall and seasonally stratified effects of fine particles on daily RR of REVs along the lags (0 to 7) and PM_{2.5} concentration level

R. Torres et al.





ours, with ranges from 0 to 30 days prior to the outcome variable. The respiratory emergency visits in our study include a number of diseases of the lower and upper tract of the respiratory system. Several studies on the Chilean population have reported greater risk in terms of morbidity and mortality related to respiratory and cardiovascular causes due to exposure to PM₁₀ and PM_{2.5} (Astudillo et al., 2007; Cifuentes et al., 2000; Ilabaca et al., 1999; Ostro et al., 1996; Ostro et al., 1999; Pino et al., 1998; Pino et al., 2004; Prieto et al., 2006; Roman et al., 2004; Sanhueza et al., 1999). Villalobos et al., (2017) studied the composition of PM₂₅ in the city of Temuco, specifically organic carbon (CO), using molecular markers that identify sources of origin, reporting that 84.6% of PM_{2,5} is smoke of wood burned by inefficient heating appliances. Jorquera et al., (2018) measured indoor air quality in 63 houses in the urban area of the same city during the year 2014, determining that 86% of indoor PM₂₅ comes from outside by infiltration. Controlled wood smoke exposure studies in humans have not been reported. However, animal wood smoke toxicology studies have been carried out. Zelikoff et al., (2002) summarized the toxicology relative to wood smoke, focusing on animal exposure but covering in part the issue from a human perspective. They concluded that the inhalation of combustion products coming from wood probably has a significant effect on pulmonary homeostasis in the exacerbation of ongoing disease processes. Wood smoke interferes with the normal development of the lungs of infants and children, increasing the risk of lower respiratory infections such as bronchitis and pneumonia (Naeher et al., 2007). Exposure to smoke can depress the immune system and damage the lung epithelial tissue responsible for protecting and cleaning the airways (Zelikoff et al., 2002). A higher frequency of coughs, headaches and eye and throat irritations is described in healthy people. Wood smoke is particularly harmful In vulnerable populations with asthma, chronic respiratory diseases and with cardiovascular disease; even short exposures can be very harmful (Guarnieri Bede-Ojimadu and Orisakwe and Balmes, 2014). (2020), in a systematic review in developing countries in Sub-Saharan Africa concludes that there is high level of exposure to wood smoke and this exposure is associated with a number of adverse health effects. On the other hand, an increase in the risk of cardiovascular events such as heart attacks and arrhythmias has been reported. Cardiopathic people may experience chest pain, palpitations, shortness of breath, fatigue and cardiovascular accidents. Exposure to wood smoke sharply exacerbates the respiratory symptoms of chronic diseases such as chronic obstructive pulmonary disease and bronchial asthma, leading to an increase in hospital admissions (Mott *et al.*, 2005; Xu *et al.*, 2008).

CONCLUSION

In the present study we evaluated the effect of PM₂₅ exposure on the relative risk (RR) of REVs in urban populations of six cities whose main source of air pollution is the use of firewood for heating and cooking, especially during the cold months. We found that during the cold months, the daily norm for PM_{3z} (50 μ g/m³) was exceeded over 90% of the time, more frequently in the southernmost cities (Valdivia, Temuco, Osorno and Coyhaique), which implies that at least 1,200,000 inhabitants are chronically exposed to harmful levels of PM₂₅ in these areas. In contrast, during the warm period the norm was only exceeded 7% of the time. The average 24-hour concentration of PM, , , during the study period, was between 3 to 6 times higher in cold months compared to warm months, reaching levels as high as 510.57 μ g/m³ in the city of Coyhaigue. The number of REVs in the cold period were on average 30% to 64% higher compared to the warm period. We found a clear non-linear, short-term positive association between the PM_{2, E} level and the number of REVs and this effect varied in size by city. These effects are especially strong in the colder months and at high levels of PM₂; they were observed during the 7-day lag period considered. On the other hand, we observed that cumulative effects of PM₂ distributed over seven days were significantly greater than the effect size reported for everyday lag in all cities, indicating clearly the delayed effects of air pollution on REVs. The average concentration of fine particles increases with the latitude of the studied area and with it the associated relative risks, in line with the above result found for individual cities. The results agree with previous analogous research and have a consistent biomedical explanation. The important differences found between the warm and cold seasons indicate the importance of performing this type of stratification suggesting the need for even more detailed seasonal analyzes in future research. This study shows clear acute harmful effects on the respiratory health of the population affected by pollution from wood smoke in the cities studied. Existing mitigation programs aimed at reducing exposure to PM should continue and be strengthened.

AUTHOR CONTRIBUTIONS

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. R. Torres, N. Baker and G. Bernal formulated the study goals and aims, data collection and statistical processing; A. Maldonado elaborated the maps and figures presented in this study; F. Peres, R. Torres and D. Cáceres analyzed the study data, made the interpretation and wrote the manuscript.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest regarding the publication of this work. In addition, the ethical issues including plagiarism, informed consent, misconduct, data fabrication and, or falsification, double publication and, or submission, and redundancy have been completely witnessed by the authors.

ABBREVIATIONS

%	Percentage
<	Less than
=	Equal
>	Greater than
>=	Greater than or equal to
3 D	Three Dimensional
°C	Degrees Celsius
° K	Degrees Kelvin
CI	Confidence Interval

CS	Cold Season
CV(%)	Coefficient of Variation
DLM	Distributed Lag Linear Models
DLNM	Distributed Lag Non-Linear Models
et al.	"and others" in latin
FAO	Food and Agriculture Organization of the United Nations
Fig.	Figure
GAM	Generalized Additive Models
GraphPad Prism	Scientific 2D graphing and statistics software
GEA	Global Energy Assessment
h	Hour
Km ²	Square kilometers
LAC	Latin America and the Caribbean
MMA	Ministry of the Enviromment
Ν	North
P<0.05	Probability that the null hypothesis is rejected
P25	25th percentile
P75	75th percentile
PM _{2.5}	Particulate Matter less than 2.5 microns in diameter
PM ₁₀	Particulate Matter less than 10 microns in diameter
RR	Relative Risk
RH	Relative Humidity
REVs	Respiratory Emergency Visits
SD	Standard Deviation
SINCA	National System of Air Quality
R	The R Project for Statistical Computing
₽Ţ	Temperature
μg/m³	Micrograms per cubic meter
U.S.	United States
USEPA	United States Environmental Protection Agency
W	West
WHO	World Health Organization
У	Year

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