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Short-term influence of environmental factors and social variables COVID-19 disease in Spain during first wave (Feb–May 2020)

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Abstract

This study aims to identify the combined role of environmental pollutants and atmospheric variables at short term on the rate of incidence (TIC) and on the hospital admission rate (TIHC) due to COVID-19 disease in Spain. This study used information from 41 of the 52 provinces of Spain (from Feb. 1, 2021 to May 31, 2021). Using TIC and TIHC as dependent variables, and average daily concentrations of PM₁₀ and NO₂ as independent variables. Meteorological variables included maximum daily temperature (Tmax) and average daily absolute humidity (HA). Generalized linear models (GLM) with Poisson link were carried out for each provinces. The GLM model controlled for trend, seasonalities, and the autoregressive character of the series. Days with lags were established. The relative risk (RR) was calculated by increases of 10 µg/m³ in PM₁₀ and NO₂ and by 1 °C in the case of Tmax and 1 g/m³ in the case of HA. Later, a linear regression was carried out that included the social determinants of health. Statistically significant associations were found between PM₁₀, NO₂, and the rate of COVID-19 incidence. NO₂ was the variable that showed greater association, both for TIC as well as for TIHC in the majority of provinces. Temperature and HA do not seem to have played an important role. The geographic distribution of RR in the studied provinces was very much heterogeneous. Some of the health determinants considered, including income per capita, presence of airports, average number of diesel cars per inhabitant, average number of nursing personnel, and homes under 30 m² could explain the differential geographic behavior. As findings indicates, environmental factors only could modulate the incidence and severity of COVID-19. Moreover, the social determinants and public health measures could explain some patterns of geographically distribution founded.

Keywords Environmental pollutants · COVID-19 · Meteorological factors · Health determinants

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Introduction

On March 11, 2020, the World Health Organization (WHO) declared a state of pandemic caused by COVID-19 (Cucinotta and Vanelli 2020). After the declaration of the state of emergency in Spain (March 14, 2020), the pandemic became the most important scientific issue around the world. Different lines of research have been established, including the origins of the virus (*WHO- Convened Global Study of Origins of SARS-CoV-2*, s. f.; Tang et al. 2020), its transmission mechanisms and treatments (Lotfi et al. 2020—*COVID-19 Transmission, prevention, and potential .pdf*, s. f.). Other lines of research have been focused on factors that could increase the transmission (Tello-Leal and Macías-Hernández 2021) and severity of infection due to COVID-19 (Jiang et al. 2020; Linares et al. 2021; Díaz et al. 2021).

Air pollution and its relationship to COVID-19 is an important area of research, and there has been study of the association between air pollutants such as PM₁₀ and NO₂. Some authors have shown that SARS-CoV-2 can attach itself to environmental pollutants such as particulate matter (PM) (Srivastava 2021). In prior studies, PM pollution has been related to infections such as severe acute respiratory syndrome (SARS) (Cui et al. 2003). Some papers reveal that the number of infected people was higher in Italian cities that exceeded the limit established for PM₁₀ and for ozone (Coccia 2021a). It was suggested that pollution could operate as a determining factor for the spread of COVID-19 in society (Coccia 2020a). There has even been investigation of a possible relationship between Saharan dust and the severity of COVID-19 (Linares et al. 2021). Another study showed that 78% of studied regions in Spain, Italy, France, and Germany had both a greater number of cases of mortality due to COVID-19 and higher concentrations of NO₂ (Ogen 2020); moreover, a study focus in Catalonia (Spain) showed a statically significant correlation between COVID-19 incidence and NO₂ (Marquès et al. 2021). Furthermore, during days with Saharan dust intrusion, there was a greater association between NO₂ and the incidence and severity of COVID-19 in eight provinces in Spain (Linares et al. 2021). In relation to the association between air pollution and the incidence and severity of COVID-19, there has also been evidence that noise pollution is a mobility indicator that has been a precursor to increased cases of COVID-19 (Díaz et al. 2021).

Despite the current evidence, there is still a lack of understanding of the association between the meteorological factors, air pollutants, and COVID-19. These differences are in many cases maintained because of methodological deficiencies in the published studies, the majority of which opt to study environmental factors and

meteorological factors separately. There are also studies that do not include the incubation period of the disease, which is on average 4 days (2–7 days) (Guan et al. 2020).

There have been contrasting results with respect to meteorological factors such as temperature and COVID-19. While some studies in China mention both a positive and negative relationship, depending on the studied provinces (Shahzad et al. 2020), others show that a lower temperature increases the number of cases of COVID-19 (Şahin 2020; Xie and Zhu 2020) and could result in an increase in the number of deaths due to the disease (Wu et al. 2020). On the other hand, other authors are simply unable to identify any type of correlation between COVID-19 and temperature (Tosepu et al. 2020).

Absolute humidity has been shown to have a weak (not robust) association with COVID-19 in Bangladesh (Islam et al. 2020), Thailand (Sangkham et al. 2021), and Turkey (Şahin 2020). Some authors have shown that the stability of SARS-CoV in climates with low humidity could facilitate the community transmission in subtropical climates in the spring (Chan et al. 2011). Furthermore, laboratory studies have shown that SARS-CoV becomes inactive with greater temperature and humidity (Casanova et al. 2010). In this sense, one study showed that an increase in humidity was related to a decrease in the number of confirmed cases of COVID-19 (Lorenzo et al. 2021). Other authors suggest that SARS-Cov-2 presents a more efficient transmission at low temperature and low humidity, as does influenza (Qi et al. 2020).

Other types of studies, mostly restricted to middle latitudes, have focused on the effect of meteorological factors—such as average temperature and absolute average humidity during the maximum incubation period—on severity and intensity of the disease during its first wave (Burra et al. 2021). Some studies have found a negative correlation between both variables. For example, a study carried out in Spain (Hervella et al., 2021) suggested that meteorological factors could have been more relevant during the initial time of COVID-19, given the lack of significant measures like social distancing and masking.

Although there are papers that analyze both, meteorological factors and air pollutants on COVID-19 incidence (Shen et al. 2021; Rahimi et al. 2021; Diao et al. 2021), there are few focused in the short-term and for a whole country. In light of the absence of studies at the Spanish national level that analyze air pollutants and atmospheric variables in a combined model, the present study was proposed to identify the short-term association between the concentrations of air pollutants (PM₁₀, NO₂) and atmospheric variables (maximum daily temperature and absolute average humidity) and the incidence and severity of COVID-19. On the other hand, there are other factors that could influence the transmission

of SARS-Cov-2 and affect the development of the disease as the government response policies (Coccia 2020b; Askitas et al. 2021) or health spending (Coccia 2021b). Even some authors propose the creation of an index to quantify environmental risks in relation to other demographic and social factors (Coccia 2020a). In this study, we try to evaluate the influence of some social determinants, and constructed a model that attempts to explain the heterogeneous geographic behavior observed for some of the impacts of the environmental variables.

Material and methods

Sample and data

This study was an ecological, longitudinal retrospective time series study of the period from February 1, 2020 through May 31, 2020. Forty-one of the Spain's 52 provinces were considered.

Inclusion criteria: the study included those provinces for which there was homogeneous information on average daily concentrations of nitrogen dioxide (NO₂), particulate matter with an aerodynamic diameter of less than 10 µm (PM₁₀), and the atmospheric variables maximum daily temperature (Tmax) and absolute average daily humidity (HA). A maximum limit was established for information loss at 10% on the study days.

Measures of variables

Dependent variables

Daily incidence rate of COVID-19 per million inhabitants (TIC) and the rate of hospital admissions due to COVID-19 (TIHC). The dependent variables were calculated based on the number of cases of patients with positive PCR tests (COVID-19) in the provinces analyzed. This information was provided by the National Center for Epidemiology of the Carlos III Health Institute. At the provincial level, the population data were provided by the National Statistics Institute (INE). Based on these data, the following were calculated:

Rate of COVID-19 incidence per 1,000,000 inhabitants: (Number of positive COVID-19 cases/population) × 1,000,000 inhabitants.

Rate of COVID-19 hospital admissions per 1,000,000 inhabitants: (Number of emergency COVID-19 positive hospital admissions/ population) × 1,000,000 inhabitants.

Independent variables

Air pollutants The average daily values of concentrations of PM₁₀ and NO₂ in µg/m³ were calculated, obtained from

the representative stations located in the provinces analyzed. These data were provided by the Ministry for Ecological Transition and Demographic Challenge (MITECO).

Meteorological variables The meteorological data used were the daily values of maximum temperature (Tmax) in °C and absolute average daily humidity (HA) in g/m³ obtained from the reference observatories of each province. As these variables presented the best behavior with the COVID-19 variables analyzed (Linares et al. 2021; Xie and Zhu 2020). The reference observatories belong to the State Meteorological Agency (AEMET).

Based on relative daily humidity (HR) and average daily temperature (T) (Gupta et al., 2020), absolute average humidity (AH) was calculated based on the Clausius Clapeyron equation, as follows (Iribarne and Cho 1980):

$$AH = \frac{6.112 * e^{[17.67 * T / + 243.5]} * HR * 2.1674}{273, 15 + T}$$

Other independent variables In order to explain the heterogeneity of the geographic distribution of the results obtained from the study of air pollutants and meteorological variables associated with COVID-19, other independent variables were analyzed. These were grouped using the Lalonde Laframboise epidemiological model of health determinants, which classifies variables in terms of those related to human biology, lifestyles, and environment and health services.

Mobility was among the included variables related to lifestyles. Mobility information was extracted from Google (*COVID-19 Community Mobility Report*, s. f.).

Other variables included the long-term exposure to chemical pollutants, such as the average value of PM_{2,5}, PM₁₀, and NO₂ from 2017 to 2019, (*informe-calidad-aire-2017.pdf*, s. f.) (*informe-calidad-aire-2018.pdf*, s. f.) (*informe-calidad-aire-2019.pdf*, s. f.). Other environmental variables were studied such as provinces with airports (*Red de aeropuertos - Aena.es*, s. f.), number of gasoline cars per inhabitant, number of gas-oil (diesel) cars per inhabitant, and total number of cars excluding zero and low-emissions vehicles (Tablas estadísticas 2019, s. f.).

Social environment variables included rurality (Ocana-Riola and Sanchez-Cantalejo 2005), homes under 30 m² (to indirectly evaluate the level of overcrowding).

In terms of socioeconomic environment, variables included income level (*INEbase / Economía / Cuentas económicas / Contabilidad regional de España / Resultados*, s. f.), deprivation index (Duque et al. 2021), and environmental expenditure (SGFAL, s. f.).

The variables related to the response of health systems included number of clinics, number of health centers, average number of ambulances per inhabitant, average number of family physicians per inhabitant, average number of nurses

per inhabitant, average number of physicians and nurses per inhabitant (*Consulta Interactiva del SNS*, s. f.), number of beds per 1000 inhabitants, number of intensive care beds per 1000 inhabitants (*Ministerio de Sanidad, Consumo y Bienestar Social - Profesionales - Datos abiertos de capacidad asistencial*, s. f.), and number of new social security personnel employed in the past year (*05m-Afi. Med. R. General por Provincia-CCAA, y Sección-Actividad*, s. f.).

Model and data analysis and procedure

Generalized linear models (GLM) with Poisson link were carried out in the 41 studied provinces, using the rate of positive COVID-19 cases and the rate of hospital admissions as the dependent variables and air pollutants and the meteorological variables as independent variables.

To control for the trend, a variable called $n1$ was used. This variable was defined as $n1 = 1$ for February 1, 2020; $n2 = 2$ for February 2, 2020 and so forth until the end of the period. To control for seasonalities of 4 months (120 days), 3 months (90 days), 2 months (60 days), and 1 month (30 days), the following variables were introduced: $\text{sen } 120 = \text{sen}(2\pi \cdot n1 / (3/365.25))$, $\text{cos } 120$, $\text{sen } 90$, $\text{sen } 60$, and $\text{sen } 30$, in addition to the corresponding cosines of the same functions. We also introduced the autoregressive of order 1 of the corresponding dependent variable.

GLM were carried out between the dependent variables and the values of the independent variables, to establish days with statistically significant lags between both variables.

In the case of Tmax and HA, the lags were considered statistically significant starting with the 5th day, up to the 28th. The existing literature does not indicate that temperature or humidity can worsen the symptoms of the disease in an immediate way; rather, they can influence the possibility of infection by the virus, whose incubation period has been established at around 5 days. Along the same lines, some authors have found a greater correlation after the fifth day (Bolaño-Ortiz et al. 2020a).

On the contrary, air pollution can contribute to worsening the symptoms of respiratory and circulatory illnesses, and in consequence, it could cause patients to seek out health services to get a PCR test. A positive result is considered a case of COVID-19 for the same day (Domingo et al., 2020). Therefore, in order to study the impact of the concentrations of PM_{10} and NO_2 , lags from day 0 through day 28 were considered.

For the purposes of the analysis, a range of lag days was established of between 0 and 28 days, from the onset of symptoms until the worsening of the disease and admission to the hospital (Lauer et al. 2020). A weekly distribution model of lags was used (Linares et al. 2021) (Díaz et al. 2021). In a first step, the lags corresponding to the

independent variables were introduced, with lags of 0 to 7 days. Second, lags of 8 to 14 days were introduced, maintaining the lags of the variables that were found to be statistically significant in step one, and so on, up to 28 days.

All of the independent and dependent variables were introduced into the same model. Relative risks (RR) were calculated using the estimators obtained, based on the absolute value of the estimators, as follows: $\text{RR} = e^{\beta}$ where β is the absolute value of the estimator.

If the coefficient of the estimator was negative, it would indicate that an increase in the dependent variable is associated with a decrease in the independent variable. The RR was calculated using an increase of $10 \mu\text{g}/\text{m}^3$ in PM_{10} and NO_2 ; of 1°C in the case of Tmax and $1 \text{ g}/\text{m}^3$ for AH.

Based on the risks obtained, the attributable risk (RA) was calculated for some of the provinces, based on the following formula: $\text{AR} = 100 \cdot (\text{RR} - 1) / \text{RR}$, which permitted calculating the incidence of each of the significant independent variables at the population level. RA has been calculated as an example, only for some of the provinces.

In order to explain the heterogeneity of the geographic distribution of the results, we carried out a linear regression model that included the other intervening independent variables already described, using the following function:

$$Y = b_0 + b_1x_1j + b_2x_2j + \dots + b_kx_kj + u_j$$

where Y = risks associated with NO_2 , PM_{10} , Tmax, and HA for each studied province; $x_1j + x_2j \dots x_kj$, represent the intervening independent variables.

Ethical considerations

Working with aggregated and anonymous data did not require the approval of the ethics committee; however, this study complied with the ethical considerations of the Declaration of Helsinki.

Software SPSS 27.0 and Stata 16.0 were used for the analysis of the time series. Maps were developed using Qgis 3.16.3, and tables were constructed using Excel.

Results

Table 1 shows the Spanish provinces studied and the days for which there was an association or lag (Lag) with TIC and with TIHC, for the environmental pollutants (PM_{10} , NO_2) and for the atmospheric variables (Tmax y AH). The day of the lag shown to be statistically significant is shown in parenthesis.

In the case of TIC, only one province failed to show a lag associated with environmental pollutants or the atmospheric

Table 1 Findings obtained from the GLM models ($p < 0.05$) by Air pollutants and meteorological variables associated with the incidence rate (TIC) or hospital admission rate (TIHC) of COVID-19 by lag days (Lag) by provinces* in Spain during First Wave (Feb.–May 2020). In brackets statistical significant lag association are showed

Spanish provinces	COVID-19 incidence rate (TIC) and associated lag days (Lag)						COVID-19 hospital admissions rate (TIHC) and associated lag days (Lag)					
	TIC			TIHC			Air pollutants			Meteorological variables		
	PM10	NO2	HA	PM10	NO2	HA	PM10	NO2	HA	Tmax	HA	
<i>A Coruña</i>	40.41	(0,7,14)	(21,26)	(-)	(8,10,18,21,23)	(-)	9.56	(26,28)	(-)	(5)	(-)	
<i>Alicant/Alicante</i>	3.03	(20)	(0,22)	(17)	(7,19,25)	(-)	0.96	(-)	(-)	(5)	(17,27)	
<i>Albacete</i>	10.14	(2)	(6,28)	(-)	(-)	(-)	3.52	(-)	(20,28)	(-)	(-)	
<i>Almería</i>	0.79	(4,8,11,12,20)	(5,16,21,25)	(8,24)	(16,18)	(-)	0.27	(-)	(12)	(-)	(-)	
<i>Araba/Álava</i>	8.34	(26)	(22)	(7)	(-)	(-)	2.62	(-)	(0)	(-)	(-)	
<i>Asturias</i>	1.97	(7,21)	(21, 24)	(17)	(8,12,14,18)	(-)	0.90	(3,19,20,28)	(1,11,14,17)	(-)	(11,13,17)	
<i>Ávila</i>	11.01	(-)	(1,7,13,21)	(-)	(11,14,18,25)	(-)	0.08	(-)	(-)	(-)	(-)	
<i>Barcelona</i>	6.99	(-)	(-)	(10,15,23)	(21)	(-)	2.29	(-)	(-)	(-)	(13)	
<i>Bizkaia</i>	5.99	(8,14,17)	(6,8,9,20)	(7,9,21)	(-)	(-)	2.36	(-)	(22,27)	(17)	(27)	
<i>Burgos</i>	6.79	(25)	(-)	(14,15)	(-)	(-)	0.32	(-)	(-)	(-)	(-)	
<i>Cádiz</i>	0.96	(2,12,19,21,23)	(24)	(-)	(-)	(-)	0.38	(-)	(-)	(27)	(-)	
<i>Cantabria</i>	3.24	(2,20,28)	(4,6,17)	(23)	(12,14,20,25)	(-)	0.14	(-)	(-)	(-)	(26)	
<i>Castelló/Castellón</i>	2.44	(-)	(21,28)	(9,13)	(6,15)	(-)	1.01	(5,12,21,26,28)	(12)	(8,13)	(-)	
<i>Ciudad Real</i>	13.21	(17,21,24)	(23,26)	(-)	(28)	(-)	3.94	(-)	(-)	(21)	(-)	
<i>Cuenca</i>	7.88	(-)	(-)	(-)	(-)	(-)	2.94	(-)	(-)	(-)	(-)	
<i>Gipuzkoa</i>	2.76	(15,24,27)	(0)	(7,9,18)	(7)	(-)	1.02	(-)	(3,14)	(12,17,20)	(28)	
<i>Guadalajara</i>	5.38	(-)	(-)	(-)	(6,24)	(-)	2.36	(-)	(28)	(-)	(-)	
<i>Huelva</i>	0.77	(19)	(21)	(7,14)	(-)	(-)	0.34	(6)	(16,19,22)	(25)	(-)	
<i>Illes Balears</i>	1.59	(18)	(7,18)	(6,16,22,25)	(-)	(-)	0.74	(-)	(-)	(17)	(23)	
<i>La Rioja</i>	9.73	(-)	(21)	(21)	(-)	(-)	2.42	(-)	(-)	(-)	(2)	
<i>León</i>	6.63	(-)	(0,2,6,15)	(7,14)	(11,16,26)	(-)	0.03	(-)	(-)	(-)	(-)	
<i>Lugo</i>	2.29	(11,28)	(14,16,20,22,24,26,28)	(10,23,24)	(21)	(-)	0.45	(4,10,15,18,21)	(13,18)	(8,14,20)	(11,15,18)	
<i>Madrid</i>	8.68	(-)	(0)	(14)	(16,18,23)	(-)	4.16	(18,24)	(-)	(7,14)	(21,24)	
<i>Málaga</i>	1.97	(0,6,12,23, 26)	(14,21,28)	(9,17,20)	(8,10,18)	(-)	0.73	(13,21)	(0,16)	(-)	(-)	
<i>Murcia</i>	1.32	(3,10,19,25)	(0,14,17)	(11)	(7,26)	(-)	0.36	(-)	(-)	(3,19)	(-)	
<i>Navarra</i>	9.70	(-)	(20)	(7)	(-)	(-)	2.61	(25,27)	(0)	(-)	(-)	
<i>Ourense</i>	4.97	(14)	(2,6,7)	(7,18,25)	(15,21)	(-)	1.54	(0,10,15,23)	(9,20)	(21,22)	(14)	
<i>Palencia</i>	6.92	(-)	(-)	(14)	(26)	(-)	0.09	(-)	(-)	(-)	(-)	
<i>Pontevedra</i>	2.69	(6)	(0,21)	(8,12)	(11,21,23,24)	(-)	0.66	(20)	(14)	(-)	(-)	
<i>Salamanca</i>	10.70	(0,3,8,18,25)	(-)	(10,19)	(-)	(-)	0.04	(-)	(-)	(-)	(-)	
<i>Segovia</i>	18.59	(-)	(14,24)	(19)	(5,10,18,23)	(-)	0.06	(-)	(-)	(-)	(-)	
<i>Sevilla</i>	1.27	(23,25,27)	(17,28)	(9,20)	(24)	(-)	0.52	(0,16,22)	(0,3,12)	(0)	(-)	
<i>Soria</i>	21.90	(6,21)	(-)	(15,21,27)	(7,17,21)	(-)	0.06	(-)	(-)	(-)	(-)	

Table 1 (continued)

Spanish provinces	COVID-19 incidence rate (TIC) and associated lag days (Lag)				COVID-19 hospital admissions rate (TIHC) and associated lag days (Lag)			
	TIC		Meteorological variables		TIHC		Meteorological variables	
	PM10	NO2	Tmax	HA	PM10	NO2	Tmax	HA
<i>Tarragona</i>	2.32 (12)	(-)	(7,14)	(6)	0.88 (28)	(1,5,12,14,21)	(-)	(-)
<i>Toledo</i>	5.98 (2,25,27)	(21,27)	(-)	(-)	2.64 (13,19,21,26)	(-)	(7,18)	(-)
<i>València/Valencia</i>	2.37 (-)	(0,3,6,8)	(-)	(-)	1.66 (-)	(13,28)	(-)	(20,27)
<i>Valladolid</i>	7.38 (24)	(7)	(11)	(11,14,23)	0.07 (-)	(-)	(-)	(-)
<i>Zamora</i>	4.98 (26,28)	(7,13,21)	(-)	(13,16)	0.36 (-)	(-)	(-)	(-)
<i>Zaragoza</i>	3.99 (9,13)	(4,7,10,16)	(8,15,17,21)	(6,12,13,17,19,21)	1.75 (3,9,14,28)	(7,14,16)	(7,15,21)	(12,18)
<i>Santa Cruz de Tenerife</i>	1.30 (-)	(1,4,14,21)	(-)	(6,12)	0.51 (2,24)	(28)	(13,23)	(-)
<i>Las Palmas</i>	0.54 (-)	(5,8)	(-)	(18,21,24)	0.22 (16,22)	(-)	(-)	(6)

*Provinces studied: 41 of 52. Not all provinces were studied due to incomplete information

(-) No association

variables. In the case of the hospital admissions rate, 10 of the studied provinces did not produce any type of associated lag (see Fig. 1).

Figures 1 and 2 and Supplementary Table 1 show the RR by province, associated with TIC and TIHC, by air pollutants and atmospheric variables. The maps show the different associations with RR stratified by terciles in natural breaks.

Figure 1 shows that the provinces that present a greater number of RR associated with PM₁₀ are found in tercile 2, and the RR present a range of between 1015 and 1050. In order to understand the contribution of PM₁₀ to TIC, by way of example, we can say that the province with the greatest value of RR associated with PM₁₀ in Spain presented an RR of 1103 (1009–1198) (see Supplementary Table 1). That is to say that for each 10 °µg/m³ increase in PM₁₀, the attributable risk (AR) of PM₁₀ to TIC is 9.4%.

The province of Lugo, located in the Northwest of Spain, was the province with the greatest value of RR associated with TIC and NO₂ (RR: 2,807 (1038–4575) (see Supplementary Table 1). The TIC of the provinces with the greatest values of RR associated with NO₂ are found in the first tercile, with RR with a range of 1000 to 1109 (see Fig. 1).

Figure 1 highlights the greatest number of provinces with RR associated with TIC and temperature, which can be found in tercile 1, with RR that ranging between 1022 and 1055.

In Fig. 1, the provinces with RR associated with TIC and HA that present the highest values—that is to say, tercile 1 (RR that range between 1477 and 2043) and tercile 2 (RR from 1477 to 2043)—are concentrated in the Northwest zone of Spain.

In general, TIHC presented a lower number of associated provinces, both for the air pollutants as well as the atmospheric variables, as shown in Fig. 2.

In Fig. 2, it can be observed that 3 of the 5 provinces with the greatest RR values associated with TIHC and PM₁₀ (tercile 1: RR of 1071 to 1127 and tercile 2: RR of 1031 to 1070) are found in the Northwest of Spain.

The greatest number of provinces that presented an association between TIHC and TIHC and NO₂ can be found in tercile 1 (with values of RR that range between 1018 and 1079) (see Fig. 2).

There is a somewhat heterogeneous geographic distraction of the provinces that presented RR associated with TIHC and temperature in all of the country (see Fig. 2).

Figure 2 shows that the provinces that presented the highest values of RR associated with TIHC and HA (tercile 1 (RRs of 1576 to 1871) and tercile 2 (RRs of 1231 to 1575)) are found in the North and Northwest of Spain.

Table 2 shows that the majority of the provinces (81%) presented a significant association between TIC and NO₂. In the same sense, 49% of the provinces presented an association between TIHC and NO₂, with NO₂ being the chemical pollutant with more association, both with TIC and TIHC.

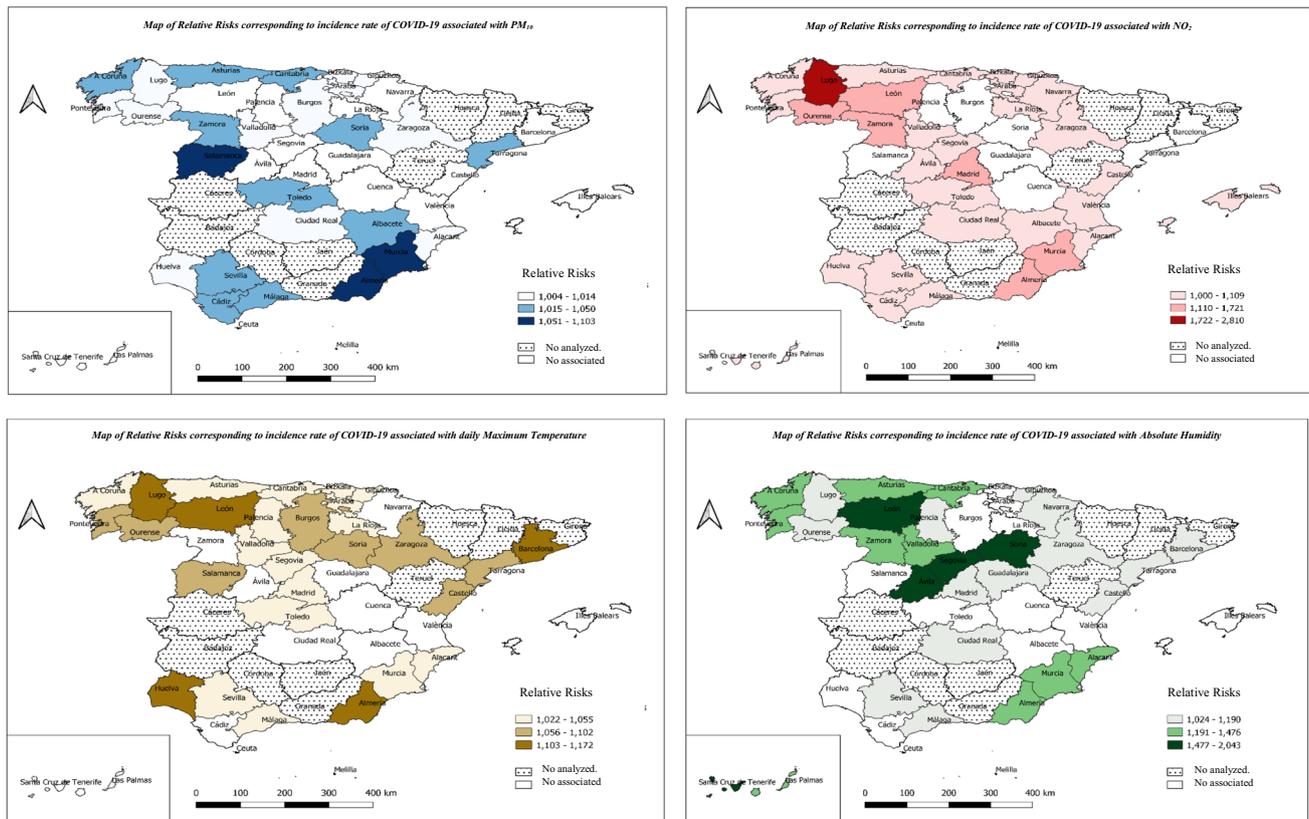


Fig. 1 Maps of Relative Risks to air pollutants and meteorological variables associated with the rate of incidence of COVID-19 (TIC) in Spain* during First Wave (Feb-May 2020). *Study provinces: 41 of 52 provinces in Spain. Not all provinces were studied due to lack of information

In order to explain the geographic differences observed at the country level, shown in Figs. 1 and 2, other health determinants were analyzed (see Supplementary Table 2) using linear regression.

Table 3 shows the analysis of the correlation between the RR of association between air pollutants and meteorological variables associated with TIC or TIHC and the determinants of health. The positive correlations (positive coefficients) indicate that when the studied variables increase, so does the health determinant; if the correlation is negative (negative coefficient), a decrease in the studied variables would indicate an increase in the health determinant, and vice versa.

Discussion

The following sections are divided according the findings obtained for the incidence rate (TIC) and hospital admission rate (TIHC) of COVID-19 and the principal variables analyzed: air pollutants, meteorological variables and social factors.

Findings obtained for NO_2

NO_2 was the pollutant with the greatest number of provinces associated with TIC. About 81% of the provinces presented an association between the concentrations of NO_2 and TIC. Forty-nine percent of the provinces presented an association between NO_2 and TIHC. These findings agree with other research carried out in the United Kingdom (UK) (Travaglio et al. 2021), in China (Zhu et al. 2020) in Wuhan (Jiang et al. 2020), and even in Catalonia (Spain) (Marquès et al. 2021). A study of Saharan dust intrusions and COVID-19 carried out in eight Spanish cities also identified a greater number of cities with an association between NO_2 and TIC (Linares et al. 2021). In our study, the province with the greatest RR associated with NO_2 and TIC was the province of Lugo (see Map 1b), and the lags were significant between 0 and 14 days. The lags reflect the days prior to the start of symptoms that present an association with NO_2 , which is related to the incubation period of the disease, and these days coincide with the physiopathology of the virus. In a study carried out in Italy, a correlation was shown between TIC and the concentrations of NO_2 , with hotspots identified in the North of Italy and the urban areas of the Center and South of Italy,

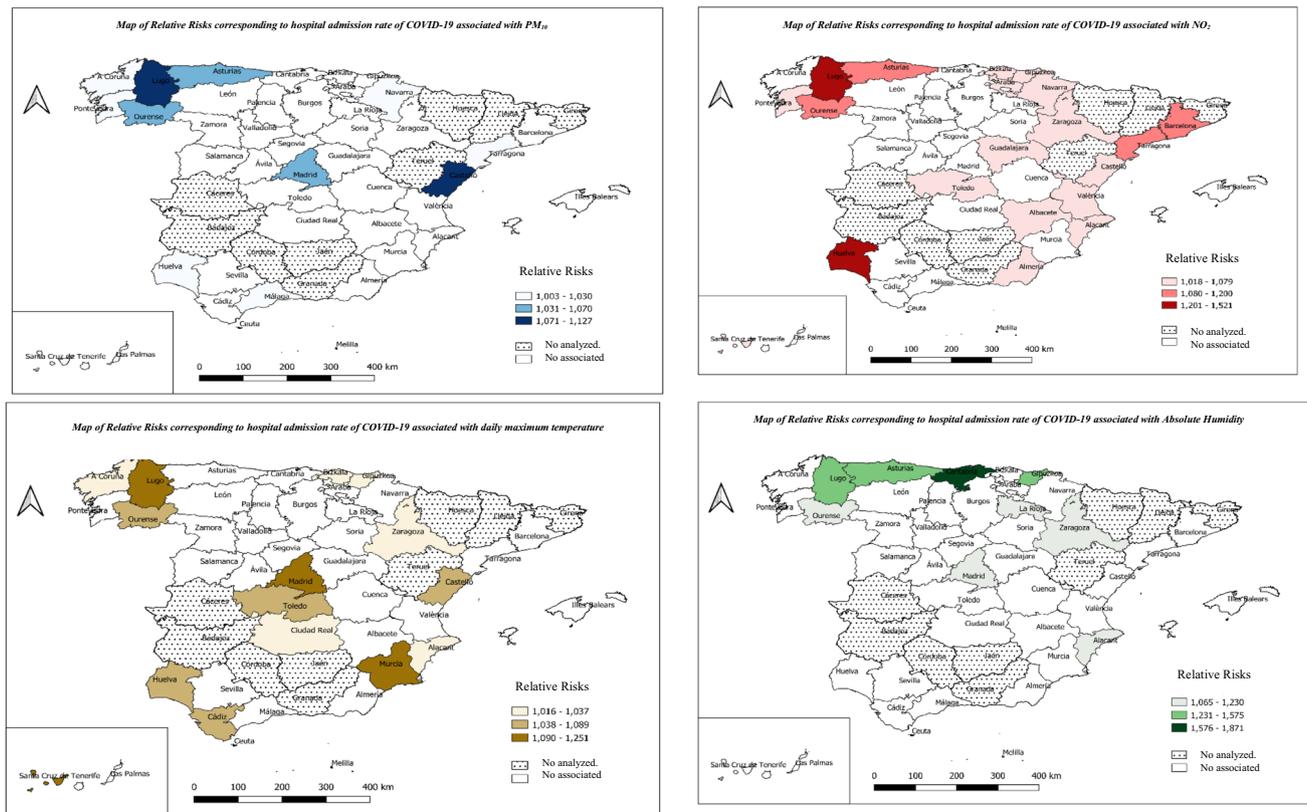


Fig. 2 Maps of Relative Risks to air pollutants and meteorological variables associated with the hospital admission rate of COVID-19 (TIHC) in Spain* during First Wave (Feb-May 2020) *Studied provinces: 41 of 52 provinces in Spain. Not all provinces were studied due to lack of information

inches: 41 of 52 provinces in Spain. Not all provinces were studied due to lack of information

Table 2 Percentage of Spanish provinces* with significant statistical association with air pollutants and meteorological variables by incidence rate (TIC) and hospital admissions rate (TIHC) of COVID-19 during the First Wave (Feb.–May 2020)

	Air pollutants		Meteorological variables	
	PM10	NO2	Tmax	HA
Incidence rate of COVID-19 (TIC)				
<i>Total number of Spanish provinces studied*</i>	41	41	41	41
<i>Number of Spanish provinces with significant statistical association</i>	26	33	29	29
<i>% of Spanish provinces with significant statistical association</i>	63.41	80.49	70.73	70.73
Hospital admission rate of COVID-19 (TIHC)				
<i>Number of Spanish provinces studied*</i>	41	41	41	41
<i>Number of Spanish provinces with significant statistical association</i>	13	20	15	9
<i>% of Spanish provinces with significant statistical association</i>	39.02	48.78	36.59	21.95

*Provinces studied: 41 of 52. Not all provinces were studied due to incomplete information.

such as Rome and Naples (Fattorini and Regoli 2020). In this study, there was no identified pattern in terms of geographic zone (see maps 1 and 2).

With respect to the mechanism of action of NO₂ and its relationship with the virus, it has been shown that environments with a greater concentration of NO₂ can influence infiltration of airways by inflammatory cells (Ghio et al. 2000). Furthermore, it is believed that the exposure to NO₂

inhibits the microbiome response and reduces the possibility of eliminating the virus in the lungs, which in consequence reduces its effectiveness (Lundborg et al. 2006). Also, it has been shown that the acute exposure to nitrogen oxides decreases pulmonary function through the mechanism of oxidative stress (Guarnieri and Balmes 2014). On the other hand, NO₂ has been associated with an increase in medical visits and hospitalizations due to bronchitis and

Table 3 Correlation between relative risks (RR) attributable to air pollution variables and meteorological variables associated with incidence rate (TIC) or hospital admissions rate (TIHC) of COVID-19 and health determinants in Spain during First Wave (Feb–May 2020) (parametric model)

Studied variable (comparison variable)	Determinants of health (comparison variable)	Coefficient	std. err.	z	P value	[95% conf.interval]	
RR of incidence rate of COVID-19 (TIC) associated with PM ₁₀	Presence of airports	.0219945	.0091323	2.41	0.016	.0040955	.0398935
	Income per capita	− 2.80e-06	1.10e-06	− 2.54	0.011	− 4.96e-06	− 6.35e-07
RR of incidence rate of COVID-19 (TIC) associated with NO ₂	Number of diesel cars per inhabitant	1,966,718	.6545239	3.00	0.003	.6838743	3,249,561
RR of hospital admissions rate of COVID-19 (TIHC) associated with PM ₁₀	Average number of nurses per inhabitant	− .0001692	.000058	− 2.92	0.004	− .0002829	− .0000556
	Number of new health personnel employees (social security contracts)	5.34e-07	2.12e-07	2.53	0.012	1.20e-07	9.49e-07
RR of hospital admissions rate of COVID-19(TIHC) associated with Tmax	Homes under 30 m ²	2,517,285	1,012,502	2.49	0.013	5,328,164	4,501,753

exacerbations of asthma (Bahrami Asl et al. 2018). It has been suggested that the angiotensin-converting enzyme (ACE2) may act as a receptor for SAR-CoV-2 (Lamas-Barreiro et al. 2020) (Yan et al. 2020). In other words, SAR-CoV-2 may interfere with the action of the ACE2 enzyme (Alifano et al. 2020). One study established a possible role of NO₂ in interfering with ACE2 due to the fact that there is a high quantity of ACE2 in epithelial cells of the lung (Alifano et al. 2020). Thus, SAR-CoV-2 may interfere in the action of ACE2, as may NO₂, but through different mechanisms. The interference results in difficulty in the degradation of ACE2 and accumulation of angiotensin II, substances that ACE2 acts upon. During COVID-19 infection, the alteration of ACE2 generates a disequilibrium in the inflammatory system involving an imbalance of vasoconstrictors, pro-inflammatory, proliferative, profibrotic, and oxidants, which could make the disease more severe. Although NO₂ levels decreased dramatically during the lock down period (Querol et al. 2021), the analysis of long-term exposure has also shown that NO₂ increases the risk of positive cases for COVID-19 (Saez et al. 2020).

Findings obtained for PM₁₀

PM₁₀ was associated with TIC in 63% of the studied provinces. It is known that the origin of the emission of PMs is 55% related to road traffic (Querol 2012) and is considered to be exclusively an oil product/fossil fuel (a product derived from gasoline and diesel fuel) (Lozhkina et al. 2016). Prior to COVID-19, it was shown that PM results in risks to health, especially respiratory infections, asthma, chronic obstructive disease, and lung cancer (Kim et al. 2018). It is known that PM₁₀ and PM_{2.5} particles can be inhaled and penetrate the lungs and circulatory system, producing difficulty in breathing, cough, and circulatory system irritation

(Kim et al. 2018). In the case of TIC, a study showed a positive relationship between the number of people infected and the provinces with daily concentrations of PM₁₀ over 50 µg/m³ up to 14 days prior to the start of the infection (Setti et al. 2020). These results coincide with ours, because we have identified that many of the lags are found between 1 and 14 days. Another study mentioned that depending on the province, there are different thresholds at which PM_{2.5} and PM₁₀ could be associated with the severity or mortality of COVID-19 (Magazzino et al. 2020), which agrees with our findings that identify different RR in the different study provinces (see Map 1 and Map 2, see Supplementary Table 1).

Some studies have identified that the number of infected people may increase in cities where the limit established for PM₁₀ and Ozone levels exceed the WHO guidelines in a significant number of days (Coccia 2021a; Saez et al. 2020; Bashir et al. 2020). Our study also controlled for long-term exposure, including the average concentration of PM₁₀ from 2017 to 2019 for PM₁₀ and PM_{2.5}; however, no association was identified when these variables were included in the final GLM model for each province.

Findings obtained for maximum daily temperature (Tmax)

Some authors consider that temperature could influence the transmission of SAR-CoV-2 (Chen et al. 2020). Other authors mention a different sort of correlation with the dissemination of the virus (Poole 2020). An Italian study identified a positive correlation between temperature and the number of cases of COVID-19 (Zoran et al. 2020), a similar relation was identified in 122 Chinese cities (Xie and Zhu 2020), other authors have identified with SARS-CoV transmission in Hong Kong and Beijing in 2003 (Bi

et al. 2007). In the case of the first wave in Spain, 70.73% of the studied provinces presented a negative association between temperature and TIC (transmission), and 36.59% presented a negative association between temperature and TIHC (severity) (see Table 2). In Spain, a strong negative correlation has been found between the expansion and severity of the disease and temperature and humidity during the time just before the outbreak of the epidemic (Luna 2021). Similar results come from other studies that are restricted to middle latitudes during the initial period of the disease (Burra et al. 2021).

Studies of temperatures show varied results. One study that included tropical zones identified a negative correlation between the number of new cases and temperature (Bolaño-Ortiz et al. 2020a). Another study carried out in China did not identify a linear relationship between temperature and the number of COVID-19 cases (Xie and Zhu 2020). Despite the fact that studies have shown that high temperatures and humidity reduce transmission of diseases like the flu and the SARs coronavirus in the respiratory tract (Park et al. 2020) (Sarkodie and Owusu 2020), evidence of the true role of temperature on SAR-CoV-2 is still inadequate (Mecenas et al. 2020) (see Maps 1c and 2c).

Findings obtained for absolute humidity

Absolute humidity (AH) was the variable that presented the lowest percentage of provinces associated with TIHC (21.95%), and there was a negative association. A study in China found that HA produced negative effects on confirmed cases of COVID-19 (Liu et al. 2020). However, another study did not show an association between HA and TIC (Araújo and Naimi 2020). Despite the fact that laboratory studies show that the transmission of SARS-CoV is more likely to be inactivated at higher temperatures and humidity (Qi et al. 2020), another study in Bangladesh identify a negative relation between humidity and temperature and the COVID-19 transmission; however, authors recognize that transmission during the summer period increased (Haque and Rahman 2020). Recent studies have not identified an association between humidity and the number of COVID-19 cases (Jiang et al. 2020). Even one study that analyzed levels of extreme humidity was unable to demonstrate inactivation of the virus (Luo et al. 2020), which confirms that there are differences between SARS-CoV-2 and other respiratory viruses. In addition, a study carried out during different seasons of the year suggested that it is possible that COVID-19 may not disappear on its own in warmer or more humid climates (Yuan et al. 2021) (see Maps 1d and 2d).

We can infer from the results of this study that both temperature and humidity play a secondary role, due to a lower number of provinces that presented an association in the GLM models (see Table 2, Maps 1c, 1d and 2c, 2d).

Despite the fact that some studies have proposed that the northern or coastal zones of some countries (Fattorini and Regoli 2020) were more affected by COVID-19. Other authors have proposed that some cities of the Italian coast are windy and showed a lower number of infected people; however, the risk of infection continued to be high due to the high percentage of the elderly population among other reasons (Coccia 2021d). In Barcelona, clusters with a greater number of infected patients were identified (Saez et al. 2020).

Our results point to a greater number of provinces with RR associations between TIC and AH in the Northwest (see Map 1d) and a greater number of provinces with RR associations between TIHC and PM_{10} in the Northwest (see Map 2a) and TIHC and HA in the North and Northwest in Spain (see Map 2d). However, we have not identified zones with a marked geographic concentration, from which we can infer that some geographic zones are much more affected than others. Thus, in general, there is a great deal of heterogeneity in the geographic distribution of the RR associated with TIC and TIHC in Spain. The geographic differences could probably be partly explained by the fact that the confinement altered the natural propagation of the virus, precluding a homogeneous distribution among all of the provinces and altering the pattern of comparison during the study period, which corresponded to the first wave of the virus in Spain.

On the other hand, during the first wave, there were insufficient tests to diagnose all of the positive cases of COVID-19. Symptomatic patients were prioritized; however, one in three patients with COVID-19 remained asymptomatic (Pollán et al. 2020). This difference could also have altered the geographic distribution of the results.

Because our results did not explain the heterogeneity in the geographic distribution of the RR association with TIC and TIHC, we carried out a complementary analysis with other health determinants, using the Lalonde Laframboise model (see Supplementary Table 2).

Findings obtained for social factors

TIC and social factors

TIC associated with PM_{10} presented a negative correlation with per capita income. It has already been suggested that the periodic appearance of other infectious disease viruses negatively correlate with socioeconomic, environmental and ecological factors (Jones et al. 2008; Coccia 2020a). One study showed that low poverty rates are related to high TIC (Bolaño-Ortiz et al. 2020b). Another study suggested that municipalities with a medium-low income level presented a greater number of mortal cases of COVID-19 (Olulana, s. f.). There has been a study of the fact that municipalities in rural areas tend to have poorer health outcomes (Anderson

et al. 2015; You et al. 2020). A study in Italy concludes that a high gross domestic product per capita, high health-care spending, and low levels of air pollution even could reduce the mortality attributable to COVID-19 (Coccia 2021b). However, our study was not able to corroborate the association between the rural/urban variable and TIC or TIHC. Some studies have even proposed race as a risk factor in increases in TIC (Millett et al. 2020), though our study did not explore race.

The presence of airports presented a positive correlation with TIC associated with PM_{10} . A short-term effect of PM_{10} has been identified, derived from air traffic, on pulmonary function in adults with asthma living near an airport in the USA (Habre et al. 2018). However, studies carried out at the airport in Barcelona have not been able to attribute the increase in PM_{10} only to the presence of the airport (Amato et al. 2010). Thus, these findings, though interesting, should be interpreted with prudence.

With respect to the positive correlation between TIC associated with NO_2 and the number of diesel cars, it is well-known that an important source of NO in urban areas is transportation emissions, diesel combustion, and domestic heating (Grange et al. 2019), which would seem to confirm that our association is not random. Our study included NO_2 pollution levels at least 14 days before the beginning of the first wave, thus we can say that average pollution levels included mobility that was prior to the first wave. However, the confinement could have altered these results. Despite the fact that the confinement could have been a modifying factor of the effect, NO_2 was associated in the majority of the studied provinces. This association was confirmed with the correlation with the number of diesel cars, which is one of the primary sources of NO_2 pollution.

TIHC and social factors

The decrease in nursing personnel per person could increase the risks of the association between TIHC and PM_{10} . In the same way, a positive relationship has been identified with the number of new health personnel. In terms of health personnel, different studies have shown a negative association with cases of death due to COVID-19 (Perone 2021). It should be noted that, considering the severity of patients admitted with COVID-19, the results are highly coherent, as PM_{10} has already been associated in other studies with an increase in hospitalizations of children due to respiratory viruses, such as respiratory syncytial virus (Zhu et al. 2020). However, there is less evidence in adults.

We observed that the presence of a lower number of homes under 30 m^2 could increase the risk of association between TIHC and temperature. In this sense, the majority of the literature does not identify a relationship between temperature and hospital admissions due to COVID-19.

However, it is probable that the presence of low temperatures during the first wave in Spain gave way to greater probability of overcrowding in homes under 30 m^2 . Similar results have been published in the USA (Ahmad et al. 2020) and in China (indoor) (Qian et al. 2021). On the other hand, there is currently more evidence about the airborne transmission of respiratory virus (Wang et al. 2021); in this context, the presence of air conditioning or inadequate ventilation could contribute to the airborne transmission of viruses in indoor environments, which could also have contributed to the increase in the association between TIHC and temperature (Li et al. 2007).

Limitations

We are aware that some variables related to human biology, such as sex or age, could not be measured due to the lack of a database that grouped this information for each Spanish province.

In addition, the lack of a polymerase chain reaction-tests and its heterogeneous provincial distribution is an important bias that may condition the results of this study, especially in the incidence rate.

The period of confinement affected the exposure to pollutants (Xu et al. 2020; Querol et al. 2021; Rahimi et al. 2021) and to environmental variables in all of the provinces, above all in the provinces with a very low incidence. This decrease in air pollution levels as a consequence of confinement may affect the association that may exist between air pollution and COVID-19.

Meteorological variables not only include variables such as temperature and absolute humidity, there are other variables such as those considered here; there are also studies that analyze the possible incidence of wind speed and wind direction (Coccia 2021c) (Coccia 2020c) (Islam et al. 2021) as well as solar radiation or precipitation (Rosario et al., 2020). However, in our study, some of these variables were not available for all the provinces studied.

Our study is limited to the first wave, and it is in this context that the results should be interpreted.

Conclusion

This is the first Spanish study that identifies a joint model of exposure risk at the province level for both air pollutants and meteorological variables on TIC and TIHC including an analysis by health determinants. The role of NO_2 is worth highlighting among the air pollutants, as it is the chemical pollutant that presented the greatest number of provinces associated with TIC and TIHC. The role of meteorological variables temperature and AH was not robust in relation to the air pollutants. The geographic distribution of the RR identified was highly heterogeneous,

and this study was unable to explain this geographic distribution, despite including other social determinants.

The health impact of epidemics does not only depend on biological and environmental factors. This study shows that environmental factors considered can modulate the incidence and severity of the pandemic; they are not determining factors that can explain by themselves the development and evolution of COVID-19. There are also economic and social factors that can alter the course of the epidemic (Coccia 2021e).

In addition, non-pharmacological public health measures such as the use of a mask, ventilation of outdoor spaces, and social distancing are proving highly effective for the control of COVID-19. Especially in places where, for many hours, a large number of people live in confined spaces such as schools (Villanueva et al. 2021). Despite the limited effect of air pollution on the incidence and severity of COVID-19 in this analysis, it is evident that the scientific literature shows the existence of robust associations. These associations at the short- and long-term support that the decrease in air pollution levels results in an improvement in the health of the population. The use of technologies that reduce social inequalities and sustainable development (Coccia 2020c) are key to the fight against this pandemic, especially in large cities.

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Data availability It is an ecological analysis, so the study does not involve human subjects. The data in relation to COVID-19 used in this study are subject to statistical secrecy and, therefore, are not freely available

Declarations

Ethics approval This study do not need to approbation by ethical committee because in this study we worked with aggregate data and we aren't including personal information.

The manuscript was not submitted to more than one journal for simultaneous consideration. The submitted work is original and have been not published elsewhere in any form or language (partially or in full).

Consent to participate This study works with aggregate data; therefore, there are no individual data, and the consent to participate is not applicable.

Consent for publication This study works with aggregate data, and there are no individual data; therefore, the consent to publish is not applicable.

Competing interests The authors declare no competing interests.

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