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2	ADMISSIONS IN MADRID AND ECONOMIC ASSESSMENT
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SHORT-TERM EFFECTS OF AIR POLLUTION AND NOISE ON EMERGENCY HOSPITAL

ABSTRACT

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29 Introduction: The aim of this study was to study the effect of air pollution and noise has on the population in Madrid Community (MAR) in the period 2013-2018, and its economic impact. 30 31 Methods: Time series study analysing emergency hospital admissions in the MAR due to all 32 causes (ICD-10: A00-R99), respiratory causes (ICD-10: J00-J99) and circulatory causes (ICD-10: 33 100-199) across the period 2013-2018. The main independent variables were mean daily PM_{2.5}, 34 PM_{10} , NO_2 , 8-hour ozone concentrations, and noise. We controlled for meteorological variables, 35 Public Holidays, seasonality, and the trend and autoregressive nature of the series, and fitted 36 generalised linear models with a Poisson regression link to ascertain the relative risks and 37 attributable risks. In addition, we made an economic assessment of these hospitalisations. 38 Results: The following associations were found: NO₂ with admissions due to natural (RR: 1.007, 39 95% CI: 1.004 – 1.011) and respiratory causes (RR: 1.012, 95% CI: 1.005 – 1.019); 8-hour ozone 40 with admissions due to natural (RR: 1.049, 95% CI: 1.014 - 1.046) and circulatory causes (RR: 41 1.088, 95% CI: 1.039 – 1.140); and diurnal noise ($L_{Aeq7-23h}$) with admissions due to natural (RR: 42 1.001, 95% CI: 1.001 - 1.002), respiratory (RR: 1.002, 95% CI: 1.001 - 1.003) and circulatory causes (RR: 1.003, 95% CI: 1.002 – 1.005). Every year, a total of 8246 (95% CI: 4580 – 11905) 43 44 natural-cause admissions are attributable to NO₂, with an estimated cost of close on €120 million 45 and 5685 (95% CI: 2533 - 8835) attributed to L_{Aeq7-23h} with an estimated cost of close on €82 46 million. 47 Conclusions: Nitrogen dioxide, ozone and noise are the main pollutants to which a large number 48 of hospitalisations in the MAR are attributed, and are thus responsible for a marked 49 deterioration in population health and high related economic impact.

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INTRODUCTION

Air pollution is a public health problem which affects a large part of the world population (Shaddick et al., 2020). The World Health Organisation (WHO) sets a series of air-pollutant concentration thresholds above which morbidity and mortality increase to an appreciable degree (WHO global air quality guideline, 2021). The effect that pollution has on the respiratory system is well known, producing exacerbations of asthma (Zheng et al., 2021) increased risk of developing chronic obstructive pulmonary disease and lung cancer (Nazar & Niedoszytko, 2022) (Bălă et al., 2021). In the circulatory system it causes coronary syndromes, cerebrovascular diseases and heart failure among others (Joshi et al., 2022) (Qin et al., 2021). There are authors who report that the effects on the human body of air pollution due to NO₂ and PM have no threshold that can be regarded as safe, and that any level of exposure amounts to a health risk (Stafoggia et al., 2022) (Strak et al., 2021). The European Environment Agency's latest report states that 94-99% of the population of the 28 European Union Member States have been exposed to nitrogen dioxide (NO₂), fine particulate matter (PM) and ozone (O₃) levels in excess of the WHO 2019 guideline values (European Environment Agency, 2021).

In addition to chemical pollution, the WHO rates acoustic pollution as one of the main environmental risks for health, with a considerable related disease burden in Europe (WHO Regional Office for Europe, 2018). The European Environmental Agency's most recent report points out that one out of every five Europeans is exposed to noise levels that could be seriously harmful to health (European Environment Agency, 2021). Although there are recent research linking noise to depression, risk of cardiovascular disease (Manukyan, 2022) (Münzel et al., 2021) and chronic obstructive pulmonary disease (Liu et al., 2021), the health effects of noise have not been as widely studied as those of chemical pollution.

Both chemical and noise pollution tends to affect extremes of age to a greater degree (Gupta et al., 2018) (United Nations Environment Programme, 2022). Affection on genes involved in the inflammatory response has been described if exposure to pollution occurs during

pregnancy and early life (Isaevska et al., 2021) and an increased risk of dementia among the elderly (Costa et al., 2020) (Delgado-Saborit et al., 2021).. Hence, a study on the effect of pollution, both chemical and acoustic, by age group, could prove highly useful and would help in designing plans that were more in line with population needs.

In recent decades, European countries have implemented policies to regulate air pollution (Rodrigues et al., 2021). This has allowed the average concentration of PM_{2.5} in all European countries to have decreased by 44% by in 2019 compared to 1990 (Juginović et al., 2021). In Spain, an annual limit for PM_{2.5} concentration came into force in 2015, which until then had been an objective and not a limit value (Evaluación de la calidad del aire en España, 2015).

Spain's large expanse of territory, the climatic differences between its regions, and the continuous changes in the socio-demographic characteristics of the population can amount to an important limitation in large-scale studies that group data on very extensive regions, by rendering extrapolation of results to specific cities difficult. What is therefore required are studies on limited regions, using updated socio-demographic data. This would allow for specific air-quality improvement plans focused on the most vulnerable population to be implemented in cities, with the aim of achieving an improvement in the quality of life of their inhabitants.

From the stance of improvement in the quality of life, rather than measuring attributable or premature mortality, it is more useful to measure morbidity based on hospital admissions, since the latter is a clear indicator of the lack of a healthy lifestyle. Moreover, this would allow for a more accurate quantification of healthcare costs. Despite its usefulness, however, there are few studies that establish the economic impact associated with hospital admissions attributed to air pollution, both chemical and acoustic.

The aim of this study was therefore to analyse the effect of chemical and acoustic pollution on hospital admissions of the resident population of the Madrid Autonomous Region (MAR) (Comunidad Autónoma de Madrid), by quantifying admissions attributable to pollution and their related economic cost.

METHODS

Study design

We conducted an ecological, retrospective, longitudinal, time series study. Unscheduled hospital admissions to hospitals in the MAR were linked to short-term air and acoustic pollution, controlling for the effect of different confounding variables, whether meteorological or control variables of seasonality and the trend and autoregressive nature of the series.

Dependent variable

As our dependent variable, we took daily unscheduled admissions as per the International Classification of Diseases, 10th edition (ICD-10), excluding accidents. For analysis purposes, the following were considered: admissions due to all causes (ICD-9:1-799; ICD-10: A00-R99) and, separately, admissions due to respiratory (ICD-9: 460-487; ICD-10: J00-J99) and circulatory causes (ICD-9: 390-459); ICD-10: I00-I99), registered in the MAR across the period 1 January 2013-31 December 2018. These data were obtained under a National Statistics Institute (Instituto Nacional de Estadística/INE) confidentiality protocol. The data were broken down by age group (<2 years, 2 to 10 years, 11 to 64 years, 65 to 79 years, and 80+ years).

Independent variables

The main independent variables were mean daily air pollution concentrations measured in $\mu g/m^3$ and acoustic pollution measured in dB(A). Air quality data were sourced from the Ministry for Ecological Transition and Demographic Challenge (Ministerio para la Transición Ecológica y Reto Demográfico) for the same period (1 January 2013-31 December 2018). Based on the data set from all the measuring stations in the MAR, we calculated the mean daily levels of particulate matter having a diameter of 2.5 microns or less (PM_{2.5}), particulate matter having a diameter of 10 microns or less (PM₁₀), nitrogen dioxide (NO₂), and 8-hour ozone (O_{3oct}: maximum value registered between 8 and 16 hours).

Acoustic pollution data were supplied by the Madrid Municipal Permanent Acoustic Pollution Monitoring Grid (Red Fija de Control de la Contaminación Acústica) and the AENA

Airports Acoustic Pollution Monitoring Grid. The data from these stations were then used to obtain the mean equivalent diurnal noise ($L_{Aeq7-23h}$), nocturnal noise ($L_{Aeq23-7h}$) and daily noise (L_{Aeq24h}) levels.

Due their importance as confounding variables, we used meteorological data drawn from readings taken at the Madrid-Retiro Observatory (MAR reference observatory) for the same period and furnished by the State Meteorological Agency (Agencia Estatal de Meteorología/AEMET). We recorded the daily values of maximum and minimum temperature (°C), air pressure (hPa), number of hours of sunlight per day, wind (km/h) and relative humidity (%). Temperature was included as two transformed variables —for low (Carmona et al 2016) and high temperature (Diaz et al 2015)— that converted lineal their non-lineal association with dependant variables. As high temperature is associated with short-term impacts, we included lagged variables of order 4 in this case (Diaz et al 2015). As low temperature is associated with long-term impacts, we include lagged variables of order 14 in their case (Díaz et al 2005). The relationship with relative humidity was linear, so no transformation was necessary. In this case, lagged variables of order 14 were included in the models. The geographical distribution of their stations could be consulted in supplementary materials figure 1.

The following control variables were also included: annual (365 days), six-monthly (180 days), four-monthly (120 days) and quarterly (90 days) seasonality using the sine and cosine functions. The trend of the series was taken into account using a counter n1, which assigns a number to each day of the series, such that n1 equals 1 for 01/01/2013, n1 equals 2 for 02/01/2013 and so on successively. We created dummy variables for the days of the week and controlled for the autoregressive nature of the dependent variable. In addition, we also controlled for Public Holidays in the MAR across the study period.

Statistical analyses

Initially, we performed a descriptive analysis of all the dependent and independent variables, by calculating the percentage of days on which the WHO's latest 2021 guideline values (WHO global

air quality guideline, 2021) and Spanish statutory limit values (RD 102/2011) (*Real Decreto* 102/2011, de 28 de enero, relativo a la mejora de la calidad del aire, 2011) were exceeded, and controlling for the presence of outliers.

According to previous studies, the functional relationships between hospital admissions and the environmental variables analysed display a linear distribution without threshold (Ortiz et al., 2017) (Linares et al., 2018), save in the case of variables of temperature and 8-hour ozone, which show a quadratic distribution (Díaz et al., 1999) (Alberdi et al., 1998). In view of this, parametrisations were only done for these last two variables.

In the case of 8-hour ozone, the functional relationship with all-cause hospital admissions was shown to be quadratic. To parametrise the function, the 8-hour ozone level corresponding to the minimum of the quadratic function was calculated by making the pertinent adjustment to a second-order polynomial, with this value being set at 147.5 μ g/m³, and a new variable was created to identify values that exceeded the threshold calculated, defined as follows:

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$$O_{3oct}high = 0, ifi [O_{3oct}] < 147.5 \,\mu\text{g/m}^3$$

$$O_{3oct}high = O_{3oct} - 147.5 \,\mu\text{g/m}^3, if [O_{3oct}] > 147.5 \,\mu\text{g/m}^3$$

For temperature, we used the threshold values set by the Ministry of Health for the definitions of heat wave (corresponding to 34°C for the maximum daily temperature) (Ministerio de Sanidad, 2022b) and cold wave in the MAR (corresponding to -2°C for the minimum daily temperature) (Dirección General de Salud Pública, 2017). Two new variables were created, defined as follows:

$$Theat = 0, if Tmax < 34$$

Theat =
$$Tmax - 34$$
°C, if $Tmax > 34$

$$Tcold = 0, if Tmin > -2$$

In the case of noise, given that there are no situations of zero noise, the minimum value of the whole series was established as the threshold, with this being set at 41.7 dB(A) for L_{Aeq7-} and 36.3 dB(A) for nocturnal noise.

Given that the health effects of independent variables on dependent variables may be lagged in time, we calculated the lags for the variables of air, acoustic and meteorological pollution in order to analyse the delayed effect. In the case of PM_{2.5}, PM₁₀, NO₂ and noise, the effect may be lagged by up to 5 days (Ortiz et al., 2017) (Linares et al., 2018), and in the case of ozone by up to 9 days (Díaz et al., 2018). For the difference in pressure, the effect is detected up to 8 days afterwards (González et al., 2001), and the effect of heat may be delayed by up to 5 days (Díaz et al., 2002). For relative humidity and cold, there were no previous studies that had analysed these jointly with the remaining meteorological variables, and we therefore allowed for a lag of 14 days.

To ascertain the impact of air and acoustic pollution on daily hospital admissions, we fitted generalised linear models (GLMs) with a Poisson regression link and controlled for overdispersion. We applied the backward method, whereby all the variables -both meteorological and pollution-related- are initially included along with their respective time lags. We also included the control variables of seasonality, and trend and autoregressive nature of the series, with those of less statistical significance then being gradually eliminated until all the variables had a significance of p<0.05. Based on the values of the significant estimators, relative risks (RRs) were calculated for every one-unit increase in the independent variables. In the case of ozone, PM_{10} , $PM_{2.5}$ and NO_2 , the increase in risk of hospital admission was calculated for every rise of 10 μ g/m³. To estimate the risk of hospital admission attributable to air and acoustic pollution, the above RRs were used to calculate the attributable risks (ARs) as per Coste and Spira's equation (1991) (Coste & Spira, 1991):

209	$AR = \frac{(RR - 1)}{RR} \times 100$
	RR

- The ARs were then used to calculate the number of admissions attributable to chemical and acoustic pollution in two cases:
- without considering any threshold (in the case of 8-hour ozone, this was considered as
 from its previously calculated health-impact value).
 - 2. based on the guideline values set by the WHO.

v17.0 and Microsoft Excel 2019 software packages.

Lastly, an economic estimate of hospital admissions was drawn up. To this end, the cost of the hospital process was first ascertained by calculating the weighted average of the mean Diagnosis Related Group (DRG) cost, using the APRGRD v.35 grouping system (2019 update). Weightings were assigned in accordance with the relative DRG weights (Ministerio de Sanidad, 2022a). We then calculated the number of admissions among the gainfully employed population (INE, 2022a) (INE, 2022b) and the cost of sick leave (Navarro-Espigares JL., 2021), and added the cost of the hospital process to the cost of sick leave.

All statistical analyses were performed using the IBM SPSS Statistics v.28 and STATA/BE

RESULTS

Emergency hospital admissions from 1 January 2013 to 31 December 2018 (total of 2191 days) were analysed. The distribution by type of admission and age group is shown in Table 1. The mean daily number of all-cause admissions (ICD: A00-R99) was 956: of these, 19.4% were admissions due to respiratory causes (ICD-10: J00-J99) and 15.6% were admissions due to circulatory causes (ICD-10: I00-I99). The descriptive analysis of air and acoustic pollution and meteorological conditions is summarised in Table 2.

Table 3 shows the percentage of days on which the WHO 2021 (WHO global air quality guideline, 2021) and Spanish statutory thresholds (RD 102/2011) (Real Decreto 102/2011, de 28

de enero, relativo a la mejora de la calidad del aire, 2011) were exceeded. All the pollutants analysed exceeded the WHO threshold at some time. In the case of $PM_{2.5}$, the threshold (15 $\mu g/m^3$) was exceeded on 11-19% of days in the 2013-2018 series, while for NO_2 the threshold (25 $\mu g/m^3$) was exceeded on 41-68% of days. In the case of 8-hour ozone, the WHO-recommended threshold (100 $\mu g/m^3$) was exceeded on 21-29% of days, and the Spanish statutory threshold (120 $\mu g/m^3$) was exceeded on 4-11% of days.

The RRs and ARs, along with their corresponding lags, which proved statistically significant (p <0.05) in the Poisson regression models for hospital admissions due to natural, respiratory and circulatory causes, are shown in Figure 1. Whereas NO₂ had a significant effect on natural- and respiratory-cause admissions, 8-hour ozone was linked to admissions due to natural and circulatory causes. No statistically significant association was however found for PM for any type of admission. With regard to noise, a significant association was observed for all three types of admissions, with the most relevant being that detected for circulatory-cause admissions attributable to $L_{Aeq7-23h}$.

Figure 2 shows the significant independent variables with the models broken down by age group for natural-cause admissions. The pollutant with the greatest effect on admissions was 8-hour ozone in the under-2 age group.

The models constructed in our study made it possible to quantify admissions attributable to chemical and acoustic pollution, along with their economic assessment, which can be seen in Tables 4 and 5. The results show that every year, 8246 (95% CI: 4580 – 11905) natural-cause admissions are attributable to overall exposure to NO₂, which accounts for 2.4% of all hospitalisations. These admissions amount to an annual hospital expenditure of close on 120 million euros. Moreover, if the thresholds established by the WHO had been complied with, 2388 (95% CI: 1326 – 3447) annual natural-cause admissions attributable to exposure to NO₂ could have been prevented. In the case of respiratory causes, 2728 (95% CI: 1231 – 4219) annual admissions were attributed to NO₂, accounting for 4% of all hospitalisations. Applying the WHO

guideline values, out of this total, 862 (95% CI: 389 – 1334) annual admissions could have been prevented.

The pollutant with the second highest number of attributable admissions was noise. Every year, 5685 (95% CI: 2533 – 8835) natural-cause admissions are attributable to exposure to acoustic pollution on the same day, accounting for 1.6% of all hospital admissions. These admissions amount to more than 82 million euros in annual hospital expenditure. The effect of noise is even greater in respiratory- and circulatory-cause admissions, 2.9% and 4.47% of which are respectively attributed to acoustic exposure on the same day.

DISCUSSION

The effect of air pollution on mortality has been widely studied in recent years (Stafoggia et al., 2022) (Orellano et al., 2020), but to be able assess the effect exerted by pollution on health it is necessary to analyse morbidity as reflected in emergency hospital admissions. In our work, NO₂ was found to be associated with an elevated risk of natural and respiratory cause admissions, and 8-hour ozone was found to be associated with an elevated risk of natural and circulatory cause admissions. These findings are closely related to both pollutants exceeding WHO recommended thresholds 20-70% of the days. A study conducted in Beijing corroborates the fact that NO₂ and ozone are the pollutants with greatest impact on health (Zhong et al., 2019).

Yet, other studies describe different magnitudes in the associations between hospital admissions and pollution. A study of a French cohort followed up for 12 years, with mean PM_{2.5} concentration levels of 10.6 μ g/m³, NO₂ concentration levels of 25.8 μ g/m³, and ozone concentration levels of 94.4 μ g/m³ -all similar to those described in our study- obtained the following RRs for natural-cause admissions: 1.107 (95% CI: 1.079 – 1.136) for PM_{2.5}; 1.029 (95% CI: 1.002 – 1.057) for NO₂; and 1.008 (95% CI: 0.974 – 1.044) for ozone (Sanyal et al., 2018). Similar results were found in a recent meta-analysis which studied countries around the world and reported RRs for respiratory-cause admissions of 1.014 (95% CI: 1.008 – 1.020) for NO₂,

1.008 (95% CI: 1.005 – 1.011) for 8-hour ozone, and 1.010 (95% CI: 1.001 – 1.020) for SO₂ (Zheng et al., 2021). Another recent meta-analysis with data on over 23 million participants described that exposure to $PM_{2.5}$, PM_{10} , SO_2 , NO_2 , CO and ozone was associated with a statistically significant increase in risk of hospital admission due to cerebrovascular disease for all pollutants (Niu et al., 2021). Contrary to what has been shown in these studies, in our work the RR of natural causes due to 8-hour ozone is much higher than the RR due to NO_2 , however, admissions attributable to NO_2 are approximately 100 times higher than admissions attributed to 8-hour ozone. This is because in Madrid the functional relationship of 8-hour ozone with hospital admissions is quadratic. The minimum value of atmospheric ozone corresponding to the minimum value of admissions is 147.5 μ g/m3, a very high value that only occurs in 0.3% of the days of the series studied.

When it comes to the percentage of admissions attributable to pollution, there are also differences in the studies published to date. A systematic review of 43 papers addressing the effects of NO_2 on hospital admissions describes a 0.57% (95% CI: 0.33 – 0.82) increase in respiratory-cause admissions for every daily rise of $10~\mu g/m^3$ in NO_2 (Mills et al., 2015). In contrast, a recent study conducted in Casablanca reported that an a $10~\mu g/m^3$ rise in NO_2 concentrations increased circulatory-cause admissions by 9% at lag 3, and respiratory-cause admissions by 3% on the same day (Nejjari et al., 2021). Seen against our Madrid-based study, this latter value is the most similar, with a 2% increase in respiratory admissions for NO_2 on the same day, though with no relationship being found between NO_2 and circulatory-cause admissions. All these differences may be due to a lack of homogeneity between the populations compared, since many health determinants, such as socio-economic level, race, education, type of dwelling, etc., were not taken into account in most of the studies.

Furthermore, when analysing the effect of pollution on the human body, one has to take into account other factors, such as temperature and other meteorological variables, which are intercorrelated (Ahad et al., 2020). For instance, the presence of NO₂, solar radiation and high

temperatures are required for the formation of ozone (WHO global air quality guideline, 2021). As regards temperatures, the effect *per se* of heat and cold waves on health is well documented (Wondmagegn et al., 2021) (López-Bueno et al., 2020), though recent studies undertaken in Spain show that mortality attributable to heat is gradually decreasing, due to adaptation to temperatures (López-Bueno et al., 2021) (Follos et al., 2020). For this reason, and in order to study the effect of atmospheric pollution as reliably and accurately as possible, meteorological variables have been included in our research, including heat and cold waves. This means that studies that do not take these variables into account may offer results that differ from ours.

Our study observed that, at present, PM are not statistically significantly associated with any type of short-term emergency hospital admission in the MAR. This may be due to the fact that the mean annual concentrations of $PM_{2.5}$ and PM_{10} in Madrid fell from 13 and 25 $\mu g/m^3$ in 2009 to 9.9 and 17.5 $\mu g/m^3$ in 2019 respectively (Dirección General de Medioambiente Sostenibilidad, 2019). One of the possible reasons for this drop is that in 2015 the annual limit for this pollutant entered into force(Evaluación de la calidad del aire en España, 2015). In Madrid, in the period 2013-2018, the SO_2 and CO pollution levels were very much below the values regarded as a health risk, with average annual concentrations of 2 $\mu g/m^3$ and 0.4 $\mu g/m^3$ respectively (Dirección General de Medioambiente Sostenibilidad, 2019), which is in fact why these pollutants were not included in our analyses.

The effect of pollution varies according to the age of the population, with children and the elderly being most vulnerable, so that an analysis broken down by age group yields valuable information. Our study found that the age groups with the highest risk of hospital admission due to pollution were children under 2 years for 8-hour ozone, followed by the elderly aged from 65 to 79 years for the same pollutant. As mentioned above, it should be borne in mind that there were only 7 days in the entire series with elevated ozone concentrations resulting in very high RRs. Moreover, the negligible number of hospitalisations occurring in the under-2 age group means that the RRs obtained are higher than in other age groups. Even so, a Texas study also

described the important effect that pollution has on children, reporting that at 4 days of 8-hour ozone exposure, children aged 5 to 14 years had a higher risk of hospitalisation due to asthma than did the older population, with an RR of 1.047 (95% CI: 1.025 – 1.069) (Zu et al., 2017).

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The effect of NO₂ concentrations is seen in all age groups, with a weaker association in terms of RR but with a greater impact on hospital admissions overall, this being the chemical pollutant to which most hospital admissions are attributed. One study undertaken in China found a statistically significant association for NO₂ at lag 5, and hospital admissions due to pneumonia in children under 15 years of age, with the effect being most marked in infants under 1 year of age (Li et al., 2018).

In addition to chemical-type air pollution, acoustic pollution has an equally relevant role in health. Its effect on short-term emergency hospital admissions is shown by the fact that our study found a statistically significant association between LAeq7-23h and all types of admissions, and for all age ranges, except children under the age of 2, of whom there were fewer. Furthermore, noise is the pollutant with which the highest proportion of attributable admissions is related, even higher than that recorded for NO2, ozone or PM. These findings are in line with those reported by other authors, such as Halonen et al., who report that L_{Aeq7-23h} increases the risk of hospitalisation due to cardiovascular disease in adults, and that nocturnal noise is responsible for the same effect in the elderly (Halonen et al., 2015). As mentioned above, children and the elderly are more vulnerable to the effect of the noise than is the rest of the population. A previous study in Madrid conducted on children under the age of 10 years described RRs of 1.02 (95% CI: 1.01 – 1.04) for natural-cause admissions and 1.05 (95% CI: 1.01 - 1.08) for respiratory- cause admissions (Linares et al., 2006) consistent with what was found in our study. More recent studies conducted in Madrid have respectively reported associations between exposure to noise and admissions due to suicide and anxiety (Díaz et al., 2020), and admissions due to exacerbations of symptoms of dementia (Linares et al., 2017).

Mention should also be made of other studies undertaken in Madrid, in which traffic noise has been linked to morbidity and mortality due to circulatory and respiratory causes (Tobías et al., 2015) (Recio et al., 2017). The common source for a very high proportion of NO₂ and noise pollution is road traffic, thereby making vehicles the main cause of hospital admissions due to circulatory and respiratory causes in Madrid (Navares et al., 2020). This highlights the fact that, while noise is a pollutant with health effects similar to those of the other chemical pollutants, scant research has targeted this pollutant, thus calling for more studies to continue assessing the effect of noise on health.

In addition to the marked impact which pollution has on population health, attention should be also drawn to the high related economic cost. Our study shows that NO₂ and noise are responsible for the highest number of attributable admissions, accompanied by an enormous hospital cost. From 2004 to 2006, the Aphekom project studied the impact of pollution in 25 European cities, and estimated that, if the threshold values annually recommended by the WHO in Europe had been observed, health systems would have saved 31 billion euros (Pascal et al., 2013). It should be borne in mind here that these data are twenty years old, so the current cost could be expected to be considerably higher. The lack of recent studies that calculate the healthcare cost associated with air and acoustic pollution highlights the need for further research to improve the welfare of the population.

Limitations

This study has a number of limitations. While the methodology used is standard for these types of studies (Samet et al., 2000), it can nevertheless give rise to a number of biases. To minimise these, we controlled for a range of variables, such as seasonality and the trend and autoregressive nature of the series. As this is an ecological study, individual inferences cannot be drawn from the results obtained, due to the ecological fallacy (Piantadosi et al., 1988). The study design only allows for collection of pollution data from a given number of stations, thus not representing real exposure at an individual level but instead obtaining average values of

daily concentrations. This approach was adopted to cover the possibility of residents who go to work at different places and are thus exposed to different levels of exposure. In the case of meteorological variables, data were obtained from a single observatory, but it should nevertheless be noted that it is the designated reference observatory for the MAR (Díaz et al., 2002).

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Madrid is an enough big city as to consider suburban areas or zones of influence associated with different stations. The exposure levels used were based on exposures determined on the basis of readings taken by external monitors and then averaged, with the result that they are not measures which represent individual exposure. Another bias from the monitors used can be the heterogeneity in the type, they are mostly urban but occasionally we used background type. Even so, this is a commonly used methodology in these types of studies (Samet et al., 2000). However, much of this residual confusion is controlled by inclusion in the model of variables such as: trend of the series, day of the week, annual, six-monthly and quarterly seasonalities and the autoregressive nature of the series. No specific validation was carried out to assess the representativeness of spatial variability in air pollutants: our study suffered from Berksontype measurement error, among other biases associated with an ecological exposure, as is common in most time-series studies of air pollution, which leads to no or little bias but decreases statistically power. At all events, most air-pollution studies address the misalignment problem (albeit only implicitly), by using a two-stage modelling procedure, or plug-in approach, where predictions from an exposure model (first stage) are used as covariates in a health-effect model (second stage) (Barceló et al., 2016).

Furthermore, there are significant correlations between particulate matter and between particulate matter and the high ozone variable (supplementary table). This problem has been controlled in the modelling process by including the control variables and excluding non-significant meteorological variables from the model.

A further limitation of this study is that use was made of hospital admission data which may have undergone coding errors: the foreseeable effect is minimal, however, since data sourced from official sources (National Statistics Institute/INE) were used across the entire study period.

Strengths

To our knowledge, this is one of the most up-to-date studies conducted in Spain in terms of the different types of pollutants analysed and their impact on short-term emergency hospital admissions. Moreover, many atmospheric variables and possible confounding factors were controlled for, in order to minimise the possibility of biases.

The study included an analysis of acoustic pollution, an aspect that is still little studied, thereby contributing to the generation of impact data on this environmental variable. No recent papers were found on the effect had by traffic-related acoustic pollution on hospital admissions due to natural causes or major disease groups, despite noise being a risk factor, similar to air pollution, that gives rise to a significant morbidity burden and related economic cost.

This study is, moreover, of great interest for national plans that seek to address the environment and health and the development of measurable and quantifiable indicators, since the effects of pollution were analysed at a regional level and their calculation can be extrapolated to other geographical areas of interest.

Conclusion

Despite the fact that air-quality control regulations have led to an improvement in the atmospheric situation in recent years, air pollutant levels continue to be high. The related morbidity is manifested in an excessive number of attributable hospital admissions, with the ensuing loss of the population's quality of life and the great financial cost that this entails. The short-term effect on hospital admissions due to NO₂ and ozone concentrations and noise levels continues to be very high in cities such as Madrid, rendering it necessary to update statutory

440 threshold limits to levels closer to those recommended by the WHO, and to implement new 441 public health policies that would continue to protect the health of the entire population. 442 **Conflicts of interest** 443 The authors declare that there are no conflicts of interest. 444 Disclaimer 445 The researchers declare that they have no conflicts of interest that would compromise the 446 independence of this research work. The views expressed by the authors are not necessarily 447 those of the institutions with which they are affiliated. 448 Acknowledgements 449 The authors would like to express their gratitude for the following grants from the Carlos III 450 Institute of Health (Instituto de Salud Carlos III/ISCIII) for the ENPY 304/20, and ENPY 436/21 451 projects.

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2	ADMISSIONS IN MADRID AND ECONOMIC ASSESSMENT
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SHORT-TERM EFFECTS OF AIR POLLUTION AND NOISE ON EMERGENCY HOSPITAL

ABSTRACT

29	Introduction: The aim of this study was to study the effect of air pollution and noise has on the
30	population in Madrid Community (MAR) in the period 2013-2018, and its economic impact.
31	Methods: Time series study analysing emergency hospital admissions in the MAR due to all
32	causes (ICD-10: A00-R99), respiratory causes (ICD-10: J00-J99) and circulatory causes (ICD-10:
33	100-199) across the period 2013-2018. The main independent variables were mean daily PM _{2.5} ,
34	PM ₁₀ , NO ₂ , 8-hour ozone concentrations, and noise. We controlled for meteorological variables,
35	Public Holidays, seasonality, and the trend and autoregressive nature of the series, and fitted
36	generalised linear models with a Poisson regression link to ascertain the relative risks and
37	attributable risks. In addition, we made an economic assessment of these hospitalisations.
38	Results: The following associations were found: NO ₂ with admissions due to natural (RR: 1.007,
39	95% CI: 1.004 – 1.011) and respiratory causes (RR: 1.012, 95% CI: 1.005 – 1.019); 8-hour ozone
40	with admissions due to natural (RR: 1.049, 95% CI: 1.014 – 1.046) and circulatory causes (RR:
41	1.088, 95% CI: 1.039 $-$ 1.140); and diurnal noise ($L_{Aeq7-23h}$) with admissions due to natural (RR:
42	1.001, 95% CI: 1.001 – 1.002), respiratory (RR: 1.002, 95% CI: 1.001 – 1.003) and circulatory
43	causes (RR: 1.003, 95% CI: 1.002 – 1.005). Every year, a total of 8246 (95% CI: 4580 – 11905)
44	natural-cause admissions are attributable to NO₂, with an estimated cost of close on €120 million
45	and 5685 (95% CI: 2533 – 8835) attributed to L _{Aeq7-23h} with an estimated cost of close on €82
46	million.
47	Conclusions : Nitrogen dioxide, ozone and noise are the main pollutants to which a large number
48	of hospitalisations in the MAR are attributed, and are thus responsible for a marked
49	deterioration in population health and high related economic impact.

INTRODUCTION

Air pollution is a public health problem which affects a large part of the world population (Shaddick et al., 2020). The World Health Organisation (WHO) sets a series of air-pollutant concentration thresholds above which morbidity and mortality increase to an appreciable degree (WHO global air quality guideline, 2021). The effect that pollution has on the respiratory system is well known, producing exacerbations of asthma (Zheng et al., 2021) increased risk of developing chronic obstructive pulmonary disease and lung cancer (Nazar & Niedoszytko, 2022) (Bălă et al., 2021). In the circulatory system it causes coronary syndromes, cerebrovascular diseases and heart failure among others (Joshi et al., 2022) (Qin et al., 2021). There are authors who report that the effects on the human body of air pollution due to NO₂ and PM have no threshold that can be regarded as safe, and that any level of exposure amounts to a health risk (Stafoggia et al., 2022) (Strak et al., 2021). The European Environment Agency's latest report states that 94-99% of the population of the 28 European Union Member States have been exposed to nitrogen dioxide (NO₂), fine particulate matter (PM) and ozone (O₃) levels in excess of the WHO 2019 guideline values (European Environment Agency, 2021).

In addition to chemical pollution, the WHO rates acoustic pollution as one of the main environmental risks for health, with a considerable related disease burden in Europe (WHO Regional Office for Europe, 2018). The European Environmental Agency's most recent report points out that one out of every five Europeans is exposed to noise levels that could be seriously harmful to health (European Environment Agency, 2021). Although there are recent research linking noise to depression, risk of cardiovascular disease (Manukyan, 2022) (Münzel et al., 2021) and chronic obstructive pulmonary disease (Liu et al., 2021), the health effects of noise have not been as widely studied as those of chemical pollution.

Both chemical and noise pollution tends to affect extremes of age to a greater degree (Gupta et al., 2018) (United Nations Environment Programme, 2022). Affection on genes involved in the inflammatory response has been described if exposure to pollution occurs during

pregnancy and early life (Isaevska et al., 2021) and an increased risk of dementia among the elderly (Costa et al., 2020) (Delgado-Saborit et al., 2021).. Hence, a study on the effect of pollution, both chemical and acoustic, by age group, could prove highly useful and would help in designing plans that were more in line with population needs.

In recent decades, European countries have implemented policies to regulate air pollution (Rodrigues et al., 2021). This has allowed the average concentration of PM_{2.5} in all European countries to have decreased by 44% by in 2019 compared to 1990 (Juginović et al., 2021). In Spain, an annual limit for PM_{2.5} concentration came into force in 2015, which until then had been an objective and not a limit value (Evaluación de la calidad del aire en España, 2015).

Spain's large expanse of territory, the climatic differences between its regions, and the continuous changes in the socio-demographic characteristics of the population can amount to an important limitation in large-scale studies that group data on very extensive regions, by rendering extrapolation of results to specific cities difficult. What is therefore required are studies on limited regions, using updated socio-demographic data. This would allow for specific air-quality improvement plans focused on the most vulnerable population to be implemented in cities, with the aim of achieving an improvement in the quality of life of their inhabitants.

From the stance of improvement in the quality of life, rather than measuring attributable or premature mortality, it is more useful to measure morbidity based on hospital admissions, since the latter is a clear indicator of the lack of a healthy lifestyle. Moreover, this would allow for a more accurate quantification of healthcare costs. Despite its usefulness, however, there are few studies that establish the economic impact associated with hospital admissions attributed to air pollution, both chemical and acoustic.

The aim of this study was therefore to analyse the effect of chemical and acoustic pollution on hospital admissions of the resident population of the Madrid Autonomous Region (MAR) (Comunidad Autónoma de Madrid), by quantifying admissions attributable to pollution and their related economic cost.

METHODS

Study design

We conducted an ecological, retrospective, longitudinal, time series study. Unscheduled hospital admissions to hospitals in the MAR were linked to short-term air and acoustic pollution, controlling for the effect of different confounding variables, whether meteorological or control variables of seasonality and the trend and autoregressive nature of the series.

Dependent variable

As our dependent variable, we took daily unscheduled admissions as per the International Classification of Diseases, 10th edition (ICD-10), excluding accidents. For analysis purposes, the following were considered: admissions due to all causes (ICD-9:1-799; ICD-10: A00-R99) and, separately, admissions due to respiratory (ICD-9: 460-487; ICD-10: J00-J99) and circulatory causes (ICD-9: 390-459); ICD-10: I00-I99), registered in the MAR across the period 1 January 2013-31 December 2018. These data were obtained under a National Statistics Institute (Instituto Nacional de Estadística/INE) confidentiality protocol. The data were broken down by age group (<2 years, 2 to 10 years, 11 to 64 years, 65 to 79 years, and 80+ years).

Independent variables

The main independent variables were mean daily air pollution concentrations measured in $\mu g/m^3$ and acoustic pollution measured in dB(A). Air quality data were sourced from the Ministry for Ecological Transition and Demographic Challenge (Ministerio para la Transición Ecológica y Reto Demográfico) for the same period (1 January 2013-31 December 2018). Based on the data set from all the measuring stations in the MAR, we calculated the mean daily levels of particulate matter having a diameter of 2.5 microns or less (PM_{2.5}), particulate matter having a diameter of 10 microns or less (PM₁₀), nitrogen dioxide (NO₂), and 8-hour ozone (O_{3oct}: maximum value registered between 8 and 16 hours).

Acoustic pollution data were supplied by the Madrid Municipal Permanent Acoustic Pollution Monitoring Grid (Red Fija de Control de la Contaminación Acústica) and the AENA

Airports Acoustic Pollution Monitoring Grid. The data from these stations were then used to obtain the mean equivalent diurnal noise ($L_{Aeq7-23h}$), nocturnal noise ($L_{Aeq23-7h}$) and daily noise (L_{Aeq24h}) levels.

Due their importance as confounding variables, we used meteorological data drawn from readings taken at the Madrid-Retiro Observatory (MAR reference observatory) for the same period and furnished by the State Meteorological Agency (Agencia Estatal de Meteorología/AEMET). We recorded the daily values of maximum and minimum temperature (°C), air pressure (hPa), number of hours of sunlight per day, wind (km/h) and relative humidity (%). Temperature was included as two transformed variables —for low (Carmona et al 2016) and high temperature (Diaz et al 2015)— that converted lineal their non-lineal association with dependant variables. As high temperature is associated with short-term impacts, we included lagged variables of order 4 in this case (Diaz et al 2015). As low temperature is associated with long-term impacts, we include lagged variables of order 14 in their case (Díaz et al 2005). The relationship with relative humidity was linear, so no transformation was necessary. In this case, lagged variables of order 14 were included in the models. The geographical distribution of their stations could be consulted in supplementary materials figure 1.

The following control variables were also included: annual (365 days), six-monthly (180 days), four-monthly (120 days) and quarterly (90 days) seasonality using the sine and cosine functions. The trend of the series was taken into account using a counter n1, which assigns a number to each day of the series, such that n1 equals 1 for 01/01/2013, n1 equals 2 for 02/01/2013 and so on successively. We created dummy variables for the days of the week and controlled for the autoregressive nature of the dependent variable. In addition, we also controlled for Public Holidays in the MAR across the study period.

Statistical analyses

Initially, we performed a descriptive analysis of all the dependent and independent variables, by calculating the percentage of days on which the WHO's latest 2021 guideline values (WHO global

air quality guideline, 2021) and Spanish statutory limit values (RD 102/2011) (*Real Decreto* 102/2011, de 28 de enero, relativo a la mejora de la calidad del aire, 2011) were exceeded, and controlling for the presence of outliers.

According to previous studies, the functional relationships between hospital admissions and the environmental variables analysed display a linear distribution without threshold (Ortiz et al., 2017) (Linares et al., 2018), save in the case of variables of temperature and 8-hour ozone, which show a quadratic distribution (Díaz et al., 1999) (Alberdi et al., 1998). In view of this, parametrisations were only done for these last two variables.

In the case of 8-hour ozone, the functional relationship with all-cause hospital admissions was shown to be quadratic. To parametrise the function, the 8-hour ozone level corresponding to the minimum of the quadratic function was calculated by making the pertinent adjustment to a second-order polynomial, with this value being set at 147.5 μ g/m³, and a new variable was created to identify values that exceeded the threshold calculated, defined as follows:

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$$O_{3oct}high = 0, ifi [O_{3oct}] < 147.5 \,\mu\text{g/m}^3$$

$$O_{3oct}high = O_{3oct} - 147.5 \,\mu\text{g/m}^3, if [O_{3oct}] > 147.5 \,\mu\text{g/m}^3$$

For temperature, we used the threshold values set by the Ministry of Health for the definitions of heat wave (corresponding to 34°C for the maximum daily temperature) (Ministerio de Sanidad, 2022b) and cold wave in the MAR (corresponding to -2°C for the minimum daily temperature) (Dirección General de Salud Pública, 2017). Two new variables were created, defined as follows:

Theat =
$$0$$
, if $Tmax < 34$

Theat =
$$Tmax - 34$$
°C, if $Tmax > 34$

$$Tcold = 0, if Tmin > -2$$

In the case of noise, given that there are no situations of zero noise, the minimum value of the whole series was established as the threshold, with this being set at 41.7 dB(A) for L_{Aeq7-} and 36.3 dB(A) for nocturnal noise.

Given that the health effects of independent variables on dependent variables may be lagged in time, we calculated the lags for the variables of air, acoustic and meteorological pollution in order to analyse the delayed effect. In the case of PM_{2.5}, PM₁₀, NO₂ and noise, the effect may be lagged by up to 5 days (Ortiz et al., 2017) (Linares et al., 2018), and in the case of ozone by up to 9 days (Díaz et al., 2018). For the difference in pressure, the effect is detected up to 8 days afterwards (González et al., 2001), and the effect of heat may be delayed by up to 5 days (Díaz et al., 2002). For relative humidity and cold, there were no previous studies that had analysed these jointly with the remaining meteorological variables, and we therefore allowed for a lag of 14 days.

To ascertain the impact of air and acoustic pollution on daily hospital admissions, we fitted generalised linear models (GLMs) with a Poisson regression link and controlled for overdispersion. We applied the backward method, whereby all the variables -both meteorological and pollution-related- are initially included along with their respective time lags. We also included the control variables of seasonality, and trend and autoregressive nature of the series, with those of less statistical significance then being gradually eliminated until all the variables had a significance of p<0.05. Based on the values of the significant estimators, relative risks (RRs) were calculated for every one-unit increase in the independent variables. In the case of ozone, PM_{10} , $PM_{2.5}$ and NO_2 , the increase in risk of hospital admission was calculated for every rise of 10 μ g/m³. To estimate the risk of hospital admission attributable to air and acoustic pollution, the above RRs were used to calculate the attributable risks (ARs) as per Coste and Spira's equation (1991) (Coste & Spira, 1991):

209	$AR = \frac{(RR - 1)}{RR} \times 100$

- The ARs were then used to calculate the number of admissions attributable to chemical and acoustic pollution in two cases:
- without considering any threshold (in the case of 8-hour ozone, this was considered as
 from its previously calculated health-impact value).
 - 2. based on the guideline values set by the WHO.

v17.0 and Microsoft Excel 2019 software packages.

Lastly, an economic estimate of hospital admissions was drawn up. To this end, the cost of the hospital process was first ascertained by calculating the weighted average of the mean Diagnosis Related Group (DRG) cost, using the APRGRD v.35 grouping system (2019 update). Weightings were assigned in accordance with the relative DRG weights (Ministerio de Sanidad, 2022a). We then calculated the number of admissions among the gainfully employed population (INE, 2022a) (INE, 2022b) and the cost of sick leave (Navarro-Espigares JL., 2021), and added the cost of the hospital process to the cost of sick leave.

All statistical analyses were performed using the IBM SPSS Statistics v.28 and STATA/BE

RESULTS

Emergency hospital admissions from 1 January 2013 to 31 December 2018 (total of 2191 days) were analysed. The distribution by type of admission and age group is shown in Table 1. The mean daily number of all-cause admissions (ICD: A00-R99) was 956: of these, 19.4% were admissions due to respiratory causes (ICD-10: J00-J99) and 15.6% were admissions due to circulatory causes (ICD-10: I00-I99). The descriptive analysis of air and acoustic pollution and meteorological conditions is summarised in Table 2.

Table 3 shows the percentage of days on which the WHO 2021 (WHO global air quality guideline, 2021) and Spanish statutory thresholds (RD 102/2011) (Real Decreto 102/2011, de 28

de enero, relativo a la mejora de la calidad del aire, 2011) were exceeded. All the pollutants analysed exceeded the WHO threshold at some time. In the case of $PM_{2.5}$, the threshold (15 $\mu g/m^3$) was exceeded on 11-19% of days in the 2013-2018 series, while for NO_2 the threshold (25 $\mu g/m^3$) was exceeded on 41-68% of days. In the case of 8-hour ozone, the WHO-recommended threshold (100 $\mu g/m^3$) was exceeded on 21-29% of days, and the Spanish statutory threshold (120 $\mu g/m^3$) was exceeded on 4-11% of days.

The RRs and ARs, along with their corresponding lags, which proved statistically significant (p <0.05) in the Poisson regression models for hospital admissions due to natural, respiratory and circulatory causes, are shown in Figure 1. Whereas NO₂ had a significant effect on natural- and respiratory-cause admissions, 8-hour ozone was linked to admissions due to natural and circulatory causes. No statistically significant association was however found for PM for any type of admission. With regard to noise, a significant association was observed for all three types of admissions, with the most relevant being that detected for circulatory-cause admissions attributable to $L_{Aeq7-23h}$.

Figure 2 shows the significant independent variables with the models broken down by age group for natural-cause admissions. The pollutant with the greatest effect on admissions was 8-hour ozone in the under-2 age group.

The models constructed in our study made it possible to quantify admissions attributable to chemical and acoustic pollution, along with their economic assessment, which can be seen in Tables 4 and 5. The results show that every year, 8246 (95% CI: 4580 - 11905) natural-cause admissions are attributable to overall exposure to NO_2 , which accounts for 2.4% of all hospitalisations. These admissions amount to an annual hospital expenditure of close on 120 million euros. Moreover, if the thresholds established by the WHO had been complied with, 2388 (95% CI: 1326 - 3447) annual natural-cause admissions attributable to exposure to NO_2 could have been prevented. In the case of respiratory causes, 2728 (95% CI: 1231 - 4219) annual admissions were attributed to NO_2 , accounting for 4% of all hospitalisations. Applying the WHO

guideline values, out of this total, 862 (95% CI: 389 – 1334) annual admissions could have been prevented.

The pollutant with the second highest number of attributable admissions was noise. Every year, 5685 (95% CI: 2533 – 8835) natural-cause admissions are attributable to exposure to acoustic pollution on the same day, accounting for 1.6% of all hospital admissions. These admissions amount to more than 82 million euros in annual hospital expenditure. The effect of noise is even greater in respiratory- and circulatory-cause admissions, 2.9% and 4.47% of which are respectively attributed to acoustic exposure on the same day.

DISCUSSION

The effect of air pollution on mortality has been widely studied in recent years (Stafoggia et al., 2022) (Orellano et al., 2020), but to be able assess the effect exerted by pollution on health it is necessary to analyse morbidity as reflected in emergency hospital admissions. In our work, NO₂ was found to be associated with an elevated risk of natural and respiratory cause admissions, and 8-hour ozone was found to be associated with an elevated risk of natural and circulatory cause admissions. These findings are closely related to both pollutants exceeding WHO recommended thresholds 20-70% of the days. A study conducted in Beijing corroborates the fact that NO₂ and ozone are the pollutants with greatest impact on health (Zhong et al., 2019).

Yet, other studies describe different magnitudes in the associations between hospital admissions and pollution. A study of a French cohort followed up for 12 years, with mean PM_{2.5} concentration levels of 10.6 μ g/m³, NO₂ concentration levels of 25.8 μ g/m³, and ozone concentration levels of 94.4 μ g/m³ -all similar to those described in our study- obtained the following RRs for natural-cause admissions: 1.107 (95% CI: 1.079 – 1.136) for PM_{2.5}; 1.029 (95% CI: 1.002 – 1.057) for NO₂; and 1.008 (95% CI: 0.974 – 1.044) for ozone (Sanyal et al., 2018). Similar results were found in a recent meta-analysis which studied countries around the world and reported RRs for respiratory-cause admissions of 1.014 (95% CI: 1.008 – 1.020) for NO₂,

1.008 (95% CI: 1.005 - 1.011) for 8-hour ozone, and 1.010 (95% CI: 1.001 - 1.020) for SO₂ (Zheng et al., 2021). Another recent meta-analysis with data on over 23 million participants described that exposure to PM_{2.5}, PM₁₀, SO₂, NO₂, CO and ozone was associated with a statistically significant increase in risk of hospital admission due to cerebrovascular disease for all pollutants (Niu et al., 2021). Contrary to what has been shown in these studies, in our work the RR of natural causes due to 8-hour ozone is much higher than the RR due to NO₂, however, admissions attributable to NO₂ are approximately 100 times higher than admissions attributed to 8-hour ozone. This is because in Madrid the functional relationship of 8-hour ozone with hospital admissions is quadratic. The minimum value of atmospheric ozone corresponding to the minimum value of admissions is 147.5 μ g/m3, a very high value that only occurs in 0.3% of the days of the series studied.

When it comes to the percentage of admissions attributable to pollution, there are also differences in the studies published to date. A systematic review of 43 papers addressing the effects of NO_2 on hospital admissions describes a 0.57% (95% CI: 0.33 – 0.82) increase in respiratory-cause admissions for every daily rise of 10 μ g/m³ in NO_2 (Mills et al., 2015). In contrast, a recent study conducted in Casablanca reported that an a 10 μ g/m³ rise in NO_2 concentrations increased circulatory-cause admissions by 9% at lag 3, and respiratory-cause admissions by 3% on the same day (Nejjari et al., 2021). Seen against our Madrid-based study, this latter value is the most similar, with a 2% increase in respiratory admissions for NO_2 on the same day, though with no relationship being found between NO_2 and circulatory-cause admissions. All these differences may be due to a lack of homogeneity between the populations compared, since many health determinants, such as socio-economic level, race, education, type of dwelling, etc., were not taken into account in most of the studies.

Furthermore, when analysing the effect of pollution on the human body, one has to take into account other factors, such as temperature and other meteorological variables, which are intercorrelated (Ahad et al., 2020). For instance, the presence of NO₂, solar radiation and high

temperatures are required for the formation of ozone (WHO global air quality guideline, 2021). As regards temperatures, the effect *per se* of heat and cold waves on health is well documented (Wondmagegn et al., 2021) (López-Bueno et al., 2020), though recent studies undertaken in Spain show that mortality attributable to heat is gradually decreasing, due to adaptation to temperatures (López-Bueno et al., 2021) (Follos et al., 2020). For this reason, and in order to study the effect of atmospheric pollution as reliably and accurately as possible, meteorological variables have been included in our research, including heat and cold waves. This means that studies that do not take these variables into account may offer results that differ from ours.

Our study observed that, at present, PM are not statistically significantly associated with any type of short-term emergency hospital admission in the MAR. This may be due to the fact that the mean annual concentrations of $PM_{2.5}$ and PM_{10} in Madrid fell from 13 and 25 $\mu g/m^3$ in 2009 to 9.9 and 17.5 $\mu g/m^3$ in 2019 respectively (Dirección General de Medioambiente Sostenibilidad, 2019). One of the possible reasons for this drop is that in 2015 the annual limit for this pollutant entered into force(Evaluación de la calidad del aire en España, 2015). In Madrid, in the period 2013-2018, the SO_2 and CO pollution levels were very much below the values regarded as a health risk, with average annual concentrations of 2 $\mu g/m^3$ and 0.4 $\mu g/m^3$ respectively (Dirección General de Medioambiente Sostenibilidad, 2019), which is in fact why these pollutants were not included in our analyses.

The effect of pollution varies according to the age of the population, with children and the elderly being most vulnerable, so that an analysis broken down by age group yields valuable information. Our study found that the age groups with the highest risk of hospital admission due to pollution were children under 2 years for 8-hour ozone, followed by the elderly aged from 65 to 79 years for the same pollutant. As mentioned above, it should be borne in mind that there were only 7 days in the entire series with elevated ozone concentrations resulting in very high RRs. Moreover, the negligible number of hospitalisations occurring in the under-2 age group means that the RRs obtained are higher than in other age groups. Even so, a Texas study also

described the important effect that pollution has on children, reporting that at 4 days of 8-hour ozone exposure, children aged 5 to 14 years had a higher risk of hospitalisation due to asthma than did the older population, with an RR of 1.047 (95% CI: 1.025 - 1.069) (Zu et al., 2017).

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The effect of NO₂ concentrations is seen in all age groups, with a weaker association in terms of RR but with a greater impact on hospital admissions overall, this being the chemical pollutant to which most hospital admissions are attributed. One study undertaken in China found a statistically significant association for NO₂ at lag 5, and hospital admissions due to pneumonia in children under 15 years of age, with the effect being most marked in infants under 1 year of age (Li et al., 2018).

In addition to chemical-type air pollution, acoustic pollution has an equally relevant role in health. Its effect on short-term emergency hospital admissions is shown by the fact that our study found a statistically significant association between LAeq7-23h and all types of admissions, and for all age ranges, except children under the age of 2, of whom there were fewer. Furthermore, noise is the pollutant with which the highest proportion of attributable admissions is related, even higher than that recorded for NO2, ozone or PM. These findings are in line with those reported by other authors, such as Halonen et al., who report that L_{Aeq7-23h} increases the risk of hospitalisation due to cardiovascular disease in adults, and that nocturnal noise is responsible for the same effect in the elderly (Halonen et al., 2015). As mentioned above, children and the elderly are more vulnerable to the effect of the noise than is the rest of the population. A previous study in Madrid conducted on children under the age of 10 years described RRs of 1.02 (95% CI: 1.01 – 1.04) for natural-cause admissions and 1.05 (95% CI: 1.01 - 1.08) for respiratory- cause admissions (Linares et al., 2006) consistent with what was found in our study. More recent studies conducted in Madrid have respectively reported associations between exposure to noise and admissions due to suicide and anxiety (Díaz et al., 2020), and admissions due to exacerbations of symptoms of dementia (Linares et al., 2017).

Mention should also be made of other studies undertaken in Madrid, in which traffic noise has been linked to morbidity and mortality due to circulatory and respiratory causes (Tobías et al., 2015) (Recio et al., 2017). The common source for a very high proportion of NO₂ and noise pollution is road traffic, thereby making vehicles the main cause of hospital admissions due to circulatory and respiratory causes in Madrid (Navares et al., 2020). This highlights the fact that, while noise is a pollutant with health effects similar to those of the other chemical pollutants, scant research has targeted this pollutant, thus calling for more studies to continue assessing the effect of noise on health.

In addition to the marked impact which pollution has on population health, attention should be also drawn to the high related economic cost. Our study shows that NO₂ and noise are responsible for the highest number of attributable admissions, accompanied by an enormous hospital cost. From 2004 to 2006, the Aphekom project studied the impact of pollution in 25 European cities, and estimated that, if the threshold values annually recommended by the WHO in Europe had been observed, health systems would have saved 31 billion euros (Pascal et al., 2013). It should be borne in mind here that these data are twenty years old, so the current cost could be expected to be considerably higher. The lack of recent studies that calculate the healthcare cost associated with air and acoustic pollution highlights the need for further research to improve the welfare of the population.

Limitations

This study has a number of limitations. While the methodology used is standard for these types of studies (Samet et al., 2000), it can nevertheless give rise to a number of biases. To minimise these, we controlled for a range of variables, such as seasonality and the trend and autoregressive nature of the series. As this is an ecological study, individual inferences cannot be drawn from the results obtained, due to the ecological fallacy (Piantadosi et al., 1988). The study design only allows for collection of pollution data from a given number of stations, thus not representing real exposure at an individual level but instead obtaining average values of

daily concentrations. This approach was adopted to cover the possibility of residents who go to work at different places and are thus exposed to different levels of exposure. In the case of meteorological variables, data were obtained from a single observatory, but it should nevertheless be noted that it is the designated reference observatory for the MAR (Díaz et al., 2002).

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Madrid is an enough big city as to consider suburban areas or zones of influence associated with different stations. The exposure levels used were based on exposures determined on the basis of readings taken by external monitors and then averaged, with the result that they are not measures which represent individual exposure. Another bias from the monitors used can be the heterogeneity in the type, they are mostly urban but occasionally we used background type. Even so, this is a commonly used methodology in these types of studies (Samet et al., 2000). However, much of this residual confusion is controlled by inclusion in the model of variables such as: trend of the series, day of the week, annual, six-monthly and quarterly seasonalities and the autoregressive nature of the series. No specific validation was carried out to assess the representativeness of spatial variability in air pollutants: our study suffered from Berksontype measurement error, among other biases associated with an ecological exposure, as is common in most time-series studies of air pollution, which leads to no or little bias but decreases statistically power. At all events, most air-pollution studies address the misalignment problem (albeit only implicitly), by using a two-stage modelling procedure, or plug-in approach, where predictions from an exposure model (first stage) are used as covariates in a health-effect model (second stage) (Barceló et al., 2016).

Furthermore, there are significant correlations between particulate matter and between particulate matter and the high ozone variable (supplementary table). This problem has been controlled in the modelling process by including the control variables and excluding non-significant meteorological variables from the model.

A further limitation of this study is that use was made of hospital admission data which may have undergone coding errors: the foreseeable effect is minimal, however, since data sourced from official sources (National Statistics Institute/INE) were used across the entire study period.

Strengths

To our knowledge, this is one of the most up-to-date studies conducted in Spain in terms of the different types of pollutants analysed and their impact on short-term emergency hospital admissions. Moreover, many atmospheric variables and possible confounding factors were controlled for, in order to minimise the possibility of biases.

The study included an analysis of acoustic pollution, an aspect that is still little studied, thereby contributing to the generation of impact data on this environmental variable. No recent papers were found on the effect had by traffic-related acoustic pollution on hospital admissions due to natural causes or major disease groups, despite noise being a risk factor, similar to air pollution, that gives rise to a significant morbidity burden and related economic cost.

This study is, moreover, of great interest for national plans that seek to address the environment and health and the development of measurable and quantifiable indicators, since the effects of pollution were analysed at a regional level and their calculation can be extrapolated to other geographical areas of interest.

Conclusion

Despite the fact that air-quality control regulations have led to an improvement in the atmospheric situation in recent years, air pollutant levels continue to be high. The related morbidity is manifested in an excessive number of attributable hospital admissions, with the ensuing loss of the population's quality of life and the great financial cost that this entails. The short-term effect on hospital admissions due to NO₂ and ozone concentrations and noise levels continues to be very high in cities such as Madrid, rendering it necessary to update statutory

440 threshold limits to levels closer to those recommended by the WHO, and to implement new 441 public health policies that would continue to protect the health of the entire population. 442 **Conflicts of interest** 443 The authors declare that there are no conflicts of interest. 444 Disclaimer 445 The researchers declare that they have no conflicts of interest that would compromise the 446 independence of this research work. The views expressed by the authors are not necessarily 447 those of the institutions with which they are affiliated. 448 Acknowledgements 449 The authors would like to express their gratitude for the following grants from the Carlos III 450 Institute of Health (Instituto de Salud Carlos III/ISCIII) for the ENPY 304/20, and ENPY 436/21 451 projects.

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TABLE 1: Description of daily hospital admissions for the 2013-2018 series, Madrid.

	Mean				_
Variable	admissions	Mean	SD	Minimum	Maximum
	per year				
All-cause admission	All-cause admissions:				
Total	349099	956	169	537	1395
Women	196530	538	89	319	785
Men	152569	418	83	201	650
<2 years	20574	56	20	12	140
2 to 10 years	12481	34	11	6	68
11 to 64 years	152655	418	67	221	573
65 to 79 years	72373	198	45	83	355
80+ years	91016	249	58	103	502
Respiratory-cause admissions:					
Total	67825	186	77	48	554
Circulatory-cause admissions:					
Total	54413	149	34	54	230

SD: standard deviation.

TABLE 2: Description of air and acoustic pollution and the meteorological conditions for the 2013-2018 series, Madrid.

Variable	Mean	SD	Minimum	Maximum
Air pollution				
$PM_{2,5} (\mu g/m^3)$	10,3	4,7	3,2	33,1
$PM_{10} (\mu g/m^3)$	19,0	9,7	2,9	85,7
$NO_2 (\mu g/m^3)$	30,7	14,5	5,8	90,9
$O_{3 \text{ oct}} (\mu g/m^3)$	78,6	28,8	9,9	171,5
Acoustic pollution:				
Diurnal noise (dB(A))	55,8	2,5	41,7	62,1
Nocturnal noise (dB(A))	48	2,6	36,3	61,4
24h noise (dB(A))	54,1	2,4	40,2	60,0
Meteorological conditions:				
Relative humidity (%)	59,7	16,3	19,0	95,2
Atmospheric pressure (hPa)	940,7	6,0	911,8	962,6
T max (°C)	21,1	9,1	2,8	40,0
T _{min} (°C)	11,1	6,8	-3,0	25,9
Wind (km/h)	6,4	3,0	0,0	18,7
No. sunlight hours per day	8,1	4,3	0,0	14,4

SD: standard deviation.

TABLE 3: Percentage of days on which the WHO 2021 and Spanish statutory (RD 102/2011) thresholds were exceeded.

	PM _{2.5}	PM ₁₀	NO ₂	O _{3 oct}
2013				
WHO 2021 threshold	12.6%	0.5%	52.3%	21.1%
Spanish statutory threshold	-	0%	-	4.4%
2014				
WHO 2021 threshold	11.2%	1.9%	55.6%	21.4%
Spanish statutory threshold	-	0.8%	-	5.2%
2015				
WHO 2021 threshold	18.6%	3.3%	64.1%	26.6%
Spanish statutory threshold	-	1.6%	-	10.7%
2016				
WHO 2021 threshold	15.8%	3.3%	65.6%	24.6%
Spanish statutory threshold	-	1.4%	-	6.3%
2017				
WHO 2021 threshold	17.0%	2.2%	68.2%	27.9%
Spanish statutory threshold	-	0.8%	-	8.2%
2018				
WHO 2021 threshold	14.8%	2.2%	40.5%	29.0%
Spanish statutory threshold	-	0.8%	-	8.5%

PM_{2.5}: WHO threshold of 15 $\mu g/m^3$.

 PM_{10} : WHO threshold of 45 $\mu g/m^3$, Spanish statutory threshold: 50 $\mu g/m^3$.

 NO_2 : threshold WHO de 25 $\mu g/m^3$.

 $O_{3 \, \text{oct}} :$ WHO threshold of 100 $\mu\text{g/m}^3$, Spanish statutory threshold: 120 $\mu\text{g/m}^3$.

TABLE 4: Admissions per year attributable to pollutant.

	Mean annual attributable admissions (95% CI)	Mean annual admissions on WHO threshold being exceeded (95% CI)	% attributable admissions
Natural-cause admissior	is:		
NO ₂ (lag 0)	5191 (2966 - 7412)	1503 (859 - 2146)	1.49%
NO ₂ (lag 4)	3055 (1614 - 4493)	885 (467 - 1301)	0.88%
O _{3 oct high} (lag 1)	31 (11 - 51)	31 (11 - 51)	0.01%
O _{3 oct high} (lag 7)	24 (4 - 44)	24 (4 - 44)	0.01%
Diurnal noise (lag 0)	5685 (2533 - 8835)	-	1.63%
Respiratory-cause admis	sions:		
NO ₂ (lag 0)	1427 (529 - 2321)	451 (167 - 734)	2.10%
NO ₂ (lag 5)	1301 (702 - 1898)	411 (222 - 600)	1.92%
Diurnal noise (lag 0)	1987 (594 - 3378)	-	2.93%
Circulatory-cause admiss	sions:		
O _{3 oct high} (lag 4)	13 (6 - 19)	13 (6 - 19)	0.02%
Diurnal noise (lag 0)	2432 (1257 - 3605)	-	4.47%

Mean annual admissions on WHO threshold being exceeded, was obtained by calculating the mean number of daily admissions that occurred on days on which the daily threshold value recommended by the WHO was exceeded (O_3 : 100 $\mu g/m^3$, NO_2 : 25 $\mu g/m^3$).

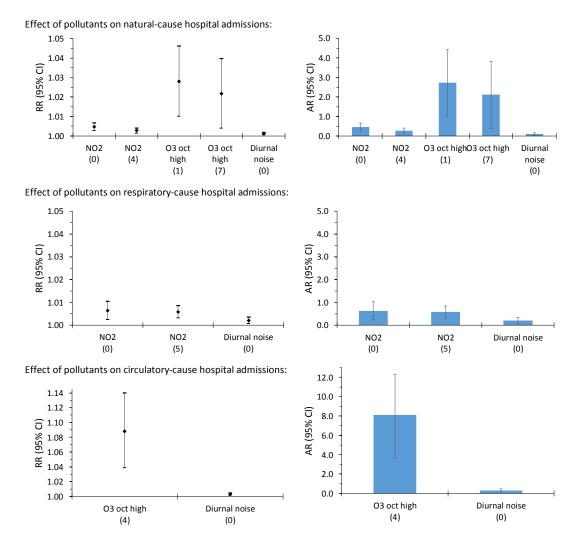


FIG 1. Relative risks (RRs) and attributable risks (ARs) with their respective 95% CIs of the significant independent variables according to type of hospital admission. Increases for every 10 μ g/m³ for air pollutants. In the case of ozone, increases for every 10 μ g/m³ above the 8-hour ozone threshold of 147.5 μ g/m³. Lags shown in brackets.

Effect of pollutants on natural-cause hospital admissions:

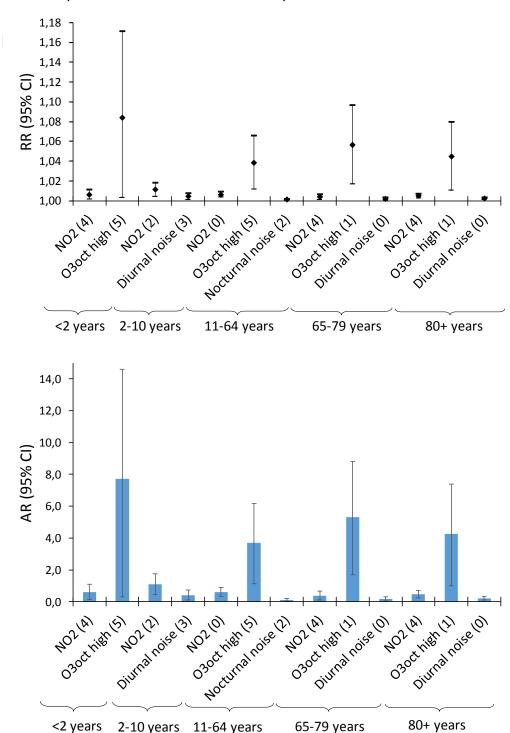


FIG 2. Relative risks (RRs) and attributable risks (ARs) with their respective 95% CIs of the significant independent variables in natural-cause admissions. Increases for every 10 $\mu g/m^3$ for air pollutants. In the case of ozone, increases for every 10 $\mu g/m^3$ above the 8-hour ozone threshold of 147.5 $\mu g/m^3$. Lags shown in brackets.