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Air pollution and human fertility rates

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ABSTRACT

Background: Some reports have suggested effects of air pollution on semen quality and success rates of in vitro fertilization (IVF) in humans and lower fertility rates in mice. However, no studies have evaluated the impact of air pollution on human fertility rates.
Aims: We assessed the association between traffic related air pollution and fertility rates in humans in Barcelona, Spain (2011–2012). We hypothesized that higher air pollution levels would be associated with lower fertility rates.
Methods: We calculated the general fertility rate which is the number of live births per 1000 women between the ages of 15 and 44 years per census tract. We used land use regression (LUR) modeling to estimate the air pollution concentrations (particulate matter, NO_2/NO_x) per census tract. We used Besag–York–Mollié models to quantify the relationship between air pollution and fertility rates with adjustment for a number of potential confounders such as maternal age and area level socio-economic status.
Results: We found a statistically significant reduction of fertility rates with an increase in traffic related air pollution levels, particularly for the coarse fraction of particulate matter (IRR = 0.87 95% CI 0.82, 0.94 per IQR).
Conclusion: This is the first study in humans to show an association between reduced fertility rates and higher traffic related air pollution levels.

1. Introduction

Exposure to air pollution has been associated with life expectancy, mortality and morbidity, including all cause mortality and cardiovascular and respiratory mortality and morbidity (Dockery et al., 1993; Hoek et al., 2013). More recently it has also been associated with adverse pregnancy outcomes such as preterm delivery and low birth weight (Dadvand et al., 2013; Pedersen et al., 2013; Stieb et al., 2012). Some reports have suggested effects of air pollution on semen quality (Guven et al., 2008; Hammoud et al., 2010; Rubes et al., 2005, 2007; Selevan et al., 2000; Srám et al., 1996), fecundability (Dejmek et al., 2000; Slama et al., 2013) and success rates of in vitro fertilization (IVF) in humans (Legro et al., 2010; Perin et al., 2010a,b) and lower fertility rates in mice (Mohallem et al., 2005; Silva et al., 2008; Veras et al., 2009). However, there is no available epidemiological study on the potential impact of air pollution on human fertility rate in a real-life setting.

This population-based study assessed the association between traffic related air pollution and fertility rates in Barcelona, Spain. We used the general fertility rate which is the number of live births per 1000 women between the ages of 15 and 44 years. We hypothesized that higher air pollution levels would be associated with low fertility rates.

2. Methods

2.1. Study area

Barcelona is the second most populated urban area in Spain with around 1.6 million inhabitants and a high population density of about 16,000 inhabitants/km^2 in a space of 101 km^2. Barcelona is a port situated on the northeastern part of the Iberian Peninsula and has a Mediterranean climate with fairly hot and humid summers and mild winters. Air pollution concentrations in Barcelona are among the highest in Europe, partly attributed to high traffic density and large proportion

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(~50%) of diesel-powered vehicles, relatively low precipitation, high population density, and its urban design characterized by semi-tall buildings (5–6 stories) and narrow streets reducing the dispersion of pollutants (Amato et al., 2009; Dirección General de Tráfico, 2008). In 2011 there were 1061 census tracts with a median area of 0.01 km^2 and an average population of 1522 people.

2.1.1. Study population

Population data by 5 year age groups per census tract were obtained from the 2011 census (Instituto Nacional de Estadística (INE), 2011). The number of all births per census tract for 2011 and 2012 was obtained from the routine data reporting (Departament d'estadística de Barcelona, 2012). We calculated both crude birth rate which is the number of live births per 1000 people and the general fertility rate which is the number of live births per 1000 women between the ages of 15 and 44 years. Only results for the latter are presented because they were very similar.

Since we could only use two years of data for the number of births because of changes in census tracts, we conducted sensitivity analyses with the numerator being the number of children in the lowest age groups (0–4) as it could be a fairly good surrogate for the number of newborns and it has a larger number of subjects. For these sensitivity analyses we also calculated the ratio of the number of children in age group of 0–4 per 1000 population and the number of children in age group of 0–4 per 1000 women between the ages of 15 and 44 years. Only results for the latter are presented because they were very similar.

2.1.2. Exposure to air pollution

Our exposure assessment was based on land use regression (LUR) modeling approach developed in the European Study of Cohorts for Air Pollution Effects (ESCAPE) framework (Beelen et al., 2013; Cyrys et al., 2012; Eeftens et al., 2012a,b). Briefly, following the ESCAPE protocol we selected 20 and 40 sites to measure PM_{10}, $PM_{2.5-10}$ (PM_{coarse}), $PM_{2.5}$, and $PM_{2.5}$ absorbance and NO_2 and NO_x respectively. These sites were a combination of both traffic and background locations representing the gradient of various land uses, emission sources, and traffic characteristics. Three monitoring campaigns, each two weeks long, were conducted in different seasons during 2009 and adjustment for temporal trends was carried out using an ESCAPE background monitoring site with continuous measurement data. European-wide and local Geographic Information System (GIS) data on land uses, traffic indicators, population density, and geographic description of monitoring sites and forecast area were obtained to create potential predictor variables. Multiple linear regression models were constructed separately for each pollutant following the ESCAPE supervised forward selection protocol (Beelen et al., 2013; Eeftens, 2012) using the annual average concentrations obtained from sampling campaign as outcomes. The adjusted R^2 of the final LUR models for PM_{10}, PM_{coarse}, $PM_{2.5}$, and $PM_{2.5}$ absorbance, and NO_2 and NO_x were 0.85, 0.72, 0.80, 0.83, 0.72 and 0.71 respectively and showed variation across Barcelona (Fig. A1) (Beelen et al., 2013; Cyrys et al., 2012; Eeftens et al., 2012a,b). We calculated the average levels per census tract for all of the pollutants.

2.2. Analyses

We included in our analyses a number of covariates: neighborhood socioeconomic status (MEDEA index Domínguez-Berjón et al., 2008), and ethnicity (% born abroad), education level (none or primary/secondary/university). The MEDEA index measures deprivation at the census tract level (Census 2001) based on five domains including percentage of manual workers, temporary workers, people with low education (overall), young population with low education, and unemployment (Domínguez-Berjón et al., 2008). These domains have been shown to explain 75% of the variability of all socioeconomic variables available in the Spanish census (Domínguez-Berjón et al., 2008).

We used Besag–York–Mollié (BYM) models (Besag et al., 1991) commonly used to analyze rates in spatial studies of small areas. This model let us incorporate the spatial information to our modeling with a smooth of the spatial distribution and a random effect of the census. At the same time, we added covariates to adjust the effect of the pollutants over the fertility rate. As our response counts, we use negative binomial regression to estimate the effects of air pollution using the number of women at fertile age as offset of the model. Also, to standardize the estimate by age we included the variables of percentage of population at each age range (0–4, 5–10, …). Air pollution estimates were given by interquartile ranges. All this modeling was done using integrated nested Laplace approximation (INLA) method (Rue et al., 2009) using the INLA package of R software (R Development Core Team, 2007).

2.3. Ethics approval

Ethics approval (no. 2008/3115/I) was obtained from the Clinical Research Ethical Committee of the Parc de Salut MAR, Barcelona, Spain, to carry out this study.

3. Results

The total population in Barcelona was 1,615,448. In 2011 and 2012 there were 13,884 and 13,733 births, respectively. There was considerable

Table 1
Description of the population by census tract.

Variable	Obs	Mean	Std.	Min	Max
Population	1061	1522.57	412.49	462.00	7211.00
General fertility rate ∗ 1000 women 15–44 years	1061	43.7	16.3	14.4	146.6
Crude fertility rate ∗ 1000 inhabitants	1061	8.8	3.0	2.5	28.9
Female population of reproductive age	1061	368.92	111.22	105.00	1730.00
Number of newborns from foreigners	1061	322.20	250.48	53.00	2270.00
Number of foreign born women	1061	160.03	96.32	26.00	881.00
Percentage foreign born women	1061	19.41	8.28	4.2	61.1
MEDEA index	1061	−0.06	0.92	−1.84	3.42
NO_2 (μg/m^3)	1061	56.59	11.40	17.39	98.79
NO_x (μg/m^3)	1061	94.33	23.83	33.69	180.11
$PM_{2.5}$ (μg/m^3)	1061	17.12	2.23	7.80	23.48
PM_{10} (μg/m^3)	1061	39.26	2.43	23.03	48.80
PM_{coarse} (μg/m^3)	1061	21.16	2.32	11.91	26.00
$PM_{2.5}$ absorbance (1 unit)	1061	2.85	0.60	1.04	4.65
Percentage women 35+	1061	65.1	4.38	45.7	83.5
Percentage women 40+	1061	57.1	5.4	26.2	79.2
Percentage women 45+	1061	49.9	6.0	17.2	72.8
Number of children between 0 and 4 years / total population ∗ 1000	1061	40.69	12.4	11.2	162.5
Number of children between 0 and 4 years / females of reproductive age ∗ 1000	1061	168.82	47.5	50.5	544.8

Table 2
Correlation between pollutants.

	NO_2	NO_x	$PM_{2.5}$	PM_{10}	PM_{coarse}
NO_x	0.79				
$PM_{2.5}$	0.59	0.76			
PM_{10}	0.43	0.69	0.75		
PM_{coarse}	0.23	0.22	0.39	0.37	
$PM_{2.5}$ absorbance	0.72	0.88	0.76	0.72	0.19

Table 3
Risk estimates for fertility (number of newborns by 1000 women of reproductive age) in Barcelona (2011–2012).

	IRR (95% CI)	DIC
NO_2 (IQR = 11.97 μg/m^3)	0.974 (0.945, 1.003)	5662.4
NO_x (IQR = 26.15 μg/m^3)	0.987 (0.957, 1.018)	5664.9
$PM_{2.5}$ absorbance (IQR = 0.71 unit)	0.992 (0.962, 1.024)	5665.3
PM_{10} (IQR = 2.88 μg/m^3)	0.994 (0.966, 1.023)	5665.8
PM_{coarse} (IQR = 3.54 μg/m^3)	0.882 (0.828, 0.942)	5660.6
$PM_{2.5}$ (IQR = 2.51 μg/m^3)	0.984 (0.954, 1.015)	5664.9

Adjusted for socioeconomic status (MEDEA), age, and women born outside Spain (%).
IQR = interquartile range.

variation in the number of people, fertility rate, the number of foreign-born women, women over a certain age and socio-economic status (MEDEA) between census tracts (Table 1).

Average levels of air pollutants showed also considerable differences, with a more than 5 fold difference between the highest and lowest levels for NO_2 and NO_x, and 2-fold difference for PM_{10} and PM_{coarse} (Table 1, Table A1). Average levels of different pollutants at census tract level were generally moderately to highly correlated, except for PM_{coarse}, which showed low correlation with other pollutants (Table 2).

Unadjusted fertility rates declined with increasing air pollution levels (Fig. 1). After adjustment for covariates, we found reduced fertility rates with increases of all pollutants, but only for the PM_{coarse} fraction was this statistically significant (Table 3). Two pollutant models including the PM_{coarse} fraction and any of the other pollutants did not change risk estimate materially for the PM_{coarse} fraction (Table A2).

Sensitivity analyses using the ratio of the number of children in age group of 0–4 and fertile women showed significantly reduced estimates for $PM_{2.5}$, PM_{10} and NO_x, but PM_{coarse} lost its statistical significance (Table A3).

4. Discussion

In this cross-sectional study using registry data at census tract level and adjusting for a number of important potential confounders, we found a statistically significant reduction of fertility rates with an increase in traffic related air pollution levels, particularly for the PM_{coarse} fraction. These results may therefore hint that air pollution could be associated with lower fertility rates in humans.

This is the first report of air pollution levels and fertility rates in humans. A reduction in the number of offspring has been reported in mice after air pollution exposure (Mohallem et al., 2005; Silva et al., 2008; Veras et al., 2009). Although it is still unclear whether the reduction in fertility rates is due to maternal or paternal factors, various studies have reported higher failure rates of IVF (Legro et al., 2010; Perin et al., 2010a,b) and effects on semen quality (Guven et al., 2008; Hammoud et al., 2010; Rubes et al., 2005, 2007; Selevan et al., 2000; Srám et al., 1996), which could lead to infertility with increasing air pollution levels. Dejmek et al. (2000) and Slama et al. (2013) found reduced fecundability with higher air pollution levels in an industrial area. There is some suggestion that exposure to traffic related pollutants may lead to an increased risk of miscarriage (Green et al., 2009). Also possible effects mediated by maternal factors, such as endocrine disruption and non-adequate endometrial preparation for nidation, have been suggested (Mohallem et al., 2005; Veras et al., 2009). Finally, some

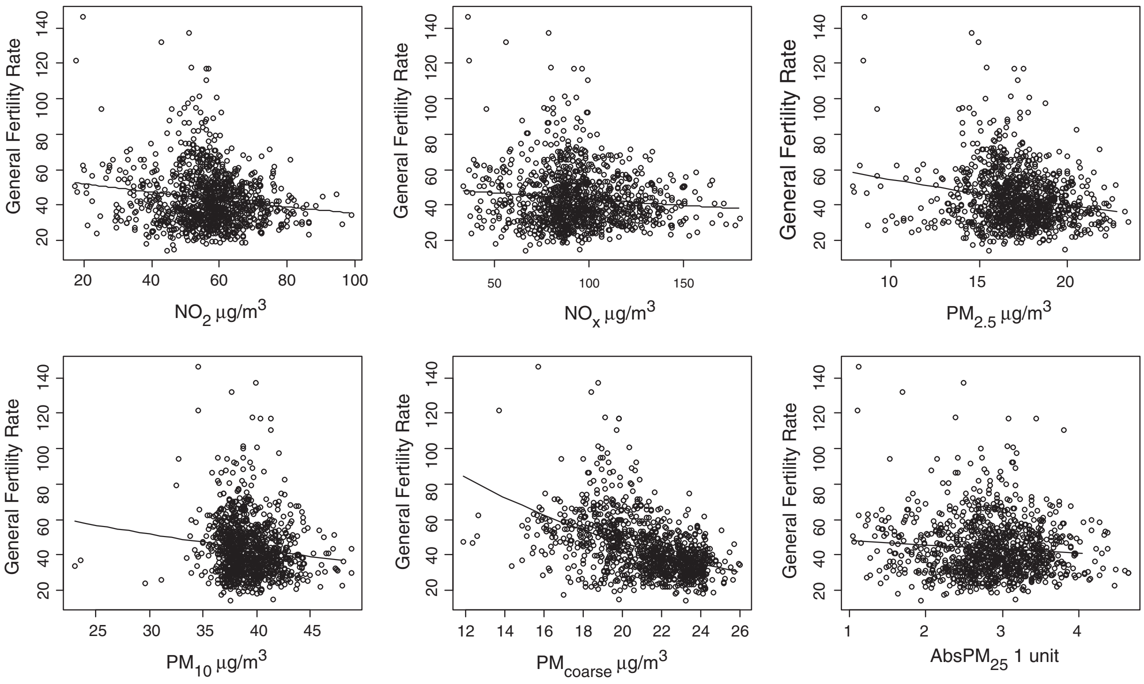

Fig. 1. Fertility rate against air pollution levels.

studies suggested a reduction in IVF implantation rates with environmental tobacco smoke, possibly sharing some mechanisms with air pollution (Benedict et al., 2011; Neal et al., 2005). Studying the effect of pollution on fertility is difficult, and the use of registry data and the cross sectional analyses are far from ideal. However, it is almost impossible to set up, or use existing cohorts to examine fertility rates, because they are not available or would require a large effort to obtain sufficient subjects. The advantage of registry data is that they are population-based, readily available, provide large numbers and may provide unbiased population counts.

We found reduced fertility rates with all the air pollutants and this may be because there was a generally moderate to high correlation between the average levels of the pollutants of the census tracts. The correlations between the PM_{coarse} and other pollutants were lower, and PM_{coarse} showed the largest reduction in risk estimates. The moderate to high correlation makes it hard to disentangle the effects of the separate pollutants, but in two pollutant models the effect of PM_{coarse} remained after adjusting for other pollutants. Furthermore, the elemental composition of the PM coarse fraction is a bit different compared to the smaller PM fraction and tends to contain more resuspended dust, mineral elements, tire-derived particles and some metals (Minguillon et al., 2014), which may explain some of the difference in observed associations in the main analyses. The $PM_{2.5}$ fraction which also showed an association with reduced fertility rates includes polyaromatic hydrocarbons (PAHs) and some metals which have endocrine disrupting properties (Jedynska et al., 2014; Minguillón et al., 2012). Further work is needed to explore this and the possible contribution of specific components of the PM.

The strengths of the study are the fairly large numbers, the detailed exposure assessment which used a standardized protocol and the relatively small size of the census tract. Although we used population and birth data from 2011 and 2012 and modeled exposure data from 2009, this is unlikely to make a substantial difference because the city spatial surface and the spatial distribution of pollutant sources have remained constant over this period. Studies in Italy, Great Britain, the Netherlands, and Canada have documented the stability of the spatial contrast over a 10-year period (Cesaroni et al., 2012; Eeftens et al., 2011; Gulliver et al., 2013; Wang et al., 2013). Furthermore in our sensitivity analyses with the ratio of children in the age from 0 to 4, we also found reduced fertility rates in association with air pollution, which were mostly statistically significant. This may be expected as the number of subjects is greater, increasing the statistical power. However, children in this age group may not have been born in this census tract, but moved there in early life, which leads to some measurement error. However, the mobility is expected to be low. A study of four Spanish birth cohorts during 2003–2008 has reported a mobility rate between 1% and 6% (Estarlich et al., 2011).

The limitation of the study is the use of registry data, the possibility for ecological bias, the limited number of covariates and the adjustment for only 5 year age periods. In our analyses we adjusted for census tract level socioeconomic status using the well established MEDEA index, the percentage of women born abroad, and the percentage of women over 35, but we could not adjust for other possible important covariates such as smoking or individual socioeconomic status. However, in a dataset with more than 8000 pregnant women residing in Barcelona City attending the obstetrics department of Hospital Clinic of Barcelona, which we have used for various studies on environmental risk factors (Dadvand et al., 2012), we found little correlation between the number of cigarettes smoked during pregnancy and PM and NO_2/NO_x exposure ($r \leq 0.06$). Furthermore, we found little difference in $PM_{2.5}$ levels between individual education levels (e.g. highest levels — $PM_{2.5}$ 16.7 $\mu g/m^3$, lowest level 17.2 $\mu g/m^3$). This suggests that there is little potential for confounding. Other possible unmeasured environmental factors which may differ between census tracts and exhibit correlations with air pollution and fertility are for example occupation, noise, soil contamination, green space, and industrial land use. Finally we did not have information whether the birth was a single birth or multiple births. The latter may be due to IVF treatment, which may be more frequent if there are fertility problems.

This is the first report on air pollution levels and fertility rates in humans. The observed associations are small and further studies are needed to confirm or refute the findings.

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Annex A

Table A1
Risk estimates for fertility (number of newborns by 1000 women of reproductive age) in Barcelona (2011–2012) for models with incremental adjustments.

	Crude model		Adjusted by SES		Adjusted for all the covariates		Adjusted by spatial component	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
NO_2 (IQR)	0.987	(0.948, 1.028)	0.984	(0.944, 1.026)	0.975	(0.935, 1.017)	0.974	(0.945, 1.003)
NO_x (IQR)	1.01	(0.969, 1.054)	1.008	(0.965, 1.053)	1.001	(0.957, 1.046)	0.987	(0.957, 1.018)
Absorbance (IQR)	1.005	(0.962, 1.051)	1.003	(0.958, 1.05)	0.998	(0.954, 1.045)	0.992	(0.962, 1.024)
PM_{10} (IQR)	0.985	(0.944, 1.028)	0.984	(0.942, 1.027)	0.98	(0.939, 1.023)	0.994	(0.966, 1.023)
PM_{coarse} (IQR)	0.894	(0.845, 0.946)	0.894	(0.845, 0.946)	0.887	(0.838, 0.938)	0.882	(0.828, 0.942)
$PM_{2.5}$ (IQR)	0.973	(0.934, 1.014)	0.969	(0.928, 1.011)	0.966	(0.925, 1.008)	0.984	(0.954, 1.015)

Table A2
Risk estimates of PM_{coarse} for fertility (number of newborns per 1000 women of reproductive age) after adjusting for other pollutants in Barcelona (2011–2012).

	PM coarse		
	IRR	LCI	UCI
NO_2	0.878	0.816	0.949
$PM_{2.5}$	0.855	0.791	0.927
NO_x	0.860	0.799	0.929
$PM_{2.5}$ absorbance	0.864	0.804	0.932
PM_{10}	0.851	0.790	0.920

Table A3
Risk estimates for the number of children between 0 and 4 years by 1000 fertile women (2011).

	IRR (95% CI)	DIC
NO_2 (IQR)	0.994 (0.982, 1.006)	7479.4
NO_x (IQR)	0.987 (0.975, 1)	7476
Absorbance (IQR)	0.988 (0.976, 1.001)	7477
PM_{10} (IQR)	0.988 (0.976, 1)	7476.2
PM_{coarse} (IQR)	0.996 (0.979, 1.013)	7480.4
$PM_{2.5}$ (IQR)	0.987 (0.975, 1)	7475.6

Adjusted for socioeconomic status (MEDEA), age, and women born outside Spain (%).
IQR = interquartile range.

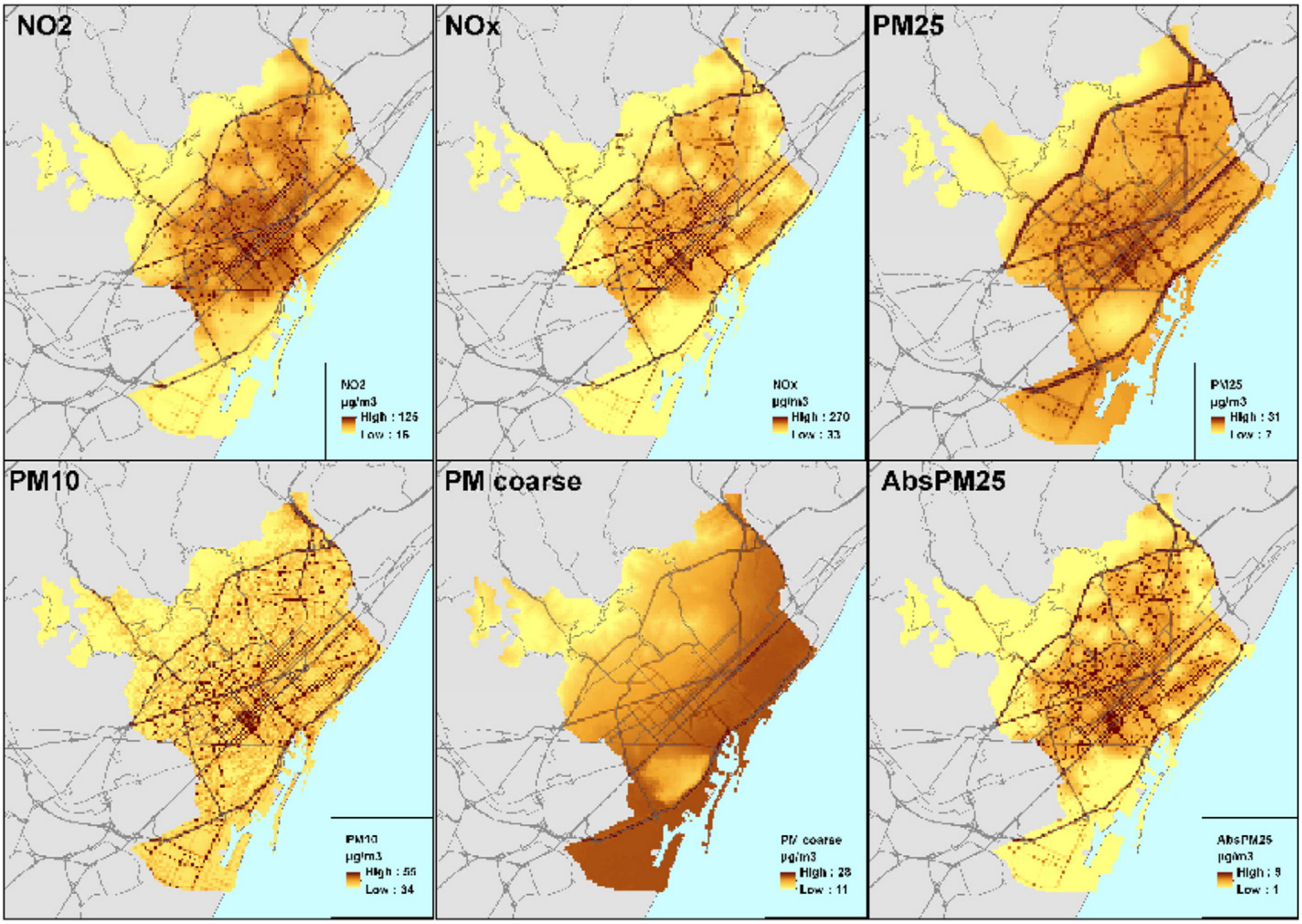

Fig. A1. Distribution of air pollution levels in Barcelona as modeled using land use regression models.

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