Air Pollution from Incinerators and Reproductive Outcomes

A Multisite Study

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Background: The few studies that have investigated the relationship between emissions from municipal solid-waste incinerators and adverse pregnancy outcomes have had conflicting results. We conducted a study to assess the effects of air emissions from the eight incinerators currently in operation in the Emilia-Romagna Region of Italy on reproductive outcomes (sex ratio, multiple births, preterm births, and small for gestational age [SGA] births).

Methods: We considered all births (n = 21,517) to women residing within a 4-km radius of an incinerator at the time of delivery during the period 2003–2010 who were successfully linked to the Delivery Certificate database. This source also provided information on maternal characteristics and deliveries. Each newborn was georeferenced and characterized by a specific level of exposure to incinerator emissions, categorized in quintiles of PM_{10}, and other sources of pollution (NO_x quartiles), evaluated by means of ADMS-Urban system dispersion models. We ran logistic regression models for each outcome, adjusting for exposure to other pollution sources and maternal covariates.

Results: Incinerator pollution was not associated with sex ratio, multiple births, or frequency of SGA. Preterm delivery increased with increasing exposure (test for trend, $P < 0.001$); for the highest versus the lowest quintile exposure, the odds ratio was 1.30 (95% confidence interval = 1.08–1.57). A similar trend was observed for very preterm babies. Several sensitivity analyses did not alter these results.

Conclusions: Maternal exposure to incinerator emissions, even at very low levels, was associated with preterm delivery.

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Several studies over the last two decades have assessed reproductive health in association with exposure to emissions from landfills[1] and to air pollution, especially traffic-related pollutants.[2–4] Only a few studies have investigated the relationship between emissions from municipal solid-waste incineration plants ("incinerators") and pregnancy outcomes.[1]

During the late 1970s and early 1980s, an excess of multiple births and altered sex ratio were observed in a population living in a region in Scotland where an incineration plant and chemical waste incinerator were located.[5,6] However, these results were not replicated in a Swedish study that evaluated the same outcomes over a longer period.[7] A subsequent study conducted in Japan investigated reproductive events within a 10-km radius of 63 incinerators with relatively high dioxin emission levels. None of the outcomes (sex ratio, low and very low birth weight, infant and neonatal deaths, including those due to congenital malformations, and spontaneous fetal deaths) was higher within a 2-km radius of the plants. However, infant mortality and the risk of infant mortality due to congenital malformations were reduced at 10 km from the incinerators.[8] Lin et al[9] examined adverse pregnancy events in an area of Taipei with high environmental exposure to dioxins and furans generated by an incinerator that began operations in 1992. The study addressed sex ratio, low birth weight, and gestational age. There were no differences in sex ratios or low birth weight, but premature birth (<37 weeks) was more frequent (odds ratio [OR] = 1.22 [95% confidence interval (CI) = 0.97–1.52]) among the most exposed subjects.

Changes in the sex ratio and frequency of multiple births are not necessarily related to a pathological mechanism, whereas increases in small for gestational age (SGA) and preterm delivery are more direct indicators of possible pathology. Sex ratio at birth may be altered by environmental and occupational chemical exposures (including dioxin, mercury, pesticides, and polychlorinated biphenyls)—possibly due, at least for some of these substances, to an endocrine-disrupting mechanism.[10] Although multiple births have seldom been associated with environmental risk factors, an increase in the twinning rate was reported in a study of a toxic-waste incinerator.[11]

We investigated the association between emissions from incinerators and pregnancy events in a recent time period (2003–2010). We considered reproductive outcomes evaluated in previous studies that could be investigated using the available administrative databases. This study is part of a larger project aimed at assessing air pollution from incinerators and their potential health effects in Emilia-Romagna, a region of northern Italy (Moniter Project: MONitoring Incinerators in the Territory of Emilia-Romagna Region).

METHODS

Area Under Study and the Plants

Almost half of the Emilia-Romagna region, including all its main cities, is located in the Po Valley, characterized by flat topography and climatic conditions with little rain and wind. These conditions do not promote the dispersion of pollutants, and air pollution levels throughout the region tend to be higher here than in Italy as a whole, particularly for particulate matter <10 µm in aerodynamic diameter (PM_{10}), nitrogen dioxide, and ozone.[12]

We defined the study area as the areas within a 4-km radius around each of the eight incinerators operating in the Emilia-Romagna region, located in Piacenza, Reggio Emilia, Modena, Bologna, Ferrara, Ravenna, Forlì-Cesena, and Rimini. These plants vary in their starting date (from 1968 to 2002), their technical characteristics, and capacity (from 56,000 to 180,000 tons per year) (eTable 1, http://links.lww.com/EDE/A719). All these plants are located in the outskirts of urban centers, with 200,000 people living within 4 km. A 4-km radius was chosen because beyond that distance it becomes difficult to assess the concentration of PM_{10} attributable to the emissions of the incinerator, whereas other pollution sources—such as traffic, industries, and domestic heating—become more prominent.

Simulations with Dispersion Models

We estimated the air concentration of pollutants around the plants using dispersion models with the quasi-Gaussian ADMS-Urban system (Cambridge Environmental Research Consultants, Cambridge, UK). We adopted homogeneous criteria for input data and for the meteorological variables.

Regarding the choice of which pollutant to use to simulate the effects of the plants, previous experiences in our region suggested that heavy metals were a suitable indicator of exposure to incinerators.[13] Unfortunately, only 2 to 5 measurements per year of emission for these pollutants were available from each site. Therefore, we used PM_{10} as a tracer of air pollution from the incinerators, with up to more than 17,000 measurements per year available per site (one measurement every 30 minutes) from the continuous monitoring systems required by law since the early 2000s. Moreover, preliminary simulations assured similar distributions of fallout for heavy metals and particulate matter.

We used hourly information on wind speed/direction, total cloud, and air temperature as input to the dispersion model to calculate atmospheric boundary layer parameters provided by the Meteorological Service of the Emilia-Romagna Regional Agency for Environmental Prevention. A reference year for each site was selected as meteorologically the most representative of the entire study period.

We ran nine yearly simulations for each plant from 2002 to 2010, which made it possible to take into account renovations of some plants (Bologna and Rimini), with changes in emission factors.

Nitrogen oxides (NO_X) were identified as the best tracer of air pollution deriving from other sources, such as traffic, industry, livestock and agricultural farms, and heating. The main reason for this choice was the completeness of emission data for this pollutant in comparison with others (particularly for industrial sites). Input data to the dispersion model were available from information on emissions from various sources collected during the study period. Pollution maps were obtained for each site and for each source mentioned above; each map was considered representative of the whole study period. Exposure to other sources was calculated as a sum of the single values derived from source-specific maps. All maps referred to yearly mean values.

Model outputs were mapped using ArcView GIS 9.0 (ESRI, Redlands, CA), and map layers for PM_{10} and NO_X were defined. Figure 1 provides an example of simulations for the incinerator (PM_{10}) and other air pollution sources (NO_X) in Bologna. Maps of other sites are provided in eFigure 1 (http://links.lww.com/EDE/A719).

Study Population

The municipal General Registry Offices in the study areas provided information (including dates of birth and addresses) for the 24,780 babies (2003–2010) born to mothers who were residents in the study area at the time of delivery. All the addresses were geocoded. All information concerning pregnancy and delivery was obtained through an individual link with the database of the Delivery Certificate for all births in the region (a formal document mandatory for all newborns in Italy, with data kept at the regional level). The linkage was possible for 21,517 babies (87%). There were some differences between linked and nonlinked infants: frequency of foreign mother (higher among the nonlinked, presumably due to spelling errors in names), site (nonlinked subjects were more frequent in Piacenza, where many deliveries take place in a contiguous Region), and exposure levels (higher among

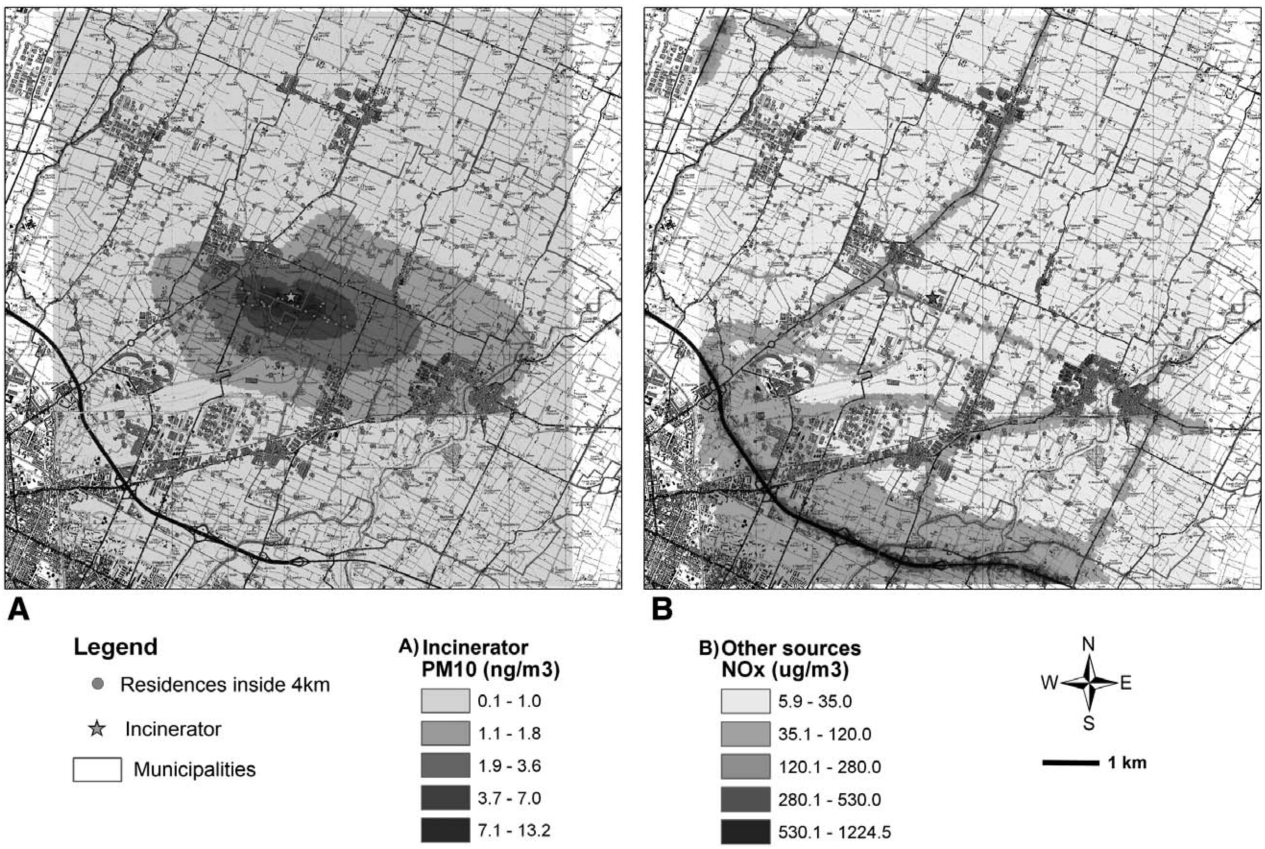

FIGURE 1. Pollutant dispersion map of Bologna site: A, PM_{10} (year 2006) for incinerator; B, NO_X for other sources.

the linked subjects) (data not shown). Children born through assisted reproduction techniques were excluded (353; 1.7%), leaving a final dataset of 21,164 newborns.

Individual Exposure Assessment

Each baby was characterized in terms of maternal exposure during pregnancy to PM_{10} emitted from the incinerators and to NO_X from other polluting sources. Based on the geocoded addresses of the residence at birth, we used modeling simulations to define exposure over the 9 months of pregnancy.

Starting with simulations of PM_{10} concentrations for each year, we estimated the monthly exposure to incinerators from the annual average considering periods when the plant was not operating. Any information on periods during which the plant was not in operation was used to weight this value on days of actual operation within the considered time period (monthly factors). To assign a value of pollutant for a given period of exposure (eg, trimester before conception), we took a weighted average of the values of up to two yearly maps:

$$Exp = \frac{\sum_{i=1}^{n1} Fi \times C_1(x,y) + \sum_{j=n1+1}^{N} Fj \times C_2(x,y)}{N}, \quad (1)$$

where

- n1 = months of pregnancy in the year before the year of birth,
- N = time-window in months (9 for the entire pregnancy),
- C_1 (x, y) = estimated PM_{10} concentration at the residence in the year before the year of birth,
- C_2 (x, y) = estimated PM_{10} concentration at the residence in the year of birth,
- Fi e Fj = monthly factors.

Quintiles of PM_{10} on the basis of the population distribution were calculated, with categories adjusted slightly to consider the natural cutoff points of pollutants.

In the 2003–2006 period, about 2,000 mothers were not exposed to incinerator emissions during pregnancy because the incinerator in Reggio Emilia was shutdown for an extended period (January 2003–June 2005). These women were assigned the lowest exposure level (set at 0).

As for all other sources, a value of exposure for each sector and for all sources was estimated at the address of residence at birth. Exposure values (μg/m^3) were then categorized in four levels, with the same criteria used for particulate matter.

Maternal Characteristics

We retrieved information from the Delivery Certificates database on maternal age, country of origin, educational level (considered an indicator of socioeconomic status [SES]), newborn birth order, and sex. Starting in 2007 an area-based Deprivation Index (census block of residence) was considered as a further SES indicator.[14] Information on smoking patterns was also available as of 2007. For the period 2007–2010, information on previous maternal morbidity was obtained from the Hospital Discharges database, considering the 3 years before the estimated conception date (all hospitalizations except those for obstetrics or trauma). Women who had been hospitalized at least once during that period were traced.

Outcomes Definition

The following pregnancy events were studied: multiple births (number of twin births); sex ratio (ratio between number of girls born and total number of newborns); preterm births (infants born before 37 weeks of gestation); very preterm (infants born before 32 weeks of gestation);[15] and SGA (newborns whose weight in grams was in the lowest 10th percentile for that gestational week and for the same sex). Because reliable Italian or European intrauterine growth curves were not available, we used Canadian curves.[16]

The complete data set was used to study multiple births and sex ratio. Twins (n = 523; 2.5%) were excluded from the analyses of preterm and SGA. For the analyses on SGA, infants born to Indian mothers (n = 266; 1.3%) were excluded because they require a different SGA referent.[17,18] The exclusion sequence can be seen in eFigure 2 (http://links.lww.com/EDE/A719).

The PM_{10} exposure of interest for multiple births and sex ratio was maternal exposure during the three months before conception, whereas for the other outcomes we examined exposure throughout pregnancy.

Statistical Analysis

For all examined outcomes (except SGA, which is not assessed by the Emilia-Romagna Delivery assistance database), we calculated prevalence rate ratios, standardized for mother's age and nationality (and 95% CIs), for each exposure level in order to compare prevalence rates of the study population with the whole Emilia-Romagna region.

We used multivariate logistic regression models to estimate ORs and 95% CIs for the association between quintiles of PM_{10} levels and reproductive outcomes, adjusting for exposure to other sources (NO_X) and for maternal covariates: age, educational level, country of origin, and newborn birth order, and sex except for sex ratio and SGA. We conducted a test for trend across categories of exposure to incinerator emissions. Because some variables were available only for the years from 2007 to 2010 (Deprivation Index, smoking during pregnancy, and comorbidity), we performed an analysis for the whole period, as well as for 2007–2010.

To test the robustness of the results, we carried out additional sensitivity analyses to exclude infants born to foreign women, newborns not exposed to emissions owing to prolonged shutdown of one incinerator, and infants born to mothers who were smokers or with unknown smoking habits. In addition, in order to assess the contribution of each site to the result, we examined regression models excluding one site at a time. Data analysis was performed using Stata IC 11 (StataCorp LP, College Station, TX).

RESULTS

The estimated annual average exposure to PM_{10} from incinerators in the study areas was 0.96 ng/m^3 (standard deviation [SD] = 1.50 ng/m^3) in 2003, decreasing to 0.26 (0.27) ng/m^3 in 2010 as plants were renovated during the study period. The mean per-person exposure level was 0.57 ng/m^3 (SD = 1.06). Mean per-person exposure to other sources, expressed as annual mean NO_X concentration calculated for the whole study period, was 53.6 mg/m^3 (SD = 34.3), with a median of 48.4 mg/m^3.

Table 1 shows the main characteristics of study population by PM_{10} categories. The level of exposure to other pollution sources was lower for subjects more exposed to the emissions from incinerators. There was no clear relationship between exposure and maternal characteristics except for nationality, with a smaller proportion of foreign women in the most-exposed categories. Twelve percent of women smoked during their pregnancy, with another 8% missing this information. Only 2% of mothers had been recently hospitalized for other reasons, in line with their young age.

Table 2 shows the distribution of outcomes by exposure categories. Preterm births and, to a lesser extent, SGA were more frequent in the most-exposed levels. The results of the multivariate analysis showed no associations between increasing exposure to PM_{10} from incinerators and sex ratio, multiple births, and SGA (Table 3). There was a trend of increasing risk of preterm birth with increasing exposure (P for trend <0.001). The ORs for the fourth and fifth quintile versus lowest exposure level were 1.42 (95% CI = 1.19–1.68) and 1.30 (1.08–1.57), respectively. When the analysis was restricted to the period 2007–2010, for which more information on some confounders was available (smoking habit, previous hospitalizations, Deprivation Index), the results for preterm births persisted (for fourth quintile, OR = 1.49 [95% CI = 1.16–1.90], and for fifth quintile, OR = 1.44 [1.11–1.85]; test for trend, $P < 0.001$) (Table 3). This association was stronger for very preterm births, both for the whole period (highest level vs. lowest, OR = 2.19 [95% CI = 1.24–3.85]; test for trend, $P = 0.001$) and for the years 2007–2010 (2.27 [1.08–4.76]; test for trend, $P = 0.002$) (Table 4).

We performed sensitivity analyses to test the robustness of these associations. Figure 2 shows the results for the highest level of exposure compared with the reference after excluding foreign women or nonexposed subjects in the whole population and after excluding both smokers and subjects with unknown smoking habit in the 2007–2010 population. Associations were maintained. Similarly, results were unchanged after excluding one site at a time. When we excluded Reggio

TABLE 1. Individual Maternal Characteristics According to the Modeled Exposure Levels to PM_{10} from the Incinerators, 2003–2010

	PM_{10} Levels Attributable to the Incinerators					
Quintiles:	**1**	**2**	**3**	**4**	**5**	**Total**
PM_{10} (ng/m^3):	**(0–0.07)**	**(0.08–0.15)**	**(0.16–0.30)**	**(0.31–0.80)**	**(>0.80)**	
	(n = 4,433)	**(n = 3,790)**	**(n = 4,196)**	**(n = 4,711)**	**(n = 4,034)**	**(n = 21,164)**
Characteristics	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Exposure to other sources						
Quartiles						
1	767 (17)	594 (16)	775 (19)	1,385 (29)	1,674 (42)	5,195 (25)
2	864 (20)	1,323 (35)	1,099 (26)	1,034 (22)	946 (24)	5,266 (25)
3	1,306 (30)	1,088 (29)	1,289 (31)	1,235 (26)	834 (21)	5,752 (27)
4	1,491 (34)	784 (21)	1,033 (25)	1,057 (22)	579 (14)	4,944 (23)
Missing	5 (0)	1 (0)	0 (0)	0 (0)	1 (0)	7 (0)
Maternal age (years)						
<20	72 (2)	58 (2)	54 (1)	70 (2)	48 (1)	302 (1)
20–34	3,191 (72)	2,575 (68)	2,863 (68)	3,156 (67)	2,830 (70)	14,615 (69)
35–40	1,027 (23)	1,020 (27)	1,116 (27)	1,307 (28)	1,043 (26)	5,513 (26)
>40	143 (3)	137 (4)	163 (4)	178 (4)	113 (3)	734 (4)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Foreigners	1,397 (32)	1,358 (36)	1,523 (36)	1,218 (26)	772 (19)	6,268 (30)
Missing	105 (2)	17 (1)	7 (0)	9 (0)	5 (0)	143 (1)
Educational level						
Low	1,636 (37)	1,241 (33)	1,461 (35)	1,597 (34)	1,126 (28)	7,061 (33)
Medium	1,788 (40)	1,475 (39)	1, 652 (39)	2,035 (43)	1,970 (49)	8,920 (42)
High	1,009 (23)	1,073 (28)	1,083 (26)	1,079 (23)	933 (23)	5,177 (25)
Missing	0 (0)	1 (0)	0 (0)	0 (0)	5 (0)	6 (0)
Primiparous	2,178 (49)	1,616 (43)	1,729 (41)	2,062 (44)	1,890 (47)	9,475 (45)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Smoking in pregnancy[a]	341 (14)	243 (13)	279 (12)	227 (10)	300 (13)	1,390 (12)
Missing	13 (1)	63 (3)	161 (7)	333 (14)	370 (17)	940 (8)
Deprivation Index[a]						
1 (least deprived)	568 (23)	346 (18)	443 (19)	457 (20)	460 (21)	2,274 (20)
2	487 (20)	383 (20)	424 (18)	404 (18)	486 (22)	2,184 (20)
3	554 (22)	352 (19)	378 (16)	454 (20)	496 (22)	2,234 (20)
4	412 (17)	380 (20)	470 (20)	447 (19)	388 (17)	2,097 (19)
5 (most deprived)	452 (18)	429 (23)	590 (26)	548 (24)	402 (18)	2,421 (22)
Missing	2 (0)	2 (0)	0 (0)	0 (0)	0 (0)	4 (0)
Previous hospitalizations[a]	48 (2)	39 (2)	45 (2)	56 (2)	36 (2)	224 (2)

[a]Available for period 2007–2010 only (n = 11,214).

Emilia, a site characterized by low exposure levels, the association was stronger.

For the period 2003–2010, we compared the frequency of all outcomes in the whole study area, as well as in each PM_{10} exposure level, with the expected values based on the regional rates (eTable 2, http://links.lww.com/EDE/A719). The standardized prevalence ratios for multiple births and sex ratio did not show any excess either in the whole study areas (1.10 [95% CI = 0.97–1.24] and 1.00 [0.98–1.02], respectively) or in the areas with highest exposure level (0.95 [0.69–1.28] and 0.98 [0.94–1.02], respectively). There was no excess of preterm births in the whole study area (0.98 [0.93–1.04]), although a slight excess was observed at the two highest exposure levels (fourth quintile, 1.18 [1.06–1.31]; fifth quintile, 1.08 [0.97–1.22]).

DISCUSSION

We examined associations between incinerator emissions and pregnancy outcomes among women living within a 4-km radius of eight incinerators operating in the Italian

TABLE 2. Frequency of the Study Outcomes According to the Modeled Exposure Levels to PM_{10} from the Incinerators, 2003–2010

	PM_{10} Levels Attributable to the Incinerators					
Quintiles:	**1**	**2**	**3**	**4**	**5**	**Total**
PM_{10} (ng/m^3):	**(0–0.07)**	**(0.08–0.15)**	**(0.16–0.30)**	**(0.31–0.80)**	**(>0.80)**	
Outcomes	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Sex ratio[a]	2,188 (49.4)	1,794 (47.3)	2,006 (47.8)	2,322 (49.3)	1,917 (47.5)	10,227 (48.3)
Multiple births[b]	53 (1.2)	43 (1.2)	58 (1.4)	63 (1.4)	43 (1.1)	260 (1.2)
Preterm births[c]	243 (5.6)	205 (5.5)	242 (5.9)	354 (7.7)	272 (6.9)	1,316 (6.4)
SGA[d]	453 (10.6)	407 (11.2)	445 (11.2)	531 (11.8)	442 (11.3)	2,278 (11.2)

[a]Ratio between number of girls born and total number of newborns.
[b]Only one twin is included, n = 20,901.
[c]Twins and 26 missing are excluded, n = 20,615.
[d]Twins, infants born to Indian mothers, and 32 missing are excluded, n = 20,343.

region of Emilia-Romagna. We did not find any association with sex ratio, multiple births, or SGA. However, we observed a relationship between maternal exposure to incinerator emissions and the frequency of preterm birth. This association was robust to several sensitivity analyses.

Our results are consistent with those from other studies of exposure to incinerators and pregnancy events. In a Taiwan study, the only one that has investigated preterm births, there was the suggestion of an association with higher levels of incinerator emissions.[9] In previous studies, the exposure to incinerator pollution has been assessed by municipality,[7] distance from the plant,[8] postcode sectors with various environmental and soil pollution,[5] and 3D smoothing mapping techniques[6] or an air-dispersion model using dioxins and furans emission.[9] Our study estimated exposure by a quasi-Gaussian dispersion model (ADMS-Urban) in which pollution data were obtained from measurements of particulate-matter emissions and exposure during each pregnancy assessed on a monthly basis. This model was previously used[9,13] to assess exposure to incinerators, and a specific validation study with measured values has demonstrated its usefulness in epidemiologic studies.[19]

The estimated values of exposure to PM_{10} from incinerators are extremely low (nanograms/m^3) and can be considered only as tracers of the exposure gradient, regardless

TABLE 3. Associations Between Modeled Exposure Levels to PM_{10} from the Incinerators and Reproductive Outcomes for the Whole Period of the Study (2003–2010) and Subset Period (2007–2010)

Incinerator Exposure	Sex Ratio[a]		Multiple Births		SGA		Preterm Births	
PM_{10} Level (ng/m^3)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
			Whole period (2003–2010)[b]					
1 (0–0.07)[c]	1.00		1.00		1.00		1.00	
2 (0.08–0.15)	0.93	(0.85–1.02)	0.94	(0.62–1.42)	1.10	(0.95–1.28)	1.00	(0.82–1.21)
3 (0.16–0.30)	0.95	(0.88–1.04)	1.17	(0.80–1.71)	1.10	(0.95–1.27)	1.05	(0.87–1.26)
4 (0.31–0.80)	1.00	(0.92–1.09)	1.12	(0.76–1.64)	1.13	(0.99–1.30)	1.42	(1.19–1.68)
5 (>0.80)	0.91	(0.83–0.99)	0.87	(0.57–1.33)	1.11	(0.96–1.28)	1.30	(1.08–1.57)
Test for trend	$P = 0.249$		$P = 0.923$		$P = 0.129$		$P < 0.001$	
			Subset period (2007–2010)[d]					
1 (0–0.09)[c]	1.00		1.00		1.00		1.00	
2 (0.10–0.15)	0.85	(0.75–0.96)	1.19	(0.65–2.16)	1.08	(0.88–1.31)	0.96	(0.73–1.27)
3 (0.16–0.27)	0.86	(0.76–0.97)	1.58	(0.92–2.73)	1.13	(0.94–1.36)	1.12	(0.87–1.44)
4 (0.28–0.55)	0.92	(0.82–1.04)	1.38	(0.77–2.45)	1.15	(0.96–1.39)	1.49	(1.16–1.90)
5 (>0.55)	0.88	(0.78–0.99)	1.12	(0.60–2.08)	1.06	(0.87–1.29)	1.44	(1.11–1.85)
Test for trend	$P = 0.190$		$P = 0.496$		$P = 0.374$		$P < 0.001$	

[a]Ratio between number of girls born and total number of newborns.
[b]ORs are adjusted for maternal age, pregnancy order, nationality, educational level, gender, exposure to other pollution sources, and period. Sex ratio and SGA are not adjusted for gender.
[c]Reference category.
[d]ORs are adjusted for maternal age, pregnancy order, nationality, educational level, gender, exposure to other pollution source, smoke, Deprivation Index, and maternal previous hospitalizations. Sex ratio and SGA are not adjusted for gender.

TABLE 4. Associations Between Modeled Exposure Levels to PM_{10} from the Incinerators and Very Preterm Birth (<32 Weeks) for the Whole Period of the Study (2003–2010) and Subset Period (2007–2010)

Incinerator Exposure PM_{10} Level (ng/m³)	Very Preterm Births (<32 Weeks)		
	No.	OR	(95% CI)
Whole period (2003–2010)[a]			
1 (0–0.07)[b]	21	1.00	
2 (0.08–0.15)	21	1.21	(0.65–2.25)
3 (0.16–0.30)	34	1.69	(0.98–2.92)
4 (0.31–0.80)	44	1.99	(1.17–3.39)
5 (>0.80)	41	2.19	(1.24–3.85)
Test for trend			$P = 0.001$
Subset period (2007–2010)[c]			
1 (0–0.09)[b]	13	1.00	
2 (0.10–0.15)	3	0.33	(0.10–1.16)
3 (0.16–0.27)	19	1.73	(0.83–3.60)
4 (0.28–0.55)	24	2.00	(0.97–4.13)
5 (>0.55)	23	2.27	(1.08–4.76)
Test for trend			$P = 0.002$

[a]ORs are adjusted for maternal age, pregnancy order, nationality, educational level gender, exposure to other pollution sources, and period.
[b]Reference category.
[c]ORs are adjusted for maternal age, pregnancy order, nationality, educational level, gender, exposure to other pollution sources, smoke, Deprivation Index, and maternal previous hospitalizations.

of their absolute quantitative value. The particles emitted by these plants are composed largely of heavy metals, dioxins and dioxin-like substances, aromatic polycyclic hydrocarbons, and other organic carbon compounds absorbed on particles. These emissions are a mix of various substances similar to those produced by other sources of combustion, though the relative contribution of each pollutant may be different.

The relation between air pollution, mainly caused by traffic, and reproductive outcomes is not yet well established. There is growing evidence that particulate matter and gaseous

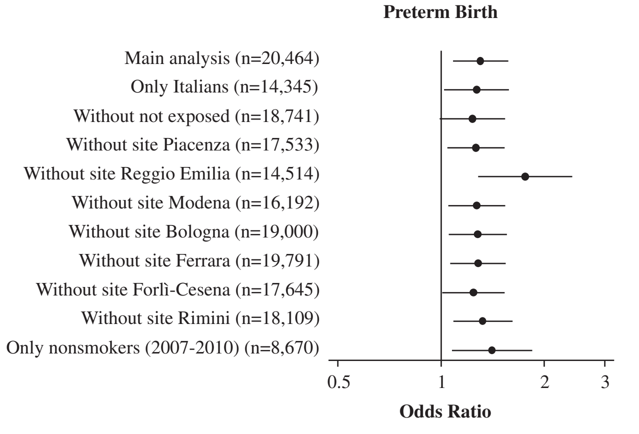

FIGURE 2. 2003–2010 preterm births, comparing highest versus lowest exposure to incinerator, for various subsets of subjects.

pollutants may be associated with low birth weight, SGA, and preterm births.[2–4] In our study, exposure to pollution from other sources tended to be inversely related to incinerator exposure because incinerators are located on the outskirts of cities.

The tracer PM_{10} was useful for characterizing the exposure to the mix of pollutants released by the incinerator plants on an ordinal scale and was considered a good proxy for the intensity of women's environmental exposure level during pregnancy, even though no information about occupational exposures or daily activities was available. Misclassification of individual exposure would tend to mask the detected association.

The association of exposure with more severe preterm delivery (gestational age <32 weeks) rules out the possibility that the observed association was due merely to near-term births, which could be the result of early medical induction of labor in women with critical health conditions or because of fetal distress. Because this practice may vary from hospital to hospital, the association considering only very preterm births is more likely to reflect an effect on the fetoplacental unit, regardless of the mode of delivery.

Socioeconomic status is a well-known determinant of adverse reproductive effects.[20] We assessed SES for the whole period using maternal educational level, which is generally a good proxy of SES for women of childbearing age. A country of origin other than Italy can also be considered a proxy for low SES. We also included Deprivation Index for the census area for the period 2007–2010.[14] Adjustment for these covariates did not alter the observed associations. Foreign women were also excluded in one sensitivity analysis test, without affecting the results. This is particularly important because a country of origin other than Italy was one of the main characteristics of subjects lost to the analysis because of data linkage failure. Because their exclusion did not alter the results, we can reasonably assume that the loss of 13% of other subjects with non-Italian origins did not markedly bias our study.

Smoking patterns are a strong determinant of morphological and biological damage on the fetoplacental unit.[21] The main adverse reproductive events are low birth weight and SGA, followed by preterm births, for which relative risks between 1.2 and 1.4 have been found.[22,23] In our study, the information on smoking (available only since 2007) is routinely collected through interview of the new mother after delivery and there is a large proportion of missing data. For this reason, this variable was considered both as a covariate in the main model and as an exclusion criterion without altering the results.

Maternal characteristics and medical or pregnancy conditions could also affect preterm births,[15,24] low birth weight,[25] and SGA.[26] For the period 2007–2010, we examined hospitalizations in the 3 years before conception as an indication of serious medical conditions. Although these conditions were present in a small proportion of cases, their distribution was not associated with the exposure.

Preterm labor is a syndrome initiated by multiple mechanisms. In general, three types of factors may contribute: social stress and race, infection and inflammation, and genetics.[15,27] Possible biological mechanisms by which air pollution might cause preterm delivery include endocrine disruption, effects mediated by arylhydrocarbon receptor, oxidative stress from free radicals and oxygen reactive compounds, and epigenetic effects. These mechanisms could determine inflammatory responses, oxidative stress, and fetoplacental dysfunctions.[2,4,28–32] Moreover, substances conveyed by particles may cause vasoconstriction and increased blood pressure or worsening of previous hypertension, which are risk factors for preeclampsia and preterm birth.[33–36]

In conclusion, our study examined a possible association between exposure to incinerator emissions and pregnancy outcomes, for which the published literature provides very limited data. We found an association between levels of exposure to incinerator emissions and preterm births, consistent with the results from the only other study on this outcome.

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REFERENCES

1. Porta D, Milani S, Lazzarino AI, Perucci CA, Forastiere F. Systematic review of epidemiological studies on health effects associated with management of solid waste. *Environ Health*. 2009;8:60.
2. Slama R, Darrow L, Parker J, et al. Meeting report: atmospheric pollution and human reproduction. *Environ Health Perspect*. 2008;116:791–798.
3. Bosetti C, Nieuwenhuijsen MJ, Gallus S, Cipriani S, La Vecchia C, Parazzini F. Ambient particulate matter and preterm birth or birth weight: a review of the literature. *Arch Toxicol*. 2010;84:447–460.
4. Shah PS, Balkhair T; Knowledge Synthesis Group on Determinants of Preterm/LBW births. Air pollution and birth outcomes: a systematic review. *Environ Int*. 2011;37:498–516.
5. Lloyd OL, Lloyd MM, Williams FL, Lawson A. Twinning in human populations and in cattle exposed to air pollution from incinerators. *Br J Ind Med*. 1988;45:556–560.
6. Williams FL, Lawson AB, Lloyd OL. Low sex ratios of births in areas at risk from air pollution from incinerators, as shown by geographical analysis and 3-dimensional mapping. *Int J Epidemiol*. 1992;21:311–319.
7. Rydhstroem H. No obvious spatial clustering of twin births in Sweden between 1973 and 1990. *Environ Res*. 1998;76:27–31.
8. Tango T, Fujita T, Tanihata T, et al. Risk of adverse reproductive outcomes associated with proximity to municipal solid waste incinerators with high dioxin emission levels in Japan. *J Epidemiol*. 2004;14:83–93.
9. Lin CM, Li CY, Mao IF. Birth outcomes of infants born in areas with elevated ambient exposure to incinerator generated PCDD/Fs. *Environ Int*. 2006;32:624–629.
10. van Larebeke NA, Sasco AJ, Brophy JT, Keith MM, Gilbertson M, Watterson A. Sex ratio changes as sentinel health events of endocrine disruption. *Int J Occup Environ Health*. 2008;14:138–143.
11. Obi-Osius N, Misselwitz B, Karmaus W, Witten J. Twin frequency and industrial pollution in different regions of Hesse, Germany. *Occup Environ Med*. 2004;61:482–487.
12. European Environment Agency. EEA Report no 4/2012. Air Quality in Europe 2012. Available at: http://www.eea.europa.eu/publications/air-quality-in-europe-2012. Accessed 13 November 2012.
13. Ranzi A, Fano V, Erspamer L, Lauriola P, Perucci CA, Forastiere F. Mortality and morbidity among people living close to incinerators: a cohort study based on dispersion modeling for exposure assessment. *Environ Health*. 2011;10:22.
14. Caranci N, Biggeri A, Grisotto L, Pacelli B, Spadea T, Costa G. The Italian deprivation index at census block level: definition, description and association with general mortality. *Epidemiol Prev*. 2010;34:167–176.
15. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008;371:75–84.
16. Kramer MS, Platt RW, Wen SW, et al.; Fetal/Infant Health Study Group of the Canadian Perinatal Surveillance System. A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics*. 2001;108:E35.
17. Ramachandran P. Nutrition and child survival in India. *Indian J Pediatr*. 2010;77:301–305.
18. Mikolajczyk RT, Zhang J, Betran AP, et al. A global reference for fetal-weight and birthweight percentiles. *Lancet*. 2011;377:1855–1861.
19. Floret N, Viel JF, Lucot E, et al. Dispersion modeling as a dioxin exposure indicator in the vicinity of a municipal solid waste incinerator: a validation study. *Environ Sci Technol*. 2006;40:2149–2155.
20. Sociodemographic and community factors contributing to preterm birth. In: Behrman RE, Stith Butler A, eds. *Preterm Birth: Causes, Consequences, and Prevention*. Washington, DC: The National Academy Press; 2007:124–147.
21. Jauniaux E, Burton GJ. Morphological and biological effects of maternal exposure to tobacco smoke on the feto-placental unit. *Early Hum Dev*. 2007;83:699–706.
22. Salihu HM, Wilson RE. Epidemiology of prenatal smoking and perinatal outcomes. *Early Hum Dev*. 2007;83:713–720.
23. Rogers JM. Tobacco and pregnancy. *Reprod Toxicol*. 2009;28:152–160.
24. Medical and pregnancy conditions associated with preterm birth. In: Behrman RE, Stith Butler A, eds. *Preterm Birth: Causes, Consequences, and Prevention.* Washington, DC: The National Academy Press; 2007:148–168.
25. Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. *Bull World Health Organ*. 1987;65:663–737.
26. McCowan L, Horgan RP. Risk factors for small for gestational age infants. *Best Pract Res Clin Obstet Gynaecol*. 2009;23:779–793.
27. Muglia LJ, Katz M. The enigma of spontaneous preterm birth. *N Engl J Med*. 2010;362:529–535.
28. Srám RJ, Binková B, Dejmek J, Bobak M. Ambient air pollution and pregnancy outcomes: a review of the literature. *Environ Health Perspect*. 2005;113:375–382.
29. Kannan S, Misra DP, Dvonch JT, Krishnakumar A. Exposures to airborne particulate matter and adverse perinatal outcomes: a biologically plausible mechanistic framework for exploring potential effect modification by nutrition. *Environ Health Perspect*. 2006;114:1636–1642.
30. Ritz B, Wilhelm M. Ambient air pollution and adverse birth outcomes: methodologic issues in an emerging field. *Basic Clin Pharmacol Toxicol*. 2008;102:182–190.
31. Henkler F, Luch A. Adverse health effects of environmental chemical agents through non-genotoxic mechanisms. *J Epidemiol Community Health*. 2011;65:1–3.
32. Stein RA. Epigenetics and environmental exposures. *J Epidemiol Community Health*. 2012;66:8–13.
33. Engel SM, Janevic TM, Stein CR, Savitz DA. Maternal smoking, preeclampsia, and infant health outcomes in New York City, 1995-2003. *Am J Epidemiol*. 2009;169:33–40.
34. Wu J, Ren C, Delfino RJ, Chung J, Wilhelm M, Ritz B. Association between local traffic-generated air pollution and preeclampsia and preterm delivery in the south coast air basin of California. *Environ Health Perspect*. 2009;117:1773–1779.
35. van den Hooven EH, de Kluizenaar Y, Pierik FH, et al. Air pollution, blood pressure, and the risk of hypertensive complications during pregnancy: the generation R study. *Hypertension*. 2011;57:406–412.
36. Pereira G, Haggar F, Shand AW, Bower C, Cook A, Nassar N. Association between pre-eclampsia and locally derived traffic-related air pollution: a retrospective cohort study. *J Epidemiol Community Health*. 2013;67:147–152.

