BMJ Open

Arson at an urban solid waste landfill in Italy: effects on human reproductive health

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027912
Article Type:	Research
Date Submitted by the Author:	14-Nov-2018
Complete List of Authors:	MAZZUCCO, WALTER; University of Palermo, Scienze Promozione Salute e Materno Infantile; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit Tavormina, Elisa; Regional Health Authority, Department of Health Services and Epidemiological Observatory Macaluso, M; Cincinnati Children's Hospital Medical Center, Division of Biostatistics and Epidemiology; University of Cincinnati College of Medicine, Department of Pediatrics Marotta, Claudia; University of Palermo, Sciences for health promotion (PROSAMI) Department Cusimano, Rosanna; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit Alba, Davide; University of Palermo, Sciences for health promotion (PROSAMI) Department Costantino, Claudio; University of Palermo, Sciences for health promotion (PROSAMI) Department Grammauta, Rosario; National Research Council, Istituto per l'Ambiente Marino Costiero (IAMC) "Capo Granitola", Cernigliaro, Achille; Regional Health Authority, Department of Health Services and Epidemiological Observatory Scondotto, Salvatore; Regional Health Authority, Department of Health Services and Epidemiological Observatory Vitale, Francesco; University of Palermo, Department of Sciences for Health Promotion "G. D'Alessandro" – Hygiene section; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit
Keywords:	PUBLIC HEALTH, Maternal medicine < OBSTETRICS, Enviromental health

Title page

Title: Arson at an urban solid waste landfill in Italy: effects on human reproductive health.

Authors

Walter Mazzucco* [a,b], Elisa Tavormina [c], Maurizio Macaluso* [d], Claudia Marotta [a], Rosanna Cusimano [f], Davide Alba [a], Claudio Costantino [a], Rosario Grammauta [g], Achille Cernigliaro [c], Salvatore Scondotto [c], Francesco Vitale [a,b].

*These authors contributed equally.

[a] Sciences for health promotion (PROSAMI) Department, University of Palermo, Palermo, Italy

[b] Clinical Epidemiology and Cancer Registry Unit, Palermo University Hospital "P. Giaccone", Palermo, Italy

[c] Department of Health Services and Epidemiological Observatory, Regional Health Authority, Sicilian Region, Palermo, Italy

[d] Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, and Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

[f] Palermo Health Agency, Palermo, Italy

[g] Istituto per l'Ambiente Marino Costiero (IAMC) "Capo Granitola", National Research Council, Via del Mare 3, 91021 Torretta Granitola, TP, Italy

Corrisponding author:

Claudia Marotta, Dipartimento Scienze Promozione della Salute e Materno Infantile "G. D'Alessandro", Università degli Studi di Palermo. Via del Vespro, 133 - 90127 Palermo, Italy

Telephone number: +393337984116 Fax: +390916553631

E-mail: marotta.claudia@gmail.com

Word count: 2.783

Abstract

Objectives: In response to increasing public health concern raising from the occurrence of arson in solid waste management plants in July 2012, a longitudinal retrospective study was performed using vital statistics data to evaluate any potential effect on pregnancies at different gestational ages of pollutants emitted from the landfill on fire.

Setting: Community, in particular a population resident nearby a landfill plant.

Participants: The study group comprised all live births and stillbirths to mothers residing within the exposed areas and conceived during a 40 weeks period intercepting the highest peak of the fire.

Primary and secondary outcome measures: Birth outcomes (gestational age <37 weeks, low birth weight, very low birth weight and small for gestational age) in the study group were compared to the birth outcomes of a reference group of women residing in areas of Sicily with similarly low population density and industrial development.

Results: There was a statistically significant excess of low birth weight singleton infants in the study group as compared to the reference group, which was limited to births to mothers exposed during peri-conception period (OR adjusted for maternal age= 4.64; 95%CI= 1.04 – 20.6) and first trimester (OR adjusted for maternal age= 3.66; 95%CI= 1.11 – 12.1).

Conclusions: The study documented an excess of very low birth weight in newborns to mothers who were exposed to the landfill fire emissions during conception or early pregnancy.

Summary

Strengths and limitations of this study

- In response to increasing public health concern raising from the occurrence of arson in solid waste management plants, we investigated the potential health effects of short term exposure to pollutants emitted from the waste on fire.
- We documented a statistically significant association between pregnancy exposure to emissions spread by urban waste landfill on fire and an excess of low birth weight singleton

infants. In particular, our findings highlighted that mothers exposed during peri-conception and first trimester of pregnancy represent a high-risk group.

- The study adds to the growing body of evidence that exposure to high concentration of pollutants emitted from solid waste landfill may have serious health effects and underscores the need for monitoring potential hazards and health outcomes in the population resident nearby the landfill plants.
- The retrospective design and the analysis of data from vital statistics do not allow a detailed assessment of the longitudinal nature of the exposure-response relation, nor a precise adjustment for potential confounding.
- As it is often the case in studies of local environmental exposure events, the outcomes of interest were limited in number, especially when stratified according to the stage of the pregnancy at exposure.

Key words: exposure to air pollutant; landfill emissions; low birth-weight; conception; early pregnancy.

Introduction

The number of studies investigating the potential human health effects on communities of pollutants released from landfills or incinerators is increasing,[1,2] showing that exposure is weakly associated with a variety of adverse health outcomes, including cancer, adverse reproductive outcomes and birth defects.[3-5] Increased risk of low birth weight and congenital malformations has been reported in communities living in proximity to landfills.[2,6] Maternal exposure to incinerator emissions was associated with preterm delivery.[7] A study of exposure to incinerator emissions containing dioxin concluded that exposure had little impact on birth weight and sex ratio, but may have been associated with gestational age at delivery.[8] Inconsistent findings across studies may be due to design issues, lack of exposure information, use of indirect surrogate measures, acute

versus long-term exposure conditions, and inadequate control of confounding.[9] Variation in risk perception among the stakeholders makes it difficult to communicate about the available evidence. In Italy, the incidence of fires in solid waste management plants is increasing,[10] addressing the need to investigate the potential health effects of short-term exposure to pollutants emitted from the combustion of solid waste.

In Sicily, the fourth most populated Italian region, 5 million residents produce about 6,000 tons of solid waste daily, which are disposed of in 4 Municipal Solid Waste Landfills (MSW-L).[11] The largest MSW-L is located in Bellolampo at 450 meters above sea level, on the hidden side of a mountain at the south-western border of Palermo (the largest city in Sicily, with 700,000 inhabitants, and its administrative capital).[11] The Bellolampo MSW-L collects solid waste from the Palermo metropolitan area, which includes the city and nearby municipalities.[12] On July 29, 2012, a fire started at multiple points within the landfill and emissions spread from the entire structure to a large populated area, becoming a threat of Public Health concern. Emissions peaked in the first 24 hours and decreased thereafter, until the fire was fully extinguished by August 16, 2012.

We analyzed vital statistics data to retrospectively evaluate the potential effects of the arson on the outcomes of pregnancies that were exposed to the emissions at different gestational ages.

Methods

In response to the arson, the Sicilian Regional Health Authority defined an area of 10 km radius around the landfill, whose resident population was considered as potentially exposed to the MSW-L emissions and placed under surveillance (**Supplementary File**).[13] Environmental monitoring of the area [14] was done through existing stationary monitoring stations.[15] A longitudinal retrospective study was designed to study the effects of exposure to the fire emissions on reproductive health outcomes. The study included all live births and stillbirths to mothers residing within the surveillance zone, whose estimated conception date occurred from 36 weeks prior to the

peak of the fire (from 2:00PM on July 29, 2012 to 2:00PM on July 30, 2012), until 4 weeks after the fire. Births were identified through the regional Certificate of Birth Attendance (CedAP) registry. The CedAP registry maintains data on all births to women of childbearing age (10-55 years old) who delivered in Sicily, including parental socio-demographic characteristics, obstetric history, prenatal care, and characteristics of pregnancy and birth. The registry does not include data on births to resident mothers who delivered outside the region (data not available) or wanted to preserve anonymity (0,4%). Date of conception was estimated using the date of birth and gestational age at birth reported in the registry.

To remove confounding by exposure to pollutants deriving from anthropic activities and vehicular traffic within metropolitan areas, we restricted the main focus of the analysis to residents of the extra-urban section of the surveillance area (**Supplementary File**). Thus, the study group included births in the extra-urban surveillance area from pregnancies that were potentially exposed to the fire around the time of conception as well as pregnancies that were exposed at later stages (through the 36th week). The reference group comprised all live births and stillbirths to mothers residing in the remaining extra-urban, low-density and unindustrialized areas of Sicily, during the same time interval.

To distinguish pregnancy periods of susceptibility to acute exposure to the fire emissions, the proportions defined above were computed separately for strata defined according to four sub-periods of exposure, corresponding to i) peri-conception (conception occurring between the beginning of the landfill fire and up to 4 weeks later), ii) first trimester (conception date 12-0 weeks before the fire), iii) second trimester (24-13 weeks before), and iv) third trimester (36-25 weeks before) (**Figure 1**). For each stage of the pregnancy at the time of exposure, we compared birth outcomes of the study group with those of the reference group. We also conducted internal comparisons of stages of pregnancy at the time of exposure within the study group.

We conducted two secondary analyses: first, we compared birth outcomes to mothers in the metropolitan area of Palermo (the main metropolitan area served by the Bellolampo MSW-L,

656,829 inhabitants) with those to mothers residing in the two other Sicilian metropolitan areas of Catania (293,104 inhabitants) and Messina (242,914 inhabitants) in the same study period. Second, to assess any systematic difference between the study group and the reference group independently from the fire, we repeated the comparison using data on births that occurred during the year preceding the arson (specifically, births conceived within -36 and +4 weeks from July 29, 2011).

Using the information available from CedAP registry, we followed European guidelines for perinatal statistics adopted by the PERISTAT system[16, 17] and evaluated the following proportions among all births (i.e., live births and stillbirths combined): proportion of stillbirths, proportions of male and female births, and proportions of singleton and multiple births. We evaluated the following proportions among live births: preterm birth (gestational age <37 weeks), low birth weight (<2,500 grams), very low birth weight (<1,500 grams) and small for gestational age (SGA) (birth weight under the tenth percentile of the national distribution of birth weights of the same gestational age or birth of gestational age ≥37 weeks weighing <2,500 grams).

To make statistical inference about the comparisons between the different study groups and the references, we used logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) of the ORs. ORs were adjusted by maternal age and newborn sex for comparisons based on all births, and by maternal age for comparisons based on singleton live births.

Statistical analyses were carried out by using STATA (version 11.2 MP, StataCorp, College Station, TX). STROBE guidelines were followed for research reporting.

Patient and Public Involvement

Patients were not involved.

Results

During the interval of interest (11/20/2011-08/26/2012) there were a total of 551 births (548 live births + 3 stillbirths) from pregnancies to mothers residing in the exposed extra-urban area (the

study group) and 22,341 births (22,264 live births + 65 stillbirths) from pregnancies to mothers residing in the remaining Sicilian low population-density, low industrialization areas (the comparison group). Among all births, there was a statistically no significant twofold excess of stillbirths in the extra-urban group (OR adjusted by gender=1.89; 95%CI = 0.59-6.03), while among singleton live births there was a two-fold, statistically significant risk excess for very low birth weight (OR adjusted for maternal age= 2.20; 95%CI= 1.02 - 4.72) (**Table 1**).

Table 1. Outcomes of 4,653 births from pregnancies to mothers residing in the Palermo metropolitan area and of 3,980 births from pregnancies to Sicilian women residing in the remaining metropolitan areas (comparison group), that were estimated to be conceived within -36 and +4 weeks from July 29, 2012.

Birth outcome	**Palermo exposed Metropolitan Area**	**Remaining Metropolitan Areas (Catania and Messina)**	**Unadjusted OR**		**Adjusted OR**	
	N (%)	**N (%)**				
All Births	4,653 (100)	3,980 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Gender						
Male	2,350 (50.51)	2,040 (51.26)	1 (ref.)		1 (ref.)	
Female	2,303 (49.49)	1,940 (48.74)	1.03	(0.94 – 1.12)	1.03	(0.94 – 1.12)
Plurality						
Singleton birth	4,492 (96.54)	3,829 (96.21)	1 (ref.)		1 (ref.)	
Multiple birth	161 (3.46)	151 (3.79)	0.91	(0.72 - 1.14)	0.91	(0.72 - 1.14)
Status at birth						
Live births	4,636 (99.63)	3,966 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	17 (0.37)	14 (0.35)	1.04	(0.51 - 2.11)	1.03	(0.51 - 2.10)
Singleton live births	4,492 (100)	3,829 (100)	**OR**	**(95%CI)**	**OR****	**(95%CI)**
Pre-term (<37 weeks)	169 (7.25)	111 (6.75)	1.08	(0.84 - 1.38)	1.08	(0.84 - 1.39)
Low birth weight (<2.500 gr)	146 (6.74)	180 (7.15)	0.86	(0.69 - 1.08)	0.86	(0.69 - 1.08)
Very low birth weight (<1500 gr)	25 (1.07)	21 (0.83)	1.28	(0.72 - 2.30)	1.28	(0.72 - 2.30)
Small for gestational age	59 (2.53)	66 (4.01)	0.62	(0.43 - 0.89)	0.62	(0.64 – 1.77)

*OR adjusted for infant gender; **OR adjusted for maternal age

Among all births, there were statistically significant differences between the study group and the comparison group that were limited to births whose pregnancies were in the third trimester when

the fire began: a twofold excess of multiple births (OR adjusted by gender= 2.42; 95%CI= 1.38-4.24) and a fourfold excess of stillbirths (OR adjusted by gender= 4.69; 95%CI= 1.40-15.6) were documented (**Table 2**). Among singleton live births there were statistically significant differences in very low birth weight rates between the extra-urban area and the remaining Sicilian low inhabitants density and unindustrialized areas for births whose pregnancies were either in peri-conception period (OR adjusted for maternal age= 4.64; 95%CI= 1.04 – 20.6) or in the first trimester (OR adjusted for maternal age= 3.66; 95%CI= 1.11 – 12.1) when the fire began (**Table 2**).

Table 2. Outcomes of 551 births from pregnancies to mothers residing in the extra-urban area and of 22,342 births from pregnancies to Sicilian women residing in low inhabitants density and unindustrialized areas (comparison group), that were estimated to be conceived within -36 and +4 weeks from July 29, 2012.

Birth outcome	**Extra-urban exposed area**	**Comparison group**	**Unadjusted OR**		**Adjusted OR**	
	N (%)	**N (%)**				
All Births	551 (100)	22,342 (100)	**OR**	**(95%CI)**	**OR****	**(95%CI)**
Gender		7 (0,03)*				
Male	299 (54.26)	11,464 (51.31)	1 (ref.)		1 (ref.)	
Female	252 (45.74)	10,871 (48.66)	0.89	(0.75 - 1.05)	0.89	(0.75 - 1.05)
Plurality						
Singleton birth	530 (96.19)	21,594 (96.65)	1 (ref.)		1 (ref.)	
Multiple birth	21 (3.81)	748 (3.35)	1.14	(0.73 - 1.78)	1.17	(0.75 - 1.82)
Status at birth		13 (0,06)*				
Live births	548 (99.46)	22,264 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	3 (0.54)	65 (0.29)	1.88	(0.59 - 5.98)	1.89	(0.59 - 6.03)
Singleton live births	530 (100)	21,525 (100)	**OR**	**(95%CI)**	**OR*****	**(95%CI)**
Pre-term (<37 weeks)	36 (6.82)	1,094 (5.13)	1.35	(0.96 - 1.91)	1.35	(0.96 - 1.90)
Low birth weight (<2.500 gr)	37 (6.99)	1,143 (5.31)	1.34	(0.95 - 1.88)	1.36	(0.97 - 1.91)
Very low birth weight (<1500 gr)	7 (1.32)	131 (0.61)	**2.19**	**(1.02 - 4.71)**	**2.20**	**(1.02- 4.72)**
Small for gestational age	15 (2.84)	578 (2.71)	1.05	(0.62 - 1.76)	1.07	(0.65 – 1.80)

*Number and percentage of non-missing values **OR adjusted for infant gender; ***OR adjusted for maternal age

Internal comparisons of the susceptibility period within the extra-urban exposed group did not reveal statistically significant differences between subgroups defined by stages of the pregnancy at the time of exposure, but these comparisons were hampered by the small size of the study group (results not shown).

Our secondary analyses did not show any significant differences in the outcomes of 4,653 births to mothers residing in the Palermo metropolitan area which were conceived during the time interval within -36 and +4 weeks from July 29, 2012 and 3,980 births to mothers residing in the other Sicilian metropolitan areas during the same time interval (**Table 3**), or in the outcomes of births from pregnancies to mothers residing in the extra-urban exposed area and births from pregnancies to Sicilian women residing in low population-density, low-industrialization areas of Sicily, conceived within -36 and +4 weeks from July 29, 2011 (one year before the arson) (**Table 4**).

Table 3. Outcomes of births from pregnancies to mothers residing in the exposed extra-urban area and of births from pregnancies to Sicilian women residing in low inhabitants density and unindustrialized are (comparison groups) by susceptibility sub-periods.

Birth outcome	Pregnancy stage as of the beginning of the fire (July 29, 2012)											
	Peri-conception			I Trimester (12-0 weeks)			II Trimester (24-13 weeks)			III Trimester (36-25 weeks)		
	Extra-urban exposed area N (%)*	Comparison Group N (%)	OR** (95%CI)	Extra-urban exposed area N (%)	Comparison Group N (%)	OR** (95%CI)	Extra-urban exposed area N (%)*	Comparison Group N (%)*	OR** (95%CI)	Extra-urban exposed area N (%)	Comparison Group N (%)	OR** (95%CI)
All Births	42 (100)	2,051 (100)		144 (100)	6,000 (100)		173 (100)	6,757 (100)		187 (100)	7,352 (100)	
Gender											6 (0,1)*	
Male	27 (64)	1,054 (51)	1 (ref.)	82 (57)	3,129 (52)	1 (ref.)	88 (51)	3,430 (51)	1 (ref.)	101 (54)	3,755 (51)	1 (ref.)
Female	15 (36)	997 (49)	0.59 (0.31-1.11)	62 (43)	2,870 (48)	0.82 (0.59-1.15)	85 (49)	3,327(49)	0.99 (0.74-1.35)	86 (46)	3,591(49)	0.89 (0.67-1.19)
Plurality												
Singleton birth	42 (100)	1993 (97)	1 (ref.)	142 (99)	5,793 (97)	1 (ref.)	168 (97)	6,535 (97)	1 (ref.)	173 (93)	7,099 (97)	1 (ref.)
Multiple birth	0 (0.0)	58 (2.8)	0 (-)	2 (1.4)	97 (3.4)	0.4 (0.09-1.62)	5 (2.9)	222 (3.3)	0.89 (0.36-2.18)	14 (7.5)	253 (3.4)	**2.42 (1.38-4.24)**
Status at birth											8 (0,11)*	
Live births	42 (100)	2.046 (99.8)	1 (ref.)	144 (100)	5,989 (99.8)	1 (ref.)	173 (100)	6,730 (99.7)	1 (ref.)	184 (98.4)	7,318 (99.54)	1 (ref.)
Stillbirths	0(0.0)	5 (0.2)	0 (-)	0(0.0)	10 (0.2)	0 (-)	0(0.0)	23 (0.34)	0 (-)	3 (1.6)	26 (0.35)	**4.69 (1.40-15.6)**
Singleton live births	42 (100)	1,983 (100)	**OR*** (95%CI)**	142 (100)	5,788 (100)	**OR*** (95%CI)**	168 (100)	6,435 (100)	**OR*** (95%CI)**	172 (100)	7,075 (100)	**OR*** (95%CI)**
Pre-term (<37 weeks)	36 (7.14)	94 (4.81)	1.46 (0.44-4.83)	11(7.75)	295 (5.16)	1.52 (0.81-2.85)	11 (6.55)	352 (5.47)	1.21 (0.65-2.26)	11 (6.43)	343 (4.88)	1.35 (0.73-2.51)
Low birth weight(<2500g)	2 (4.76)	116 (5.85)	0.83 (0.20-3.48)	12 (8.45)	327 (5.65)	1.57 (0.86-2.88)	11 (6.55)	353 (5.42)	1.22 (0.66-2.27)	12 (6.98)	341 (4.82)	1.52 (0.83-2.76)
Very low birth weight(<1500g)	2 (4.76)	20 (1.01)	**4.64 (1.04-20.6)**	3 (2.11)	34 (0.59)	**3.66 (1.11-12.1)**	0 (0.0)	37 (0.57)	0 (-)	2 (1.16)	39 (0.55)	2.18 (0.52-9.12)
Small for gestational age	0 (0.0)	61 (3.1)	0 (-)	4 (2.82)	167 (2.92)	1.00 (0.36-2.74)	5 (2.98)	173 (2.69)	1.11 (0.45-2.75)	6 (3.51)	175 (2.49)	1.45 (0.63-3.31)

*Number and percentage of non-missing values; **OR adjusted for infant gender; ***OR adjusted for maternal age

Table 4. Outcome of 536 births from pregnancies to mothers residing in the exposed extra-urban area and of 23,373 births from pregnancies to Sicilian women residing in low inhabitants density and unindustrialized areas of Sicily (comparison group), that were estimated to be conceived within -36 and +4 weeks from July 29, 2011 (in last year before the arson).

Birth outcome	Extra-urban exposed area	Comparison group	Unadjusted OR		Adjusted OR	
	N (%)	N (%)				
All Births	536 (100)	23,373 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Gender						
Male	272 (50.75)	12,041 (51.52)	1 (ref.)		1 (ref.)	
Female	264 (49.25)	11,329 (48.57)	1.03	(0.87 - 1.22)	1.03	(0.87 - 1.22)
Plurality						
Singleton birth	520 (97.01)	22,632 (96.83)	1 (ref.)		1 (ref.)	
Multiple birth	16 (2.99)	741 (3.17)	0.94	(0.57 - 1.56)	0.96	(0.58 - 1.58)
Status at birth						
Live births	534 (99.63)	23,291 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	2 (0.37)	79 (0.34)	1.10	(0.27 - 4.50)	1.10	(0.27 - 4.50)
			OR	**(95%CI)**	**OR****	**(95%CI)**
Pre-term (<37 weeks)	30 (5.78)	1,226 (5.44)	1.06	(0.731 - 1.54)	1.07	(0.74 - 1.55)
Low birth weight (<2.500 gr)	35 (6.74)	1,226 (5.44)	1.26	(0.88 - 1.78)	1.26	(0.89 - 1.79)
Very low birth weight (<1500 gr)	4 (0.77)	133 (0.59)	1.31	(0.48 - 3.55)	1.31	(0.48- 3.56)
Small for gestational age	15 (2.89)	616 (2.75)	1.05	(0.62 - 1.77)	1.05	(0.63– 1.77)

*OR adjusted for infant gender; **OR adjusted for maternal age

Discussion

This retrospective study investigated birth outcomes among women residing near one of the largest Italian solid waste landfills (the Bellolampo MSW-L), who were pregnant during a fire that started on July 29, 2012 and lasted for about a two-week period before being completely extinguished. The population potentially affected by the emissions comprising women residing both in metropolitan and low population-density, low-industrialization areas of Sicily, who were pregnant during the same time interval. As we were not able to estimate the impact of confounding by exposure to pollutants deriving from anthropic activities and vehicular traffic for the metropolitan areas, our

primary analysis focused on the potential impact of the fire on births to mothers residing in the extra-urban area adjacent to the landfill. As compared to births occurring during the same interval to mothers residing in other areas of Sicily with similar population density and level of industrialization, we observed a statistically significant differences suggesting that the landfill arson could have had an adverse impact on pregnancy outcomes. Our secondary analysis did not highlight statistically significant differences between the metropolitan exposed area and the other metropolitan populations in Sicily. In the study group, the analysis documented a two-fold, statistically significant excess risk of very low birth weight (<1500g) among singleton live births. The effect appeared to be concentrated among births whose conception date was between 12 weeks prior to the beginning of the fire to 4 weeks after, indicating that the largest impact of the exposure may have been on pregnancies that were conceived during the fire (OR adjusted for maternal age= 4.64; 95%CI= 1.04 – 20.6) or were exposed to the fire during the first trimester (OR adjusted for maternal age= 3.66; 95%CI= 1.11 – 12.1). As this type of outcome is typically associated with very early pre-term birth (gestational age <32 weeks), these findings are compatible with a toxic effect on placentation or early embryo development leading to premature delivery.[18,19] Maternal exposure to ambient concentrations of air pollutants, particularly to fine particulate matter, has been identified as a risk factor for preterm birth, low birth weight and SGA births.[20] Multiple studies have documented an association between fine particulate exposure and preterm birth.[21-23] Exposure to wildfires has been proposed as a risk factor for preterm birth [20] and reduced average birth weight.[24, 25]

In a multi-site Italian study, maternal exposure to incinerator emissions was associated with preterm delivery even at very low levels.[7] Moreover, a study conducted in Taiwan concluded that exposure to emissions from an incinerator generating dioxin had little effects on birth weight and female birth, but may have a modest effect on gestational age.[8]

The mechanisms proposed to explain the effect of fine particulate exposure on preterm birth include oxidative stress, pulmonary and placental inflammation, coagulopathy, endothelial dysfunction and

hemodynamic responses,[20, 26] as well as intrauterine inflammation.[20] Of interest, adverse pregnancy outcomes including pre-term delivery, intrauterine growth restriction and impaired infant weight gain are associated with exposure to polychlorinateddibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like PCBs (DL-PCBs).[1] Recently, The Hokkaido Study on Environment and Children's Health has demonstrated the effects of environmental chemical exposures (dioxins, polychlorinated biphenyls, organochlorine pesticides, perfluoroalkyl substances, phthalates, bisphenol A, and methylmercury) on genetically susceptible populations and on DNA methylation,[28] while other research suggests that exposure to tetrachlorodibenzo-*p*-dioxin (TCDD) may induce shifts in the immune response that enhance a proinflammatory phenotype at the maternal-fetal interface, increasing the risk of infection-mediated preterm birth.[29]

The body of published evidence, taken together with the statistically significant excess risk concentrated in a relatively narrow period of susceptibility, lends credibility to the hypothesis that the Bellolampo arson adversely affected pregnancies exposed during conception or in the first trimester, causing an excess of deliveries of very low birth weight infants in the extra-urban area. The study also documented in the same area a significant four-fold excess of stillbirths among pregnancies that were exposed to the landfill fire during the third trimester. This finding is based on a total of three stillbirths that occurred in the extra-urban study group, all of which were concentrated to the subgroup exposed during the third trimester, and it is possible that the observed excess is due to chance even if it was statistically significant. On the other hand, long-term exposure to PCBs was associated with increased proportions of miscarriage and stillbirth in animal studies,[30] and exposure to emissions from solid-waste incinerators was associated with increased risk of miscarriage in an epidemiologic study in Italy.[31] Thus, the excess of stillbirths to mothers exposed during the third trimester could be causally related to the arson.

The excess of multiple births from pregnancies exposed during the third trimester in the study group is unlikely to be caused by exposure to the landfill fire, as plurality must have been established long

before the arson. The literature provides conflicting evidence on the association between exposure to air pollution from incinerators and multiple births.[32]

Long-term exposure of the study area to pollutants (independently from the fire) was already known and was confirmed by the detection of TCCD and heavy metals at concentrations above the limits permitted by law [33] in sub-soil samples collected by the regional environment protection agency after the fire.[34] However, the secondary analysis comparing birth outcomes in the same extra-urban groups in the year before the arson did not highlight any potential effect related to a long-term exposure to pollutants emitted from the landfill.

The findings of this study should be interpreted in light of some limitations. First, the retrospective design and the analysis of data from vital statistics do not allow a detailed assessment of the longitudinal nature of the exposure-response relation, or precise adjustment for potential confounding. Although environmental monitoring was performed in response to the arson, we had limited access to the data and could only confirm the increase in air particulate concentrations after the beginning of the fire. Thus, we could not assess specific exposure levels of individual pregnancies at multiple points in time. Lastly, as it is often the case in studies of local environmental exposure events, the outcomes of interest were limited in number, especially when stratified according to the stage of the pregnancy at exposure. Nevertheless, the observations made in this study are of general interest. While previous studies conducted in Italy have suggested associations between exposure to incinerator emissions and increased risk of miscarriages and preterm births,[31] to our knowledge, the present study is the first in Europe to investigate the effects of exposure emissions on birth outcomes evaluating pregnancies exposed at different stages of development. Despite the limited information base and sample size, the excess of very low birth weight infants achieved statistical significance and was confined to early-stage pregnancies.

The study adds to the growing body of evidence that exposure to emissions from solid waste landfill operations may have serious health effects and underscores the need for monitoring potential hazards and health outcomes in the resident population.[35] The arsons at the Bellolampo

MSW-L,[36] as well as the ones that occurred in other Italian solid waste treatment plants in proximity to populated areas,[10] and the public concern they caused, exemplify the important role that integration of environmental monitoring and epidemiologic surveillance may have in this realm.[37-39] The questionable strength of the evidence collected in this and in similar studies also underscores the need for better planning of monitoring and surveillance activities (more detailed exposure information, better definition and monitoring of reproductive and other health outcomes, assessment of long-term effects and better control for potential confounders), and highlights the difficulty of conveying results to the various stakeholders [9] and the related need for effective methods to transfer study results to policy makers and the public.[40]

Finally, our study highlights the importance to promote an integrated management of urban solid waste alternatives to landfills, including waste to energy plants or other newly available technologies such as pyrolysis and gasification.[41]

Ethics

Ethical approval was obtained by the "Palermo Ethical Committee 1" on February 14, 2018 (protocol number: 02/2018).

Data sharing

No additional data available.

Funding

No funding received.

Competing interests

The authors declare they have no actual or potential competing interests.

Authors' contributions

All individuals listed as authors have contributed substantially to designing, performing or reporting the study and every specific contribution is indicated as follows. Conception and design of the study: WM, MM, RC, AC. Data collection: ET, AC, SS. Statistical analysis: ET, AC, RG, MM, WM. Interpretation of data: CC, CM, WM, MM, AC, ET. Manuscript writing and drafting: WM,

MM, CM, AC, DA. Revision of the manuscript: WM, CM, MM, SS, FV. Approval of the final version of the manuscript: WM, ET, MM, CM, RC, DA, CC, RG, AC, SS, FV.

Acknowledgments

The authors are grateful to the Regional Environmental Protection Agency of Sicily (ARPA Sicilia) for technical assistance with the study design.

References

1 Vrijheid M. Health effects of residence near hazardous waste landfill sites: a review of epidemiologic literature. *Environ Health Perspect* 2000;108(suppl 1):101-112.

2 Saunders P. A systematic review of the evidence of an increased risk of adverse birth outcomes in populations living in the vicinity of landfill waste disposal sites. In Population health and waste management: scientific data and policy options. Report of a WHO workshop Rome, Italy, 29-30 March 2007 Edited by: Mitis F, Martuzzi M. WHO, Regional Office for Europe, Copenhagen; 2007:25-27.

3 Williams FL, Lawson AB, Lloyd OL. Low sex ratios of births in areas at risk from air pollution from incinerators, as shown by geographical analyis and 3-dimensional mapping. *Int J Epidemiol* 1992;21:311.

4 Dummer TJ, Dickinson HO, Parker L. Adverse pregnancy outcomes around incinerators and crematoriums in Cumbria, north west England, 1956-93. *J Epidemiol Community Health* 2003;57:456-461.

5 Cordier S, Chevrier C, Robert-Gnansia E, Lorente C, Brula P, Hours M. Risk of congenital anomalies in the vicinity of municipal solid waste incinerators. *Occup Environ Med* 2004;61:8-15.

6 Elliot P, Richardson S, Abellan JJ, et al. Geographic density of landfill sites and risk of congenital anomalies in England. *Occup Environ Med* 2009;66:81-89.

7 Candela S, Ranzi A, Bonvicini L, et al. Air pollution from incinerators and reproductive outcomes: a multisite study. *Epidemiology* 2013;24(6):863-70.

8 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(5):624-9.

9 Porta D, Milani S, Lazzarino AI, et al. Systematic review of epidemiological studies on health effects associated with management of solid waste. *Environmental Health* 2009;8:60.

10 Regioni.it. 2018. Incendi negli impianti di smaltimento rifiuti: il 20% è doloso. 17 January 2018

Available: http://www.regioni.it/newsletter/n-3303/del-17-01-2018/incendi-negli-impianti-di-smaltimento-rifiuti-il-20-e-doloso-17570/ [accessed 3 February 2018].

11 ISTAT (National Institute for Statistics) Population Data. Available: http://demo.istat.it/ [accessed 3 February 2018].

12 Di Bella G, Di Trapani D, Viviani G. Evaluation of methane emissions from Palermo municipal landfill: Comparison between field measurements and models. *Waste Management* 211;1820–1826.

13 UNINETLAB - University of Palermo, ARPA Sicily (Sicilian Regional Environmental Protection Agency). 2012. Studio per la valutazione della dispersione di contaminanti in atmosfera in seguito all'incendio nella discarica di Bellolampo avvenuta dal 29 Luglio al 17 Agosto 2012. Available: http://www.arpa.sicilia.it/wp-content/uploads/2014/03/Allegato_3.pdf [accessed 3 February 2018].

14 Sicilian Regional Health Authority. Department of health activities and epidemiological observatory. D.D.G n°01690/2012, adopted on 29.08.2012 with regard to "Zona di protezione da diossina nell'area di Bellolampo (Palermo). Misure sanitarie per la sicurezza alimentare".

15 Sicilian Region Environmental Department; ARPA Sicily (Sicialian Regional Environmental Protection Agency). 2014. Sistema di Rilevamento Regionale della Qualità dell'Aria della Regione Sicilia. Progetto di Razionalizzazione del monitoraggio della qualità dell'aria in Sicilia e relativo Programma di Valutazione (art.5, comma 6, del Decreto Legislativo 13 agosto 2010, n.155).

16 Zeitlin J, Wildman K, Bréart G, et al. PERISTAT: Indicators for monitoring and evaluating perinatal health in Europe. *Eur J Public Health* 2003;13(3):29-37.

17 Mazzucco W, Cusimano R, Macaluso M, et al. A retrospective follow up study on maternal age and infant mortality in two Sicilian districts. *BMC Public Health* 2011;19;11:817.

18 Maisonet M, Correa A, Misra D, et al. A review of the literature on the effects of ambient air pollution on fetal growth. *Environ Res* 2004;95:106-115.

19 Srám RJ, Binková B, Dejmek J, et al.. Ambient air pollution and pregnancy outcomes: a review of the literature. *Environ Health Perspect* 2005;113:375-382.

20 Shah PS, BalkhairT, Knowledge Synth Grp Determinants P. Air pollution and birth outcomes: a systematic review. *Environ*. 2011;Int.37:498–516. http://dx.doi.org/10.1016/j.envint.2010.10.009.

21 Qian Z, Liang S, Yang S, et al. Ambient air pollution and preterm birth: a prospective birth cohort study in Wuhan, China. Int. J. Hyg. *Environ. Health* 2016;219:195–203. http://dx.doi.org/10.1016/j.ijheh.2015.11.003.

22 Ha S, Hu H, Roussos-Ross D, et al. The effects of air pollution on adverse birth outcomes. *Environ Res* 2014;134:198–204. http://dx.doi.org/10.1016/j.envres.2014.08.002.

23 Fleischer NL, Merialdi M, van Donkelaar A, et al. Outdoor air pollution, preterm birth, and low birth weight: analysis of the World Health Organization global survey on maternal and perinatal health. *Environ Health Perspect* 2014;122:425–430. http://dx.doi.org/10.1289/ehp.1306837.

24 Holstius DM, Reid CE, Jesdale BM, et al. Birth weight following pregnancy during the 2003 southern California wildfires. *Environ Health Perspec* 2012;120:1340–1345. http://dx.doi.org/10.1289/ehp.1104515.

25 Rich DQ, Liu K, Zhang J, et al. Differences in birth weight associated with the 2008 Beijing Olympics air pollution reduction: results from a natural experiment. *Environ Health Perspect* 2015;123:880–887.http://dx.doi.org/10.1289/ehp.1408795.

26 Kannan S, Misra DP, Dvonch JT, et al. 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. http://dx.doi.org/10.1289/ehp.9081.

27 Nachman RM, Mao G, Zhang X, et al. Intrauterine inflammation and maternal exposure to ambient PM2.5 during preconception and specific periods of pregnancy: the Boston birth cohort. *Environ Health Perspect* 2016;124,1608–1615.

28 Kishi R, Araki A, Minatoya M, et al. The Hokkaido Birth Cohort Study on Environment and Children's Health: cohort profile—updated 2017. *Environ Health Prev Med* 2017;22(1):46.

29 Peltier MR, Arita Y, Klimova NG, et al. 2, 3, 7, 8-Tetrachlorodibenzo-p-dioxin (TCDD) enhances placental inflammation. *J Reprod Immunol* 2013;98(1-2):10-20.

30 Tsukimori K, Tokunaga S, Shibata S, et al. Long-term effects of polychlorinated biphenyls and dioxins on pregnancy outcomes in women affected by the Yusho incident. *Environ Health Perspect* 2008May;116(5):626-30. doi: 10.1289/ehp.10686.

31 Candela S, Bonvicini L, Ranzi A, et al. Exposure to emissions from municipal solid waste incinerators and miscarriages: A multisite study of the MONITER Project. *Environ Int* 2015;Mar9;78:51-60. doi: 10.1016/j.envint.2014.12.008.

32 Lloyd OL, Lloyd MM, Williams FL, et al. Twinning in human populations and in cattle exposed to air pollution from incinerators. *Br J Ind Med Aug* 1988;45(8):556-60.

33 Legislative decree n. 152 of 2006. Norme in materia ambientale. 2006.

34 ARPA Sicily (Sicilian Regional Environmental Protection Agency). 2012. Studio preliminare sullo stato di qualità dei comparti ambientali (suolo e acque sotterranee) all'esterno della discarica di Bellolampo. Available: http://www.arpa.sicilia.it/wp-content/uploads/2014/03/Allegato_1.pdf [accessed 3 February 2018].

35 Domingo JL, Rovira J, Vilavert L, et al. Health risks for the population living in the vicinity of an Integrated Waste Management Facility: Screening environmental pollutants. *Sci Total Environ 2015;*Mar 12;518-519C:363-370. doi: 10.1016/j.scitotenv.2015.03.010.

36 Marchese I. Maxi incendio nella discarica di Bellolampo. Giornale di Sicilia 8 July 2015. Available: http://palermo.gds.it/2015/07/08/maxi-incendio-nella-discarica-di-bellolampo-minacciata-dalle-fiamme-la-sesta-vasca_379946/ [accessed 3 February 2018].

37 Barchitta M, Fragapane S, Quattrocchi A, et al. Environmental health risk communication in the case "Terra dei Fuochi": content analysis of online newspaper articles. *Ann Ig* 2015;Jan-Feb;27(1):30-8. doi: 10.7416/ai.2015.2020.

38 Mazzucco W, Cusimano R, Zarcone M, et al. Funnel plots and choropleth maps in cancer risk communication: a comparison of tools for disseminating population-based incidence data to stakeholders. *BMJ open* 2017Mar1;7(3):e011502.

39 Mazzucco W, Cusimano R, Mazzola S, et al. Childhood and Adolescence Cancers in the Palermo Province (Southern Italy): Ten Years (2003–2012) of Epidemiological Surveillance. *Int J Environ Res Public Health* 2018;*15*(7),p.1344.

40 Briggs DJ. A framework for integrated environmental health impact assessment of systemic risks. *Environ Health* 2008;7:61.

41 Cotana F, Messineo A, Petrozzi A, et al. Comparison of ORC turbine and stirling engine to produce electricity from gasified poultry waste. *Sustainability* 2014;6(9),5714-5729, doi: 10.3390/su6095714, ISSN: 2071-1050, MDPI Publisher, Switzerland.

Figure 1. Area potentially exposed to emissions deriving from the Bellolampo municipal solid waste landfill: **a**) Under surveillance area; **b**) Metropolitan area (Palermo) and extra-urban area (in red).

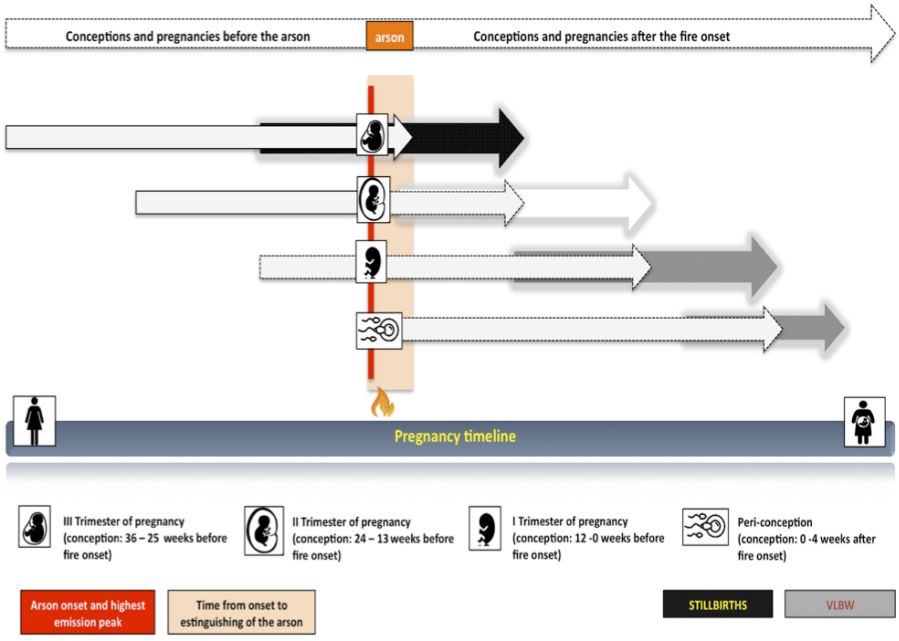
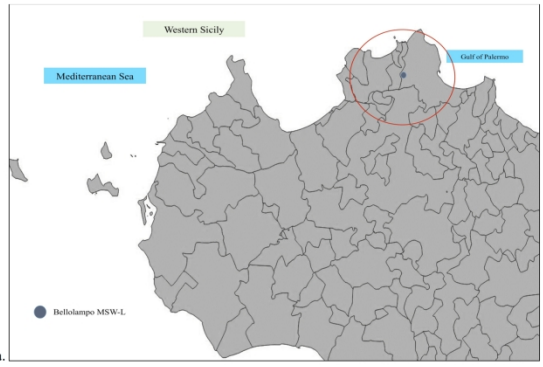


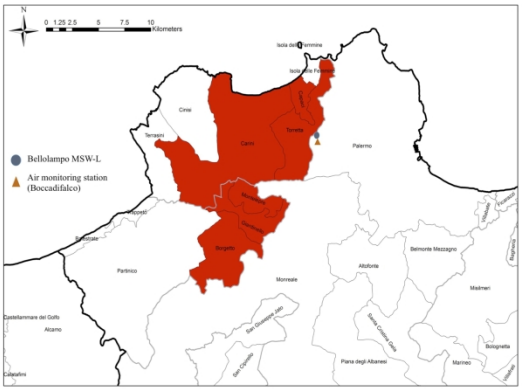
Figure 1. Area potentially exposed to emissions deriving from the Bellolampo municipal solid waste landfill: a) Under surveillance area; b) Metropolitan area (Palermo) and extra-urban area (in red).

185x130mm (150 x 150 DPI)

Supplementary file. Area potentially exposed to emissions deriving from the Bellolampo municipal solid waste landfill: **a**) Under surveillance area; **b**) Metropolitan area (Palermo) and extra-urban area (in red).



a.



b.

209x296mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 - 6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*7-9*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*NA*
		Cross-sectional study—Report numbers of outcome events or summary measures	*NA*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Do emissions from landfill fires affect pregnancy outcomes? A retrospective study after arson at a solid waste facility in Sicily.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027912.R1
Article Type:	Research
Date Submitted by the Author:	21-May-2019
Complete List of Authors:	MAZZUCCO, WALTER; University of Palermo, Scienze Promozione Salute e Materno Infantile; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit Tavormina, Elisa; Regional Health Authority, Department of Health Services and Epidemiological Observatory Macaluso, M; Cincinnati Children's Hospital Medical Center, Division of Biostatistics and Epidemiology; University of Cincinnati College of Medicine, Department of Pediatrics Marotta, Claudia; University of Palermo, Sciences for health promotion (PROSAMI) Department Cusimano, Rosanna; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit Alba, Davide; University of Palermo, Sciences for health promotion (PROSAMI) Department Costantino, Claudio; University of Palermo, Sciences for health promotion (PROSAMI) Department Grammauta, Rosario; National Research Council, Istituto per l'Ambiente Marino Costiero (IAMC) "Capo Granitola", Cernigliaro, Achille; Regional Health Authority, Department of Health Services and Epidemiological Observatory Scondotto, Salvatore; Regional Health Authority, Department of Health Services and Epidemiological Observatory Vitale, Francesco; University of Palermo, Department of Sciences for Health Promotion "G. D'Alessandro" – Hygiene section; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Reproductive medicine
Keywords:	PUBLIC HEALTH, Maternal medicine < OBSTETRICS, Enviromental health, exposure to air pollutant

Title page

Title: Do emissions from landfill fires affect pregnancy outcomes? A retrospective study after arson at a solid waste facility in Sicily.

Authors

Walter Mazzucco* [a,b], Elisa Tavormina [c], Maurizio Macaluso* [d], Claudia Marotta [a], Rosanna Cusimano [f], Davide Alba [a], Claudio Costantino [a], Rosario Grammauta [g], Achille Cernigliaro [c], Salvatore Scondotto [c], Francesco Vitale [a,b].

*These authors contributed equally.

[a] Sciences for health promotion (PROSAMI) Department, University of Palermo, Palermo, Italy

[b] Clinical Epidemiology and Cancer Registry Unit, Palermo University Hospital "P. Giaccone", Palermo, Italy

[c] Department of Health Services and Epidemiological Observatory, Regional Health Authority, Sicilian Region, Palermo, Italy

[d] Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, and Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

[f] Palermo Health Agency, Palermo, Italy

[g] Istituto per l'Ambiente Marino Costiero (IAMC) "Capo Granitola", National Research Council, Via del Mare 3, 91021 Torretta Granitola, TP, Italy

Corresponding author:

Claudia Marotta, Dipartimento Scienze Promozione della Salute e Materno Infantile "G. D'Alessandro", Università degli Studi di Palermo. Via del Vespro, 133 - 90127 Palermo, Italy

Telephone number: +393337984116 Fax: +390916553631

E-mail: marotta.claudia@gmail.com

Word count: 2.783

Abstract

Objectives: In response to public health concern about effects of arson at solid waste management plants in July 2012, we analysed vital statistics data to evaluate any potential effect on pregnancies at different gestational ages of pollutants emitted from the landfill on fire.

Setting: A community living near the largest landfill plant in Sicily.

Participants: The study group comprised 551 births live births and stillbirths from pregnancies of mothers residing in the extra-urban exposed area, conceived during a 40-week period during which the highest fire's peak might have influenced pregnancy.

Primary and secondary outcome measures: Birth outcomes (gestational age <37 and <32 weeks, low birth weight, very low birth weight and small for gestational age) in the study group were compared to the ones of a reference group of women residing in areas of Sicily with similarly low population density and industrial development.

Results: Among singleton live births we observed a three-fold increase in risk of very preterm birth between the extra-urban area and the remaining low inhabitants density and unindustrialized areas for births whose pregnancies were in the third trimester (OR adjusted for maternal age and infant gender= 3.41; 95%CI= 1.04 - 11.16). There was an excess of very low birth weight singleton infants in the study group as compared to the reference group, which was limited to births to mothers exposed during peri-conception period (OR adjusted for maternal age and infant gender= 4.64; 95%CI= 1.04 – 20.6) and first trimester (OR adjusted for maternal age and infant gender = 3.66; 95%CI= 1.11 – 12.1). The association estimates were imprecise due to the small number of outcomes recorded.

Conclusions: The study documented an excess of very preterm and very low birth weight among infants born to mothers exposed to the landfill fire emissions during conception or early pregnancy.

Strengths and limitations of this study

- Vital statistics were used to investigate the potential reproductive health effects of short term exposure to pollutants emitted from an arson at an urban solid waste facility.
- The study documented the effects of the emissions from urban solid waste management plant on birth outcomes evaluating pregnancies exposed at different stages of development.
- The study added to the growing body of evidence that exposure to pollutants emitted from solid waste landfills may have serious health effects and underscores the need for monitoring potential hazards and health outcomes in the population living near landfills.
- The retrospective design and the limited vital statistics data available for analysis did not allow a detailed assessment of the longitudinal nature of the exposure-response relation, nor a precise adjustment for potential confounding.
- As it is often the case in studies of local environmental exposure events, the number of relevant outcomes was limited, especially when stratified according to the stage of the pregnancy at exposure, and association estimates were imprecise.

Key words: exposure to air pollutant; landfill emissions; low birth-weight; conception; early pregnancy.

Introduction

The number of studies investigating the potential human health effects on communities of pollutants released from landfills or incinerators is increasing,[1,2] showing that exposure is weakly associated with a variety of adverse health outcomes, including cancer, adverse reproductive outcomes and birth defects.[3-5] Increased risk of low birth weight and congenital malformations has been reported in communities living in proximity to landfills.[2,6] Maternal exposure to incinerator emissions was associated with preterm delivery.[7] A study of exposure to incinerator emissions containing dioxin concluded that exposure had little impact on birth weight and sex ratio, but may have been associated with gestational age at delivery.[8] Inconsistent findings across studies may

be due to design issues, lack of exposure information, use of indirect surrogate measures, acute versus long-term exposure conditions, and inadequate control of confounding.[9] Variation in risk perception among the stakeholders makes it difficult to communicate about the available evidence. In Italy, the incidence of fires in solid waste management plants is increasing,[10] addressing the need to investigate the potential health effects of short-term exposure to pollutants emitted from the combustion of solid waste.

In Sicily, the fourth most populated Italian region, 5 million residents produce about 6,000 tons of solid waste daily, which are disposed of in 4 Municipal Solid Waste Landfills (MSW-L).[11] The largest MSW-L is located in Bellolampo at 450 meters above sea level, on the hidden side of a mountain at the south-western border of Palermo (the largest city in Sicily, with 700,000 inhabitants, and its administrative capital).[11] The Bellolampo MSW-L collects solid waste from the Palermo metropolitan area, which includes the city and nearby municipalities.[12] On July 29, 2012, a fire started at multiple points within the landfill and emissions spread to a large populated area, causing concern for the public's health. Emissions peaked in the first 24 hours and decreased thereafter, until the fire was fully extinguished by August 16, 2012.

We analyzed vital statistics data to retrospectively evaluate the potential effects of the arson on the outcomes of pregnancies that were exposed to the emissions at different gestational ages.

Methods

In response to the arson, the Sicilian Regional Health Authority defined an administrative area around the landfill, whose resident population was considered as potentially exposed to the MSW-L emissions and placed under surveillance (**Supplementary file**).[13] Environmental monitoring of the area [14] was done through existing stationary monitoring stations.[15] A longitudinal retrospective study was designed to study the effects of exposure to the fire emissions on reproductive health outcomes. We obtained limited data from the regional Certificate of Birth Attendance (CedAP) registry, which collects information on all births to women of childbearing age

(10-55 years old) who deliver in Sicily, including parental socio-demographic characteristics, obstetric history, prenatal care, and characteristics of pregnancy and birth. The CedAP registry does not include data on births to resident mothers who delivered outside the region or wanted to preserve anonymity (0.4%). Date of conception was estimated using the date of birth and gestational age at birth reported in the registry. The study included all live births and stillbirths to mothers residing within the surveillance zone, whose estimated conception date occurred from 36 weeks prior to the peak of the fire (from 2:00PM on July 29, 2012 to 2:00PM on July 30, 2012), until 4 weeks after the fire. To remove confounding by exposure to pollutants deriving from anthropic activities and vehicular traffic within metropolitan areas, we restricted the main focus of the analysis to residents of the extra-urban section of the surveillance area (**Supplementary file**). Thus, the study group included all live births and stillbirths in the extra-urban surveillance area from pregnancies that were potentially exposed to the fire around the time of conception as well as pregnancies that were exposed at later stages (through the 36th week). The reference group comprised all live births and stillbirths to mothers residing in the remaining extra-urban, low-density and unindustrialized areas of Sicily, during the same time interval. To distinguish pregnancy periods of susceptibility to acute exposure to the fire emissions, we stratified the study group and the reference population according to the following four sub-periods of exposure (**Figure 1**):

i) peri-conception (conception occurring on July 29, 2012 or up to 4 weeks later);

ii) first trimester (conception date 12-0 weeks before July 29, 2012);

iii) second trimester (24-13 weeks before July 29, 2012);

iv) third trimester (36-25 weeks before July 29, 2012).

For each stage of the pregnancy at the time of exposure, we compared birth outcomes of the study group with those of the reference group. We also carried out internal comparisons within the study group, contrasting outcomes across the four sub-periods of exposure.

We conducted two supplementary analyses: first, we compared birth outcomes to mothers in the metropolitan area of Palermo (the main metropolitan area served by the Bellolampo MSW-L,

656,829 inhabitants) with those to mothers residing in the two other Sicilian metropolitan areas (Catania, 293,104 inhabitants, and Messina, 242,914 inhabitants) in the same study period. Second, to assess any systematic difference between the study group and the reference group independently from the fire, we repeated the comparison using data on births that occurred during the year preceding the arson (specifically, births conceived within -36 and +4 weeks from July 29, 2011).

For each comparison, we evaluated the following proportions, defined according to European guidelines for perinatal statistics adopted by the PERISTAT system[16,17]: a) among all births (i.e., live births and stillbirths combined): proportion of stillbirths, proportions of male and female births, and proportions of singleton and multiple births; b) among live births: preterm birth (gestational age <37 weeks), very preterm birth (gestational age <32 weeks), low birth weight (<2,500 grams), very low birth weight (<1,500 grams) and small for gestational age (SGA) (birth weight under the tenth percentile of the national distribution of birth weights of the same gestational age or birth of gestational age ≥37 weeks weighing <2,500 grams).

Because of CedAP data flow at the time in study was relatively new, we were only able to use the limited information described in this manuscript.

To make statistical inference about the comparisons between the different study groups and the references, we used logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) of the ORs, with and without adjusting for maternal age and infant gender, the only two potential confounders made available to us. Throughout this paper we treated the OR as an estimate of the risk ratio. This is appropriate as the absolute risks for most of the outcomes considered are well below 10%, and under these conditions the OR closely approximates the RR. Statistical analyses were carried out using STATA (version 11.2 MP, StataCorp, College Station, TX).

STROBE guidelines were followed for research reporting.

Patient and Public Involvement

Patients were not involved.

Results

Mothers residing in the exposed extra-urban area (the study group) gave birth to a total of 551 infants (548 live born + 3 stillborn) conceived during the interval of interest (11/20/2011-08/26/2012). There were 22,341 births (22,264 live births + 65 stillbirths) from pregnancies conceived during the same period by mothers residing in the remaining Sicilian low population-density, low industrialization areas (the comparison group). We observed a two-fold increase in risk of very preterm birth (OR adjusted for maternal age and infant gender= 2.29; 95%CI= 1.12 - 4.68) and a two-fold increase in risk of very low birth weight (OR adjusted for maternal age and infant gender= 2.20; 95%CI= 1.02 - 4.72) among singleton live births (**Table 1**).

Table 1. Outcomes of 551 births from pregnancies to mothers residing in the extra-urban area (study group) and of 22,342 births from pregnancies to Sicilian women residing in similar low population density, low industrialization areas (comparison group), conceived between 36 weeks before and 4 weeks after July 29, 2012.

Birth outcome	**Extra-urban exposed area**	**Comparison group**	**Unadjusted OR**		**Adjusted OR**	
	N (%)	**N (%)**				
All Births	551 (100)	22,342 (100)	**OR**	**(95%CI)**	**OR****	**(95%CI)**
Gender		7 (0,03)*				
Male	299 (54.26)	11,464 (51.31)	1 (ref.)		1 (ref.)	
Female	252 (45.74)	10,871 (48.66)	0.89	(0.75 - 1.05)	0.8	(0.75 - 1.05)
Plurality						
Singleton birth	530 (96.19)	21,594 (96.65)	1 (ref.)		1 (ref.)	
Multiple birth	21 (3.81)	748 (3.35)	1.14	(0.73 - 1.78)	1.17	(0.75 - 1.82)
Status at birth		13 (0,06)*				
Live births	548 (99.46)	22,264 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	3 (0.54)	65 (0.29)	1.88	(0.59 - 5.98)	1.89	(0.59 - 6.03)
Singleton live births	530 (100)	21,525 (100)	**OR**	**(95%CI)**	**OR****	**(95%CI)**
Preterm (<37 weeks)	36 (6.82)	1,094 (5.13)	1.35	(0.96 - 1.91)	1.35	(0.96 - 1.90)
Very preterm (<32 weeks)	8 (1.52)	144 (0.68)	**2.26**	**(1.10 – 4.63)**	**2.29**	**(1.12 – 4.68)**
Low birth weight (<2.500 gr)	37 (6.99)	1,143 (5.31)	1.34	(0.95 - 1.88)	1.36	(0.97 - 1.91)
Very low birth weight (<1500 gr)	7 (1.32)	131 (0.61)	**2.19**	**(1.02 - 4.71)**	**2.20**	**(1.02- 4.72)**
Small for gestational age	15 (2.84)	578 (2.71)	1.05	(0.62 - 1.76)	1.07	(0.65 – 1.80)

*Number and percentage of non-missing values **OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Among all births, we observed differences between the study group and the comparison group that were limited to births whose pregnancies were in the third trimester when the fire began: a twofold excess of multiple births (OR adjusted by gender= 2.42; 95%CI= 1.38-4.24) and a fourfold excess of stillbirths (OR adjusted by gender= 4.69; 95%CI= 1.40-15.6) (**Table 2**).

Among singleton live births we observed a three-fold increase in risk of very preterm between the extra-urban area and the remaining Sicilian low inhabitants density and unindustrialized areas for births whose pregnancies were in the third trimester (OR adjusted for maternal age and infant gender= 3.41; 95%CI= 1.04 - 11.16) when the fire began (**Table 2**).

Among singleton live births there were differences in very low birth weight rates between the extra-urban area and the remaining Sicilian low inhabitants density and unindustrialized areas for births whose pregnancies were either in peri-conception period (OR adjusted for maternal age and infant gender= 4.64; 95%CI= 1.04 – 20.6) or in the first trimester (OR adjusted for maternal age and infant gender= 3.66; 95%CI= 1.11 – 12.1) when the fire began (**Table 2**). Additional analyses of the risk of very low birth weight stratified by gestational age revealed that the excess of very low birth weight overlapped only in part with very preterm birth: remarkably, the infants accounting for the excess of very low birth weight from pregnancies conceived around the time of exposure were born after 32 weeks of gestation (results not shown in detail). Internal comparisons of the susceptibility period within the extra-urban exposed group did not reveal clear differences between subgroups defined by stages of the pregnancy at the time of exposure, but these comparisons were hampered by the small size of the study group (results not shown).

Our supplementary analyses did not show differences between the outcomes of 4,653 births to mothers residing in the Palermo metropolitan area which were conceived between 36 weeks before and 4 weeks after July 29, 2012 and the outcomes of 3,980 births to mothers residing in the other Sicilian metropolitan areas conceived during the same time interval (**Table 3**). Similarly, we

observed no differences between the outcomes of births from pregnancies to mothers residing in the extra-urban exposed area and the outcomes of births from pregnancies to Sicilian women residing in low population-density, low-industrialization areas of Sicily, conceived between 36 weeks before and 4 weeks after July 29, 2011 (one year before the arson) (**Table 4**).

Table 2. Outcomes of births from pregnancies to mothers residing in the exposed extra-urban area and of births from pregnancies to Sicilian women residing in similar low population density, low industrialization areas (comparison groups) by susceptibility sub-periods.

Birth outcome	Pregnancy stage as of the beginning of the fire (July 29, 2012)											
	Peri-conception			I Trimester (12-0 weeks)			II Trimester (24-13 weeks)			III Trimester (36-25 weeks)		
	Extra-urban exposed area N (%)*	Comparison Group N (%)	OR** (95%CI)	Extra-urban exposed area N (%)	Comparison Group N (%)	OR** (95%CI)	Extra-urban exposed area N (%)*	Comparison Group N (%)*	OR** (95%CI)	Extra-urban exposed area N (%)	Comparison Group N (%)	OR** (95%CI)
All Births	42 (100)	2,051 (100)		144 (100)	6,000 (100)		173 (100)	6,757 (100)		187 (100)	7,352 (100)	
Gender											6 (0,1)*	
Male	27 (64)	1,054 (51)	1 (ref.)	82 (57)	3,129 (52)	1 (ref.)	88 (51)	3,430 (51)	1 (ref.)	101 (54)	3,755 (51)	1 (ref.)
Female	15 (36)	997 (49)	0.59 (0.31-1.11)	62 (43)	2,870 (48)	0.82 (0.59-1.15)	85 (49)	3,327(49)	0.99 (0.74-1.35)	86 (46)	3,591(49)	0.89 (0.67-1.19)
Plurality												
Singleton birth	42 (100)	1993 (97)	1 (ref.)	142 (99)	5,793 (97)	1 (ref.)	168 (97)	6,535 (97)	1 (ref.)	173 (93)	7,099 (97)	1 (ref.)
Multiple birth	0 (0.0)	58 (2.8)	0 (-)	2 (1.4)	97 (3.4)	0.4 (0.09-1.62)	5 (2.9)	222 (3.3)	0.89 (0.36-2.18)	14 (7.5)	253 (3.4)	**2.42 (1.38-4.24)**
Status at birth											8 (0,11)*	
Live births	42 (100)	2.046 (99.8)	1 (ref.)	144 (100)	5,989 (99.8)	1 (ref.)	173 (100)	6,730 (99.7)	1 (ref.)	184 (98.4)	7,318 (99.54)	1 (ref.)
Stillbirths	0 (0.0)	5 (0.2)	0 (-)	0(0.0)	10 (0.2)	0 (-)	0 (0.0)	23 (0.34)	0 (-)	3 (1.6)	26 (0.35)	**4.69 (1.40-15.6)**
Singleton live births	42 (100)	1,983 (100)	**OR** (95%CI)**	142 (100)	5,788 (100)	**OR** (95%CI)**	168 (100)	6,435 (100)	**OR** (95%CI)**	172 (100)	7,075 (100)	**OR** (95%CI)**
Preterm (<37 weeks)	36 (7.14)	94 (4.81)	1.46 (0.44-4.83)	11(7.75)	295 (5.16)	1.52 (0.81-2.85)	11 (6.55)	352 (5.47)	1.21 (0.65-2.26)	11 (6.43)	343 (4.88)	1.35 (0.73-2.51)
Very preterm (<32 weeks)	2 (4,76)	18 (0,92)	3,99 (0.90-17.66)	3 (2,11)	43 (0,75)	2,88 (0,88-9,39)	0	42 (0,65)	-	3 (1,75)	39 (0,55)	**3,41 (1,04-11,16)**
Low birth weight (<2500g)	2 (4.76)	116 (5.85)	0.83 (0.20-3.48)	12 (8.45)	327 (5.65)	1.57 (0.86-2.88)	11 (6.55)	353 (5.42)	1.22 (0.66-2.27)	12 (6.98)	341 (4.82)	1.52 (0.83-2.76)

Very low birth weight (<1500g)	2 (4.76)	20 (1.01)	**4.64 (1.04-20.6)**	3 (2.11)	34 (0.59)	**3.66 (1.11-12.1)**	0 (0.0)	37 (0.57)	0 (-)	2 (1.16)	39 (0.55)	2.18 (0.52-9.12)
Small for gestational age	0 (0.0)	61 (3.1)	0 (-)	4 (2.82)	167 (2.92)	1.00 (0.36-2.74)	5 (2.98)	173 (2.69)	1.11 (0.45-2.75)	6 (3.51)	175 (2.49)	1.45 (0.63-3.31)

*Number and percentage of non-missing values **OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Table 3. Outcomes of 4,653 births from pregnancies to mothers residing in the Palermo metropolitan area and of 3,980 births from pregnancies to Sicilian women residing in the remaining metropolitan areas (comparison group), conceived between 36 weeks before and 4 weeks after July 29, 2012.

.

Birth outcome	Palermo exposed Metropolitan Area	Remaining Metropolitan Areas (Catania and Messina)	Unadjusted OR		Adjusted OR	
	N (%)	N (%)				
All Births	4,653 (100)	3,980 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Gender						
Male	2,350 (50.51)	2,040 (51.26)	1 (ref.)		1 (ref.)	
Female	2,303 (49.49)	1,940 (48.74)	1.03	(0.94 – 1.12)	1.03	(0.94 – 1.12)
Plurality						
Singleton birth	4,492 (96.54)	3,829 (96.21)	1 (ref.)		1 (ref.)	
Multiple birth	161 (3.46)	151 (3.79)	0.91	(0.72 - 1.14)	0.91	(0.72 - 1.14)
Status at birth						
Live births	4,636 (99.63)	3,966 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	17 (0.37)	14 (0.35)	1.04	(0.51 - 2.11)	1.03	(0.51 - 2.10)
Singleton live births	4,492 (100)	3,829 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Preterm (<37 weeks)	169 (7.25)	111 (6.75)	1.08	(0.84 - 1.38)	1.08	(0.84 - 1.39)
Low birth weight (<2.500 gr)	146 (6.74)	180 (7.15)	0.86	(0.69 - 1.08)	0.86	(0.69 - 1.08)
Very low birth weight (<1500 gr)	25 (1.07)	21 (0.83)	1.28	(0.72 - 2.30)	1.28	(0.72 - 2.30)
Small for gestational age	59 (2.53)	66 (4.01)	0.62	(0.43 - 0.89)	0.62	(0.64 – 1.77)

*OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Table 4. Outcome of 536 births from pregnancies to mothers residing in the exposed extra-urban area and of 23,373 births from pregnancies to Sicilian women residing in low inhabitants density and unindustrialized areas of Sicily (comparison group), conceived between 36 weeks before and 4 weeks after July 29, 2011 (the same calendar period during the previous year).

Birth outcome	Extra-urban exposed area	Comparison group	Unadjusted OR		Adjusted OR	
	N (%)	N (%)				
All Births	536 (100)	23,373 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Gender						
Male	272 (50.75)	12,041 (51.52)	1 (ref.)		1 (ref.)	
Female	264 (49.25)	11,329 (48.57)	1.03	(0.87 - 1.22)	1.03	(0.87 - 1.22)
Plurality						
Singleton birth	520 (97.01)	22,632 (96.83)	1 (ref.)		1 (ref.)	
Multiple birth	16 (2.99)	741 (3.17)	0.94	(0.57 - 1.56)	0.96	(0.58 - 1.58)
Status at birth						
Live births	534 (99.63)	23,291 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	2 (0.37)	79 (0.34)	1.10	(0.27 - 4.50)	1.10	(0.27 - 4.50)
Singleton live births			**OR**	**(95%CI)**	**OR***	**(95%CI)**
Preterm (<37 weeks)	30 (5.78)	1,226 (5.44)	1.06	(0.731 - 1.54)	1.07	(0.74 - 1.55)
Low birth weight (<2.500 gr)	35 (6.74)	1,226 (5.44)	1.26	(0.88 - 1.78)	1.26	(0.89 - 1.79)
Very low birth weight (<1500 gr)	4 (0.77)	133 (0.59)	1.31	(0.48 - 3.55)	1.31	(0.48- 3.56)
Small for gestational age	15 (2.89)	616 (2.75)	1.05	(0.62 - 1.77)	1.05	(0.63– 1.77)

*OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Discussion

This retrospective study investigated birth outcomes among women residing near one of the largest Italian solid waste landfills (the Bellolampo MSW-L), who were pregnant during a fire that started on July 29, 2012 and lasted for about a two-week period before being completely extinguished. As compared to births occurring during the same interval to mothers residing in other areas of Sicily

with similar population density and level of industrialization, we observed statistically significant differences suggesting that the landfill arson could have had an adverse impact on pregnancy outcomes. Our secondary analysis did not highlight statistically significant differences between the metropolitan exposed area and the other metropolitan populations in Sicily. In the study group, the analysis documented a three-fold excess risk of very preterm birth (<32weeks, OR adjusted for maternal age and infant gender= 3.41; 95%CI= 1.04 - 11.16) and a two-fold excess risk of very low birth weight (<1500g) among singleton live births. The effect on very low birth weight appeared to be concentrated among births whose conception date was between 12 weeks prior to the beginning of the fire to 4 weeks after, suggesting that the largest impact of the exposure may have been on pregnancies that were conceived during the fire (OR adjusted for maternal age and infant gender= 4.64; 95%CI= 1.04 – 20.6) or were exposed to the fire during the first trimester (OR adjusted for maternal age and infant gender = 3.66; 95%CI= 1.11 – 12.1). On the other hand, the effect on the risk of very pre-term birth did not appear to be confined to any particular subgroup at risk. These findings are compatible with a toxic effect on placentation or early embryo development leading to restricted intrauterine growth and premature delivery.[18,19] Maternal exposure to ambient concentrations of air pollutants, particularly to fine particulate matter, has been identified as a risk factor for preterm birth, low birth weight and SGA births.[20] Multiple studies have documented an association between fine particulate exposure and preterm birth.[21-23] Exposure to wildfires has been proposed as a risk factor for preterm birth [20] and reduced average birth weight.[24, 25] In a multi-site Italian study, maternal exposure to incinerator emissions was associated with preterm delivery even at very low levels.[7] Moreover, a study conducted in Taiwan concluded that exposure to emissions from an incinerator generating dioxin had little effects on birth weight and female birth, but may have a modest effect on gestational age.[8]

The mechanisms proposed to explain the effect of fine particulate exposure on preterm birth include oxidative stress, pulmonary and placental inflammation, coagulopathy, endothelial dysfunction and hemodynamic responses,[20, 26] as well as intrauterine inflammation.[20] Of interest, adverse

pregnancy outcomes including pre-term delivery, intrauterine growth restriction and impaired infant weight gain are associated with exposure to polychlorinateddibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like PCBs (DL-PCBs).[1] Recently, The Hokkaido Study on Environment and Children's Health has demonstrated the effects of environmental chemical exposures (dioxins, polychlorinated biphenyls, organochlorine pesticides, perfluoroalkyl substances, phthalates, bisphenol A, and methylmercury) on genetically susceptible populations and on DNA methylation,[27, 28] while other research suggests that exposure to tetrachlorodibenzo-*p*-dioxin (TCDD) may induce shifts in the immune response that enhance a proinflammatory phenotype at the maternal-fetal interface, increasing the risk of infection-mediated preterm birth.[29]

The body of published evidence, taken together with the statistically significant excess risk concentrated in a relatively narrow period of susceptibility, lends credibility to the hypothesis that the Bellolampo arson adversely affected pregnancies exposed during conception or in the first trimester, causing an excess of deliveries of very low birth weight infants in the extra-urban area. The study also documented in the same area a significant four-fold excess of stillbirths among pregnancies that were exposed to the landfill fire during the third trimester. This finding is based on a total of three stillbirths that occurred in the extra-urban study group, all of which were concentrated to the subgroup exposed during the third trimester, and it is possible that the observed excess is due to chance even if it was statistically significant. On the other hand, long-term exposure to PCBs was associated with increased proportions of miscarriage and stillbirth in animal studies,[30] and exposure to emissions from solid-waste incinerators was associated with increased risk of miscarriage in an epidemiologic study in Italy.[31] Thus, the excess of stillbirths to mothers exposed during the third trimester could be associated with the arson.

The excess of multiple births from pregnancies exposed during the third trimester in the study group is unlikely to be caused by exposure to the landfill fire, as plurality must have been established long

before the arson. The literature provides conflicting evidence on the association between exposure to air pollution from incinerators and multiple births.[32]

Long-term exposure of the study area to pollutants (independently from the fire) was already known and was confirmed by the detection of TCCD and heavy metals at concentrations above the limits permitted by law [33] in sub-soil samples collected by the regional environment protection agency after the fire.[34] However, the secondary analysis comparing birth outcomes in the same extra-urban groups in the year before the arson did not highlight any potential effect related to a long-term exposure to pollutants emitted from the landfill.

The findings of this study should be interpreted in light of some limitations. First, the retrospective design and the analysis of data from vital statistics do not allow a detailed assessment of the longitudinal nature of the exposure-response relation, or precise adjustment for potential confounding. Although environmental monitoring was performed in response to the arson, we had limited access to the data and could only confirm the increase in air particulate concentrations after the beginning of the fire. Thus, we could not assess specific exposure levels of individual pregnancies at multiple points in time. Lastly, as it is often the case in studies of local environmental exposure events, the outcomes of interest were limited in number, especially when stratified according to the stage of the pregnancy at exposure. Nevertheless, the observations made in this study are of general interest. While previous studies conducted in Italy have suggested associations between exposure to incinerator emissions and increased risk of miscarriages and preterm births,[31] to our knowledge, the present study is the first in Europe to investigate the effects of exposure emissions on birth outcomes evaluating pregnancies exposed at different stages of development. Despite the limited information base and sample size, the excess of very low birth weight infants achieved statistical significance and was confined to early-stage pregnancies.

The study adds to the growing body of evidence that exposure to emissions from solid waste landfill operations may have serious health effects and underscores the need for monitoring potential hazards and health outcomes in the resident population.[35] The arsons at the Bellolampo

MSW-L,[36] as well as the ones that occurred in other Italian solid waste treatment plants in proximity to populated areas,[10] and the public concern they caused, exemplify the important role that integration of environmental monitoring and epidemiologic surveillance may have in this realm.[37-39] The questionable strength of the evidence collected in this and in similar studies also underscores the need for better planning of monitoring and surveillance activities (more detailed exposure information, better definition and monitoring of reproductive and other health outcomes, assessment of long-term effects and better control for potential confounders), and highlights the difficulty of conveying results to the various stakeholders [9] and the related need for effective methods to transfer study results to policy makers and the public.[40]

Finally, our study highlights the importance to promote an integrated management of urban solid waste alternatives to landfills, including waste to energy plants or other newly available technologies such as pyrolysis and gasification.[41]

Ethics

Ethical approval was obtained by the "Palermo Ethical Committee 1" on February 14, 2018 (protocol number: 02/2018).

Data sharing

No additional data available.

Funding

No funding received.

Competing interests

The authors declare they have no actual or potential competing interests.

Authors' contributions

All individuals listed as authors have contributed substantially to designing, performing or reporting the study and every specific contribution is indicated as follows. Conception and design of the study: WM, MM, RC, AC. Data collection: ET, AC, SS. Statistical analysis: ET, AC, RG, MM, WM. Interpretation of data: CC, CM, WM, MM, AC, ET. Manuscript writing and drafting: WM,

MM, CM, AC, DA. Revision of the manuscript: WM, CM, MM, SS, FV. Approval of the final version of the manuscript: WM, ET, MM, CM, RC, DA, CC, RG, AC, SS, FV.

Acknowledgments

The authors are grateful to the Regional Environmental Protection Agency of Sicily (ARPA Sicilia) for technical assistance with the study design.

References

1 Vrijheid M. Health effects of residence near hazardous waste landfill sites: a review of epidemiologic literature. *Environ Health Perspect* 2000;108(suppl 1):101-112.

2 Saunders P. A systematic review of the evidence of an increased risk of adverse birth outcomes in populations living in the vicinity of landfill waste disposal sites. In Population health and waste management: scientific data and policy options. Report of a WHO workshop Rome, Italy, 29-30 March 2007 Edited by: Mitis F, Martuzzi M. WHO, Regional Office for Europe, Copenhagen; 2007:25-27.

3 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.

4 Dummer TJ, Dickinson HO, Parker L. Adverse pregnancy outcomes around incinerators and crematoriums in Cumbria, north west England, 1956-93. *J Epidemiol Community Health* 2003;57:456-461.

5 Cordier S, Chevrier C, Robert-Gnansia E, Lorente C, Brula P, Hours M. Risk of congenital anomalies in the vicinity of municipal solid waste incinerators. *Occup Environ Med* 2004;61:8-15.

6 Elliot P, Richardson S, Abellan JJ, et al. Geographic density of landfill sites and risk of congenital anomalies in England. *Occup Environ Med* 2009;66:81-89.

7 Candela S, Ranzi A, Bonvicini L, et al. Air pollution from incinerators and reproductive outcomes: a multisite study. *Epidemiology* 2013;24(6):863-70.

8 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(5):624-9.

9 Porta D, Milani S, Lazzarino AI, et al. Systematic review of epidemiological studies on health effects associated with management of solid waste. *Environmental Health* 2009;8:60.

10 Regioni.it. 2018. Incendi negli impianti di smaltimento rifiuti: il 20% è doloso. 17 January 2018

Available: http://www.regioni.it/newsletter/n-3303/del-17-01-2018/incendi-negli-impianti-di-smaltimento-rifiuti-il-20-e-doloso-17570/ [accessed 3 February 2018].

11 ISTAT (National Institute for Statistics) Population Data. Available: http://demo.istat.it/ [accessed 3 February 2018].

12 Di Bella G, Di Trapani D, Viviani G. Evaluation of methane emissions from Palermo municipal landfill: Comparison between field measurements and models. *Waste Management* 211;1820–1826.

13 UNINETLAB - University of Palermo, ARPA Sicily (Sicilian Regional Environmental Protection Agency). 2012. Studio per la valutazione della dispersione di contaminanti in atmosfera in seguito all'incendio nella discarica di Bellolampo avvenuta dal 29 Luglio al 17 Agosto 2012. Available: http://www.arpa.sicilia.it/wp-content/uploads/2014/03/Allegato_3.pdf [accessed 3 February 2018].

14 Sicilian Regional Health Authority. Department of health activities and epidemiological observatory. D.D.G n°01690/2012, adopted on 29.08.2012 with regard to "Zona di protezione da diossina nell'area di Bellolampo (Palermo). Misure sanitarie per la sicurezza alimentare".

15 Sicilian Region Environmental Department; ARPA Sicily (Sicialian Regional Environmental Protection Agency). 2014. Sistema di Rilevamento Regionale della Qualità dell'Aria della Regione Sicilia. Progetto di Razionalizzazione del monitoraggio della qualità dell'aria in Sicilia e relativo Programma di Valutazione (art.5, comma 6, del Decreto Legislativo 13 agosto 2010, n.155).

16 Zeitlin J, Wildman K, Bréart G, et al. PERISTAT: Indicators for monitoring and evaluating perinatal health in Europe. *Eur J Public Health* 2003;13(3):29-37.

17 Mazzucco W, Cusimano R, Macaluso M, et al. A retrospective follow up study on maternal age and infant mortality in two Sicilian districts. *BMC Public Health* 2011;19;11:817.

18 Maisonet M, Correa A, Misra D, et al. A review of the literature on the effects of ambient air pollution on fetal growth. *Environ Res* 2004;95:106-115.

19 Srám RJ, Binková B, Dejmek J, et al.. Ambient air pollution and pregnancy outcomes: a review of the literature. *Environ Health Perspect* 2005;113:375-382.

20 Shah PS, BalkhairT, Knowledge Synth Grp Determinants P. Air pollution and birth outcomes: a systematic review. *Environ*. 2011;Int.37:498–516. http://dx.doi.org/10.1016/j.envint.2010.10.009.

21 Qian Z, Liang S, Yang S, et al. Ambient air pollution and preterm birth: a prospective birth cohort study in Wuhan, China. Int. J. Hyg. *Environ. Health* 2016;219:195–203. http://dx.doi.org/10.1016/j.ijheh.2015.11.003.

22 Ha S, Hu H, Roussos-Ross D, et al. The effects of air pollution on adverse birth outcomes. *Environ Res* 2014;134:198–204. http://dx.doi.org/10.1016/j.envres.2014.08.002.

23 Fleischer NL, Merialdi M, van Donkelaar A, et al. Outdoor air pollution, preterm birth, and low birth weight: analysis of the World Health Organization global survey on maternal and perinatal health. *Environ Health Perspect* 2014;122:425–430. http://dx.doi.org/10.1289/ehp.1306837.

24 Holstius DM, Reid CE, Jesdale BM, et al. Birth weight following pregnancy during the 2003 southern California wildfires. *Environ Health Perspec* 2012;120:1340–1345. http://dx.doi.org/10.1289/ehp.1104515.

25 Rich DQ, Liu K, Zhang J, et al. Differences in birth weight associated with the 2008 Beijing Olympics air pollution reduction: results from a natural experiment. *Environ Health Perspect* 2015;123:880–887. http://dx.doi.org/10.1289/ehp.1408795.

26 Kannan S, Misra DP, Dvonch JT, et al. 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. http://dx.doi.org/10.1289/ehp.9081.

27 Nachman RM, Mao G, Zhang X, et al. Intrauterine inflammation and maternal exposure to ambient PM2.5 during preconception and specific periods of pregnancy: the Boston birth cohort. *Environ Health Perspect* 2016;124,1608–1615.

28 Kishi R, Araki A, Minatoya M, et al. The Hokkaido Birth Cohort Study on Environment and Children's Health: cohort profile—updated 2017. *Environ Health Prev Med* 2017;22(1):46.

29 Peltier MR, Arita Y, Klimova NG, et al. 2, 3, 7, 8-Tetrachlorodibenzo-p-dioxin (TCDD) enhances placental inflammation. *J Reprod Immunol* 2013;98(1-2):10-20.

30 Tsukimori K, Tokunaga S, Shibata S, et al. Long-term effects of polychlorinated biphenyls and dioxins on pregnancy outcomes in women affected by the Yusho incident. *Environ Health Perspect* 2008May;116(5):626-30. doi: 10.1289/ehp.10686.

31 Candela S, Bonvicini L, Ranzi A, et al. Exposure to emissions from municipal solid waste incinerators and miscarriages: A multisite study of the MONITER Project. *Environ Int* 2015;Mar9;78:51-60. doi: 10.1016/j.envint.2014.12.008.

32 Lloyd OL, Lloyd MM, Williams FL, et al. Twinning in human populations and in cattle exposed to air pollution from incinerators. *Br J Ind Med Aug* 1988;45(8):556-60.

33 Legislative decree n. 152 of 2006. Norme in materia ambientale. 2006.

34 ARPA Sicily (Sicilian Regional Environmental Protection Agency). 2012. Studio preliminare sullo stato di qualità dei comparti ambientali (suolo e acque sotterranee) all'esterno della discarica di Bellolampo. Available: http://www.arpa.sicilia.it/wp-content/uploads/2014/03/Allegato_1.pdf [accessed 3 February 2018].

35 Domingo JL, Rovira J, Vilavert L, et al. Health risks for the population living in the vicinity of an Integrated Waste Management Facility: Screening environmental pollutants. *Sci Total Environ 2015;*Mar 12;518-519C:363-370. doi: 10.1016/j.scitotenv.2015.03.010.

36 Marchese I. Maxi incendio nella discarica di Bellolampo. Giornale di Sicilia 8 July 2015. Available: http://palermo.gds.it/2015/07/08/maxi-incendio-nella-discarica-di-bellolampo-minacciata-dalle-fiamme-la-sesta-vasca_379946/ [accessed 3 February 2018].

37 Barchitta M, Fragapane S, Quattrocchi A, et al. Environmental health risk communication in the case "Terra dei Fuochi": content analysis of online newspaper articles. *Ann Ig* 2015;Jan-Feb;27(1):30-8. doi: 10.7416/ai.2015.2020.

38 Mazzucco W, Cusimano R, Zarcone M, et al. Funnel plots and choropleth maps in cancer risk communication: a comparison of tools for disseminating population-based incidence data to stakeholders. *BMJ open* 2017Mar1;7(3):e011502.

39 Mazzucco W, Cusimano R, Mazzola S, et al. Childhood and Adolescence Cancers in the Palermo Province (Southern Italy): Ten Years (2003–2012) of Epidemiological Surveillance. *Int J Environ Res Public Health* 2018;*15*(7),p.1344.

40 Briggs DJ. A framework for integrated environmental health impact assessment of systemic risks. *Environ Health* 2008;7:61.

41 Cotana F, Messineo A, Petrozzi A, et al. Comparison of ORC turbine and stirling engine to produce electricity from gasified poultry waste. *Sustainability* 2014;6(9),5714-5729, doi: 10.3390/su6095714, ISSN: 2071-1050, MDPI Publisher, Switzerland.

Figure 1. Bellolampo solid waste landfill arson: pregnancy stage at exposure among resident mothers and key statistically significant findings documented for the extra-urban area (the arrows represent the health outcomes associated to the exposure to the pollutants emitted by the arson).

Supplementary File. Under surveillance area exposed to emissions deriving from the Bellolampo municipal solid waste landfill (Borgetto, Capaci, Carini, Giardinello, Montelepre, Torretta): Metropolitan area (Palermo) and extra-urban area (in red).

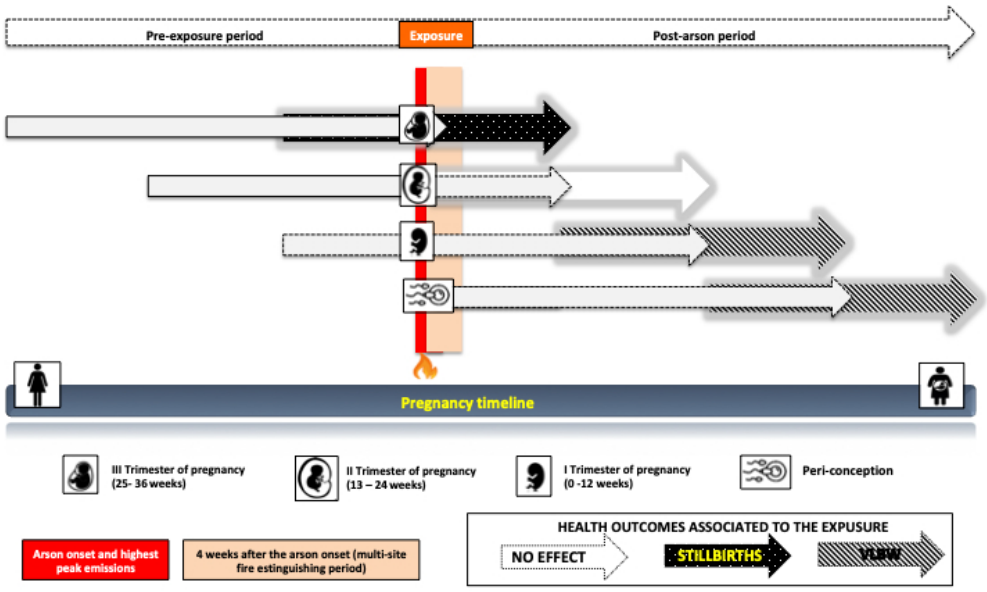
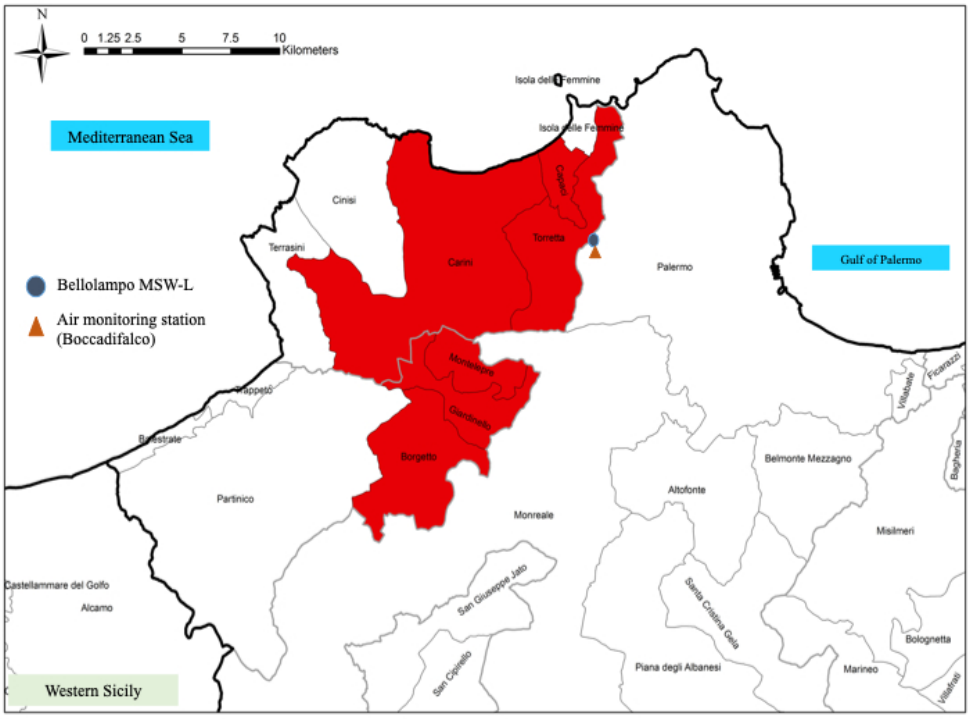


Figure 1. Bellolampo solid waste landfill arson: pregnancy stage at exposure among resident mothers and key statistically significant findings documented for the extra-urban area (the arrows represent the health outcomes associated to the exposure to the pollutants emitted by the arson).

254x158mm (72 x 72 DPI)



254x190mm (72 x 72 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 - 6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*7-9*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*NA*
		Cross-sectional study—Report numbers of outcome events or summary measures	*NA*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Do emissions from landfill fires affect pregnancy outcomes? A retrospective study after arson at a solid waste facility in Sicily.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-027912.R2
Article Type:	Research
Date Submitted by the Author:	19-Jun-2019
Complete List of Authors:	MAZZUCCO, WALTER; University of Palermo, Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE) Department, University of Palermo, Palermo, Italy; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit, Palermo University Hospital "P. Giaccone", Palermo, Italy Tavormina, Elisa; Regional Health Authority, Department of Health Services and Epidemiological Observatory Macaluso, M; Cincinnati Children's Hospital Medical Center, Division of Biostatistics and Epidemiology; University of Cincinnati College of Medicine, Department of Pediatrics Marotta, Claudia; University of Palermo, Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE) Department, University of Palermo, Palermo, Italy Cusimano, Rosanna; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit, Palermo University Hospital "P. Giaccone", Palermo, Italy Alba, Davide; University of Palermo, Sciences for health promotion (PROSAMI) Department Costantino, Claudio; University of Palermo, Sciences for health promotion (PROSAMI) Department Grammauta, Rosario; National Research Council, Institute for the Study of Anthropogenic Impacts and Sustainability in the Marine Environment (IAS), National Research Council Cernigliaro, Achille; Regional Health Authority, Department of Health Services and Epidemiological Observatory Scondotto, Salvatore; Regional Health Authority, Department of Health Services and Epidemiological Observatory Vitale, Francesco; University of Palermo, Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE) Department, University of Palermo; Palermo University Hospital "P. Giaccone", Clinical Epidemiology and Cancer Registry Unit, Palermo University Hospital "P. Giaccone"
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Reproductive medicine
Keywords:	PUBLIC HEALTH, Maternal medicine < OBSTETRICS, Enviromental health, exposure to air pollutant

Title page

Title: Do emissions from landfill fires affect pregnancy outcomes? A retrospective study after arson at a solid waste facility in Sicily.

Authors

Walter Mazzucco* [a,b], Elisa Tavormina [c], Maurizio Macaluso* [d], Claudia Marotta [a], Rosanna Cusimano [f], Davide Alba [a], Claudio Costantino [a], Rosario Grammauta [g], Achille Cernigliaro [c], Salvatore Scondotto [c], Francesco Vitale [a,b].

*These authors contributed equally.

[a] Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE) Department, University of Palermo, Palermo, Italy

[b] Clinical Epidemiology and Cancer Registry Unit, Palermo University Hospital "P. Giaccone", Palermo, Italy

[c] Department of Health Services and Epidemiological Observatory, Regional Health Authority, Sicilian Region, Palermo, Italy

[d] Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, and Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA

[f] Palermo Health Agency, Palermo, Italy

[g] Institute for the Study of Anthropogenic Impacts and Sustainability in the Marine Environment (IAS), National Research Council, Torretta Granitola (Trapani), Italy

Corresponding author:

Claudia Marotta, Dipartimento Scienze Promozione della Salute e Materno Infantile "G. D'Alessandro", Università degli Studi di Palermo. Via del Vespro, 133 - 90127 Palermo, Italy

Telephone number: +393337984116 Fax: +390916553631

E-mail: marotta.claudia@gmail.com

Word count: 4.156

Abstract

Objectives: In response to public health concern about effects of arson at solid waste management plants in July 2012, we analysed vital statistics data to evaluate any potential effect on pregnancies at different gestational ages of pollutants emitted from the landfill on fire.

Setting: A community living near the largest landfill plant in Sicily.

Participants: The study group comprised 551 births live births and stillbirths from pregnancies of mothers residing in the extra-urban exposed area, conceived during a 40-week period during which the highest fire's peak might have influenced pregnancy.

Primary and secondary outcome measures: Birth outcomes (gestational age <37 and <32 weeks, low birth weight, very low birth weight and small for gestational age) in the study group were compared to the ones of a reference group of women residing in areas of Sicily with similarly low population density and industrial development.

Results: Among singleton live births we observed a three-fold increase in risk of very preterm birth between the extra-urban area and the remaining low inhabitants density and unindustrialized areas for births whose pregnancies were in the third trimester (OR adjusted for maternal age and infant gender= 3.41; 95%CI= 1.04 - 11.16). There was an excess of very low birth weight singleton infants in the study group as compared to the reference group, which was limited to births to mothers exposed during peri-conception period (OR adjusted for maternal age and infant gender= 4.64; 95%CI= 1.04 – 20.6) and first trimester (OR adjusted for maternal age and infant gender = 3.66; 95%CI= 1.11 – 12.1). The association estimates were imprecise due to the small number of outcomes recorded.

Conclusions: The study documented an excess of very preterm and very low birth weight among infants born to mothers exposed to the landfill fire emissions during conception or early pregnancy.

Strengths and limitations of this study

- Arson at an urban solid waste facility allowed us to investigate the potential reproductive health effects of short-term exposure to pollutants emitted from the combustion of solid waste.
- The analysis of vital records data allowed us to assess birth outcomes of pregnancies exposed at distinct stages of development, from conception to the time of delivery.
- Data obtained from the regional Certificate of Birth Attendance registry allowed comparing exposed and non-exposed groups employing standardized information on birth outcomes.
- The retrospective design and the limited vital statistics data available for analysis did not allow a detailed assessment of the longitudinal nature of the exposure-response relation, or a precise adjustment for potential confounding.
- As it is often the case in studies of local environmental exposure events, the number of relevant outcomes was limited, especially when stratified according to the stage of the pregnancy at exposure, and association estimates were imprecise.

Key words: exposure to air pollutant; landfill emissions; low birth-weight; conception; early pregnancy.

Introduction

The number of studies investigating the potential human health effects on communities of pollutants released from landfills or incinerators is increasing,[1,2] showing that exposure is weakly associated with a variety of adverse health outcomes, including cancer, adverse reproductive outcomes and birth defects.[3-5] Increased risk of low birth weight and congenital malformations has been reported in communities living in proximity to landfills.[2,6] Maternal exposure to incinerator

emissions was associated with preterm delivery.[7] A study of exposure to incinerator emissions containing dioxin concluded that exposure had little impact on birth weight and sex ratio, but may have been associated with gestational age at delivery.[8] Inconsistent findings across studies may be due to design issues, lack of exposure information, use of indirect surrogate measures, acute versus long-term exposure conditions, and inadequate control of confounding.[9] Variation in risk perception among the stakeholders makes it difficult to communicate about the available evidence. In Italy, the incidence of fires in solid waste management plants is increasing,[10] addressing the need to investigate the potential health effects of short-term exposure to pollutants emitted from the combustion of solid waste.

In Sicily, the fourth most populated Italian region, 5 million residents produce about 6,000 tons of solid waste daily, which are disposed of in 4 Municipal Solid Waste Landfills (MSW-L).[11] The largest MSW-L is located in Bellolampo at 450 meters above sea level, on the hidden side of a mountain at the south-western border of Palermo (the largest city in Sicily, with 700,000 inhabitants, and its administrative capital).[11] The Bellolampo MSW-L collects solid waste from the Palermo metropolitan area, which includes the city and nearby municipalities.[12] On July 29, 2012, a fire started at multiple points within the landfill and emissions spread to a large populated area, causing concern for the public's health. Emissions peaked in the first 24 hours and decreased thereafter, until the fire was fully extinguished by August 16, 2012.

We analyzed vital statistics data to retrospectively evaluate the potential effects of the arson on the outcomes of pregnancies that were exposed to the emissions at different gestational ages.

Methods

In response to the arson, the Sicilian Regional Health Authority defined an administrative area around the landfill, whose resident population was considered as potentially exposed to the MSW-L emissions and placed under surveillance (**Supplementary file**).[13] Environmental monitoring of the area [14] was done through existing stationary monitoring stations.[15] A longitudinal

retrospective study was designed to study the effects of exposure to the fire emissions on reproductive health outcomes. We obtained limited data from the regional Certificate of Birth Attendance (CedAP) registry, which collects information on all births to women of childbearing age (10-55 years old) who deliver in Sicily, including parental socio-demographic characteristics, obstetric history, prenatal care, and characteristics of pregnancy and birth. The CedAP registry does not include data on births to resident mothers who delivered outside the region or wanted to preserve anonymity (0.4%). Date of conception was estimated using the date of birth and gestational age at birth reported in the registry. The study included all live births and stillbirths to mothers residing within the surveillance zone, whose estimated conception date occurred from 36 weeks prior to the peak of the fire (from 2:00PM on July 29, 2012 to 2:00PM on July 30, 2012), until 4 weeks after the fire. To remove confounding by exposure to pollutants deriving from anthropic activities and vehicular traffic within metropolitan areas, we restricted the main focus of the analysis to residents of the extra-urban section of the surveillance area (**Supplementary file**). Thus, the study group included all live births and stillbirths in the extra-urban surveillance area from pregnancies that were potentially exposed to the fire around the time of conception as well as pregnancies that were exposed at later stages (through the 36th week). The reference group comprised all live births and stillbirths to mothers residing in the remaining extra-urban, low-density and unindustrialized areas of Sicily, during the same time interval. To distinguish pregnancy periods of susceptibility to acute exposure to the fire emissions, we stratified the study group and the reference population according to the following four sub-periods of exposure (**Figure 1**):

i) peri-conception (conception occurring on July 29, 2012 or up to 4 weeks later);

ii) first trimester (conception date 12-0 weeks before July 29, 2012);

iii) second trimester (24-13 weeks before July 29, 2012);

iv) third trimester (36-25 weeks before July 29, 2012).

For each stage of the pregnancy at the time of exposure, we compared birth outcomes of the study group with those of the reference group. We also carried out internal comparisons within the study group, contrasting outcomes across the four sub-periods of exposure.

We conducted two supplementary analyses: first, we compared birth outcomes to mothers in the metropolitan area of Palermo (the main metropolitan area served by the Bellolampo MSW-L, 656,829 inhabitants) with those to mothers residing in the two other Sicilian metropolitan areas (Catania, 293,104 inhabitants, and Messina, 242,914 inhabitants) in the same study period. Second, to assess any systematic difference between the study group and the reference group independently from the fire, we repeated the comparison using data on births that occurred during the year preceding the arson (specifically, births conceived within -36 and +4 weeks from July 29, 2011).

For each comparison, we evaluated the following proportions, defined according to European guidelines for perinatal statistics adopted by the PERISTAT system[16,17]: a) among all births (i.e., live births and stillbirths combined): proportion of stillbirths, proportions of male and female births, and proportions of singleton and multiple births; b) among live births: preterm birth (gestational age <37 weeks), very preterm birth (gestational age <32 weeks), low birth weight (<2,500 grams), very low birth weight (<1,500 grams) and small for gestational age (SGA) (birth weight under the tenth percentile of the national distribution of birth weights of the same gestational age or birth of gestational age ≥37 weeks weighing <2,500 grams).

Because of CedAP data flow at the time in study was relatively new, we were only able to use the limited information described in this manuscript.

To make statistical inference about the comparisons between the different study groups and the references, we used logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) of the ORs, with and without adjusting for maternal age and infant gender, the only two potential confounders made available to us. Throughout this paper we treated the OR as an estimate of the risk ratio. This is appropriate as the absolute risks for most of the outcomes considered are well below 10%, and under these conditions the OR closely approximates the RR. Statistical

analyses were carried out using STATA (version 11.2 MP, StataCorp, College Station, TX). STROBE guidelines were followed for research reporting.

Patient and Public Involvement

Patients were not involved.

Results

Mothers residing in the exposed extra-urban area (the study group) gave birth to a total of 551 infants (548 live born + 3 stillborn) conceived during the interval of interest (11/20/2011-08/26/2012). There were 22,341 births (22,264 live births + 65 stillbirths) from pregnancies conceived during the same period by mothers residing in the remaining Sicilian low population-density, low industrialization areas (the comparison group). We observed a two-fold increase in risk of very preterm birth (OR adjusted for maternal age and infant gender= 2.29; 95%CI= 1.12 - 4.68) and a two-fold increase in risk of very low birth weight (OR adjusted for maternal age and infant gender= 2.20; 95%CI= 1.02 - 4.72) among singleton live births (**Table 1**).

Table 1. Outcomes of 551 births from pregnancies to mothers residing in the extra-urban area (study group) and of 22,342 births from pregnancies to Sicilian women residing in similar low population density, low industrialization areas (comparison group), conceived between 36 weeks before and 4 weeks after July 29, 2012.

Birth outcome	**Extra-urban exposed area**	**Comparison group**	**Unadjusted OR**		**Adjusted OR**	
	N (%)	**N (%)**				
All Births	551 (100)	22,342 (100)	**OR**	**(95%CI)**	**OR****	**(95%CI)**
Gender		7 (0,03)*				
Male	299 (54.26)	11,464 (51.31)	1 (ref.)		1 (ref.)	
Female	252 (45.74)	10,871 (48.66)	0.89	(0.75 - 1.05)	0.8	(0.75 - 1.05)
Plurality						
Singleton birth	530 (96.19)	21,594 (96.65)	1 (ref.)		1 (ref.)	
Multiple birth	21 (3.81)	748 (3.35)	1.14	(0.73 - 1.78)	1.17	(0.75 - 1.82)
Status at birth		13 (0,06)*				
Live births	548 (99.46)	22,264 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	3 (0.54)	65 (0.29)	1.88	(0.59 - 5.98)	1.89	(0.59 - 6.03)
Singleton live births	530 (100)	21,525 (100)	**OR**	**(95%CI)**	**OR****	**(95%CI)**
Preterm (<37 weeks)	36 (6.82)	1,094 (5.13)	1.35	(0.96 - 1.91)	1.35	(0.96 - 1.90)

Very preterm (<32 weeks)	8 (1.52)	144 (0.68)	**2.26**	**(1.10 – 4.63)**	**2.29**	**(1.12 – 4.68)**
Low birth weight (<2.500 gr)	37 (6.99)	1,143 (5.31)	1.34	(0.95 - 1.88)	1.36	(0.97 - 1.91)
Very low birth weight (<1500 gr)	7 (1.32)	131 (0.61)	**2.19**	**(1.02 - 4.71)**	**2.20**	**(1.02- 4.72)**
Small for gestational age	15 (2.84)	578 (2.71)	1.05	(0.62 - 1.76)	1.07	(0.65 – 1.80)

*Number and percentage of non-missing values **OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Among all births, we observed differences between the study group and the comparison group that were limited to births whose pregnancies were in the third trimester when the fire began: a twofold excess of multiple births (OR adjusted by gender= 2.42; 95%CI= 1.38-4.24) and a fourfold excess of stillbirths (OR adjusted by gender= 4.69; 95%CI= 1.40-15.6) (**Table 2**).

Among singleton live births we observed a three-fold increase in risk of very preterm between the extra-urban area and the remaining Sicilian low inhabitants density and unindustrialized areas for births whose pregnancies were in the third trimester (OR adjusted for maternal age and infant gender= 3.41; 95%CI= 1.04 - 11.16) when the fire began (**Table 2**).

Among singleton live births there were differences in very low birth weight rates between the extra-urban area and the remaining Sicilian low inhabitants density and unindustrialized areas for births whose pregnancies were either in peri-conception period (OR adjusted for maternal age and infant gender= 4.64; 95%CI= 1.04 – 20.6) or in the first trimester (OR adjusted for maternal age and infant gender= 3.66; 95%CI= 1.11 – 12.1) when the fire began (**Table 2**). Additional analyses of the risk of very low birth weight stratified by gestational age revealed that the excess of very low birth weight overlapped only in part with very preterm birth: remarkably, the infants accounting for the excess of very low birth weight from pregnancies conceived around the time of exposure were born after 32 weeks of gestation (results not shown in detail). Internal comparisons of the susceptibility period within the extra-urban exposed group did not reveal clear differences between

subgroups defined by stages of the pregnancy at the time of exposure, but these comparisons were hampered by the small size of the study group (results not shown).

Our supplementary analyses did not show differences between the outcomes of 4,653 births to mothers residing in the Palermo metropolitan area which were conceived between 36 weeks before and 4 weeks after July 29, 2012 and the outcomes of 3,980 births to mothers residing in the other Sicilian metropolitan areas conceived during the same time interval (**Table 3**). Similarly, we observed no differences between the outcomes of births from pregnancies to mothers residing in the extra-urban exposed area and the outcomes of births from pregnancies to Sicilian women residing in low population-density, low-industrialization areas of Sicily, conceived between 36 weeks before and 4 weeks after July 29, 2011 (one year before the arson) (**Table 4**).

Table 2. Outcomes of births from pregnancies to mothers residing in the exposed extra-urban area and of births from pregnancies to Sicilian women residing in similar low population density, low industrialization areas (comparison groups) by susceptibility sub-periods.

Birth outcome	Pregnancy stage as of the beginning of the fire (July 29, 2012)											
	Peri-conception			I Trimester (12-0 weeks)			II Trimester (24-13 weeks)			III Trimester (36-25 weeks)		
	Extra-urban exposed area N (%)*	Comparison Group N (%)	OR** (95%CI)	Extra-urban exposed area N (%)	Comparison Group N (%)	OR** (95%CI)	Extra-urban exposed area N (%)*	Comparison Group N (%)*	OR** (95%CI)	Extra-urban exposed area N (%)	Comparison Group N (%)	OR** (95%CI)
All Births	42 (100)	2,051 (100)		144 (100)	6,000 (100)		173 (100)	6,757 (100)		187 (100)	7,352 (100)	
Gender											6 (0,1)*	
Male	27 (64)	1,054 (51)	1 (ref.)	82 (57)	3,129 (52)	1 (ref.)	88 (51)	3,430 (51)	1 (ref.)	101 (54)	3,755 (51)	1 (ref.)
Female	15 (36)	997 (49)	0.59 (0.31-1.11)	62 (43)	2,870 (48)	0.82 (0.59-1.15)	85 (49)	3,327(49)	0.99 (0.74-1.35)	86 (46)	3,591(49)	0.89 (0.67-1.19)
Plurality												
Singleton birth	42 (100)	1993 (97)	1 (ref.)	142 (99)	5,793 (97)	1 (ref.)	168 (97)	6,535 (97)	1 (ref.)	173 (93)	7,099 (97)	1 (ref.)
Multiple birth	0 (0.0)	58 (2.8)	0 (-)	2 (1.4)	97 (3.4)	0.4 (0.09-1.62)	5 (2.9)	222 (3.3)	0.89 (0.36-2.18)	14 (7.5)	253 (3.4)	**2.42 (1.38-4.24)**
Status at birth											8 (0,11)*	
Live births	42 (100)	2.046 (99.8)	1 (ref.)	144 (100)	5,989 (99.8)	1 (ref.)	173 (100)	6,730 (99.7)	1 (ref.)	184 (98.4)	7,318 (99.54)	1 (ref.)
Stillbirths	0 (0.0)	5 (0.2)	0 (-)	0(0.0)	10 (0.2)	0 (-)	0 (0.0)	23 (0.34)	0 (-)	3 (1.6)	26 (0.35)	**4.69 (1.40-15.6)**
Singleton live births	42 (100)	1,983 (100)	**OR** (95%CI)**	142 (100)	5,788 (100)	**OR** (95%CI)**	168 (100)	6,435 (100)	**OR** (95%CI)**	172 (100)	7,075 (100)	**OR** (95%CI)**
Preterm (<37 weeks)	36 (7.14)	94 (4.81)	1.46 (0.44-4.83)	11(7.75)	295 (5.16)	1.52 (0.81-2.85)	11 (6.55)	352 (5.47)	1.21 (0.65-2.26)	11 (6.43)	343 (4.88)	1.35 (0.73-2.51)
Very preterm (<32 weeks)	2 (4,76)	18 (0,92)	3,99 (0.90-17.66)	3 (2,11)	43 (0,75)	2,88 (0,88-9,39)	0	42 (0,65)	-	3 (1,75)	39 (0,55)	**3,41 (1,04-11,16)**
Low birth weight (<2500g)	2 (4.76)	116 (5.85)	0.83 (0.20-3.48)	12 (8.45)	327 (5.65)	1.57 (0.86-2.88)	11 (6.55)	353 (5.42)	1.22 (0.66-2.27)	12 (6.98)	341 (4.82)	1.52 (0.83-2.76)

Very low birth weight (<1500g)	2 (4.76)	20 (1.01)	**4.64 (1.04-20.6)**	3 (2.11)	34 (0.59)	**3.66 (1.11-12.1)**	0 (0.0)	37 (0.57)	0 (-)	2 (1.16)	39 (0.55)	2.18 (0.52-9.12)
Small for gestational age	0 (0.0)	61 (3.1)	0 (-)	4 (2.82)	167 (2.92)	1.00 (0.36-2.74)	5 (2.98)	173 (2.69)	1.11 (0.45-2.75)	6 (3.51)	175 (2.49)	1.45 (0.63-3.31)

*Number and percentage of non-missing values **OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Table 3. Outcomes of 4,653 births from pregnancies to mothers residing in the Palermo metropolitan area and of 3,980 births from pregnancies to Sicilian women residing in the remaining metropolitan areas (comparison group), conceived between 36 weeks before and 4 weeks after July 29, 2012.

.

Birth outcome	Palermo exposed Metropolitan Area	Remaining Metropolitan Areas (Catania and Messina)	Unadjusted OR		Adjusted OR	
	N (%)	N (%)				
All Births	4,653 (100)	3,980 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Gender						
Male	2,350 (50.51)	2,040 (51.26)	1 (ref.)		1 (ref.)	
Female	2,303 (49.49)	1,940 (48.74)	1.03	(0.94 – 1.12)	1.03	(0.94 – 1.12)
Plurality						
Singleton birth	4,492 (96.54)	3,829 (96.21)	1 (ref.)		1 (ref.)	
Multiple birth	161 (3.46)	151 (3.79)	0.91	(0.72 - 1.14)	0.91	(0.72 - 1.14)
Status at birth						
Live births	4,636 (99.63)	3,966 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	17 (0.37)	14 (0.35)	1.04	(0.51 - 2.11)	1.03	(0.51 - 2.10)
Singleton live births	4,492 (100)	3,829 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Preterm (<37 weeks)	169 (7.25)	111 (6.75)	1.08	(0.84 - 1.38)	1.08	(0.84 - 1.39)
Low birth weight (<2.500 gr)	146 (6.74)	180 (7.15)	0.86	(0.69 - 1.08)	0.86	(0.69 - 1.08)
Very low birth weight (<1500 gr)	25 (1.07)	21 (0.83)	1.28	(0.72 - 2.30)	1.28	(0.72 - 2.30)
Small for gestational age	59 (2.53)	66 (4.01)	0.62	(0.43 - 0.89)	0.62	(0.64 – 1.77)

*OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Table 4. Outcome of 536 births from pregnancies to mothers residing in the exposed extra-urban area and of 23,373 births from pregnancies to Sicilian women residing in low inhabitants density and unindustrialized areas of Sicily (comparison group), conceived between 36 weeks before and 4 weeks after July 29, 2011 (the same calendar period during the previous year).

Birth outcome	Extra-urban exposed area	Comparison group	Unadjusted OR		Adjusted OR	
	N (%)	N (%)				
All Births	536 (100)	23,373 (100)	**OR**	**(95%CI)**	**OR***	**(95%CI)**
Gender						
Male	272 (50.75)	12,041 (51.52)	1 (ref.)		1 (ref.)	
Female	264 (49.25)	11,329 (48.57)	1.03	(0.87 - 1.22)	1.03	(0.87 - 1.22)
Plurality						
Singleton birth	520 (97.01)	22,632 (96.83)	1 (ref.)		1 (ref.)	
Multiple birth	16 (2.99)	741 (3.17)	0.94	(0.57 - 1.56)	0.96	(0.58 - 1.58)
Status at birth						
Live births	534 (99.63)	23,291 (99.65)	1 (ref.)		1 (ref.)	
Stillbirths	2 (0.37)	79 (0.34)	1.10	(0.27 - 4.50)	1.10	(0.27 - 4.50)
Singleton live births			**OR**	**(95%CI)**	**OR***	**(95%CI)**
Preterm (<37 weeks)	30 (5.78)	1,226 (5.44)	1.06	(0.731 - 1.54)	1.07	(0.74 - 1.55)
Low birth weight (<2.500 gr)	35 (6.74)	1,226 (5.44)	1.26	(0.88 - 1.78)	1.26	(0.89 - 1.79)
Very low birth weight (<1500 gr)	4 (0.77)	133 (0.59)	1.31	(0.48 - 3.55)	1.31	(0.48- 3.56)
Small for gestational age	15 (2.89)	616 (2.75)	1.05	(0.62 - 1.77)	1.05	(0.63– 1.77)

*OR adjusted for maternal age and infant gender (OR contrasting male and female gender adjusted for maternal age, only)

Discussion

This retrospective study investigated birth outcomes among women residing near one of the largest Italian solid waste landfills (the Bellolampo MSW-L), who were pregnant during a fire that started on July 29, 2012 and lasted for about a two-week period before being completely extinguished. As compared to births occurring during the same interval to mothers residing in other areas of Sicily

with similar population density and level of industrialization, we observed statistically significant differences suggesting that the landfill arson could have had an adverse impact on pregnancy outcomes. Our secondary analysis did not highlight statistically significant differences between the metropolitan exposed area and the other metropolitan populations in Sicily. In the study group, the analysis documented a three-fold excess risk of very preterm birth (<32weeks, OR adjusted for maternal age and infant gender= 3.41; 95%CI= 1.04 - 11.16) and a two-fold excess risk of very low birth weight (<1500g) among singleton live births. The effect on very low birth weight appeared to be concentrated among births whose conception date was between 12 weeks prior to the beginning of the fire to 4 weeks after, suggesting that the largest impact of the exposure may have been on pregnancies that were conceived during the fire (OR adjusted for maternal age and infant gender= 4.64; 95%CI= 1.04 – 20.6) or were exposed to the fire during the first trimester (OR adjusted for maternal age and infant gender = 3.66; 95%CI= 1.11 – 12.1). On the other hand, the effect on the risk of very pre-term birth did not appear to be confined to any particular subgroup at risk. These findings are compatible with a toxic effect on placentation or early embryo development leading to restricted intrauterine growth and premature delivery.[18,19] Maternal exposure to ambient concentrations of air pollutants, particularly to fine particulate matter, has been identified as a risk factor for preterm birth, low birth weight and SGA births.[20] Multiple studies have documented an association between fine particulate exposure and preterm birth.[21-23] Exposure to wildfires has been proposed as a risk factor for preterm birth [20] and reduced average birth weight.[24, 25] In a multi-site Italian study, maternal exposure to incinerator emissions was associated with preterm delivery even at very low levels.[7] Moreover, a study conducted in Taiwan concluded that exposure to emissions from an incinerator generating dioxin had little effects on birth weight and female birth, but may have a modest effect on gestational age.[8]

The mechanisms proposed to explain the effect of fine particulate exposure on preterm birth include oxidative stress, pulmonary and placental inflammation, coagulopathy, endothelial dysfunction and hemodynamic responses,[20, 26] as well as intrauterine inflammation.[20] Of interest, adverse

pregnancy outcomes including pre-term delivery, intrauterine growth restriction and impaired infant weight gain are associated with exposure to polychlorinateddibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like PCBs (DL-PCBs).[1] Recently, The Hokkaido Study on Environment and Children's Health has demonstrated the effects of environmental chemical exposures (dioxins, polychlorinated biphenyls, organochlorine pesticides, perfluoroalkyl substances, phthalates, bisphenol A, and methylmercury) on genetically susceptible populations and on DNA methylation,[27, 28] while other research suggests that exposure to tetrachlorodibenzo-*p*-dioxin (TCDD) may induce shifts in the immune response that enhance a proinflammatory phenotype at the maternal-fetal interface, increasing the risk of infection-mediated preterm birth.[29]

The body of published evidence, taken together with the statistically significant excess risk concentrated in a relatively narrow period of susceptibility, lends credibility to the hypothesis that the Bellolampo arson adversely affected pregnancies exposed during conception or in the first trimester, causing an excess of deliveries of very low birth weight infants in the extra-urban area. The study also documented in the same area a significant four-fold excess of stillbirths among pregnancies that were exposed to the landfill fire during the third trimester. This finding is based on a total of three stillbirths that occurred in the extra-urban study group, all of which were concentrated to the subgroup exposed during the third trimester, and it is possible that the observed excess is due to chance even if it was statistically significant. On the other hand, long-term exposure to PCBs was associated with increased proportions of miscarriage and stillbirth in animal studies,[30] and exposure to emissions from solid-waste incinerators was associated with increased risk of miscarriage in an epidemiologic study in Italy.[31] Thus, the excess of stillbirths to mothers exposed during the third trimester could be associated with the arson.

The excess of multiple births from pregnancies exposed during the third trimester in the study group is unlikely to be caused by exposure to the landfill fire, as plurality must have been established long

before the arson. The literature provides conflicting evidence on the association between exposure to air pollution from incinerators and multiple births.[32]

Long-term exposure of the study area to pollutants (independently from the fire) was already known and was confirmed by the detection of TCCD and heavy metals at concentrations above the limits permitted by law [33] in sub-soil samples collected by the regional environment protection agency after the fire.[34] However, the secondary analysis comparing birth outcomes in the same extra-urban groups in the year before the arson did not highlight any potential effect related to a long-term exposure to pollutants emitted from the landfill.

The findings of this study should be interpreted in light of some limitations. First, the retrospective design and the analysis of data from vital statistics do not allow a detailed assessment of the longitudinal nature of the exposure-response relation, or precise adjustment for potential confounding. Although environmental monitoring was performed in response to the arson, we had limited access to the data and could only confirm the increase in air particulate concentrations after the beginning of the fire. Thus, we could not assess specific exposure levels of individual pregnancies at multiple points in time. Lastly, as it is often the case in studies of local environmental exposure events, the outcomes of interest were limited in number, especially when stratified according to the stage of the pregnancy at exposure. Nevertheless, the observations made in this study are of general interest. While previous studies conducted in Italy have suggested associations between exposure to incinerator emissions and increased risk of miscarriages and preterm births,[31] to our knowledge, the present study is the first in Europe to investigate the effects of exposure emissions on birth outcomes evaluating pregnancies exposed at different stages of development. Despite the limited information base and sample size, the excess of very low birth weight infants achieved statistical significance and was confined to early-stage pregnancies.

The study adds to the growing body of evidence that exposure to emissions from solid waste landfill operations may have serious health effects and underscores the need for monitoring potential hazards and health outcomes in the resident population.[35] The arsons at the Bellolampo

MSW-L,[36] as well as the ones that occurred in other Italian solid waste treatment plants in proximity to populated areas,[10] and the public concern they caused, exemplify the important role that integration of environmental monitoring and epidemiologic surveillance may have in this realm.[37-39] The questionable strength of the evidence collected in this and in similar studies also underscores the need for better planning of monitoring and surveillance activities (more detailed exposure information, better definition and monitoring of reproductive and other health outcomes, assessment of long-term effects and better control for potential confounders), and highlights the difficulty of conveying results to the various stakeholders [9] and the related need for effective methods to transfer study results to policy makers and the public.[40]

Finally, our study highlights the importance to promote an integrated management of urban solid waste alternatives to landfills, including waste to energy plants or other newly available technologies such as pyrolysis and gasification.[41]

Ethics

Ethical approval was obtained by the "Palermo Ethical Committee 1" on February 14, 2018 (protocol number: 02/2018).

Data sharing

No additional data available.

Funding

No funding received.

Competing interests

The authors declare they have no actual or potential competing interests.

Authors' contributions

All individuals listed as authors have contributed substantially to designing, performing or reporting the study and every specific contribution is indicated as follows. Conception and design of the study: WM, MM, RC, AC. Data collection: ET, AC, SS. Statistical analysis: ET, AC, RG, MM, WM. Interpretation of data: CC, CM, WM, MM, AC, ET. Manuscript writing and drafting: WM,

MM, CM, AC, DA. Revision of the manuscript: WM, CM, MM, SS, FV. Approval of the final version of the manuscript: WM, ET, MM, CM, RC, DA, CC, RG, AC, SS, FV.

Acknowledgments

The authors are grateful to the Regional Environmental Protection Agency of Sicily (ARPA Sicilia) for technical assistance with the study design.

References

1 Vrijheid M. Health effects of residence near hazardous waste landfill sites: a review of epidemiologic literature. *Environ Health Perspect* 2000;108(suppl 1):101-112.

2 Saunders P. A systematic review of the evidence of an increased risk of adverse birth outcomes in populations living in the vicinity of landfill waste disposal sites. In Population health and waste management: scientific data and policy options. Report of a WHO workshop Rome, Italy, 29-30 March 2007 Edited by: Mitis F, Martuzzi M. WHO, Regional Office for Europe, Copenhagen; 2007:25-27.

3 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.

4 Dummer TJ, Dickinson HO, Parker L. Adverse pregnancy outcomes around incinerators and crematoriums in Cumbria, north west England, 1956-93. *J Epidemiol Community Health* 2003;57:456-461.

5 Cordier S, Chevrier C, Robert-Gnansia E, Lorente C, Brula P, Hours M. Risk of congenital anomalies in the vicinity of municipal solid waste incinerators. *Occup Environ Med* 2004;61:8-15.

6 Elliot P, Richardson S, Abellan JJ, et al. Geographic density of landfill sites and risk of congenital anomalies in England. *Occup Environ Med* 2009;66:81-89.

7 Candela S, Ranzi A, Bonvicini L, et al. Air pollution from incinerators and reproductive outcomes: a multisite study. *Epidemiology* 2013;24(6):863-70.

8 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(5):624-9.

9 Porta D, Milani S, Lazzarino AI, et al. Systematic review of epidemiological studies on health effects associated with management of solid waste. *Environmental Health* 2009;8:60.

10 Regioni.it. 2018. Incendi negli impianti di smaltimento rifiuti: il 20% è doloso. 17 January 2018

Available: http://www.regioni.it/newsletter/n-3303/del-17-01-2018/incendi-negli-impianti-di-smaltimento-rifiuti-il-20-e-doloso-17570/ [accessed 3 February 2018].

11 ISTAT (National Institute for Statistics) Population Data. Available: http://demo.istat.it/ [accessed 3 February 2018].

12 Di Bella G, Di Trapani D, Viviani G. Evaluation of methane emissions from Palermo municipal landfill: Comparison between field measurements and models. *Waste Management* 211;1820–1826.

13 UNINETLAB - University of Palermo, ARPA Sicily (Sicilian Regional Environmental Protection Agency). 2012. Studio per la valutazione della dispersione di contaminanti in atmosfera in seguito all'incendio nella discarica di Bellolampo avvenuta dal 29 Luglio al 17 Agosto 2012. Available: http://www.arpa.sicilia.it/wp-content/uploads/2014/03/Allegato_3.pdf [accessed 3 February 2018].

14 Sicilian Regional Health Authority. Department of health activities and epidemiological observatory. D.D.G n°01690/2012, adopted on 29.08.2012 with regard to "Zona di protezione da diossina nell'area di Bellolampo (Palermo). Misure sanitarie per la sicurezza alimentare".

15 Sicilian Region Environmental Department; ARPA Sicily (Sicialian Regional Environmental Protection Agency). 2014. Sistema di Rilevamento Regionale della Qualità dell'Aria della Regione Sicilia. Progetto di Razionalizzazione del monitoraggio della qualità dell'aria in Sicilia e relativo Programma di Valutazione (art.5, comma 6, del Decreto Legislativo 13 agosto 2010, n.155).

16 Zeitlin J, Wildman K, Bréart G, et al. PERISTAT: Indicators for monitoring and evaluating perinatal health in Europe. *Eur J Public Health* 2003;13(3):29-37.

17 Mazzucco W, Cusimano R, Macaluso M, et al. A retrospective follow up study on maternal age and infant mortality in two Sicilian districts. *BMC Public Health* 2011;19;11:817.

18 Maisonet M, Correa A, Misra D, et al. A review of the literature on the effects of ambient air pollution on fetal growth. *Environ Res* 2004;95:106-115.

19 Srám RJ, Binková B, Dejmek J, et al.. Ambient air pollution and pregnancy outcomes: a review of the literature. *Environ Health Perspect* 2005;113:375-382.

20 Shah PS, BalkhairT, Knowledge Synth Grp Determinants P. Air pollution and birth outcomes: a systematic review. *Environ*. 2011;Int.37:498–516. http://dx.doi.org/10.1016/j.envint.2010.10.009.

21 Qian Z, Liang S, Yang S, et al. Ambient air pollution and preterm birth: a prospective birth cohort study in Wuhan, China. Int. J. Hyg. *Environ. Health* 2016;219:195–203. http://dx.doi.org/10.1016/j.ijheh.2015.11.003.

22 Ha S, Hu H, Roussos-Ross D, et al. The effects of air pollution on adverse birth outcomes. *Environ Res* 2014;134:198–204. http://dx.doi.org/10.1016/j.envres.2014.08.002.

23 Fleischer NL, Merialdi M, van Donkelaar A, et al. Outdoor air pollution, preterm birth, and low birth weight: analysis of the World Health Organization global survey on maternal and perinatal health. *Environ Health Perspect* 2014;122:425–430. http://dx.doi.org/10.1289/ehp.1306837.

24 Holstius DM, Reid CE, Jesdale BM, et al. Birth weight following pregnancy during the 2003 southern California wildfires. *Environ Health Perspec* 2012;120:1340–1345. http://dx.doi.org/10.1289/ehp.1104515.

25 Rich DQ, Liu K, Zhang J, et al. Differences in birth weight associated with the 2008 Beijing Olympics air pollution reduction: results from a natural experiment. *Environ Health Perspect* 2015;123:880–887. http://dx.doi.org/10.1289/ehp.1408795.

26 Kannan S, Misra DP, Dvonch JT, et al. 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. http://dx.doi.org/10.1289/ehp.9081.

27 Nachman RM, Mao G, Zhang X, et al. Intrauterine inflammation and maternal exposure to ambient PM2.5 during preconception and specific periods of pregnancy: the Boston birth cohort. *Environ Health Perspect* 2016;124,1608–1615.

28 Kishi R, Araki A, Minatoya M, et al. The Hokkaido Birth Cohort Study on Environment and Children's Health: cohort profile—updated 2017. *Environ Health Prev Med* 2017;22(1):46.

29 Peltier MR, Arita Y, Klimova NG, et al. 2, 3, 7, 8-Tetrachlorodibenzo-p-dioxin (TCDD) enhances placental inflammation. *J Reprod Immunol* 2013;98(1-2):10-20.

30 Tsukimori K, Tokunaga S, Shibata S, et al. Long-term effects of polychlorinated biphenyls and dioxins on pregnancy outcomes in women affected by the Yusho incident. *Environ Health Perspect* 2008May;116(5):626-30. doi: 10.1289/ehp.10686.

31 Candela S, Bonvicini L, Ranzi A, et al. Exposure to emissions from municipal solid waste incinerators and miscarriages: A multisite study of the MONITER Project. *Environ Int* 2015;Mar9;78:51-60. doi: 10.1016/j.envint.2014.12.008.

32 Lloyd OL, Lloyd MM, Williams FL, et al. Twinning in human populations and in cattle exposed to air pollution from incinerators. *Br J Ind Med Aug* 1988;45(8):556-60.

33 Legislative decree n. 152 of 2006. Norme in materia ambientale. 2006.

34 ARPA Sicily (Sicilian Regional Environmental Protection Agency). 2012. Studio preliminare sullo stato di qualità dei comparti ambientali (suolo e acque sotterranee) all'esterno della discarica di Bellolampo. Available: http://www.arpa.sicilia.it/wp-content/uploads/2014/03/Allegato_1.pdf [accessed 3 February 2018].

35 Domingo JL, Rovira J, Vilavert L, et al. Health risks for the population living in the vicinity of an Integrated Waste Management Facility: Screening environmental pollutants. *Sci Total Environ 2015;*Mar 12;518-519C:363-370. doi: 10.1016/j.scitotenv.2015.03.010.

36 Marchese I. Maxi incendio nella discarica di Bellolampo. Giornale di Sicilia 8 July 2015. Available: http://palermo.gds.it/2015/07/08/maxi-incendio-nella-discarica-di-bellolampo-minacciata-dalle-fiamme-la-sesta-vasca_379946/ [accessed 3 February 2018].

37 Barchitta M, Fragapane S, Quattrocchi A, et al. Environmental health risk communication in the case "Terra dei Fuochi": content analysis of online newspaper articles. *Ann Ig* 2015;Jan-Feb;27(1):30-8. doi: 10.7416/ai.2015.2020.

38 Mazzucco W, Cusimano R, Zarcone M, et al. Funnel plots and choropleth maps in cancer risk communication: a comparison of tools for disseminating population-based incidence data to stakeholders. *BMJ open* 2017Mar1;7(3):e011502.

39 Mazzucco W, Cusimano R, Mazzola S, et al. Childhood and Adolescence Cancers in the Palermo Province (Southern Italy): Ten Years (2003–2012) of Epidemiological Surveillance. *Int J Environ Res Public Health* 2018;*15*(7),p.1344.

40 Briggs DJ. A framework for integrated environmental health impact assessment of systemic risks. *Environ Health* 2008;7:61.

41 Cotana F, Messineo A, Petrozzi A, et al. Comparison of ORC turbine and stirling engine to produce electricity from gasified poultry waste. *Sustainability* 2014;6(9),5714-5729, doi: 10.3390/su6095714, ISSN: 2071-1050, MDPI Publisher, Switzerland.

Figure 1. Bellolampo solid waste landfill arson: pregnancy stage at exposure among resident mothers and key statistically significant findings documented for the extra-urban area (the arrows represent the health outcomes associated to the exposure to the pollutants emitted by the arson).

Supplementary File. Under surveillance area exposed to emissions deriving from the Bellolampo municipal solid waste landfill (Borgetto, Capaci, Carini, Giardinello, Montelepre, Torretta): Metropolitan area (Palermo) and extra-urban area (in red).

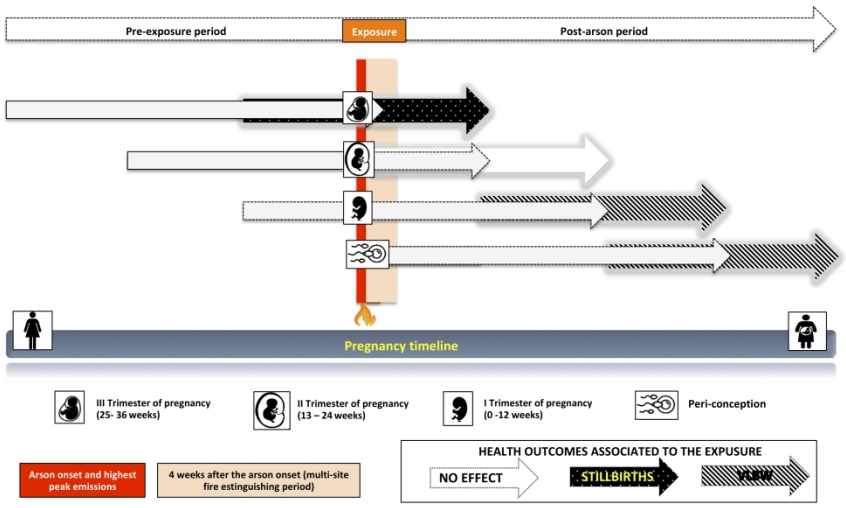
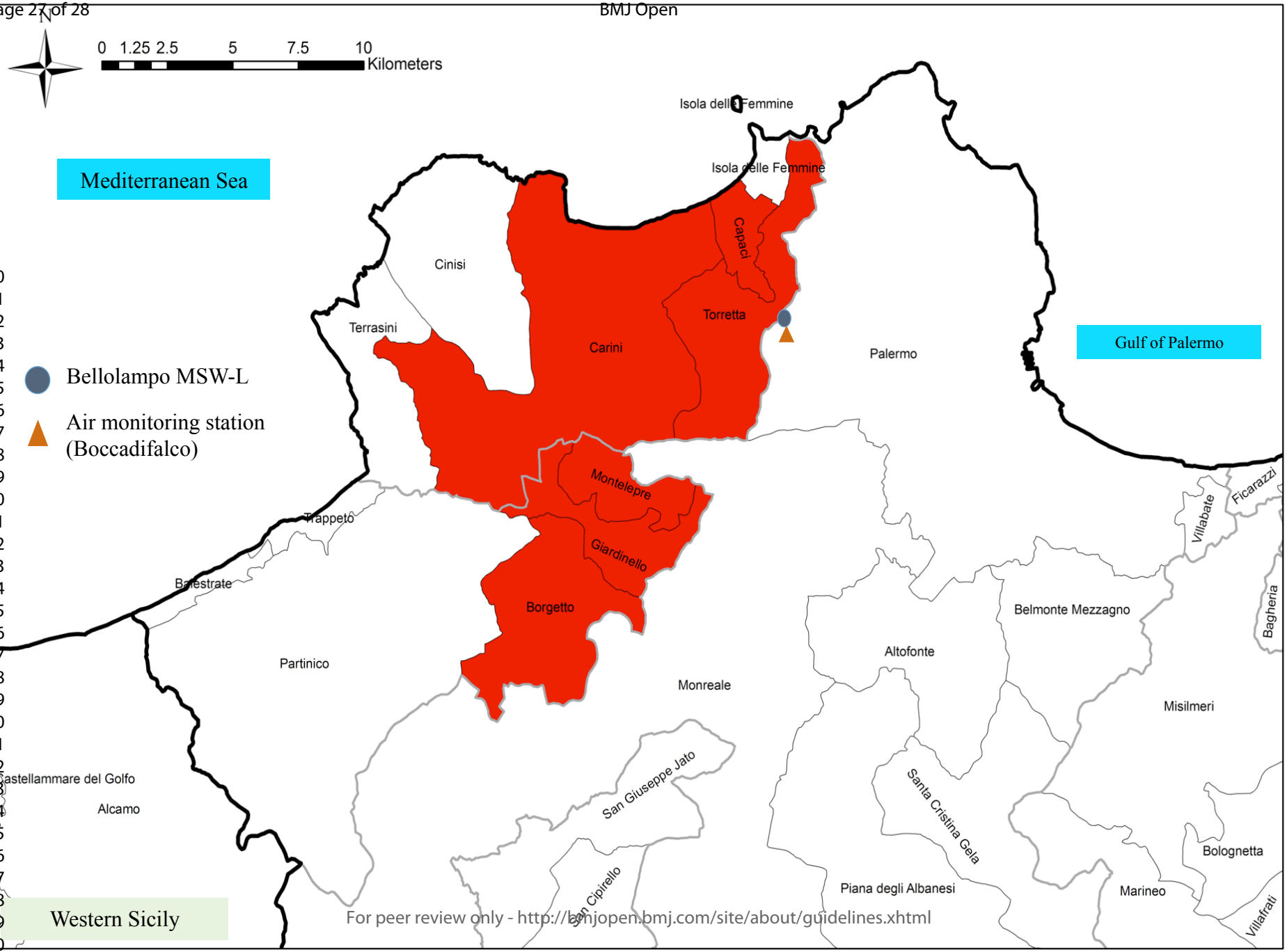


Figure 1. Bellolampo solid waste landfill arson: pregnancy stage at exposure among residentmothers and key statistically significant findings documented for the extra-urban area (the arrows represent the health outcomes associated to the exposure to the pollutants emitted by the arson).

297x209mm (300 x 300 DPI)



STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 - 6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	NA
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-7
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*7-9*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*NA*
		Cross-sectional study—Report numbers of outcome events or summary measures	*NA*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.