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Review

Waste incineration and adverse birth and neonatal outcomes: a systematic review☆

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ABSTRACT

Background: Public concern about potential health risks associated with incineration has prompted studies to investigate the relationship between incineration and risk of cancer, and more recently, birth outcomes. We conducted a systematic review of epidemiologic studies evaluating the relationship between waste incineration and the risk of adverse birth and neonatal outcomes.

Methods: Literature searches were performed within the MEDLINE database, through PubMed and Ovid interfaces, for the search terms; incineration, birth, reproduction, neonatal, congenital anomalies and all related terms. Here we discuss and critically evaluate the findings of these studies.

Results: A comprehensive literature search yielded fourteen studies, encompassing a range of outcomes (including congenital anomalies, birth weight, twinning, stillbirths, sex ratio and infant death), exposure assessment methods and study designs. For congenital anomalies most studies reported no association with proximity to or emissions from waste incinerators and "all anomalies", but weak associations for neural tube and heart defects and stronger associations with facial clefts and urinary tract defects. There is limited evidence for an association between incineration and twinning and no evidence of an association with birth weight, stillbirths or sex ratio, but this may reflect the sparsity of studies exploring these outcomes.

Conclusions: The current evidence-base is inconclusive and often limited by problems of exposure assessment, possible residual confounding, lack of statistical power with variability in study design and outcomes. However, we identified a number of higher quality studies reporting significant positive relationships with broad groups of congenital anomalies, warranting further investigation. Future studies should address the identified limitations in order to help improve our understanding of any potential adverse birth outcomes associated with incineration, particularly focussing on broad groups of anomalies, to inform risk assessment and waste policy.

Contents

☆ This paper has not previously been published, in whole or in part. As far as we are aware no similar papers are in press or under review elsewhere.

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1. Introduction

Waste treatment methods vary in environmental desirability and sustainability. These methods include: (1) disposal (landfilling); (2) recovery (incineration); (3) recycling; (4) preparation for re-use, and (5) prevention (Department for Environment Food and Rural Affairs, 2011). Incineration, defined as the controlled burning of waste at high temperatures, eliminates pathogens, reduces the volume of waste and recovers energy from waste (Crowley et al., 2003; Rushton, 2003). By-products of incineration include solid waste residues, fly and bottom ash, and stack emissions, such as: acidic gases (carbon dioxide, carbon monoxide, oxides of sulphur and nitrogen), persistent organic compounds (dioxins and furans), heavy metals (cadmium, thallium, mercury, antimony, arsenic, chromium, cobalt, copper, manganese, nickel, vanadium and lead) and particulates (Crowley et al., 2003).

The evidence exploring possible health risks associated with waste management has been reviewed a number times, focused primarily on landfilling and cancer risk (Crowley et al., 2003; Enviros Consulting Ltd et al., 2004; Porta et al., 2009; Redfearn and Roberts, 2002; Rushton, 2003; Saunders, 2007; Vrijheid, 2000), but also incineration and other health outcomes including respiratory symptoms, reparatory illness, lung function, symptoms of physical health, skin diseases, developmental disorders and birth outcomes, as well as blood levels of chemicals (Crowley et al., 2003; Enviros Consulting Ltd et al., 2004; Franchini et al., 2004; Hu and Shy, 2001; Porta et al., 2009; Rushton, 2003; Staines and Crowley, 2007). The potential health effects from municipal solid waste incinerators (MSWIs) have been reviewed by the UK Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment in 2000, updated in 2009, "*.....any potential risk of cancer due to residency near to municipal solid waste incinerators was exceedingly low and probably not measureable by the most modern epidemiological techniques*" (Committee on Carcinogenity of Chemicals in Food Consumer Products and the Environment, 2000, 2009), supported by the UK Health Protection Agency in 2009 which concluded that "*.....While it is not possible to rule out adverse health effects from modern, well regulated municipal incinerators with complete certainty, any potential damage to the health of those living close-by is likely to be very small, if detectable*" (Health Protection Agency, 2009).

Questions on potential risk of adverse birth outcomes associated with incineration are largely unaddressed. Studies of birth outcomes benefit from the short window of exposure (relative to, for example, cancer risk) and the monitoring of fetal and newborn health that takes place during pregnancy and around the time of birth. Here we report a systematic review of the published evidence on incineration and birth and neonatal outcomes, including sex ratio and twinning rates, and make recommendations for future work.

2. Methods

2.1. Search strategy and study inclusion criteria

Literature searches were performed in the MEDLINE database through PubMed and Ovid interfaces. The search strategy used to identify epidemiological studies examining the association between incineration and birth outcomes is summarised in Fig. 1. Searches were conducted using both key words and MESH terms (Fig. 1). The following keywords were used: incinerat*, waste incinerat*, MSWI, birth*, reproduct*, neonat* and the MeSH term for congenital anomalies/malformations/birth defects in both interfaces was "congenital abnormalities". The asterisk allows the interface to capture all words that start with the letters provided, for example incinerat* would include studies with both incinerator and incineration within the title or abstract. Additionally, references were sourced from the bibliographies of identified papers. The first screen assessed the relevance of a study based on its title and abstract. The second screen involved obtaining the paper's full text and examining its eligibility using the study inclusion criteria. Studies were deemed relevant if: (1) they were human studies (2) the paper was written in English (3) incineration (all types) was defined as the exposure source (4) they examined any birth or neonatal outcome. Selected studies were grouped according to birth outcome and the following information was abstracted (by D.C.A.): study design, location, study period, type and number of incinerators, study participants, exposure assessment methods, confounders identified, main findings and risk estimates.

2.2. Study quality assessment

To assess the reporting and general standard of each study, the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement was used (von Elm et al., 2007). The STROBE checklist was designed to encourage complete and adequate reporting of observational studies (von Elm et al., 2007). This checklist provides a way to assess what the study has reported, without weighting items.

We additionally created a checklist for this review to help assess the quality of the selected studies (Khan et al., 2011). The items included within the quality checklist were deemed the areas with greatest potential for uncertainty and included all items assessed within the STROBE methods section (von Elm et al., 2007). The scores assigned to each item within this quality checklist reflected the authors' judgment as to their relative importance; all items selected are widely reported as areas of concern in epidemiologic studies. As exposure assessment is often referred to as the 'Achilles heel' of environmental epidemiology (Elliott and Wartenberg, 2004; Steenland and Savitz, 1997), the method and quality of exposure assessment was assigned the strongest weight (7 points); other areas assessed were: study design (5 points), quality of health data (2 points) and adequate control for potential confounding (3 points). The maximum score achievable for each study was thus 17.

The quality scores were used to help rank the evidence rather than to weight the results of individual studies. Due to the heterogeneous nature of the studies reviewed, and the diverse range of study designs, and reporting, no attempt was made to provide a quantitative summary of the evidence.

3. Results

The initial search resulted in the identification of 309 studies, of which 14 met the inclusion criteria (Cordier et al., 2004, 2010; Cresswell et al., 2003; Dummer et al., 2003; Jansson, 1998; Lin et al., 2006; Lloyd et al., 1988; Obi-Osius et al., 2004; Rydhstroem, 1998; Tango et al., 2004; ten Tusscher et al., 2000; Vinceti et al., 2008, 2009; Williams et al., 1992). Fig. 1 outlines the search method and the number of studies identified and selected during each phase of the search. Table 1 provides a detailed overview of the 14 reviewed studies including information on the health outcomes investigated, study design and participants, exposure assessment methods and adjustment for confounders and Table 2 summarises the main findings of these epidemiological studies identified. Supplementary Table 1 summarises each study according to the STROBE checklist. Table 3 gives a breakdown of the quality scores assigned to each study.

Of the 14 studies, eight examined congenital anomalies (Cordier et al., 2004, 2010; Cresswell et al., 2003; Dummer et al., 2003; Jansson, 1998; ten Tusscher et al., 2000; Vinceti et al., 2008, 2009) of which one included spontaneous abortions (Vinceti et al., 2008) and one stillbirths and neonatal deaths(Dummer et al., 2003); three examined twinning (Lloyd et al., 1988; Obi-Osius et al., 2004; Rydhstroem, 1998); two examined fetal growth (Lin et al., 2006; Tango et al., 2004), as well as neonatal, infant and spontaneous deaths (Tango et al., 2004), sex ratio at birth (Lin et al., 2006; Tango et al., 2004) and preterm delivery (Lin et al., 2006); and one examined sex ratio only (Williams et al., 1992). Studies varied in: (1) number of incinerators: six single site (Cresswell et al., 2003; Lin et al., 2006; Obi-Osius et al., 2004; ten Tusscher et al., 2000; Vinceti et al., 2008, 2009) and eight multi-site (Cordier et al.,

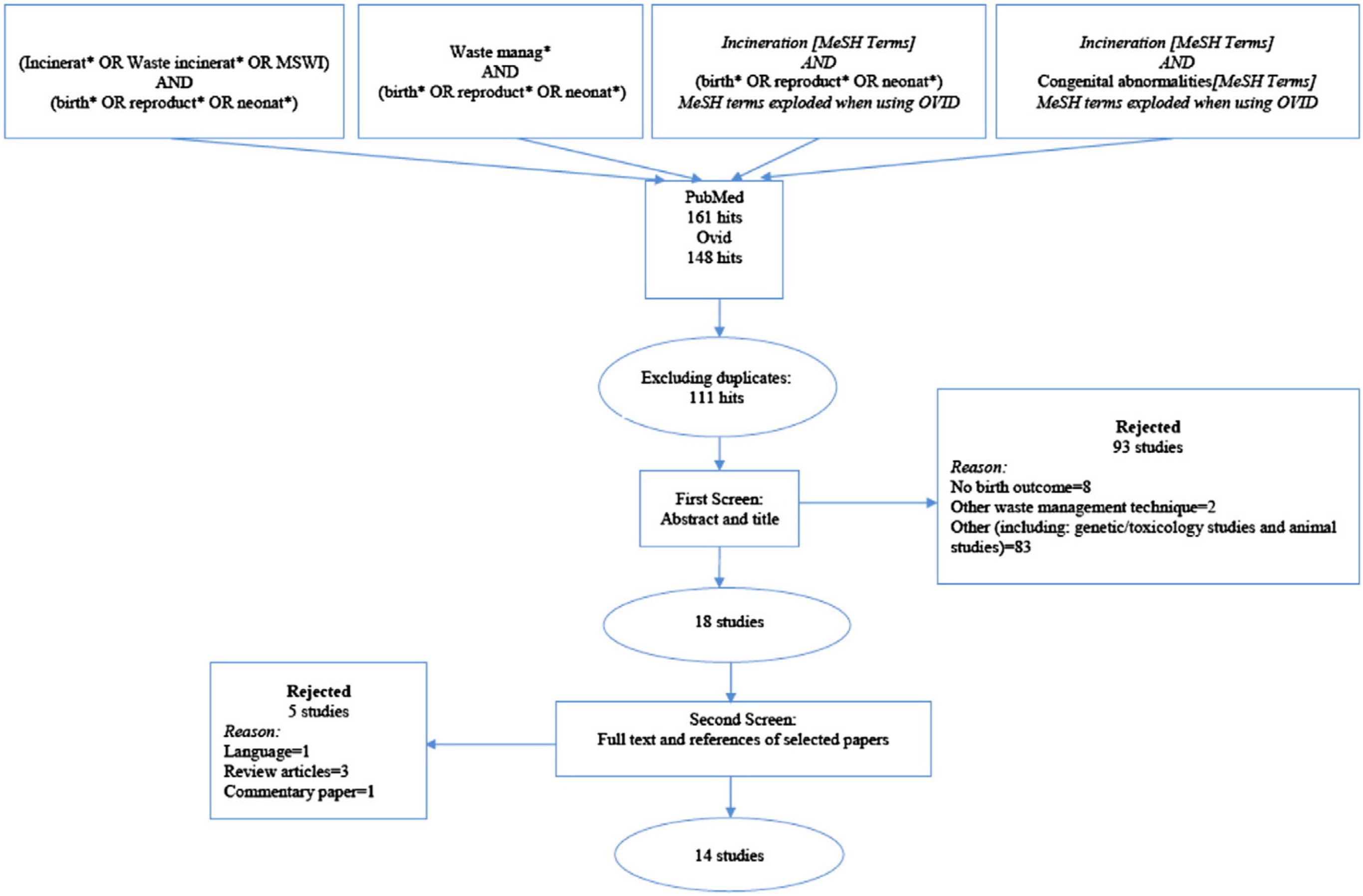

Fig. 1. Selection and review method for all identified studies.

2004, 2010; Dummer et al., 2003; Jansson, 1998; Lloyd et al., 1988; Rydhstroem, 1998; Tango et al., 2004; Williams et al., 1992) ranging from two (Lloyd et al., 1988; Williams et al., 1992) to 70 incinerators (Cordier et al., 2004); (2) design: two case-control studies (Cordier et al., 2010; Vinceti et al., 2008), three cohort studies (Dummer et al., 2003; ten Tusscher et al., 2000; Vinceti et al., 2009), of which one was a hospital based retrospective cohort (ten Tusscher et al., 2000), and nine geographic studies (Cordier et al., 2004; Cresswell et al., 2003; Jansson, 1998; Lin et al., 2006; Lloyd et al., 1988; Obi-Osius et al., 2004; Rydhstroem, 1998; Tango et al., 2004; Williams et al., 1992).

The majority of the studies met most of the requirements of the STROBE reporting checklist (Supplementary Table 1). Using the quality checklist (Table 3), the studies' overall scores ranged from 2 to 14, with a mean of 7.6. The six studies scoring above the mean (Cordier et al., 2004, 2010; Dummer et al., 2003; Lin et al., 2006; Vinceti et al., 2008, 2009) reported incineration to be significantly associated with facial clefts (Cordier et al., 2004), urinary tract anomalies (Cordier et al., 2004, 2010), lethal neural tube (Dummer et al., 2003) and lethal heart defects (Dummer et al., 2003). These studies found no associations with all congenital anomalies combined, stillbirths and neonatal deaths, spontaneous abortions, low birth weight, preterm delivery and sex ratio (Cordier et al., 2004; Dummer et al., 2003; Lin et al., 2006; Vinceti et al., 2008, 2009). The highest scoring study was a population based case-control study by Cordier et al. (2010) that examined the relationship between maternal exposure to dioxins and heavy metals, based on modelled exposures, and risk of babies born with urinary tract defects (Cordier et al., 2010).

The sections below present the study results grouped by the birth outcome investigated.

3.1. Congenital anomalies

Five studies examined the association between all congenital anomalies combined (including lethal anomalies and major anomalies) and incineration (Cordier et al., 2004; Cresswell et al., 2003; Dummer et al., 2003; Vinceti et al., 2008, 2009) of which only one Dummer et al. (2003) reported a significant association for all anomalies.

Two of these studies were located in Northern Italy and defined areas of increasing exposure according to modelled concentrations of dioxins from a MSWI, estimated through stochastic dispersion models (Vinceti et al., 2008, 2009). The first, a cohort study (Quality = 8), found no excess risk of major congenital anomalies based on birth defects registry data (which exclude minor anomalies when isolated) (European Surveillance of Congenital Anomalies (EUROCAT), 2005); the study compared risks for mothers resident in areas near the incinerator classified as high/intermediate exposure, with those resident in the municipal population (Vinceti et al., 2008) (relative risk [RR] 0.64; 95% confidence interval 0.20–1.55). Although a large excess risk was observed for mothers working near the incinerator (RR 2.26; 0.57–6.14), the number of cases included was small, reflected in wide confidence intervals. The second was a population based case-control study (quality = 11); it found a non significant excess risk of major congenital anomalies for mothers living in areas near the MSWI classified as medium/high exposure (RR 1.11; 0.60–2.04) (Vinceti et al., 2009).

One was a geographic study in South Eastern France (quality = 10) with findings consistent with the Italian studies. Cordier et al. (2004) examined the association between 70 MSWIs and the risk of major congenital anomalies within 2,872 communities (<50,000 inhabitants) (Cordier et al., 2004); they found no difference in the rate of all

Table 1
Summary of epidemiological studies on incineration and risk of adverse birth and neonatal outcomes grouped by outcome.

Birth outcomes investigated	Author(s) and location of study	Study design	Study period	Study participants	Exposure source	Exposure assessment	Confounders
All congenital anomalies (Broad groups of anomalies)	Cordier et al., 2004, France	Geographic study (comparing communities)	1988–1997	Communities with <50,000 inhabitants surrounding 70 MSWIs Within the 194 exposed communities: Births = 94,239 Congenital anomalies = 1481 Within the 2678 unexposed communities: Births = 470,369 Congenital anomalies = 6730	70 MSWIs	Communities assigned exposure index's calculated as the product of "immission" score (proxy for annual ambient air concentrations from incinerator flue) and years of operation Exposure assessment based on maternal community of residence at birth (or medical termination) Three classes of exposure	Year of birth, maternal age, department of birth, population density, average family income *Exposed communities only;* other sources of dioxin exposure, local road traffic
Urinary tract birth defects	Cordier et al., 2010, France	Population-based case-control	2001–2003	Live births/stillbirths/medical termination with renal birth defect or obstructive uropathy (cases) = 304 (187 interviewed) Live births/stillbirths/medical termination without defect or low birth weight (controls) = 226 Controls frequency matched for sex, year and district of birth	21 MSWIs	Modelled atmospheric dioxins, dioxin deposits and heavy metals concentrations Exposure assessment based on maternal place of residence for a 4 month period (from 1 month before conception until the end of the first trimester) Three classes of exposure- Exposed families split into groups; above median and below median exposure. Exposed participants had modelled concentration above a threshold (10 km away from the most heavily polluting MSWI)	Population density, deprivation score, industrial dioxin sources, past MSWI activity, maternal age, parental geographic origin, educational level, employment status during pregnancy, treatment for chronic disease during first trimester of pregnancy, folic acid supplementation, family history of urinary tract defects, parity, obesity, tobacco use during pregnancy, alcohol use during pregnancy, environmental tobacco smoke exposure *Four identified confounder;* parental geographic origin, family history of urinary tract defects, parity, maternal alcohol use during pregnancy
Major congenital anomalies	Cresswell et al., 2003, England	Geographic study	1985–1999	Live births within the study area = 81,225 Live births, stillbirths, induced abortions and fetal death after 14 weeks gestation with a major congenital anomaly within study area = 1,508	1 waste combustion plant	Exposure assessment based on distance to plant from maternal residence at birth Two classes of exposure- Inner zone; 3 km from the plant, Outer zone, 3–7 km from the plant	Socio-economic deprivation
Lethal congenital anomalies i) All neural tube defects ii) Heart defects iii) All other anomalies Stillbirths Neonatal death Stillbirths & neonatal death	Dummer et al., 2003, England	Retrospective cohort	1956–1993	Births = 244,758 Lethal congenital anomalies = 2000 All neural tube defects = 734 Anecephalus = 295 Spina bifida = 304 Other central nervous system anomalies = 135 Heart defects = 351 All other anomalies = 484 Stillbirths = 3234 Neonatal deaths = 2663 Stillbirth & neonatal deaths = 5897	4 industrial & domestic incinerators	Exposure assessment based on distance to incinerator from maternal residence at birth	Social class, year of birth, birth order, multiple births
Cleft lip/palate	Jansson and Voog, 1998, Sweden	Geographic study Study A. Case study Study B. Register study	Study A. 1987 Study B. 1975–1987	Study A. Cleft lip/palate = 6 Study B. Cleft lip/palate within the boroughs in Skaraborg with an incinerator = 82	Study B. 18 boroughs in Sweden with a refuse incinerator	Study A. Case analysis, exposure assessment and meteorological dispersion calculations Study B. Exposure assessment based on maternal residence in a borough with a refuse incinerator	
Birth weight LBW Gestational age		Geographic study (ecological study-	1991 & 1997	Births in 1991 (1 year before incinerator opened) =6,697 neonates	1 MSWI	Modelled dioxin concentrations as a proxy for ambient dioxin exposure	Gender, birth order, maternal age, maternal education level

(continued on next page)

Table 1 (*continued*)

Birth outcomes investigated	Author(s) and location of study	Study design	Study period	Study participants	Exposure source	Exposure assessment	Confounders
PTD Sex ratio	Lin et al., 2006, Taiwan	before and after the introduction of an incinerator)		LBW = 247 PTD = 562 Females/males = 3092/3604 Births in 1997 (5 years after incinerator opened) =6,282 neonates LBW = 237 PTD = 753 Females/males = 3002/3280		Exposure assessment based on maternal residence at birth Three classes of exposure- Exposed districts had modelled average annual dioxin concentrations ≥0.03 pg TEQ/m^3 Two classes of increasing exposure: 0.03–0.05 pg TEQ/m^3 and >0.05 pg TEQ/m^3	
Twinning	Lloyd et al., 1988, Scotland	Geographic study	1975–1983	1976–9: Births = 12,295 Pairs of twins = 113 1980–3: Births = 13,029 Pairs of twins = 122 Controls where resident in neighbouring areas	1 MSWI & 1 chemical waste incinerator	Exposure assessment based on maternal residence near incinerators (postcode sector) Three classes of exposure – Wind patterns, distance from the incinerator and soil concentrations of polychlorinated hydrocarbons used to categorise postcode sectors exposure categories	Maternal age
Twinning	Obi-Osius et al., 2004, Germany	Geographic study Study A. Retrospective cross-sectional study Study B. Geographic study	Study A. 1994–1995 Study B. 1994–1997	Study A. Total births = 636 Twin births = 24 Study B. Total births = 20,603 Twin births = ~200	1 toxic waste incinerator	Exposure assessment based on maternal residence within municipalities surrounding the incinerator and industrial site Study A. Exposure assessment based on maternal residence Study B. Exposure assessment based on maternal residence at time of delivery	Study B. Maternal age, parity, nationality (German or non-German)
Spatial clustering of twins	Rydhstroem, 1998, Sweden	Geographic study (before and after the introduction of an incinerator)	1973–1990	Twin deliveries in 1,224 parishes = 17,067 (Included parishes/municipalities had ≥4 expected twin deliveries or <1 expected and >4 observed)	14 refuse incinerators	Exposure assessment based on maternal residence within the municipalities and parishes surrounding the 14 incinerators	Year of delivery, maternal age
Female live birth LBW Very LBW Infant death and those due to congenital anomalies Neonatal deaths and those due to congenital anomalies (additionally early neonatal deaths) Spontaneous fetal deaths and those due to congenital anomalies	Tango et al., 2004, Japan	Geographic study	1997–1998	Live births = 225,215 Female live births = 110,044 LBW = 18,167 Very LBW = 1394 Infant deaths = 835 Infant deaths due to congenital anomalies = 310 Neonatal deaths (early) = 471 (314) Neonatal deaths due to congenital anomalies (early) = 186 (121) Spontaneous deaths = 3,380 Spontaneous deaths due to congenital anomalies = 202	63 MSWIs	Exposure assessment based on distance to incinerator from maternal residence (within 10 km) MSWIs selected for inclusion were those reported by the Ministry of Health and Welfare of Japan as high dioxin emitting (>80 ng TEW/m^3)	*All outcomes, except female sex, were stratified for:* maternal age, gestational age, birth weight, previous deliveries, past experience of fetal deaths, paternal occupation
Non-syndromal orofacial clefts	ten Tusscher et al., 2000, The Netherlands	Hospital based retrospective cohort study	1960–1969	Zeeburg clinic births = 8,803 Zeeburg clinic non-syndromal orofacial clefts = 22 Zeeburg clinic syndromal orofacial cleft = 2 Wilhelmina clinic births = 21,078 Wilhelmina clinic non-syndromal orofacial	1 open chemical incinerator	Exposure assessment based on maternal residence of participants giving birth at either the Zeeburg maternity clinic (located near the incinerator) or the	Smoking, socioeconomic status, genetic encaves, anti-epileptic medication use, alcohol consumption

Table 1 (*continued*)

Birth outcomes investigated	Author(s) and location of study	Study design	Study period	Study participants	Exposure source	Exposure assessment	Confounders
				clefts = 25 Wilhelmina clinic syndromal orofacial clefts = 10		Wilhelmina Gasthuis maternity clinic (located12km from the incinerator)	
Spontaneous abortions (miscarriages) Congenital anomalies	Vinceti et al., 2008, Italy	Cohort	2003–2006	All females between 16–49 resident or working in areas categorized as medium or high exposed areas All cases of birth defects and spontaneous abortions in Modena municipal population Spontaneous abortions = 28 Birth defects = 7	1 MSWI	Modelled dioxin concentrations Exposure assessment based on females residing or working in areas defined as "exposed" to incinerator dioxins (based on modelled dioxin concentrations) Three classes of exposure- Exposed areas had annual average modelled concentrations $\geq 0.5*10^{-9}$ µg/m^3 Two classes of increasing exposure: Intermediate = $0.5–1*10^{-9}$ µg/m^3 & High = $\geq 1*10^{-9}$ µg/m^3	Socio-economic status
All major anomalies Cardiovascular system Nervous system Chromosomal Genito-urinary Musculoskeletal Clefts Eye Other and unspecified anomalies	Vinceti et al., 2009, Italy	Population based case-control	1998–2006	Live/stilbirths/induced abortions with one or more congenital anomaly (cases) = 228 Cardiovascular system = 96 Nervous system = 23 Chromosomal = 41 Genito-urinary = 21 Musculoskeletal = 39 Eye = 7 Other and unspecified anomalies = 14 Controls = live births randomly selected from hospital discharge directory Matched for; year of diagnosis, municipality, hospital referral, and maternal age	1 MSWI	Modelled dioxin concentrations Exposure assessment based on maternal residence during first three months of pregnancy Three classes of exposure- Exposed areas had annual average modelled concentrations $\geq 0.5*10^{-9}$ µg/m^3 Two classes of increasing exposure: Intermediate = $0.5–1*10^{-9}$ µg/m^3 & High = $\geq 1*10^{-9}$ µg/m^3	Education, maternal age
Sex ratio	Williams et al., 1992, Scotland	Geographic study	1975–1983	Births within the Falkirk District Males births = 1788 Female births = 1789	2 waste incinerators	Exposure assessment based on postcode district at place of birth Exposure assigned to districts based on: -Wind direction -Topography -Reporting of nuisance by nearby communities -Soil concentrations	Other industrial sources (comparison areas selected outside at-risk postcode district and excluded the industrial towns)

Abbreviations: LBW (low birth weight); PTD (preterm delivery).

Table 2
Summary of findings for epidemiological studies on incineration and risk of adverse birth and neonatal outcomes.

Author(s)	Birth outcomes	Summary estimate: Risk estimates for significant findings (95% CI)	Number of cases
Cordier et al., 2004	1. All congenital anomalies 2. Broad groups of anomalies	1. The rate of congenital anomalies was not significantly higher in exposed communities compared with unexposed communities *Relative risk* 104 (0.97–1.11) 2. The rate of anomaly subgroups, facial clefts and renal dysplasia, were significantly higher in exposed communities compared with unexposed A dose response trend of risk with increasing exposure was observed for obstructive uropathies *Relative risk* i) Facial clefts 1.30 (1.06–1.59) ii) Renal dysplasia 1.55 (1.10–2.20) iii) Obstructive uropathies- 1.22 (0.90–1.65) Exposure related dose response trend of risk Low exposure index: 1 Medium exposure index: 1.38 (0.65–2.93) High exposure index: 1.93 (0.94–3.94)	8,211
Cordier et al., 2010	Urinary tract birth defects 1. All participants 2. Participants interviewed (62%)	Mothers exposed to dioxins above median at the beginning of pregnancy were at increased risk of urinary tract birth defects compared with mothers unexposed to dioxins *1. Odds ratio* *Atmospheric dioxin:* Exposed 1.99 (1.17–3.40) Above the median 2.84 (1.32–6.09) *Dioxin deposits:* Exposed 1.83 (1.13–2.96) Above the median 2.95 (1.47–5.92) *Heavy metals:* Exposed 2.30 (0.93–5.68) *2. Odds ratio* *Dioxin deposits:* Exposed 2.05 (0.92- 4.57)	1. 304 2. 187
Cresswell et al., 2003	Major congenital anomalies	No increases in risk of congenital anomalies for residents living within 3 km from the combustion plant, following the plant opening *Inner/outer zone rate ratio:* *1.11 (0.96–1.28)* Marginally significant increasing trend in rate ratios over time *Inner/outer zone rate ratio:* 1995: 1.73 (1.10–2.72) 1998: 1.56 (1.01–2.41) 1999: 2.05 (1.20–3.52)	1,508
Dummer et al., 2003	1. Lethal congenital anomalies i)All neural tube defects Anecephalus Spina bifida Other central nervous system anomalies ii) Heart defects iii) All other anomalies 2. Stillbirths 3. Neonatal death 4. Stillbirths & neonatal death	1. Increased risk of all lethal congenital anomalies, in particular for spina bifida and heart defects, with proximity to the incinerator, following the incinerator opening *Continuous odds ratio (at a distance, D,* $OR^{1/(D+0.1)^2-1/3.1^2}$*)* Lethal congenital anomaly 1.10 (1.03–1.19) i) All neural tube defects 1.13 (1.04–1.23) Anencephalus 1.08 (0.99–1.18) Spina bifida 1.17 (1.07–1.28) Other central nervous system anomalies 0.73 (0.34–1.56) ii) Heart defects 1.12 (1.03–1.22) iii) All other anomalies 0.90 (0.67–1.22) 2–4 No increase in risk of stillbirths and/or neonatal deaths with proximity to incinerators *Continuous odds ratio(at a distance, D,* $OR^{1/(D+0.1)^2-1/3.1^2}$*)* Stillbirths 1.04 (0.90–1.19) Neonatal death 1.02 (0.90–1.14) Stillbirths & neonatal death 1.03 (0.93–1.13)	1. 2000 2. 3234 3. 2663 4. 5897
Jansson and Voog, 1998	Cleft lip and palate	No increased risk of cleft lip and palate following the start of refuse incineration *Ratio before and after introduction of incinerator* 1.02 (0.71–1.47)	Study A. 6 Study B. 82
Lin et al., 2006	1. Birth weight LBW (<2500 g) 2. Gestational age PTD 3. Sex ratio	Modelled incinerator generated dioxins were not significantly associated with birth weight, gestational age or sex ratio *Odds ratio five years after incinerator was introduced (Highest exposure category)* LBW 1.06 (0.71–1.57) PTD 1.22 (0.97–1.52) Sex ratio 0.90 (0.78–1.05)	1991 1. 247 2. 562 3. 3092/3604 1997 1. 237

Table 2 (*continued*)

Author(s)	Birth outcomes	Summary estimate: Risk estimates for significant findings (95% CI)	Number of cases
		Small significant decrease in gestational weeks, in exposed districts compared to unexposed districts following the introduction of the incinerator (−0.09 weeks)	2. 753 3. 3002/3280
Lloyd et al., 1988	Twinning	The frequency of twinning was increased in areas at greatest risk of exposure to pollutants from incinerators 1976–1979: Area with highest exposure: 7.3 twins per 1000 births Area with second highest exposure: 12.4 twins per 1000 births Background rate varied between 5–10.4 twins per 1000 births 1980–1983: Area with highest exposure: 16 twins per 1000 births Area with second highest exposure: 19.9 twins per 1000 births Background rate ranged from 3.3–12.5 twins per 1000 births	1976–9: 113 1980–3: 122
Obi-Osius et al., 2004	Twinning	Twinning was significantly higher in mothers within areas surrounding incinerator Study A. *Proportion of twins (%)* Toxic waste incinerator region 5.3% Two comparison areas-1.6% and 2.3% Study B. *Incidence of twinning (per 100 births)* Toxic waste incinerator region-1.4–1.6 per 100 births Reference areas-0.8 per 100 births *Odds Ratio of frequency of twinning* Toxic waste incinerator region – 2.03 (1.28–3.22)	Study A. 24 Study B. 200
Rydhstroem, 1998	Spatial clustering of twins 1. Total at risk area 2. Individual municipalities	1. No spatial clustering, or excess in, twin delivery in areas near incinerators, following their commission 2. Significant increase in the number of twin deliveries in a municipality near one incinerator, RR 1.72 (1.22–2.43). A significant decrease in the number of twin deliveries found in another municipality near another incinerator, 0.46 (0.29–0.73)	17,067
Tango et al., 2004	1. Female live birth (male/female) 2. LBW/very LBW 3. Infant death and those due to congenital anomalies 4. Neonatal deaths and those due to congenital anomalies (additionally early neonatal deaths) 5. Spontaneous fetal deaths and those due to congenital anomalies	1,2,4,5 No significant excess of female births, LBW babies, infant deaths, neonatal deaths or spontaneous deaths found within 2 km from the incinerators *Ratio of observed divided by expected rates at 0–1 km* Female live births 1.04 (0.98–1.10) LBW 1.02 (0.87–1.18) Neonatal deaths 0.91 (0.25–2.32) Neonatal deaths due to congenital anomalies 1.20 (0.15–4.32) Early neonatal deaths 0.96 (0.20–2.81) Early neonatal deaths due to congenital anomalies 0.99 (0.03–5.51) Spontaneous deaths 0.82 (0.54–1.20) Spontaneous deaths due to congenital anomalies 1.75 (0.48–4.48) 3. Small statistically significant peak decline in risk with distance from incinerators for infant deaths and infant deaths due to congenital anomalies	1. 110,044 2. 18,167 1394 3. 835 310 4. 471 (314) 186 (121) 5. 3,380 202
ten Tusscher et al., 2000	Non-syndromal orofacial clefts	A relationship between open chemical incineration and local increased risk of orofacial clefts found Zeeburg clinic: Birth prevalence of non-syndromal orofacial clefts = 2.5 per 1000 births. Peak in birth prevalence found between 1963- 65, (peak 7.1 per 1000 births in 1964), then prevalence plateaus, averaging at 1.3 per 1000 births Wilhelmina clinic: Birth prevalence of non-syndromal orofacial clefts 1.2 per 1000 births (peak 2.3 per 1000 births in 1964). Small peak in birth prevalence observed between 1963–65, at Zeeburg clinic. A low trend in birth prevalence found between 1966–69 (0.66 per 1000 births)	Zeeburg 24 Wilhelmina clinic 35
Vinceti et al., 2008	1. Spontaneous abortions (miscarriages) 2. Congenital anomalies	1. No excess in risk of miscarriage detected for women residing in two areas close to the incinerator plant, or female workers employed in factories located in exposed areas, both compared with the municipal population *Relative risk* Women residing near incinerator 1.00 (0.65–1.48) Women working near incinerator 1.04 (0.38–2.30) 2. No excess in risk of congenital anomalies detected for women residing in two areas close to the incinerator plant, compared to the municipal population.	1. 28 2. 7

(continued on next page)

Table 2 (*continued*)

Author(s)	Birth outcomes	Summary estimate: Risk estimates for significant findings (95% CI)	Number of cases
		Small, statistically insignificant, excess in birth prevalence of congenital anomalies for female workers employed in factories in exposed regions compared to the municipal population *Relative risk* Women residing near incinerator 0.64 (0.20–1.55) Women working near the incinerator 2.26 (0.57–6.14)	
Vinceti et al., 2009	1. All major anomalies 2. Cardiovascular system 3. Nervous system 4. Chromosomal 5. Genito-urinary 6. Musculoskeletal 7. Clefts 8. Eye 9. Other and unspecified anomalies	Women residing in areas with high and medium exposure had no increase in prevalence of congenital anomalies compared with the control population. No change in risk observed during a prolonged shut-down period of the MSWI *Odds ratio* All major anomalies 1.11 (0.60–2.04) Cardiovascular system 0.86 (0.40–1.86) Nervous system 0.41 (0.05–3.17) Chromosomal 1.82 (0.70–4.72) Genito-urinary 0.82 (0.18–3.67) Musculoskeletal 1.13 (0.41–3.10) Eye 1.78 (0.20–5.65) Other and unspecified anomalies 1.11 (0.24–5.10)	1. 228 2. 96 3. 23 4. 41 5. 21 6. 39 7. 4 8. 7 9. 14
Williams et al., 1992	Sex ratio 1. Total at risk areas 2. Individual districts	1. No differences in sex ratio found between at risk area and comparison areas 2. Most at risk sector saw an excess of female births. District most at risk (FK4)- 1981–83 Sex ratio (F/M) = 0.87 Sector most at risk (FK4.1)- 1975–78: Sex ratio = 0.89 1980–83: Sex ratio = 0.90	Males births = 1788 Female births = 1789

Abbreviations: LBW (low birth weight); PTD (preterm delivery).

congenital anomalies for those in the exposed communities compared with unexposed — with exposure defined by "immission" scores, calculated from ambient concentrations of pollutants released from an incinerator based on dispersion modelling multiplied by the number of years the MSWI was in operation.

The remaining two studies were UK based using distance to incinerators as a proxy for exposure (Cresswell et al., 2003; Dummer et al., 2003). In a retrospective cohort study (Quality = 9), Dummer et al.(2003) calculated the odds of lethal congenital anomalies for mothers resident near four industrial and domestic incinerators,

Table 3
Checklist for quality of research.

Study (author, date)	Design (max 5 points) ***Number of cases:*** • Number of cases (births with outcome of interest) > 500 = 1 • Number of cases (births with outcome of interest) < 30 = −1 *Single site or multi-site study:* • Single site study = 0 • Multi-site study = 1 *Study design:* • Geographic = 1 • Case-control = 2 • Cohort = 3	Health data (max 2 points) • Appropriate denominator = 1 • > 1 source of data = 1	Exposure assessment (max 7 points) ***Exposure assessment method:*** • Distance from source = 1 • Distance from source-with additional information = 2 • Dispersion modelled exposure = 3 *Additional information considered:* • Critical period of exposure accounted for = 1 • Maternal migration considered = 1 • Multiple sources of emissions considered = 1 • Different routes of exposure considered = 1	Confounders (max 3 points) • No confounders = −2 • Socio-economic deprivation/ social class/income/education = 1 • Ethnicity (maternal or baby) = 1 • Parity/maternal age/alcohol/ tobacco = 1	TOTAL (max 17 points)
Cordier et al. (2004)	3	1	4	2	10
Cordier et al. (2010)	3	2	6	3	14
Cresswell et al. (2003)	2	2	1	1	6
Dummer et al. (2003)	5	1	1	2	9
Jansson and Voog (1998)	2	1	1	−2	2
Lin et al. (2006)	2	1	4	2	9
Lloyd et al. (1988)	2	1	2	1	6
Obi-Osius et al. (2004)	1	2	1	2	6
Rydhstroem (1998)	3	1	1	1	6
Tango et al. (2004)	3	2	1	1	7
ten Tusscher et al. (2000)	3	1	1	2	7
Vinceti et al. (2008)	3	1	3	1	8
Vinceti et al. (2009)	2	2	5	2	11
Williams et al. (1992)	3	1	3	−2	5

reporting a continuous odds ratio [OR] of 1.10 (1.03–1.19) compared with the odds of living 3 km or further from the incinerators (continuous OR calculated as $OR^{1/(D+0.1)^2-1/3.1^2}$, where D is the distance from the incinerator). The continuous OR formula implies that the odds ratio of the risk of lethal congenital anomalies at 500 m from incinerator compared with that at 3 km or further would be 1.3. The geographic study by Cresswell et al. (2003) (Quality = 6) investigated the prevalence of 'major' congenital anomalies within 3 km from a waste combustion plant compared to residents 3–7 km from the plant, before and after the site was in operation. They found no significant association between proximity to the plant and the risk of major congenital anomalies (RR 1.11; 0.96–1.28), but concluded that a more comprehensive, multi-site investigation was required.

Two (Cordier et al., 2004; Dummer et al., 2003) of the three studies (Cordier et al., 2004; Dummer et al., 2003; Vinceti et al., 2009) investigating broad groups of anomalies reported significant increased risks with incineration. Although Cordier et al. (2004) (Quality = 10) reported no increase in the risk of all anomalies combined, for specific congenital anomalies, the exposed communities (based on the "immission" score) had increased risks of facial clefts (RR 1.30; 1.06–1.59) and renal dysplasia (RR 1.55; 1.10–2.20). Additionally, within the exposed communities a dose response trend in risk of obstructive uropathies was found based on exposure indices (low, medium and high) estimated using dispersion models. Dummer et al. (2003) (Quality = 9) subcategorised lethal congenital anomalies into congenital heart defects and neural tube defects. They reported significant continuous odds ratios of neural tube defects (OR 1.13; 1.04–1.23, OR 1.39 at 0.5 km compared to 3 km or further), spina bifida (OR 1.17; 1.07–1.28, OR 1.52 at 0.5 km compared to 3 km or further) and congenital heart defects (OR 1.12; 1.03–1.22, OR 1.35 at 0.5 km compared to 3 km or further). Vinceti et al. (2009) (quality = 11) reported no association between modelled dioxin levels from incinerators and the risk of cardiovascular, nervous, chromosomal, genito-urinary, musculoskeletal, eye and other unspecified congenital anomalies, but only a small numbers of cases were included for these rare defects.

Of the three studies examining the association between incineration and a single anomaly (Cordier et al., 2010; Jansson, 1998; ten Tusscher et al., 2000), two reported a significant increased risk with incineration (Cordier et al., 2010; ten Tusscher et al., 2000). Two studies investigated refuse and chemical incinerator emissions and orofacial clefts with conflicting results (Jansson, 1998; ten Tusscher et al., 2000). The first, a hospital based retrospective cohort in Amsterdam (quality = 7), examined the birth prevalence of non-syndromal orofacial clefts at two maternity clinics between 1960–1969 near which a chemical incinerator opened in 1961 (ten Tusscher et al., 2000). The clinic situated closer to the incinerator showed a peak in birth prevalence of non-syndromal orofacial clefts at 7.1 per 1000 births in 1964 compared to the average rate of 2.5 per 1000 births at this clinic. For the clinic further away from the incinerator no peak was observed; birth prevalence never exceeded 2.3 per 1000 births with an average of 1.2 per 1000 births. The second study conducted in response to a cluster of orofacial clefts at a maternity clinic in the county of Skaraborg in Sweden (quality = 2),found no increase in the rates of orofacial clefts after a refuse incinerator was commissioned within the study area (Jansson, 1998).

A population based case-control study (quality = 14) by Cordier et al. (2010) substantially improved on all preceding studies in terms of study design, exposure assessment and adjustment for potential confounders. Individual exposures were assigned using dispersion models to map concentrations of pollutants surrounding 21 MSWIs and information on individual risk factors was collected at interview for 62% of the participants, providing individual level data on potential confounders. The study found a significant increased risk of urinary tract defects (OR 2.84; 1.32–6.09) among offspring of mothers exposed to atmospheric dioxins during early pregnancy (Cordier et al., 2010).

3.2. Fetal growth and preterm birth

Two studies examined the relationship between incineration and birth weight; neither found an association (Lin et al., 2006; Tango et al., 2004). The first by Tango et al. (2004) (quality = 7) included 63 "high dioxin emitting" MSWIs within their study with distance in 1 km concentric rings used as a proxy for dioxin exposure. The MSWIs selected recorded dioxin measurements above 80 ng TEQ/m^3 as part of a survey by the Ministry of Health and Welfare of Japan in 1997. The second study by Lin et al. (2006) (quality = 9) modelled ambient dioxin concentrations from one incinerator in Taiwan and examined the relationship with low birth weight (defined as a weight less than 2500 g excluding birth weights below 500 g, births by unmarried women, multiple births, and births with a gestation period less than 20 weeks) at two periods in time, one year before the incinerator began operating and six years following. Lin et al. (2006), also investigated the risk of preterm delivery (<37 weeks) and found a non-significant increase in the risk of preterm delivery for mothers resident in areas of highest exposure (estimated from modelling) to dioxins and furans concentrations, >0.05 pg TEQ/m^3, compared to areas of lowest exposure (OR 1.22; 95% CI:0.97–1.52). Following the operation of the MSWI a lower gestational age in exposed compared with reference areas was also observed.

3.3. Stillbirths, neonatal deaths, infant deaths, spontaneous abortions and spontaneous fetal deaths

No associations were reported between incineration and stillbirths (Dummer et al., 2003) or neonatal deaths (Dummer et al., 2003; Tango et al., 2004) although the evidence base remains very sparse. Tango et al. (2004) (Quality = 7) examined rates of infant deaths for mothers resident within 10 km of 63 incinerators in Japan compared with national rates and found no significant difference. However, using Tango's conditional test they reported a significant peak-decline in risk for 0–1 km, 1–2 km and 2–3 km from the incinerators. Two studies reported no association between incineration and spontaneous abortions and spontaneous fetal deaths (Tango et al., 2004; Vinceti et al., 2008).

3.4. Twinning

The frequency of human twinning in areas potentially exposed to incinerator emissions was explored in two geographic studies, in central Scotland (Lloyd et al., 1988) (quality = 6) and Hesse Germany (Obi-Osius et al., 2004) (quality = 6); both studies reported that areas with greater likelihood of exposure to incinerator emissions had increased rates of twinning. Obi-Osius et al. (2004) reported a significantly higher birth prevalence of twins in the areas surrounding a toxic waste incinerator (1.4–1.6 per 100 births) compared to references areas with little or no industry (0.8 per 100 births). A third study (quality = 6) of spatial and temporal clustering of twins near 14 refuse incinerators in Sweden (Rydhstroem, 1998), found no clustering of twinning overall, though there was a significantly higher rate of twin deliveries surrounding one incinerator and a lower rate around another.

3.5. Sex ratio at birth

Three studies included an analysis of sex ratio at birth and incineration (Lin et al., 2006; Tango et al., 2004; Williams et al., 1992). Overall, the study findings did not suggest an association at the individual level; however, Williams et al. (1992) (quality = 5) reported a significant excess in female births in one of three "at risk" districts compared to the Scottish average (Williams et al., 1992).

4. Discussion

We provide an up to date review of the epidemiological evidence on potential birth outcomes associated with incineration. The available studies are few in number and are not fully consistent. Four (Cordier et al., 2010; Lloyd et al., 1988; Obi-Osius et al., 2004; ten Tusscher et al., 2000) reported significant associations for all outcomes examined and a further five studies (Cordier et al., 2004; Dummer et al., 2003; Rydhstroem, 1998; Tango et al., 2004; Williams et al., 1992) reported an association for at least one outcome. Of the six studies scoring above the mean for data quality (Cordier et al., 2004, 2010; Dummer et al., 2003; Lin et al., 2006; Vinceti et al., 2008, 2009), three reported a significant association with one of the congenital anomalies outcomes examined (Cordier et al., 2004, 2010; Dummer et al., 2003), while the remaining three studies found no association with sex ratio, low birth weight, gestational age or congenital anomalies (Lin et al., 2006; Vinceti et al., 2008, 2009).

Most of the epidemiologic evidence to date is weak, with potential exposure misclassification, low statistical power and inadequate control for confounding. Additionally, the evidence-base is difficult to synthesise due to heterogeneity between studies in their design, location, time period, number of incinerators and the health outcomes explored. Despite this, in the small number of studies we have identified of better quality, significant positive associations with incineration have been reported for a number of broad groups of anomalies including, neural tube defects (Dummer et al., 2003), lethal heart defects (Dummer et al., 2003), facial clefts (Cordier et al., 2004; ten Tusscher et al., 2000) and urinary tract defects (Cordier et al., 2010). Potential confounders most commonly accounted for were maternal age (Cordier et al., 2004; Lin et al., 2006; Obi-Osius et al., 2004; Rydhstroem, 1998; Tango et al., 2004; Vinceti et al., 2009) and surrogate measures of socio-economic status (Cordier et al., 2004; Cresswell et al., 2003; Dummer et al., 2003; Jansson, 1998; Lin et al., 2006; Tango et al., 2004; ten Tusscher et al., 2000; Vinceti et al., 2009). Cordier et al. (2010) included four potential confounders; geographical location, parity, family alcohol consumption, as well as family history of urinary tract defects, but most other studies had only limited control for confounding.

Exposure assessment methods ranged from use of distance as a proxy for ambient exposure to incinerator emissions in seven of the 14 studies (Cresswell et al., 2003; Dummer et al., 2003; Jansson, 1998; Obi-Osius et al., 2004; Rydhstroem, 1998; Tango et al., 2004; ten Tusscher et al., 2000), to modelling of dioxin exposures (Cordier et al., 2004, 2010; Lin et al., 2006; Vinceti et al., 2008, 2009). Five studies used dispersion models (Cordier et al., 2004, 2010; Lin et al., 2006; Vinceti et al., 2008, 2009) which incorporated information on stack characteristics, stack emissions, meteorological and topographic data. Although the majority of the studies reviewed used distance as a proxy for exposure, considered to be a crude exposure assessment method, nonetheless distance to source is highly correlated with modelled exposure estimates (Ashworth et al., 2013). However, any inaccuracy and imprecision of such methods and resultant exposure misclassification would most likely lead to attenuation of any association if present. None of the reviewed studies included measured exposure levels or biomonitoring data as a method of exposure assessment or to validate the exposure models.

As well as the exposure assessment methods there are a number of additional considerations when assessing exposure from incinerators. Overall these were not well addressed within the epidemiological evidence. These include consideration of: multiple sources — five studies acknowledged and discussed the issue of multiple exposure sources (Cordier et al., 2004, 2010; Lin et al., 2006; Vinceti et al., 2009; Williams et al., 1992), but only Cordier et al. (2004, 2010) identified and assessed exposure to other sources of dioxins within their study population; multiple pollutants — seven studies used aggregate exposure measures, e.g., distance from source (Cresswell et al., 2003; Dummer et al., 2003; Jansson, 1998; Obi-Osius et al., 2004; Rydhstroem, 1998; Tango et al., 2004; ten Tusscher et al., 2000), of which two included information on dioxins levels (Lloyd et al., 1988; Tango et al., 2004) and five studies modelled incinerator released dioxins (Cordier et al., 2004, 2010; Lin et al., 2006; Vinceti et al., 2008, 2009); different routes of exposure — only one study accounted for dietary intake (Cordier et al., 2010) which is the main route of dioxin exposure (Papke, 1998); exposure period — two studies (Cordier et al., 2010; Vinceti et al., 2009) considered the timing of *in utero* exposure in relation to embryonic and fetal development. The critical window of exposure for congenital anomalies is likely to be the first trimester, when all the major organs are developing, whereas second and third trimester exposures are likely to have greater impact on stillbirth and fetal outcomes (Rothman and Greenland, 1998); and maternal migration — three studies (Cordier et al., 2010; Vinceti et al., 2008) considered residential history during the study period, thereby taking into account changes in exposure status, and only one study (Vinceti et al., 2009) thoroughly explored this issue by investigating the long-term residential history of a sample of the study population. If residential mobility is not accounted for, exposure measurement error and related biases may be introduced into the epidemiological analyses; for example, some incinerator exposures, such as dioxins, accumulate over long periods of time and reflect exposures prior to as well as during pregnancy.

Our review found limited evidence for an association between incineration and twinning and no evidence, based on few studies, of an association with low birth weight, stillbirths or sex ratio. Most studies report no association with all major congenital anomalies combined, but this may be too crude a measure to be meaningful in this context; however, some studies point towards weak associations for neural tube and heart defects, with stronger associations for facial clefts and urinary tract defects. The finding by Cordier et al. (2010) of a two to three fold excess risk of urinary tract defects among mothers exposed to dioxins at the beginning of pregnancy was the strongest of the reported associations. This related to older generation MSWIs in France. Since then, the newer generation of MSWIs is more strictly regulated with dioxin emission limits required to be one tenth of previous standards (Royal Commission on Environmental Pollution, 1993; The European parliment and the council of the European Union, 2000).

Dioxins are generated as one of the end-products of combustion and are emitted from incinerators; they are widespread persistent organic pollutants with lipophillic properties enabling them to accumulate in adipose tissue for many years (Milbrath et al., 2009). The toxicological evidence for any adverse effects of dioxins in human studies is sparse and largely focused on the health effects in adults exposed to high doses of dioxins at the work place or from industrial accidents such as Seveso, Italy, and contamination incidents such as Yusho, Japan and Yu-Cheng, Taiwan (Milbrath et al., 2009). Animal studies have shown that dioxin exposure in high and prolonged doses can induce structural malformations (cleft palate and hydrophronesis) (Couture et al., 1990) and adverse effects on the reproductive system (sperm production and morphology (Committee on Toxicity of Chemicals in Food Consumer Products and The Environment, 2001)). The binding of dioxins to the ligand activated receptor, aryl hydrocarbon receptor, and consequent changes in gene expression and cell function, are thought to be responsible for their toxicity, though a detailed understanding of this process remains unknown (Committee on Toxicity of Chemicals in Food Consumer Products and The Environment, 2001; World Health Organisation (WHO), 1998). However, it is unclear to what extent the animal and mechanistic findings are relevant to low dose exposures in humans (Couture et al., 1990).

Incinerators additionally emit a number of heavy metals including mercury, lead and cadmium, most widely documented as metals associated with adverse human reproductive health effects. These three metals share two main routes of exposure; inhalation and ingestion. Mercury accumulates in the kidneys (Health Protection Agency, 2012; International Programme on Chemical Safety, 1991) and there is evidence that maternal occupational exposure to mercury (mothers working in mercury smelting plants and dental practices) increases the risk of spontaneous abortions (Sikorski et al., 1987). Studies have additionally reported that prenatal mercury exposure from maternal fish consumption is associated with impaired child neurological development (Oken and Bellinger, 2008), preterm delivery (Xue et al., 2007) and congenital anomalies (Elghany et al., 1997). Lead is distributed by the blood accumulating in the bone (Health Protection Agency, 2012). Maternal occupational exposure to lead has been reported to increase risk of spontaneous abortions (Borja-Aburto et al., 1999), preterm delivery, low birth weight (Health Protection Agency, 2012) and adverse neurodevelopment in early life (Tong et al., 1998; Wigg et al., 1988). Cadmium accumulates in the kidneys and liver, and is associated with preterm delivery and low birth weight (Health Protection Agency, 2011; Nishijo et al., 2002; Salpietro et al., 2002).

Our report has a number of strengths. It includes more studies and more individuals than previous reviews. No previously published systematic reviews have specifically focused on birth and neonatal outcomes and incineration. The broader focus of other reviews has included a variety of waste management options (Crowley et al., 2003; Enviros Consulting Ltd et al., 2004; Porta et al., 2009; Rushton, 2003) and health outcomes (Crowley et al., 2003; Enviros Consulting Ltd et al., 2004; Franchini et al., 2004; Hu and Shy, 2001; Porta et al., 2009; Rushton, 2003). This review also has limitations. Only papers written in English and published in the peer-reviewed literature were included, introducing the potential for publication bias. Additionally, synthesizing the evidence base was complicated by significant heterogeneity between the reviewed studies, in their design, exposure assessment and methods of assessment, confounder adjustment, and health outcomes. This heterogeneity meant that we were unable to conduct a meta-analysis of the epidemiological studies to date and provide a quantitative summary of the current evidence.

Incineration is becoming more widely used as a method of waste disposal reflecting a shift away from landfill (Redfearn and Roberts, 2002; Vrijheid, 2000), so potentially more people will be exposed to low-level incinerator emissions in the future. We conclude that the overall evidence base for adverse birth outcomes is weak, however, in the small number of studies we identified of better quality, significant positive associations with incineration were shown for a number of broad groups of anomalies. Moreover, the established reproductive toxicity of dioxins and heavy metals, present in emissions from incinerators, provides plausible biological mechanisms for these observed associations, although doses received by individuals at ground level are likely to be low. We therefore propose that further epidemiological investigation is warranted, with better control for confounding and more accurate exposure assessment. Exposure assessment methods are recommended to include at the least atmospheric dispersion modelling, with consideration of multiple exposure sources through thorough investigation of nearby sources and identification of the specific incinerator related exposures, in addition to validation of exposure models through individual biomonitoring. In the European Union, incinerators are required, by law, to adhere to the regulations prescribed by the European Waste Incineration Directive (2000/76/EC) (WID) (The European parliment and the council of the European Union, 2000). This directive sets operational standards and tight emission limit values to prevent or limit, where possible, negative effects on the environment and human health (The European parliment and the council of the European Union, 2000). The change in policy for incinerators with the introduction of the Waste Incineration Directive provides the opportunity to carry out 'natural experiment' studies investigating possible health effects before and after the introduction of new regulatory standards. Additionally multi site studies with clearly defined birth outcomes are recommended to increase statistical power.

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