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Risk of congenital anomalies near municipal waste incinerators in England and Scotland: Retrospective population-based cohort study

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ABSTRACT

Background: Few studies have investigated congenital anomalies in relation to municipal waste incinerators (MWIs) and results are inconclusive.
Objectives: To conduct a national investigation into the risk of congenital anomalies in babies born to mothers living within 10 km of an MWI associated with: i) modelled concentrations of PM_{10} as a proxy for MWI emissions more generally and; ii) proximity of residential postcode to nearest MWI, in areas in England and Scotland that are covered by a congenital anomaly register.
Methods: Retrospective population-based cohort study within 10 km of 10 MWIs in England and Scotland operating between 2003 and 2010. Exposure was proximity to MWI and log of daily mean modelled ground-level particulate matter $\leq 10\,\mu m$ diameter (PM_{10}) concentrations.
Results: Analysis included 219,486 births, stillbirths and terminations of pregnancy for fetal anomaly of which 5154 were cases of congenital anomalies. Fully adjusted odds ratio (OR) per doubling in PM_{10} was: 1·00 (95% CI 0·98–1·02) for all congenital anomalies; 0·99 (0·97–1·01) for all congenital anomalies excluding chromosomal anomalies. For every 1 km closer to an MWI adjusted OR was: 1·02 (1·00–1·04) for all congenital anomalies

Abbreviations: ADMS, atmospheric dispersion modelling system; BINOCAR, British and Irish Network of Congenital Anomaly Researchers; CAROBB, Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire; COA, census output area; Dioxin, polychlorinated dibenzo-p-dioxins; DH, Department of Health (now called Department of Health and Social Care); EA, Environment Agency; EMSYCAR, East Midlands & South Yorkshire Congenital Anomaly Register; EU, European Union; EUROCAT, European surveillance of congenital anomalies; EU-WID, European Union Waste Incineration Directive; ICD, International Classification of Diseases; ISD, Information Services Division Scotland; LCAR, local congenital anomaly register; MSOA, Middle Super Output Area; MWI, municipal waste incinerator; NOx, oxides of nitrogen; NHS, National Health Service; NorCAS, Northern Congenital Abnormality Survey; NN4B, Numbers for Babies; ONS, Office for National Statistics.; OR, odds ratio; PAHs, polycyclic aromatic hydrocarbons; PCB, polychlorinated biphenyls; PCDD/Fs, polychlorinated dibenzo-p-dioxins and furans; PM_{10}, particulate matter 10 µm or less in diameter; RCAR, Regional Congenital Anomaly Register; SO_2, sulphur dioxide; SWCAR, South West Congenital Anomaly Register; TOPFA, termination of pregnancy for fetal anomaly; WANDA, Wessex Antenatally Detected Anomalies Register

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combined; 1·02 (1·00–1·04) for all congenital anomalies excluding chromosomal anomalies; and, for specific anomaly groups, 1·04 (1·01–1·08) for congenital heart defect sand 1·07 (1·02–1·12) for genital anomalies.
Discussion: We found no increased risk of congenital anomalies in relation to modelled PM_{10} emissions, but there were small excess risks associated with congenital heart defects and genital anomalies in proximity to MWIs. These latter findings may well reflect incomplete control for confounding, but a possible causal effect cannot be excluded.

1. Introduction

Over the last 20 years, the move to reduce landfill waste has driven an increase in waste incineration in the European Union (EU) (Vehlow et al., 2007). Municipal waste incinerators (MWIs) burn non-hazardous waste mostly from households and commercial establishments, at high temperatures. Emissions from MWIs are currently regulated under the EU Industrial Emissions Directive (IED) (2010/75/EU) (European Union, 2010), which incorporated the Waste Incineration Directive (EU-WID) (2000/76/EC) implemented in Great Britain (GB) on 28 December 2002 and 28 December 2005 for new and existing MWIs respectively. Emissions include particulates, sulphur dioxide (SO_2), nitrogen oxides (NO_x), heavy metals, polychlorinated dibenzo-p-dioxins and furans (PCDD/Fs), polycyclic aromatic hydrocarbon (PAH) and polychlorinated biphenyls (PCBs). Limits for MWI emissions are set by the EU under the IED. However, there remains public concern and scientific uncertainty about possible health effects on the population exposed to emissions from MWIs (Health Protection Agency, 2009).

In a recent systematic review (subsequently updated for this research) of the association between municipal waste incineration and birth outcomes, results were inconsistent and inconclusive (Ashworth et al., 2014; Candela et al., 2013; Candela et al., 2015; Santoro et al., 2016). There are few investigations of municipal waste incineration and health specifically focussed on congenital anomalies (Cordier et al., 2004; Cordier et al., 2010; Cresswell et al., 2003; Dummer et al., 2003; Jansson and Voog, 1988; Tango et al., 2004; ten Tusscher et al., 2000; Vinceti et al., 2008; Vinceti et al., 2009; Vinceti et al., 2018). The start dates of all these studies pre-date the implementation of the Industrial Emissions Directive for existing MWIs (28 December 2005). Five separate studies have found some increased risks with specific congenital anomaly groups, and include facial clefts (Cordier et al., 2004; ten Tusscher et al., 2000), renal and urological anomalies (Cordier et al., 2004; Cordier et al., 2010) neural tube defects, spina bifida and lethal congenital heart defects (CHDs) (Dummer et al., 2003) and deaths due to all congenital anomalies combined (Tango et al., 2004). These inconsistent findings may reflect chance findings related to small numbers of cases in some studies, different types of MWIs with differing exposure profiles, varying study designs and limitations in exposure assessment.

The study aim was to conduct a national investigation into the risk of congenital anomalies in babies born to mothers living within 10 km of an MWI associated with: i) modelled concentrations of PM_{10} as a proxy for MWI emissions more generally and; ii) proximity of residential postcode to nearest MWI, in areas in England and Scotland that are covered by a congenital anomaly register.

2. Methods

2.1. Study area

The study area was defined as all centroids of postcodes (representing on average 12 households) occurring within a 10 km radius of at least one MWI in a region of England or Scotland covered by a participating Regional Congenital Anomaly Register (RCAR) during the study period 1 April 2003 to 31 December 2010 (the RCAR for Wales did not take part in this study). Fig. 1 shows the 11 MWIs and RCARs eligible for inclusion in the study, covering approximately 24·5 million of the population of England and Scotland. Grundon MWI commenced operation in February 2010 so there were too few congenital anomalies during the study period to be included.

2.2. Outcomes

The primary outcome groups analysed were:

- One or more congenital anomalies (International Classification of Diseases tenth revision (ICD_{10}) codes: Q00 – Q99, D215, D821, D1810, P350, P351, P371)
- Specific congenital anomaly groups based on previous evidence (nervous System (Q00-Q07 excl. Q0461, Q0782), congenital heart defects (CHDs) (Q20-Q26 excluding Q2111, Q2541, Q261, Q250 (< 37 weeks gestation), Q256 (< 37 weeks gestation)), abdominal wall defects (Q792, Q793, Q795, Q7950, Q7951, Q7959), orofacial clefts (Q35-Q37), limb defects (Q65-Q74 excluding Q653-Q656, Q662-Q678, Q680–685, Q7400), digestive system (Q790, Q38-Q45 excluding Q381, Q382, Q3850, Q400, Q401, Q4021, Q430, Q4320, Q4381, Q4382), urinary (Q60-Q64, Q794 excluding Q610, Q627, Q633), genital organs (Q50-Q52, Q54-Q56 excluding Q523, Q525, Q527, Q5520, Q5521))

Secondary outcome groups analysed were:

- One or more congenital anomalies excluding chromosomal congenital anomalies (Q90-Q99).
- Specific congenital anomaly sub-groups (neural tube defects (Q00, Q01, Q05), severe CHDs (Q200-Q204, Q212, Q213, Q220, Q224 -Q226, Q230, Q232-Q234, Q251, Q252, Q262), gastroschisis (Q793), cleft palate (Q35), cleft lip with or without cleft palate (Q36, Q37), limb reduction defects (Q71-Q73), oesophageal atresia (Q390, Q391, Q3911), anomalies of the renal system (Q60-Q61 excluding Q610), obstructive defects of renal pelvis (Q62, Q64 excluding Q627), hypospadias (Q54)).

Descriptions of ICD_{10} codes are listed in Table S1. Congenital anomalies data were provided by the participating RCARs, five in England (Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire (CAROBB); East Midlands & South Yorkshire Congenital Anomaly Register (EMSYCAR); Northern Congenital Abnormality Survey (NorCAS); South West Congenital Anomaly Register (SWCAR); Wessex Antenatally Detected Anomalies Register (WANDA)), and data for the whole of Scotland, collated from multiple sources linking Scottish Stillbirth and Infant Death Survey (SSBID), Scottish Birth Record (SBR), SMR11 (historic version of SBR), SMR01 (hospital activity) and National Records Scotland Still Birth & Infant Deaths.

Denominator data for England and Scotland were obtained from the Office for National Statistics (ONS) Births and Stillbirths register and the Information Services Division (ISD) Scotland Scottish Birth Record

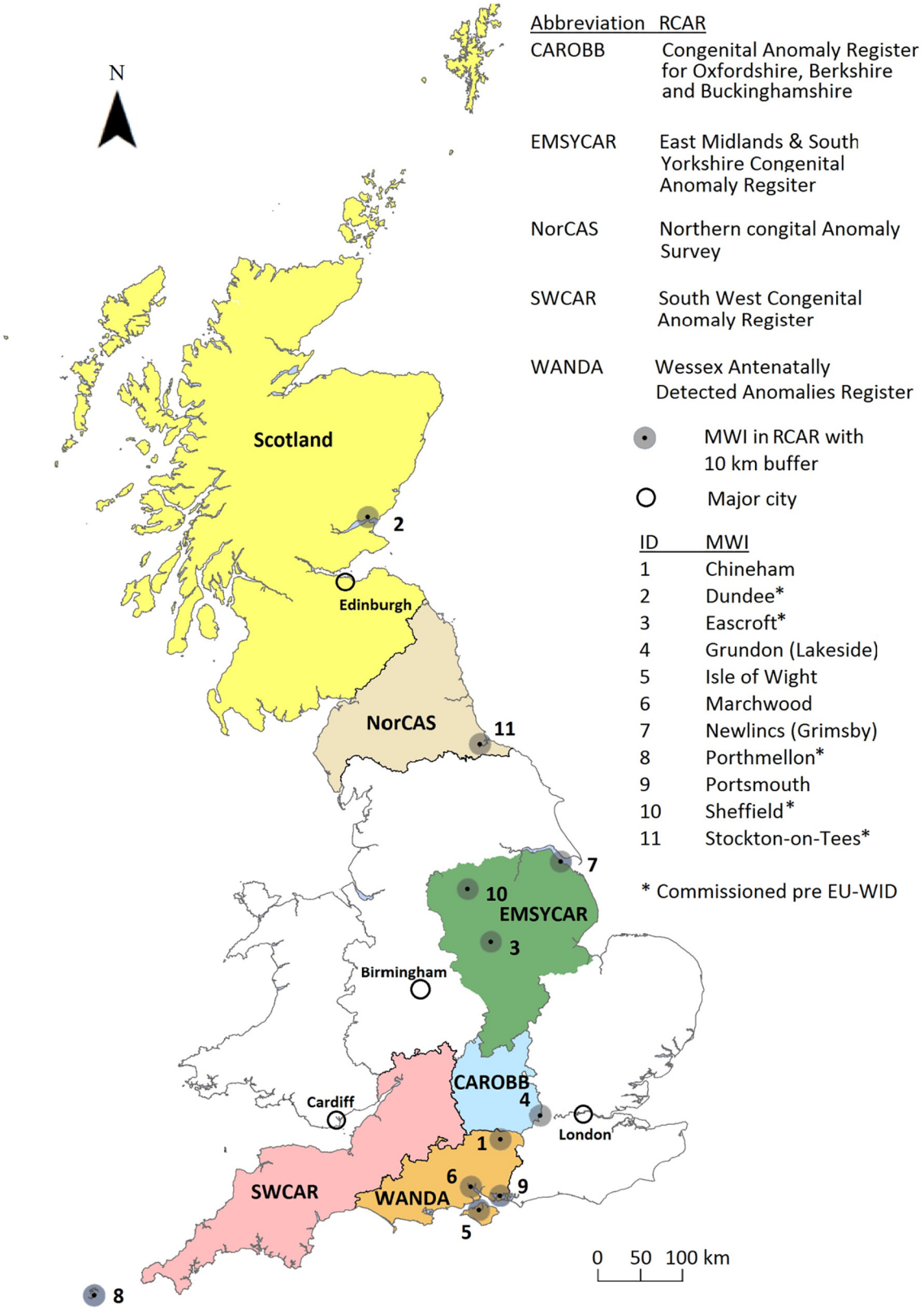

Fig. 1. Map of England, Wales and Scotland showing the regional congenital anomaly register (RCAR) areas and the locations of the 10 municipal waste incinerators (MWIs) in the study. The Grundon (Lakeside) MWI commenced operation in February 2010; there were too few congenital anomalies during the study period to include this site. All MWIs in the study operate to the European Union Waste Incinerator Directive (EU-WID).

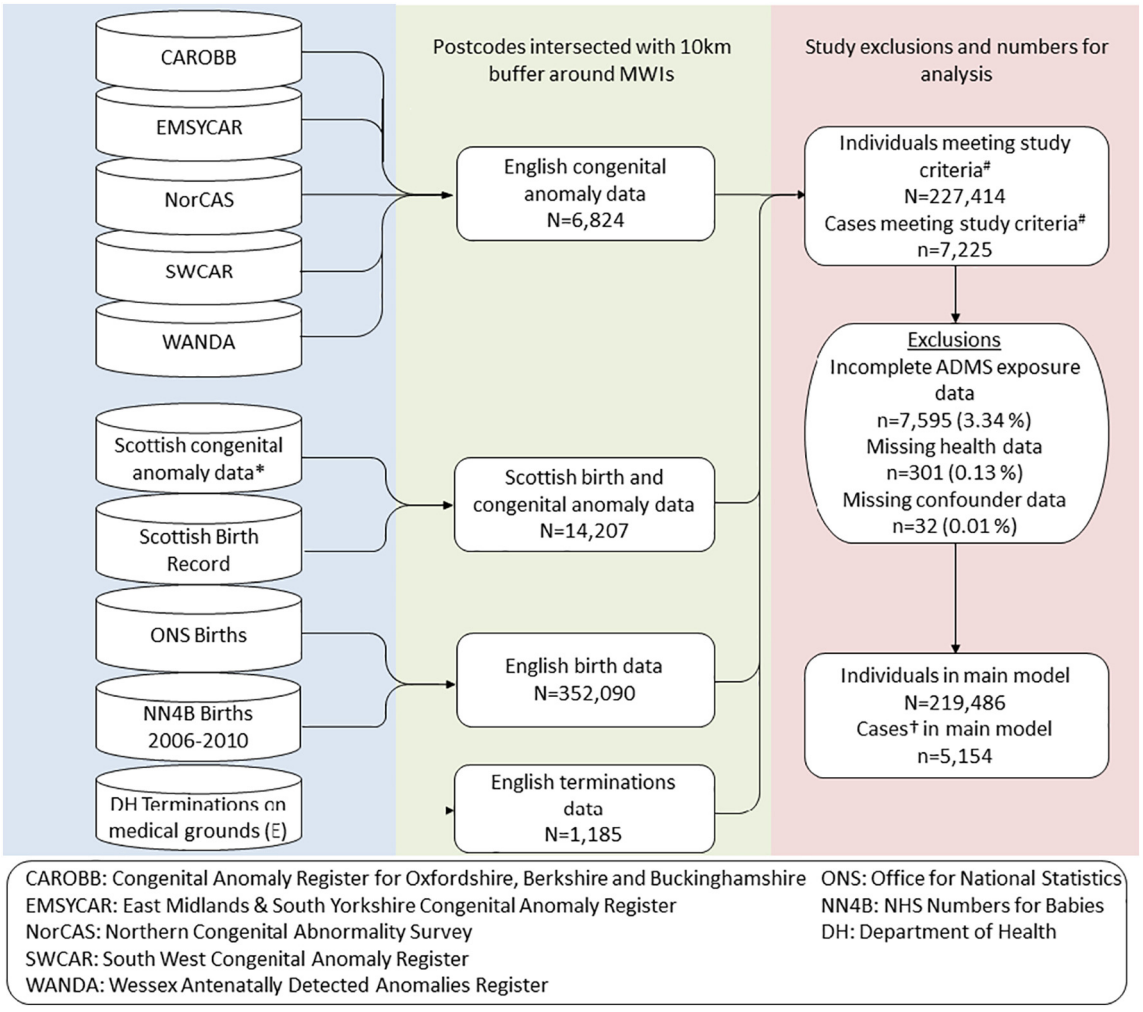

Fig. 2. Schematic of the health datasets used for the congenital anomalies study.
* Scottish congenital anomalies data created by linking Scottish Stillbirth and Infant Death Survey (SSBID), Scottish Birth Record (SBR), General/Acute Inpatient and Day Case dataset (SMR01) and National Records of Scotland Still Birth & Infant Deaths.
# Birth records meet the study criteria if 91 day pre-pregnancy period starts after the MWI commenced operation.
† The number of cases (5154) shown in Fig. 2 indicates births with at least one major congenital anomaly.

respectively. Data about terminations of pregnancy for fetal anomaly (TOPFAs) for England were provided by the Department of Health (now called Department of Health and Social Care). Ethnicity information was obtained by linking the National Health Service (NHS) Numbers for Babies (NN4B) births data to the ONS data for 2006 to 2010 (the years available).

For data governance reasons, we were unable to link records in the English RCARs with other datasets; consequently all live-born babies affected by a congenital anomaly in England (estimated to be 2·3% by the British Isles Network of Congenital Anomaly Registers (BINOCAR)) are duplicated in the denominator dataset. Data from Scotland were provided in a single dataset, avoiding duplicates. Fig. 2 summarises the datasets involved and how they were combined.

The English RCAR data are supplied to the European surveillance of congenital anomalies (EUROCAT) which requires the exclusion of minor anomalies. In Scotland the data are not supplied to EUROCAT and, due to a technical issue, the Scottish congenital anomaly data supplied to us did not include the 5th character of the ICD_{10} code, meaning it was not possible to be certain if all cases can be correctly identified as minor or major. No data on TOPFAs are available for Scotland resulting in a potential underestimation of congenital anomaly rates in Scotland.

Harmonising the English and Scottish data involved:

- Removing cases of congenital anomalies from the Scottish data that could be identified as minor based on the EUROCAT codes.
- Identifying inconsistencies of rates of certain anomalies between the English and Scottish data, e.g. excluding 70 cases of ICD_{10} Q828 (other specified congenital malformations of skin) in Scotland as these were likely to be minor. Higher rates for certain ICDs in England compared to Scotland could be explained by the absence of TOPFA and prenatal data for Scotland.

Cases with multiple congenital anomalies were counted once for each case when analysing all congenital anomalies combined and all congenital anomalies excluding chromosomal, and under each outcome when analysing specific congenital anomalies groups and sub-groups. So an individual with multiple congenital anomalies may appear more than once when analysing separate congenital anomalies groups and sub-groups. When excluding chromosomal anomalies, it was assumed that the presence of a chromosomal anomaly was the underlying cause of any additional (non-chromosomal) anomalies (Garne et al., 2011).

All birth records (births, stillbirths and TOPFAs) in the study area were included if conception was after 1 April 2003 and birth or

termination was before 31 December 2010 and the mother's residence at birth or termination was within 10 km of an operational MWI.

2.3. Exposure assessment

We used two metrics to represent 'exposure' to MWI emissions: i) dispersion modelling using ADMS-Urban software from Cambridge Environmental Research Consultants (CERC), taking account of meteorological factors including wind direction – to estimate daily mean ground-level PM_{10} concentrations from MWI emissions at each postcode centroid within 10 km of the included MWIs (as a proxy for MWI emissions more generally), as previously described by Douglas et al. (2017) and references therein; ii) proximity to nearest MWI – calculated as a continuous measure of straight line distance of the MWI coordinates to the postcode centroid of mother's residence at time of birth.

Most congenital anomalies are known to occur in the first trimester of pregnancy (Rankin et al., 2009); hence we defined the critical window of exposure for the dispersion modelling as the 91 days prior to calculated/estimated date of conception (to cover the sperm regeneration cycle) plus the first trimester of pregnancy (with exposure represented by mean PM_{10} concentration over the period). Two separate sensitivity analyses were run using just the 91 days prior to calculated/estimated date of conception and just the first trimester as exposure periods (see supplemental table S5 for details of sensitivity analyses). For births after the start of 2006, the gestational age at birth was available allowing us to estimate the conception date by subtracting the gestational age from the date of birth. For births prior to 2006, the pregnancy was assumed to be 279 days which was the median pregnancy duration for the births in our dataset 2006–2010. Exposure could not be estimated for all individuals as not all MWIs in the study were operational by the start of 2003; some MWIs had periods of non-operation and data from SWCAR were only available from the start of 2005 (see Douglas et al. (2017) for details of MWI operating dates). As the distribution of the modelled PM_{10} concentrations was heavily right-skewed, PM_{10} concentrations were log transformed prior to analysis. We used mother's residential postcode at birth for the distance-based analyses.

2.4. Potential confounders

Potential confounders were selected a priori to reflect factors that have previously been associated with risk of congenital anomalies (see supplemental table S2). Individual level confounders were maternal age (categories in years: <20; 20–29; 30–39; >40) and year of birth or termination. Area-level confounders were deprivation by fifths of the Carstairs deprivation index (comprising lack of car ownership, low occupational social class, overcrowded households and male unemployment at the census output area (COA) level – comprising 40–250 households) and area-level ethnicity (% of white women aged 16–49 at the middle layer super output area (MSOA) level – 2000–6000 households). In addition, major road density (length of motorways, A-roads and B-roads) within 10 km of the MWI, major road density within 250 m of mother's postcode and other sources of emissions were used as proxies for background air pollution. The data for 'other sources of emissions' were based on the total number of industries in operation within 10 km of each MWI for each year of operation, obtained from the Environment Agency in England and the Scottish Pollutant Release Inventory (Table S3).

Sensitivity analyses additionally adjusted for: sex; individual level ethnicity (only available for England after 2006); tobacco sales (not available in Scotland) at COA level, as a proxy for smoking; and multiple births (see Supplemental Material, Table S5 for details of sensitivity analyses).

2.5. Statistical analysis

We used logistic regression to examine associations between each measure of exposure and outcome, adjusting for available potential confounders listed above. We did not have information on MWI feedstocks; these were likely to be heterogeneous with relative pollutant concentrations emitted varying between MWIs; we therefore included a random slope for the PM_{10} exposure variable in all models. We also included a random intercept for MWI to allow for possible unmeasured confounding effects e.g. other local sources of pollution for which only area level proxies were available. As PM_{10} data were log transformed, odds ratios (ORs) indicate the risk associated with a multiplicative increase in PM_{10} concentrations; here we report the risk associated with a doubling (100% increase) in MWI emission-related PM_{10}, i.e. an OR of 1·1 would indicate a 10% increase in risk each time the PM_{10} concentration is doubled. Our primary analysis was fully adjusted logistic regression with a random intercept for MWI and random slope for the PM_{10} exposure variable.

To evaluate associations of MWI emissions and proximity, we present odds ratios and 95% confidence intervals. In view of the large number of analyses, we also present *p*-values adjusted for multiple testing using the procedure proposed by Simes which is recommended when several tests may be highly correlated (Simes, 1986). All analyses were conducted in R version 3.2.2 (available from: https://www.R-project.org) (R Core Team, 2015). See Supplemental Material for details of regression models.

3. Results

After exclusions (Fig. 2) we included 219,486 births, stillbirths and terminations of pregnancy for fetal anomaly of which 5154 were cases of congenital anomalies (Table 1). Mean modelled PM_{10} concentrations for 91 day pre-pregnancy period and first trimester was $0{\cdot}64\ 10^{-3}$ μg/m^3 [IQR 0·14–0·76] and $0{\cdot}67\ 10^{-3}$ μg/m^3 [IQR 0·14–0·80] for the births and congenital anomaly cases respectively (Table 2). Mean distance from postcode of maternal residence to nearest MWI was 5·44 km [IQR 3·57–7·23] and 5·28 km [IQR 3·45–7·03] for births and cases respectively. No births were within 10 km of more than one MWI (Fig. 1). Numbers of congenital anomaly cases by ICD group and sub-group are listed in table S10.

There was limited correlation between proximity to nearest MWI and modelled PM_{10}, percent of non-white women and deprivation (Pearson correlation = 0·31 (95% CI 0·30–0·31) for PM_{10}, 0·45 (0·45–0·46) ethnicity and 0·22 (0·22–0·22) deprivation) (table S4).

We found no associations between modelled PM_{10} concentrations from MWIs and all congenital anomalies when fully adjusted for confounders (Table 3a, Table S11a). However, with proximity to nearest MWI, there was a small (2%) excess risk of all congenital anomalies combined for each kilometre closer to the MWI [OR 1·02; 95% CI 1·00–1·04] (Table 3b, Table S11b).

There were no significant associations between modelled PM_{10} and any of the individual congenital anomalies groups and sub-groups after fully adjusting for confounders (Table 4a). Associations with proximity to nearest MWI were found for CHDs [OR 1·04; 95% CI 1·01–1·08] and genital anomalies [OR 1·07; 95% CI 1·02–1·12] (Table 4b) which make up the majority of the excess risk found when analysing all congenital anomalies. For hypospadias, which make up 85·6% of genital anomalies, there was a 7% excess risk for each kilometre closer to the MWI [OR 1·07; 95% CI 1·01–1·12].

After Simes procedure adjustment for multiple testing, *p*-values were robust to adjustment for genital anomalies but not for CHDs (table S12). Findings from sensitivity analyses showed no material difference to those from main models (table S6), other than addition of individual ethnicity as a confounder; this is likely due to bias introduced by the difference in completeness of individual ethnicity data between numerator (38·3%) and denominator (73·8%) datasets. Additionally, the

Table 1
Characteristics of the study population.

Variable	Total[a] n (%)	All congenital anomalies n (%)	All congenital anomalies excl. chromosomal n (%)
Total n (%)	219,486	5154 (2·35%)	4172 (1·90%)
Sex n (%)			
Male	112,650 (51·3%)	2800 (54·3%)	2315 (55·5%)
Female	106,573 (48·6%)	2093 (40·6%)	1615 (38·7%)
Indeterminate sex/unknown	263 (0·12%)	261 (5·06%)	242 (5·80%)
Maternal age n (%)			
< 20 years	18,830 (8·58%)	440 (8·54%)	395 (9·47%)
20–29 years (ref)	109,460 (49·9%)	2421 (47·0%)	2136 (51·2%)
30–39 years	84,644 (38·6%)	1978 (38·4%)	1502 (36·0%)
≥ 40 years	6552 (2·99%)	315 (6·11%)	139 (3·33%)
Percentage non-white ethnicity[b] n (%)			
< 5%	68,806 (31·3%)	1522 (29·5%)	1231 (29·5%)
5–14%	80,986 (36·9%)	1928 (37·4%)	1512 (36·2%)
15–30%	41,385 (18·9%)	919 (17·8%)	762 (18·3%)
> 30%	28,309 (12·9%)	785 (15·2%)	667 (16·0%)
Year of birth n (%)			
2003[c]	70 (0·039%)	55 (1·07%)	33 (0·791%)
2004	18,473 (8·42%)	459 (8·91%)	382 (9·15%)
2005	22,039 (10·0%)	591 (11·5%)	472 (11·3%)
2006	30,982 (14·1%)	771 (15·0%)	622 (14·9%)
2007	36,629 (16·7%)	907 (17·6%)	750 (18·0%)
2008	37,466 (17·1%)	857 (16·6%)	711 (17·0%)
2009	37,607 (17·1%)	837 (16·2%)	669 (16·0%)
2010	36,220 (16·5%)	677 (13·1%)	533 (12·8%)
Deprivation quintile[d] n (%)			
1 - least deprived	25,124 (11·4%)	557 (10·9%)	395 (9·47%)
2	32,340 (14·7%)	740 (14·4%)	550 (13·2%)
3	38,153 (17·4%)	850 (16·5%)	663 (15·9%)
4	41,691 (19·0%)	995 (19·3%)	795 (19·1%)
5 - most deprived	82,178 (37·4%)	2052 (39·8%)	1769 (42·4%)
Mean major road length within 250 m of maternal residence·			
0 m	116,490 (53·1%)	2677 (51·9%)	2147 (51·5%)
1–250 m	12,168 (5·54%)	307 (5·96%)	255 (6·11%)
251–500 m	59,688 (29·2%)	1372 (26·6%)	1125 (27·0%)
> 500 m	31,140 (14·2%)	798 (15·5%)	645 (15·5%)
Other sources of emissions[e]			
< 1	81,036 (36·9%)	1540 (29·9%)	1178 (28·2%)
1–2	82,322 (37·5%)	2274 (44·1%)	1872 (44·9%)
≥ 2	56,128 (25·6%)	1340 (26·0%)	1122 (26·9%)

[a] Live births, stillbirths and TOPFAs, including congenital anomaly cases.
[b] Defined as % of non-white women aged 16–49 at the middle layer super output area (MSOA) level (2000 to 6000 households).
[c] Emission data for the MWIs was only available from the start of 2003, this means very few births in 2003 are included in the study because the 91 day pre-pregnancy period would have started in 2002 for almost all 2003 births.
[d] Defined as the Carstairs deprivation quintile at the census output area (COA) level (40 to 250 households).
[e] Defined as number of industries divided by years of incinerator operation (see Table S3).

analysis that excluded area-level covariates (deprivation and ethnicity) showed a slightly larger association between all congenital anomalies and proximity to nearest MWI [OR 1·03; 95% CI 1·01–1·04]. The majority of exclusions (3.3%) were due to incomplete exposure data (Fig. 2), because birth events were excluded if > 10% of ADMS data was missing for the exposure period. To investigate the effect of this we ran 2 sensitivity analyses with exclusion criteria of 5% and 15% as the cut-off points for missing ADMS data. The results were similar to those using the default 10% cut-off point for missing ADMS data (see supplemental table S6).

4. Discussion

With inclusion of 219,486 births, including 5154 cases, this study is one of the largest to examine the risk of congenital anomalies near MWIs. Both modelled concentrations of PM_{10} from MWI emissions and incinerator proximity were used as indicators of potential exposure to pollution from MWIs. We found no increased risk of congenital anomalies associated with modelled concentrations of PM_{10} but small increases in risk across all congenital anomalies, CHDs and genital anomalies with proximity to the nearest MWI. The limited correlation between proximity to nearest MWI and modelled PM_{10} (Pearson correlation = 0·31) suggests that they are estimating different entities and may at least partly explain the differing results for the two metrics.

4.1. Comparison with related studies

In line with our study findings, no previous studies have found associations of MWI emissions with all congenital anomalies combined or all congenital anomalies excluding chromosomal anomalies. Dummer et al. (2003) in their study examining congenital anomalies in relation to four incinerators in a county of England in 1956–1993, found an association between proximity and lethal CHDs [OR: 1·12; 95% CI 1·03–1·22, continuous odds ratio using the distance function 1/(D + 0·1) where D is the distance in km from the incinerator]. Similarly, in our study, we found a 4% excess risk of CHDs (95% CI 1·01–1·08) for every 1 km closer to an MWI when considering proximity to nearest MWI; however, there was no association between severe CHDs and proximity to nearest MWI

Table 2
Distribution of PM_{10} exposure and distance to nearest MWI.

a) Distribution by exposure variables

Variable	All birth records[a] n (%)	All congenital anomalies n (%)	All congenital anomalies excl. chromosomal n (%)
Total n (%)	219,486	5154 (2·35)	4172 (1·90)
Distance to nearest MWI (km)[b]			
<1	3464 (1·6)	104 (2·0)	86 (2·1)
≥1 to <2	12,256 (5·6)	289 (5·6)	228 (5·5)
≥2 to <3	21,101 (9·6)	538 (10·4)	451 (10·8)
≥3 to <4	31,644 (14·4)	784 (15·2)	627 (15·0)
≥4 to <5	28,906 (13·2)	730 (14·2)	612 (14·7)
≥5 to <6	31,554 (14·4)	773 (15·0)	623 (14·9)
≥6 to <7	29,531 (13·5)	626 (12·2)	511 (12·3)
≥7 to <8	22,680 (10·3)	500 (9·7)	394 (9·4)
≥8 to <9	20,352 (9·3)	420 (8·2)	342 (8·2)
≥9 to ≤10	17,998 (8·2)	390 (7·6)	298 (7·1)
Estimated[c] PM_{10} distribution (10^{-3} µg/m^3)			
<0·00625	482 (0·2)	8 (0·2)	5 (0·1)
0·00625–0·0125	1644 (0·8)	29 (0·6)	25 (0·6)
0·0125–0·025	4361 (2·2)	115 (2·2)	92 (2·2)
0·025–0·05	9272 (4·4)	202 (3·9)	167 (4·0)
0·05–0·1	21,553 (9·8)	524 (10·2)	412 (9·88)
0·1–0·2	36,369 (16·6)	855 (16·6)	713 (17·1)
0·2–0·4	47,448 (21·6)	1059 (20·6)	855 (20·5)
0·4–0·8	45,819 (20·9)	1069 (20·8)	845 (20·2)
0·8–1·6	31,741 (14·9)	779 (15·1)	639 (15·3)
1·6–3·2	15,545 (7·1)	388 (7·5)	314 (7·5)
3·2–6·4	3924 (1·8)	103 (2·0)	90 (2·2)
≥6·4	873 (0·4)	23 (0·5)	17 (0·4)

b) Distribution by quantile

Variable	All birth records[a]	All congenital anomalies	All congenital anomalies excl. chromosomal
Distance to nearest MWI[b] (km)			
Minimum	0·12	0·36	0·36
1st quartile	3·57	3·45	3·43
Median	5·38	5·16	5·11
Mean	5·44	5·28	5·25
3rd quartile	7·23	7·05	6·98
Maximum	10·0	10·0	10·0
Estimated[c] PM_{10} quartiles (10^{-3} µg/m^3)			
Minimum	0·00	$5{\cdot}30 \times 10^{-5}$	$1{\cdot}40 \times 10^{-3}$
1st quartile	0·143	0·144	0·145
Median	0·339	0·348	0·348
Mean	0·643	0·666	0·670
3rd quartile	0·764	0·804	0·810
Maximum	20·4	15·7	15·7

[a] Live births, stillbirths and TOPFAs, including congenital anomaly cases.
[b] Proximity of the nearest MWI was calculated as a continuous measure of linear distance (km) from the postcode centroid of maternal residence at birth.
[c] Mean estimated PM_{10} concentration from ADMS dispersion modelling over 91 day pre-pregnancy period plus first trimester of pregnancy.

[OR: 1·02; 95% CI 0·97–1·07] (Table 4b). While a previous study found a link between CHDs and landfill sites (Elliott et al., 2009) causality has been debated (COT, 2010).

All four previous studies investigating the risk of congenital anomalies by modelling exposure from MWI emissions (Cordier et al., 2004; Cordier et al., 2010; Vinceti et al., 2008; Vinceti et al., 2009; Vinceti et al., 2018) used modelled maternal exposure to dioxins. Of these, only the studies by Cordier et al. (2004, 2010) found evidence of increased risk of some congenital anomalies subgroups (facial clefts, renal dysplasia and urinary tract defects). We did not find excess of these specific anomalies and modelled PM_{10} concentrations in our study, although we did not model maternal exposure to dioxins.

No published study on MWIs to date has found associations with genital anomalies and/or hypospadias. The aetiology of hypospadias is largely unknown (van der Zanden et al., 2012); it has been suspected that maternal exposure to endocrine disrupting chemicals is a risk factor, but evidence is inconsistent (Ormond et al., 2009). Elevated risks of hypospadias have been reported near landfill sites but may reflect residual confounding (Elliott et al., 2009).

4.2. Strength and limitations

In this large retrospective cohort study we included all available live birth, stillbirth, termination and congenital anomaly registration data in the study area and period thus minimising selection bias (< 3.5% exclusions). We used modelled PM_{10} concentrations as a means to investigate effects of MWI emissions, as well as proximity to a MWI. These were based on postcode centroid of the mother's residence although not the exact address, and do not account for migration during pregnancy or paternal residence and exposure prior to the exposure period, all of which may have led to misclassification bias (Hodgson et al., 2015). The PM_{10} concentrations were modelled using a Gaussian dispersion model treated deterministically rather than probabilistically, potentially narrowing the confidence intervals for the analysis results.

Table 3
Risk of all congenital anomalies and all congenital anomalies without chromosomal congenital anomalies for modelled emissions and proximity to nearest MWI.

a.) Modelled emissions from nearest MWI

Outcome	n cases/n total[a]	Unadjusted OR[b](95% CI)	Fully adjusted[c] OR[b] (95% CI)
All congenital anomalies	5154/219,486	1·01 (1·00–1·03)	1·00 (0·98–1·02)
All congenital anomalies excl. chromosomal	4172/219,020	1·02 (1·00–1·03)	0·99 (0·97–1·01)

b.) Proximity to nearest MWI

Outcome	n cases/n total[a]	Unadjusted OR[d] (95% CI)	Fully adjusted[c] OR[d] (95% CI)
All congenital anomalies	5154/219,486	1·03 (1·02–1·04)	1·02 (1·00–1·04)
All congenital anomalies excl. chromosomal	4172/219,020	1·04 (1·02–1·05)	1·02 (1·00–1·04)

Note: OR, odds ratio; CI, confidence interval. *P*-values for these results are reported in Table S11.

[a] Live births, stillbirths and TOPFAs, including congenital anomaly cases.

[b] Risk per doubling in modelled mean PM_{10} over exposure period. Modelled exposure to mothers (10^{-3} μg m^{-3}): range 0–20·4, IQR 0·14–0·76, median 0·34, mean 0·64. Exposure is mean modelled PM_{10} concentration over 91 day pre-pregnancy period plus first trimester of pregnancy.

[c] Adjusted for maternal age, year of birth, area level ethnicity, area-level deprivation, other potential sources of emissions, MWI road density (length of motorways, A-roads and B-roads within 10 km of the MWI), individual road density (length of motorways, A-roads and B-roads within 250 m of mother's postcode); random effect for MWI area and random slope for the exposure.

[d] Risk per km closer to nearest MWI (continuous).

Our models adjusted for other sources of pollution based on permits to pollute in the vicinity of the MWI, and for road density which has been shown to be a useful proxy for road traffic air pollution (Rose et al., 2009), but these will not capture exposure to all local sources of pollutants. We were reliant on modelling since we did not have individual-level measurements of exposures to MWI emissions for the hundreds of thousands of mothers included in the study, nor would it be feasible to collect such data. Use of a dispersion model assuming primary airborne exposure (as in our study) has been recommended to reduce exposure misclassification (Cordioli et al., 2013). We found statistically significant correlations between in-stack measurements of PM_{10} and some heavy metals, polycyclic aromatic hydrocarbons and polychlorinated biphenyls (Douglas et al., 2017; Ghosh et al., 2018), all of which have previously been associated with risks of congenital anomalies (Dolk and Vrijheid, 2003). However, based on limited measurement data, we found weaker correlations between in-stack measurements of PM_{10} and compounds of mercury or polychlorinated dibenzo-p-dioxins and furans (PCDD/Fs) (Spearman's correlation values of $r = 0{\cdot}11$–$0{\cdot}15$) (Douglas et al., 2017; Ghosh et al., 2018), which have been associated with increased risks of congenital anomalies (Dolk and Vrijheid, 2003; van der Zanden et al., 2012), specifically with modelled waste incinerator dioxin emissions (Cordier et al., 2010).

Distance is a cruder measure but may pick up other potentially toxic emissions accumulating through non-airborne exposure pathways or from local (non-stack) emissions. These might include, for example, emissions from waste handling including waste transportation to the MWI (estimated at 2% to 10% of MWI emissions in a hypothesised case study by Ciuta et al., 2012), which may not be picked up by the stack emissions modelling.

We found a weak correlation between proximity to nearest MWI and both deprivation and ethnicity (table S4) and between all congenital anomalies combined and proximity to nearest MWI; while we adjusted at area level for deprivation and ethnicity, previously linked with increased risks of CHD and hypospadias respectively (van der Zanden et al., 2012; Varela et al., 2009), we did not have the relevant data to adjust for these potential confounders at individual level, and it is possible that association of proximity with these outcomes reflects residual confounding rather than 'true' (causal) effects.

Further considerations include the potential for bias in outcome ascertainment and ambiguity of ICD_{10} coding, inconsistent reporting of the severity of certain anomalies across registries and differences between English and Scottish datasets (e.g. lack of TOPFA data in the Scottish data). Of particular relevance is the surveillance of hypospadias cases which is known to be inconsistent with differences in ascertainment between registries (Dolk et al., 2004). In 2004, Dolk et al. suggested that the reporting systems in place were unlikely to provide effective surveillance of hypospadias and notably these systems had not changed during our study period.

5. Conclusions

This study found no increased risk of congenital anomalies in relation to mean modelled PM_{10} concentrations from MWIs in England and Scotland as a proxy for MWI emissions more generally. Small increased risks (2–7%) with proximity to the nearest MWI were observed for all congenital anomalies combined, congenital heart defects and genital anomalies, specifically hypospadias. These findings in proximity to MWI might reflect residual confounding, although it is not possible from these data to exclude a potential causal effect even in the absence of associations with modelled PM_{10} emissions; further monitoring of exposures and health outcomes near MWIs appears warranted.

Data

Births and deaths data were from the Office for National Statistics (ONS) National Mortality, Births and Stillbirth register for England and Wales and the National Health Service (NHS) Numbers for Babies (NN4B). Scottish births and deaths were from the Information Services Division (ISD) Scotland. TOPFAs were from the Department of Health (now called Department of Health and Social Care).

English data on congenital anomalies are from the British and Irish Network of Congenital Anomaly Researchers (BINOCAR) as well as individual regional congenital anomaly registers (RCARs): Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire (CAROBB); East Midlands & South Yorkshire Congenital Anomaly Register (EMSYCAR); Northern Congenital Abnormality Survey (NorCAS); South West Congenital Anomaly Register (SWCAR); Wessex Antenatally Detected Anomalies Register (WANDA).

Incinerator emissions data came from the Environment Agency (EA), and Scottish Environment Protection Agency (SEPA).

Data on industrial sites came from the Environment Agency Environmental Permitting Regulations – Industrial sites (England), and the Scottish Pollutant Release Inventory.

Road length data came from Meridian 2014 road lengths. Ordnance

Table 4
Risk of congenital anomaly outcomes by congenital anomalies grouping (chromosomal anomalies excluded) for modelled emissions and proximity to nearest MWI.

a.) Modelled exposure to PM_{10} from nearest MWI

	n cases/n total[a]	Unadjusted OR[b] (95% CI)	Fully adjusted[c] OR[b] (95% CI)
Congenital anomaly groups			
Nervous system	543/215,863	1·02 (0·97–1·07)	0·97 (0·92–1·02)
Congenital heart defects	1232/216,644	1·08 (1·05–1·12)	0·99 (0·93–1·05)
Abdominal wall defects	222/215,788	0·99 (0·93–1·07)	1·00 (0·92–1·08)
Oro-facial clefts	339/215,931	1·04 (0·98–1·10)	1·00 (0·94–1·07)
Limb defects	746/216,252	0·92 (0·89–0·96)	1·01 (0·94–1·08)
Digestive system	355/215,928	1·04 (0·98–1·10)	1·00 (0·92–1·09)
Urinary system	534/216,037	1·03 (0·98–1·08)	1·00 (0·94–1·07)
Genital system	472/216,053	0·96 (0·92–1·01)	1·03 (0·95–1·13)
Congenital anomaly sub-groups			
Neural tube defects	264/215,695	1·04 (0·97–1·11)	1·00 (0·92–1·07)
Severe congenital heart defects	436/215,954	1·07 (1·02–1·13)	1·03 (0·97–1·10)
Gastroschisis	133/215,753	1·04 (0·95–1·15)	1·04 (0·94–1·15)
Cleft palate	124/215,749	1·03 (0·94–1·14)	1·02 (0·92–1·13)
Cleft lip with or without cleft palate	217/215,822	1·04 (0·96–1·12)	1·00 (0·93–1·08)
Limb reduction defects	122/215,725	1·04 (0·94–1·15)	1·02 (0·91–1·14)
Oesophageal atresia	51/215,681	1·07 (0·92–1·25)	1·04 (0·88–1·22)
Anomalies of the renal system	241/215,803	1·04 (0·97–1·12)	1·02 (0·95–1·10)
Obstructive defects of renal pelvis	255/215,840	0·97 (0·91–1·04)	0·97 (0·90–1·04)
Hypospadias	407/216,004	0·96 (0·91–1·01)	1·00 (0·90–1·12)

b.) Proximity to nearest MWI

	n cases/n total[a]	Unadjusted OR[d] (95% CI)	Fully Adjusted[c] OR[d] (95% CI)
Congenital anomaly groups			
Nervous system	543/215,863	1·02 (0·98–1·05)	0·97 (0·93–1·02)
Congenital heart defects	1232/216,644	1·04 (1·01–1·06)	1·04 (1·01–1·08)
Abdominal wall defects	222/215,788	0·97 (0·92–1·03)	1·00 (0·94–1·07)
Oro-facial clefts	339/215,931	0·99 (0·95–1·04)	0·99 (0·94–1·05)
Limb defects	746/216,252	1·06 (1·03–1·09)	1·02 (0·97–1·08)
Digestive system	355/215,928	0·98 (0·93–1·02)	1·00 (0·95–1·06)
Urinary system	534/216,037	1·02 (0·98–1·06)	1·02 (0·97–1·06)
Genital system	472/216,053	1·10 (1·06–1·15)	1·07 (1·02–1·12)
Congenital anomaly sub-groups			
Neural tube defects	264/215,695	1·00 (0·95–1·05)	0·97 (0·91–1·03)
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Cleft palate	124/215,749	0·96 (0·89–1·03)	0·98 (0·90–1·06)
Cleft lip with or without cleft palate	217/215,822	1·01 (0·95–1·07)	1·00 (0·94–1·07)
Limb reduction defects	122/215,725	1·04 (0·96–1·12)	0·98 (0·90–1·08)
Oesophageal atresia	51/215,681	0·95 (0·85–1·07)	0·92 (0·80–1·05
Anomalies of the renal system	241/215,803	1·00 (0·95–1·05)	1·00 (0·93–1·07)
Obstructive defects of renal pelvis	255/215,840	1·04 (0·99–1·10)	1·03 (0·97–1·10
Hypospadias	407/216,004	1·11 (1·07–1·16)	1·07 (1·01–1·12)

Note: OR, odds ratio; CI, confidence interval. P-values and P-values after Simes procedure adjustment for multiple testing for these results are reported in Table S12.

[a] Live births, stillbirths and TOPFAs, including congenital anomaly cases.

[b] Risk per doubling in modelled mean PM_{10} over exposure period. Modelled exposure to mothers (10^{-3} μg m^{-3}): range 0–20·4, IQR 0·14–0·76, median 0·34, mean 0·64. Exposure is mean modelled PM_{10} concentration over 91 day pre-pregnancy period plus first trimester of pregnancy.

[c] Adjusted for maternal age, year of birth, area level ethnicity, area-level deprivation, other potential sources of emissions, MWI road density (length of motorways, A-roads and B-roads within 10 km of the MWI), individual road density (length of motorways, A-roads and B-roads within 250 m of mother's postcode); random effect for MWI area and random slope for the exposure.

[d] Risk per km closer to nearest MWI (continuous).

Data sharing

Health data are available from the data providers on application with appropriate ethics and governance permissions, but we do not hold data provider, ethics, or governance permissions to share the health datasets with third parties.

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Contributors

REG, BP, ALH, MBT, PE contributed to study conception and design; REG, BP, ALH, MBT, DW, JR and JK to the statistical analysis plan; REG, MBT, ALH, DF, DW, JK and JR to acquisition of health and confounder data; and PD, REG, KdH, GF to initial data analysis and exposure assessment. BP conducted the data analyses and drafted the initial report. All authors contributed to interpreting the analyses and critically revising the article and approved the final draft. BP, ALH, REG, PD had full access to the data and can take responsibility for the integrity of the data and the accuracy of the data analysis. BP, ALH, PE, MBT agree to be accountable for all aspects of the work. MBT is the guarantor of this paper. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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PPI statement

Patients and members of the public were not directly involved in setting the research question or outcome measures, but the study was designed to include outcomes of public concern such as congenital anomalies. The study design and dissemination issues were discussed with the MRC-PHE Centre for Environment and Health's Community Advisory Board, which includes lay members, and a lay study protocol was made available on the SAHSU website. Following this publication, the public and patients will be informed by press reports, and information on the PHE and SAHSU homepages.

Ethical approval

The study uses SAHSU data, supplied from the Office for National Statistics; data use and link between UK National Births and Stillbirth register data and NHS Numbers for Babies (NN4B), BINOCAR/LCAR data covered by approval from the National Research Ethics Service REC Reference 17/L0/0846 and by the Health Research Authority Confidentiality Advisory Group (HRA-CAG) for Section 251 support (HRA – 14/CAG/1039). Approval for Scottish data was covered by SAHSU's existing ethics and from the NHS National Services Scotland Privacy Advisory Committee (PAC) reference - PAC 17/14.

Transparency

The manuscript's guarantor affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Declaration of Competing Interest

Anna Hansell declares a Greenpeace membership but has not received any money from the organisation nor been involved in campaigns; nor other relationships or activities that could appear to have influenced the submitted work. Brandon Parkes declares a Friends of the Earth membership but has not been involved in campaigns; nor other relationships or activities that could appear to have influenced the submitted work. The other authors declare they have no actual or potential competing financial interests.

The views expressed are those of the author(s) and not necessarily those of the NIHR, MRC, the Department of Health (now called Department of Health and Social Care) or PHE.

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Appendix A. Supplementary data

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References

Ashworth, D.C., Elliott, P., Toledano, M.B., 2014. Waste incineration and adverse birth and neonatal outcomes: a systematic review. Environment International 69, 120–132.

Candela, S., Ranzi, A., Bonvicini, L., et al., 2013. Air pollution from incinerators and reproductive outcomes: a multisite study. Epidemiology 24 (6), 863–870.

Candela, S., Bonvicini, L., Ranzi, A., et al., 2015. Exposure to emissions from municipal solid waste incinerators and miscarriages: A multisite study of the MONITER Project. Environment International 78, 51–60.

Ciuta, S., Schiavon, M., Chiste, A., et al., 2012. Role of feedstock transport in the balance of primary PM emissions in two case-studies: RMSW incineration vs. sintering plant. *UPB Sci Bull* Series D 74 (1), 8.

Cordier, S., Chevrier, C., Robert-Gnansia, E., Lorente, C., Brula, P., Hours, M., 2004. Risk of congenital anomalies in the vicinity of municipal solid waste incinerators. Occupational and Environmental Medicine 61 (1), 8–15.

Cordier, S., Lehebel, A., Amar, E., et al., 2010. Maternal residence near municipal waste incinerators and the risk of urinary tract birth defects. Occupational and Environmental Medicine 67 (7), 493–499.

Cordioli, M., Ranzi, A., De Leo, G.A., Lauriola, P., 2013. A review of exposure assessment methods in epidemiological studies on incinerators. Journal of Environmental and Public Health 2013, 129470.

COT, 2010. Committee on toxicity of chemicals in food, consumer producs and the environment. Second statement on landfill sites. Available at. https://cot.food.gov.uk/sites/default/files/cot/cotstatementlandfill201001.pdf.

Cresswell, P.A., Scott, J.E.S., Pattenden, S., Vrijheid, M., 2003. Risk of congenital anomalies near the Byker waste combustion plant. Journal of Public Health Medicine 25 (3), 237–242.

Dolk, H., Vrijheid, M., 2003. The impact of environmental pollution on congenital anomalies. British Medical Bulletin 68 (1), 25–45.

Dolk, H., Vrijheid, M., Scott, J.E.S., et al., 2004. Toward the effective surveillance of hypospadias. Environmental Health Perspectives 112 (3), 398–402.

Douglas, P., Freni-Sterrantino, A., Sanchez, M.L., et al., 2017. Estimating Particulate Exposure from Modern Municipal Waste Incinerators in Great Britain. Environmental Science & Technology 51 (13), 7511–7519.

Dummer, T.J.B., Dickinson, H.O., Parker, L., 2003. Adverse pregnancy outcomes around incinerators and crematoriums in Cumbria, north west England, 1956-93. Journal of Epidemiology and Community Health 57 (6), 456–461.

Elliott, P., Richardson, S., Abellan, J.J., et al., 2009. Geographic density of landfill sites and risk of congenital anomalies in England. Occupational and Environmental Medicine 66 (2), 81–89.

European Union, 2010. Directive 2010/75/EU on Industrial Emissions (Integrated Pollution Prevention and Control).

Garne, E., Dolk, H., Loane, M., et al., 2011. Paper 5: Surveillance of Multiple Congenital Anomalies: Implementation of a Computer Algorithm in European Registers for Classification of Cases. *Birth Defects Research Part a-Clinical and Molecular* Teratology 91, S44–S50.

Ghosh, R.E., Freni-Sterrantino, A., Douglas, P., et al., 2018. Fetal growth, stillbirth, infant mortality and other birth outcomes near UK municipal waste incinerators; retrospective population based cohort and case-control study. Environ. Int. 122, 151–158.

Health Protection Agency, 2009. The impact on health of emissions to air from municipal waste incinerators. Health Research Board, Dublin, Irelandhttps://www.gov.uk/government/uploads/system/uploads/attachment_data/file/384592/The_impact_on_health_emissions_to_air_from_municipal_waste_incinerators.pdf, Accessed date: 10 February 2019.

Hodgson, S., Lurz, P.W., Shirley, M.D., Bythell, M., Rankin, J., 2015. Exposure misclassification due to residential mobility during pregnancy. International Journal of Hygiene and Environmental Health 218 (4), 414–421.

Jansson, B., Voog, L., 1988. Dioxin from Swedish municipal incinerators and the occurrence of cleft lip and palate malformations. International Journal of Environmental Studies 34 (1-2), 99–104.

Ormond, G., Nieuwenhuijsen, M.J., Nelson, P., et al., 2009. Endocrine disruptors in the workplace, hair spray, folate supplementation, and risk of hypospadias: case–control study. Environmental health perspectives 117 (2), 303.

R Core Team, 2015. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria Available from: https://www.R-project.org.

Rankin, J., Chadwick, T., Natarajan, M., Howel, D., Pearce, M.S., Pless-Mulloli, T., 2009. Maternal exposure to ambient air pollutants and risk of congenital anomalies. Environmental Research 109 (2), 181–187.

Rose, N., Cowie, C., Gillett, R., Marks, G.B., 2009. Weighted road density: A simple way of assigning traffic-related air pollution exposure. Atmospheric Environment 43 (32), 5009–5014.

Santoro, M., Minichilli, F., Linzalone, N., et al., 2016. Adverse reproductive outcomes associated with exposure to a municipal solid waste incinerator. Ann Ist Super Sanita 52 (4), 576–581.

Simes, R.J., 1986. An improved Bonferroni procedure for multiple tests of significance. Biometrika 73 (3), 751–754.

Tango, T., Fujita, T., Tanihata, T., et al., 2004. Risk of adverse reproductive outcomes associated with proximity to municipal solid waste incinerators with high dioxin emission levels in Japan. Journal of Epidemiology 14 (3), 83–93.

ten Tusscher, G.W., Stam, G.A., Koppe, J.G., 2000. Open chemical combustions resulting in a local increased incidence of orofacial clefts. Chemosphere 40 (9-11), 1263–1270.

van der Zanden, L.F.M., van Rooij, I., Feitz, W.F.J., Franke, B., Knoers, N., Roeleveld, N., 2012. Aetiology of hypospadias: a systematic review of genes and environment. Human Reproduction Update 18 (3), 260–283.

Varela, M., Nohr, E.A., Llopis-Gonzalez, A., Andersen, A.M.N., Olsen, J., 2009. Socio-occupational status and congenital anomalies. European Journal of Public Health 19 (2), 161–167.

Vehlow, J., Bergfeldt, B., Visser, R., Wilen, C., 2007. European Union waste management strategy and the importance of biogenic waste. Journal of Material Cycles and Waste Management 9 (2), 130–139.

Vinceti, M., Malagoli, C., Teggi, S., et al., 2008. Adverse pregnancy outcomes in a population exposed to the emissions of a municipal waste incinerator. Science of the Total Environment 407 (1), 116–121.

Vinceti, M., Malagoli, C., Fabbi, S., et al., 2009. Risk of congenital anomalies around a municipal solid waste incinerator: a GIS-based case-control study. International Journal of Health Geographics 8.

Vinceti, M., Malagoli, C., Werler, M., et al., 2018. Adverse pregnancy outcomes in women with changing patterns of exposure to the emissions of a municipal waste incinerator. Environmental Research 164 (8).