IMPROVING EXPOSURE ASSESSMENT AND DEFINING HEALTH OUTCOMES IN THE REPRODUCTIVE EPIDEMIOLOGY OF MUNICIPAL SOLID WASTE INCINERATORS

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ABSTRACT

The last decade has seen a shift away from disposal of waste in landfills to more environmentally desirable methods of waste management, such as recycling, composting and incineration. There is ongoing public concern about health risks associated with incineration. Epidemiological studies investigating exposure to incinerator emissions and risk of adverse birth outcomes are limited by poor exposure assessment lack of information on uptake of these emissions and the small numbers of birth outcomes explored.

The aim of this thesis was to estimate population exposure to emissions from four municipal solid waste incinerators (MSWI) in England. Also, at an individual level, to design and undertake a study to ascertain the exposure profile to dioxins for women resident near two MSWIs. Finally, to compare the availability and quality of national birth data in England and make recommendations on their use in epidemiological studies of birth outcomes. The findings of this thesis have contributed to the ongoing national study being conducted by the Small Area Health Statistics Unit (SAHSU), investigating the association between MSWI emissions and the risk of adverse birth and neonatal outcomes in Great Britain (GB).

Atmospheric dispersion modelling was undertaken to estimate population exposure to particulate matter as a proxy for all MSWI emissions. Model outputs presented will be used in the SAHSU study and the model developed rolled out for all MSWIs in GB. The Incinerators Biomonitoring Study achieved a study database of 97 participants, each providing breast milk samples and questionnaire information. The study showed variability in participation by demographic and lifestyle factors, alongside dietary dioxin intake estimates. The findings of this study will help to interpret the results of SAHSU's study, providing an insight into the relationship between MSWI exposure and total body burden of dioxins. Finally, a comparison of routine national birth data revealed variation in completeness and fields of information collected by dataset. Hospital birth data compared favourability with registry data at a national scale after 2002, with considerable improvements in quality between 2001 and 2010. However, large differences between datasets were observed at small area level, reflecting the influence of hospital provider effects on this dataset.

DECLARATION OF ORIGINALITY

I declare that this thesis is my own work and that where work conducted by others is presented, it is fully referenced and/or acknowledged as appropriate.

This multi-disciplinary thesis required the collaboration of others for it to be carried out. Under the supervision of Dr Kees De Hoogh, the dispersion modelling of was conducted using stack emissions data collected by the UK Environment Agency. Models for all other incinerators in Great Britain were subsequently rolled out by Maria Leal Sanchez

The author has been involved in each stage of the Incinerators Biomonitoring Study. With the supervision of Dr Mireille B. Toledano and Professor Paul Elliott, the author wrote the study protocol, all study materials, the ethical, R&D, and Clinical Research Network portfolio applications and co-ordinated the study on a daily basis (involving liaison with collaborating midwives and participants) and undertook the data collection and subsequent data analyses. Potential participants for the biomonitoring study were identified by collaborating midwives using hospital records.

Dr Kevin Garwood, a member of the SAHSU database team, extracted the routine birth data. A small area level comparison of birth registration and hospital birth records was undertaken by Dr Rebecca Ghosh.

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CHAPTER 1: INTRODUCTION & LITERATURE REVIEW

1.1 BACKGROUND

Burning waste has been undertaken for millennia but it was not until the 19th Century that legislation was enacted to regulate this practice. This was in response to the vast increase in waste generated during the industrial revolution, the increasing global population and the recognition of health risks associated with inadequate waste disposal [1]. Since the first incinerator was commissioned in 1874, incineration has principally functioned as a means to reduce the volume of waste, with additional benefits including diverting waste from disposal in landfills, eliminating pathogens within the waste and recovering energy in the form of heat or electricity from the combustion process [2]. The first incinerator (previously known as "destructors") was commissioned in England, which remains at the forefront of pioneering and developing incinerator technology.

In England incineration of waste is the third most common method of waste management, with the proportion of total waste incinerated more than doubling in the last decade [3]. This rise in waste incineration and consequently in population exposure to incinerator emissions, has led to public concern about any associated potential health risks.

The epidemiological evidence exploring potential links between incineration and adverse health outcomes has, to date, focused primarily on cancer. Recently studies have begun to explore associated risks to more vulnerable subgroups of the population, such as the developing fetus, but the evidence as a whole is both inconsistent and inconclusive.

This chapter provides an introduction to incineration in the United Kingdom (UK), specifically municipal solid waste incinerators (MSWIs) and their emissions, before a review of the epidemiological and toxicological evidence investigating the associations between incineration and birth and neonatal outcomes. The epidemiological review presented was published in Environment International in 2014 [4] **(Appendix A).**

1.2 WASTE MANAGEMENT - INCINERATION

There are a number of waste management methods, all of which vary in their environmental impact and thus desirability and sustainability. Waste legislation and policy provide an order of priority for these waste management methods- the waste hierarchy. Waste prevention is ranked as the most desirable management method, followed by preparing for re-use, recycling (includes composting), other recovery (includes incineration with energy recovery) and finally the least desirable method waste disposal (includes landfill and incineration without energy recovery) (Figure 1.1) [5, 6].

A wide variety of types of waste are incinerated. These include chemical, municipal and clinical waste, refuse derived fuel, sewage sludge and animal carcasses [7]. For these purposes there are four main types of incinerators: clinical waste incinerators, hazardous waste incinerators, sewage sludge incinerators and municipal waste incinerators; 66% of the overall volume of waste incinerated is by municipal waste incinerators [8].

While the urban population continues to grow the amount of local authority generated waste in England has decreased. From 2000 to 2013 there was a 10% decrease in waste volume generated, with 25,120,000 tonnes of waste in 2013 (Figure 1.2) [3]. Figure 1.2 displays how waste management practices have changed between 2000 and 2013, with a movement away from disposal of waste in landfills (78.6% in 2001/01 and 33.9% in 2012/13) towards more environmentally desirable options such as recycling and composting (12.3% in 2001/01 and 42.1% in 2012/13) and incineration (8.5% in 2001/01 and 21.9% in 2012/13) [3].

1.3 MUNICIPAL SOLID WASTE INCINERATORS (MSWIs)

There is controversy surrounding the issue of what constitutes municipal waste. Within waste policy and reporting, municipal waste is waste collected by the local authority, however in legislation it is defined as *"waste from households, as well as other waste which, because of its nature or composition, is similar to waste from household"* [9], which includes waste, usually commercial and industrial, which is not necessarily collected by local authorities [10]. For either definition the greatest proportion of municipal waste is from households (over 90% of waste collected by local authority in 2012/2013 was household waste [3]). The composition of household waste in 2006/07 was reported as predominantly paper/card (23%), followed by food (18%), garden waste (14%), plastic (10%) and glass (7%) (Figure 1.3) [11].

In Europe approximately 400 Waste-to-Energy plants (excluding hazardous waste incinerators) were operational in 2001 across 18 countries. By 2011 this number increased to over 450 plants across 21 countries [12]. In 2011, Italy, France, the Netherlands and Germany were the only countries with greater waste capacities than the UK [12].

Table 1.1 provides an overview of the characteristics of all operational MSWIs in the UK in 2010. In addition to the MSWIs reported in Table 1.1 three MSWIs are currently under construction and due to become operational by the end of 2014 (Ardley in Oxfordshire, Runcorn in Cheshire, and Exeter in Devon, - all operated by Viridor). One additional MSWI site in Cornwall is currently applying for planning permission (their application was refused by Cornwall County council in 2009, this decision was then appealed to the Secretary of State and granted permission in 2011, subsequently challenged at high court, then appealed by the Secretary of State, after which the planning permission was confirmed in 2012) [13].

1.3.1 Technology

Figure 1.4 provides a basic overview of the different stages within the incineration process, applicable to all waste types. Although there are a number of different combustion technologies for MSWIs, the stages within the process are the same. Waste is fed into a primary combustion chamber by a feed hopper, where air is supplied through the waste into this chamber for effective combustion. Products of incomplete combustion move into a secondary chamber where more air is supplied, to ensure all products are combusted [14].

There are three main combustion technologies, or furnace types, used in MSWIs within the UK; grate technology, fluidised bed and rotary kiln/furnace. The most common of these is grate technology, whereby waste deposited onto a grate is transported through the primary combustion chamber (Figure 1.5) with air (primary air) moving upwards through the grate. To allow movement and loosening of waste there are a number of different types of grates. These include rollers, rockers/vibration and inclined grates which rotate backwards [14, 15]. The second most common technology in the UK is fluidised bed technology. Air is propelled through a combustion chamber lined with a bed of inert material, usually sand or silica, which acts to agitate or fluidise and mobilise the waste. This technology requires a homogenous waste feed, and so normally involves waste being pre-treated through crushing and shredding. For this reason, fluidised bed technology is more widely used for sewage sludge incineration but can also be used for MSW with examples in the UK including both Dundee and Allington MSWIs (Table 1.1) [7, 13, 14]. The third technology is rotary kiln which works to agitate and tumble

waste through the rotation of a horizontally inclined kiln (cylinder and primary combustion chamber). The high temperatures used in this technology mean that they are well suited for incineration of hazardous waste although rotary kiln incinerators are also used in MSWI - for example Newlincs/Grimsby MSWI [7, 13].

Table 1.1 indicates the presence and type of energy recovery used for all operational MSWIs in the UK. Most commonly energy is recovered within the incineration process using the heat from combustion to generate steam which turns turbines and produces electricity [13]. This electricity is then often used internally, i.e. within the plant, but can also be sold externally.

1.3.2 Legislation

Within waste management, policies are continuously being updated. There are however two key directives which have the greatest influence on currently operational incinerators in the UK.

Firstly, the council of the European Union's Landfill Directive (1999/31/EC). This EU directive set out a number of targets to reduce the volume of biodegradable municipal waste landfilled, with an ultimate target of reducing the total weight of waste in 2020 to 35% of that in 1995 [9]. This directive has had a significant effect on driving the diversion of waste away from landfills towards more sustainable methods such as incineration, through guidance of the waste hierarchy (Figure 1.1) [16].

Secondly, the European Union's Waste Incineration Directive (WID) (Directive 2000/76/EC) [17]. The WID aims to *"prevent or to limit as far as practicable negative effects on the environment, in particular pollution by emissions into air, soil, surface water and groundwater, and the resulting risk to human health, from the incineration and co-incineration of waste"* through *"stringent operational conditions and technical requirements, through setting emission limit values for waste incineration and co-incineration plants within the Community"* [17]. Conditions prescribed by the WID for MSWIs include; a minimum combustion temperature of 850°C, a residence time of 2 seconds (time the pollutant is inside the incinerator), a limit on the proportion of organic carbon within bottom ash (<3%) and limits on the atmospheric emissions (discussed in detail in section 1.3.4). The WID was implemented in the UK through The Waste Incineration (England and Wales) Regulation in December 2002 and legally enforced within the Pollution Prevention and Control regime. In the UK, new incinerators were required to abide by these regulations from 28th December 2002 and previously existing incinerators from 28th December 2005.

1.3.3 Planning and permit permissions

Under the Land Use planning regime, planning permission for new MSWI sites has to be sought from the local authority within which the proposed site lies. Local authorities assess a number of criteria, including; location, size, traffic, emissions, odour, noise and how energy recovery has been considered and maximised [7]. In addition to planning permissions, the UK Environment Agency (EA), under the Environmental Permitting Regulations, issue permits for new incinerators. The complexity of an incinerator permit depends on the surrounding local environment, the requirements of both the incinerator site and neighbouring industry. Once a plant has been issued a permit, it is required to adhere to the conditions prescribed in the permit which may include future improvement plans such as upgrades to emerging technology [13]. Although local authorities issue planning permissions and the EA issue permits, information is exchanged between these two bodies and applications are usually made simultaneously.

1.3.4 Outputs

Incinerators have two main outputs, a solid residue known as bottom ash (approximately 20-30% in weight of waste input), and gaseous emissions into the atmosphere (the remaining 70-75% in weight of waste input) [13]. Additional outputs include: fly ash, reagents, waste water, metals [13], odour, noise and vibration.

Incinerators release a variety of compounds into the atmosphere including volatile organic compounds (VOCs), sulphur oxides (SOx), nitrogen oxides (NOx), carbon oxides (COx), hydrogen chloride (HCl), ammonia (NH_3), particulates (PM), polychlorinated dibenzo-dioxins (PCDDs), polychlorinated dibenzo-furans (PCDFs) and heavy metals. Of these emissions it is PCDDs/PCDFs, from now on referred to as “dioxins” and a number of heavy metals that make a significant contribution to total atmospheric concentrations [14].

The WID stipulates limits on the concentration of a subset of incinerator emissions, but additionally details requirements in their chemical composition and how they are dispersed [7, 14]. Factors influencing the type and concentration of these emissions include; the type of waste incinerated, a plant’s combustion technology and design (operating conditions, capacity and abatement techniques used). The WID emission limits, frequency in which the emissions are monitored and abatement techniques used for particulates, acidic gases, dioxins and mercury

are detailed in Tables 1.2 and 1.3. It is noted that because dioxins adhere to particulate matter, it is particulate abatement and the control of combustion conditions that are most influential on the amount and concentration of dioxins released [7].

1.3.5 Public concern & response

There is public concern and resistance to commissioning of new incinerators. These concerns fall into two categories: environmental/local services concerns and health concerns. Environmental concerns largely relate to the aesthetics of the plants themselves; their odour, dust, noise and the additional road traffic experienced both during construction and subsequently for the transportation of waste to the plant [13]. Additionally the vast cost of building and running an incinerator diverts resources away from local amenities. The cost of building an energy from waste facility with a moving grate technology has been estimated at between £145- £200 million with a running cost of between £44-£101 per tonne of waste incinerated [13]. Concerns about health risks associated with incinerators are principally focused on the pollutants emitted. In response to these concerns the independent advisory committee, the committee on carcinogenicity of chemicals in food, consumer products and the environment (COC), who are responsible for advising the government on the carcinogenicity of chemicals, issued a statement in 2000, updated in 2009, on cancer risk and MSWIs concluding that *"The Committee was reassured that any potential risk of cancer due to residency (for periods in excess of 10 years) near to a municipal solid waste incinerators was exceedingly low and probably not measurable by the most modern epidemiological technique"* and *"at the present time, there was no need for any further epidemiological investigations of cancer incidence near municipal solid waste incinerators"* [18]. Additionally the Health Protection Agency which had a statutory responsibility to advise government and local authorities on possible health impacts of air pollutants and who are consultees for environmental permits, reported in 2009 that *"any potential damage to the health of those living close-by is likely to be very small, if detectable*" [19].

1.4 EXPOSURE INCINERATOR EMISSIONS

Appropriately identifying and measuring exposures from environmental sources in order to mitigate or eliminate any associated risk is fundamental in heath protection. The methods used to assess exposure to incinerator emissions can be classified as direct or indirect. The goal for all exposure assessment methods is to accurately, precisely and most cost effectively acquire exposure estimates.

1.4.1 Direct measures of exposure

Direct measures of exposure determine the concentration of the pollutant reaching the population of interest. These methods include personal monitoring (concentration of the pollutant reaching the individual) and biological monitoring (concentration of the pollutant within the body). Personal monitoring involves study subjects wearing monitors or sensors that measure the polluantant of interest reaching the subject. Biological monitoring of pollutants indicates the concentration of the pollutant within the body, quantifying the amount of an environmental pollutant taken up into the body ('dose'). Although uncommonly used to assess exposure to incinerators, measuring biomarkers of environmental chemicals provides an individual level direct measure of exposure and is considered the most conclusive tool, the "gold standard", in exposure assessment [20]. The strength of these direct exposure measures lie in their ability to include a multitude of different exposure pathways and the individual nature of these measures. Biological monitoring is also further advantaged by accounting for all routes of exposure and individual level differences in uptake/absorption. This is of particular importance for low level environmental exposures [21] where environmental monitoring is often not possible. However the weaknesses of these direct assessments relate in large to the difficulty in obtaining samples due to their intrusive collection process. These techniques additionally are costly to implement, both financially and with regard to the resources and staff expertise required to collect and store samples. Biological samples also suffer the additional disadvantage of not reflecting long-term exposures, which is of particular importance when samples are not continuously collected.

1.4.2 Indirect measures of exposure

Indirect measures of exposure estimate the concentration of the pollutant reaching the population of interest. Indirect measures of exposure are usually divided into environmental monitoring and modelling and information extracted from study questionnaires.

For exposure to MSWI pollutants the most commonly used indirect measures are proximity to the MSWI as a proxy for exposure and dispersion modelling of MSWI emissions. Proximity to an incinerator, as a proxy for exposure to incinerator emissions, is a widely used, indirect exposure measure [22]. The strength of this measure is that it requires limited resources and therfore is frequently used in ecological studies. It is however disadvantaged by providing a crude

assessment (commonly assuming emissions from the source decrease uniformly with distance from the source) limited most crucially in that it does not account for concentration levels reflecting emissions from the source, nor variation in local topographic and metrological conditions [22, 23]. These limitations mean that there is a risk of significant exposure misclassification, likely to bias the results towards the null.

The use and development of environmental models in exposure assessment is ongoing. These models provide a way of improving the exposure assessment and reducing the risk of exposure misclassification [23]. The applicability of these models is not confined to scientific research and they are frequently used for regulatory purposes, policy support, and to provide information to the public [24].

Atmospheric dispersion models use emissions rate data, local topography and meteorology conditions alongside accounting for point source characteristics such as stack height and diameter, to provide estimates of ground level pollutant concentrations and the dispersion pattern of these pollutants [23, 25]. These models are continuously being updated and developed, differing mostly in how turbulence and atmospheric boundary layer structure are modelled [22]. First-generation dispersion models were limited by their oversimplified assumptions regarding the Pasquill stability classification system, normal dispersion patterns, and the state of the atmospheric boundary layer (based on meteorological conditions) [26]. Recent developments in the understanding of atmospheric turbulence and dispersion, have led to advances in these models and the creation of second-generation dispersion models such as Atmospheric Dispersion Modelling System (ADMS-Urban) developed by Cambridge Environmental Research Consultant. ADMS-Urban builds on previous models, using updated scientific components which incorporate the most current understanding of the atmospheric boundary layer structure. Within ADMS-Urban, boundary layer structure is more precisely and accurately defined using boundary layer depth. It makes use of the Monin-Obukhov length (LMO), going beyond the Pasquill stability categories. LMO is a parameter defined by heat flux at ground and friction velocity [26, 27]. This allows dispersion characteristics to change with height and therefore the vertical profile of plume concentrations has a skewed normal distribution (turbulence increases initially with height then decreases at the top of the boundary layer) [22]. These features make ADMS-Urban capable of monitoring air quality and simulating the atmospheric dispersion patterns of pollutants from a number of different emission sources, using an array of different models and scales [28], within numerous complex urban settings. This widely applicable model is used in a variety of settings, for example, in the

assessment and review of new legislation and guidelines, planning of new management schemes, and making future predictions [27].

The performance of ADMS-Urban models has been evaluated within a number of studies [29-32]. Comparisons have been made with other dispersion models, field observations and monitoring stations data [29-32]. Despite model performance measures for ADMS continuing to be found satisfactory, pollutant concentrations are consistently underestimated by ~15-30% [29, 30, 32, 33].

The advantages of using atmospheric dispersion modelling are they use emissions data and take into account local topographic and meteorological conditions. However, atmospheric dispersion models as a whole are subject to a number of limitations. First, because environmental exposures are exceptionally complex, assuming a perfect Gaussian dispersion pattern in these environments is over simplistic. Secondly, data acquisition can be problematic and the extensive inputs can be costly. This is a particular issue for emissions data, when the purpose of collection is rarely for research. Thirdly, the great computation power and expertise required to successfully run these models are a major constraint to their use. Fourthly, the temporality of the input data can show considerable variation. For incinerators, emissions data are most frequently recorded on a quarterly basis whereas meteorological conditions are available hourly [23]. This discrepancy leads to the averaging out of modelled outputs thereby increasing the likelihood of errors in estimates. Finally as stated above the model has been found to under-estimate pollutant concentrations by ~15-30% and therefore true exposure concentrations cannot be assumed [29, 30, 32, 33].

1.4.3 Pathways of exposure

The pathways by which MSWI emissions commonly enter the body are displayed in Figure 1.6. The most common of these pathways is direct inhalation of emissions and indirect ingestion through the food chain [34]. It is noted that the primary route of exposure to dioxins is through ingestion (estimated to make up 90% of dioxin exposure [35]) for which the main source of exposure is remote, for example fish consumption. However exposure from MSWIs through ingestion would likely occur through local contamination i.e. foods grown or animals reared near MSWIs. Therefore information on both the location of the MSWIs and, because food consumed is often imported, where food is grown/reared are important factors.

1.5 BIOLOGICAL MONITORING OF DIOXINS

As discussed in section 1.3.4 MSWIs emit a number of pollutants, of which, dioxins are one of the key exposures of concern. This is due to their proportionally large contribution to total atmospheric levels alongside their reported toxicity (discussed in section 1.7). Dioxins are a group name for approximately 75 congeners of PCDD's and 135 PCDF's. Dioxins are widespread persistent organic pollutants generated as one of the end-products of combustion. Although the primary sources of dioxins are anthropogenic, they are produced from a limited number of natural sources such as forest fires and volcanic eruptions.

Dioxins have lipophilic properties that mean that once in the body they accumulate in adipose tissue [35, 36] with each congener possessing a different half-life in the human body. These half-lives are influenced by congener, age, body fat, smoking and breast feeding [37], and estimated at between 7-11 years [35]. Biomarkers of dioxins are detected in blood (serum and plasma) and adipose tissue (within adipose tissue itself and within breast milk). Although dioxin congeners partition from breast milk in a different way to blood [38], studies investigating the relationship between dioxin concentrations in both media show very similar distribution trends. Wittsiepe *et al* [39] reported a Pearsons correlation coefficient of 0.83 for dioxin concentrations measured in breast milk after delivery and bloods during pregnancy among 160 study participants. WHO- toxic equivalency (TEQ) ranged from 2.73 to 55.07pg/glipid base (mean:16.79, median:15.32) in blood and 1.80 to 34.70pg/glipid base (mean:13.84 and median:13.30) in breast milk. Dioxin analysis in blood and breast milk are compared in table 1.4.

Breast milk dioxins levels have been documented in the UK within three studies. The first two were conducted by the Ministry of Agriculture, Fisheries and Food (MAFF) between 1987-88 and 1993-94 and the third, by the University of Leeds which undertook the SUREmilk study between 2001-02 [40]. The first MAFF study recruited 80 women in Birmingham and Glasgow and the second, 60 women in Birmingham, Glasgow and Cambridge. SUREmilk recruited 188 women in North and West Yorkshire. All three studies reported a decreasing trend in dioxin concentrations over time; however, it remains unclear as to whether this decrease was a result of population difference or a true population decline. The Food Standards Agency (FSA) support the conclusion that population levels of dioxins are declining, reporting a reduction in total dietary dioxin intake in adults, schoolchildren and toddlers and also in the proportion of people exceeding the Tolerable Daily Intake (TDI) between 1997 and 2001 [41].

Dioxins stored in women's fat reserves (which make up their lifetime's body burden) are mobilised during milk production and delivered to infants during feeding [40, 42, 43]. Therefore breastfeeding infants are of particular concern because not only do dioxins accumulate in the body, they also accumulate in the food chain. Therefore infants, who are at the top of the food chain i.e. feeding from other humans, are more likely to be exposed to higher dioxin levels. Additionally breast milk for many infants, is their only source of nutrition for a significant period of time and compared to adults they consume a much higher proportion per kilogram of body weight [42, 43]. However it is noted that dioxin levels in breastfed infants are a step down from their mother, with their levels additionally dependent on a number of factors including the volume of milk consumed, efficiency of uptake and susceptibility of the infant.

Current guidance on dioxins in breast milk state that the benefits of breastfeeding outweigh any risk associated with dioxin intake. However these recommendations are both outdated and based on a limited pool of studies. The WHO reported that "*The advantages of breastfeeding far outweigh the potential risks from environmental Pollutants*" [44]; the La Leche League "*Scientific research shows consistently that even in a world exposed to so many chemicals, breastfeeding offers advantages which outweigh the risk of ingesting possible contaminants"* [45]; the Scientific Committee on Food (SCF) " *In this context, the Committee reiterated the conclusions of the WHO meetings on the health significance of contamination of human milk with dioxins and PCBs, namely that the current evidence does not justify altering recommendations on the promotion of, and support for, breast-feeding"* [46] and the US Environment Protection Agency "*Although breast milk appears to be a significant source of dioxin exposure for nursing infants, the overwhelming body of evidence supports the health benefits of breastfeeding despite the potential presence of dioxin*" [47].

1.5.1 A systematic review – Biological monitoring of dioxins from incinerators

Aim and rationale of this review

As detailed above levels of dioxins can be measured in blood and adipose tissue, providing an objective measure of internal dose. In this section all published biomonitoring studies of dioxin emissions from incinerators are synthesised and discussed.

Search strategy and inclusion criteria

Figure 1.7 displays the search strategy undertaken in the MEDLINE database through PubMed and Ovid interfaces until 13th June 2014. Searches were filtered by species, human studies, and language. Papers were additionally screened for three criteria: inclusion of dioxin biomarkers, incineration (all types) defined as the exposure source and finally exposure was non occupational. Despite excluding occupational studies on incinerator workers, the findings of these studies which additionally included non-occupationally exposed participants (often using a comparator population), were included in the review. References of selected articles were also screened for inclusion.

Included papers were grouped according to matrices of biomarker and information on the study aim, design and study findings extracted.

Included studies

Initial searches identified 326 papers, of these 184 were duplicates and 47 met the inclusion criteria, Figure 1.7.

Included papers are described in Tables 1.5 and 1.6. Table 1.5 provides an overview of the identified papers measuring dioxins in blood (plasma and serum) and Table 1.6 in adipose tissue and breast milk. Information on study location, design, study period, number and type of incinerators, population, biological matrix, biomarkers measured, aim and finally dioxin levels measured and study conclusions were extracted.

Dioxins in blood

Table 1.5 provides an overview of the 26 studies in which dioxins from incinerators were monitored in blood. Studies are categorised into those comparing "exposed" and "unexposed" populations to incinerator emissions; exploring levels over time i.e. before and after the operation of an incinerator and investigating population concentration levels.

Comparing "exposed" and "unexposed" populations

Of the 19 papers in which populations were categorised as "exposed" or "unexposed" to incinerator emissions, 15 found no evidence of a difference in blood dioxin levels.

Nine of these papers were non-European conducted in South Korea, Taiwan, USA and Japan. In South Korea no significant difference in blood dioxin levels were detected for populations categorised as exposed compared with unexposed to incinerator emissions, within two studies around industrial waste incinerators (IWI). Both Leem *et al* (2006) and Park *et al* (2004) categorised exposure based on distance from an IWI. Leem *at al* (2006) reported a mean TEQ level of dioxins for subjects within 5 km from the plant at 11.9 pg TEQ/g lipid (n=40), compared with subjects over 20 km away, 11.2 pg TEQ/g lipid (n=20)) [48]. Park *et al* (2004) reported mean TEQ for subjects within 5 km of the plant at 12.2 pg I- TEQ/g lipid (n=40), compared with subjects 7-12 km from the plant, 11.0 pg I- TEQ/g lipid (n=20) [49]. Both studies did however find significantly higher dioxin levels in both groups when compared with a small sample, n=5, of subjects resident in an adjacent agricultural area defined as an area with no industrial activity present (1-6.3 pg I- TEQ/g lipid [48] and 4 pg I- TEQ/g lipid [49]). Similarly these findings have been replicated around two MSWIs in South Korea (subjects near the plants 13.63 pg TEQ/g lipid (n=28); subjects > 10 km from the plant 6.91 pg TEQ/g lipid) [50]. More recently Park *et al* (2013) evaluated the less commonly measured mono- to octa-chlorinated dibenzo-p-dioxin and dibenzofurans and found residents within 300 m from a MSWI had mean dioxin levels of 12.9 pg I-TEQ/g lipid (n=49) compared with 12.6 pg I-TEQ/g lipid (n=11) in residents more than 10 km from the plant [51].

There is a large resource of data on blood dioxin levels from Taiwan, where the Taiwanese Environment Protection Agency have undertaken large scale biomonitoring studies since 1999 [52] around their 19 MSWIs. Within the six identified papers from Taiwan, three explored serum dioxin levels within exposure groups. Exposure was defined by atmospheric dispersion modelled concentrations [52-54]. Each study reported no difference in levels by exposure group in addition to lack of adherence and correlation of serum levels with the dispersion modelled ambient dioxin levels [52, 54]. In a comparison of blood levels by modelled zones, zone A defined as high modelled dioxin levels and zone D low modelled dioxin levels, Chen *et al* 2004 reported that for 1 MSWI levels at site (A) were 12.3 pg TEQ/g lipid (n=24) compared with 13.6 pg TEQ/g lipid (n=19) at (D) [52]; Huang *et al* 2007 for 19 MSWI reported levels at site (A) were 18.7 pg TEQ/g lipid (n=270) compared with 19.6 pg TEQ/g lipid (n=445) at (D) [53].

In Missouri, USA, Evans *et al* (2000) explored exposure to a hazardous waste incinerator (HWI) emissions and reported no significant difference between subjects resident within 4 km of the plant (9.89 pg TEQ/g lipid (n=76)) and subjects in a comparison city (10.29 pg TEQ/g lipid (n=74)) [55].

One of the three studies (four papers) which reported significant differences in blood levels of dioxin between exposure groups was conducted in Japan. Kitamura *et al* (2001) compared blood dioxin levels among residents within 2 km from moderately high dioxin emitting incinerators compared with residents within 2 km from high dioxin emitting incinerators and residents further than 5 km from all incinerators. Dioxin levels were similar between residents over 5 km from incinerators (23.8 pg TEQ/g lipid (n=80)) and those within 2 km from moderately high dioxin emitting incinerators (25.6 pg TEQ/g lipid (n=95)); however, these were both significantly lower than dioxin blood levels for residents within 2 km around high dioxin emitting MSWIs (39.1 pg TEQ/g lipid (n=50)) [56].

Ten of the identified papers were from studies undertaken in Europe. In Portugal, Reis *et al* (2007) found no difference in blood dioxin levels between exposure groups (exposed: 15.8 pg WHO TEQ/g lipid (n=65); control 15.3 pg WHO TEQ/g lipid (n=51)) [57] supported by De Felip *et al* (2008) who conducted a study in Italy around 2 MSWI (MSWI 1:9.3 pg WHO-TEQ/g lipid (n=8) compared with 9.1 & 8.5 pg WHO-TEQ/g lipid (n=20); MSWI 2: 8.6 pg WHO-TEQ/g lipid (n=8) compared with 8.0 pg WHO-TEQ/g lipid (n=9)) [58]. Further Frery et al (2012) reported a geometric mean of 13.7 pg WHO-TEQ/g lipid (n=1030) across all subjects with no differences between residents living near the 3 MSWI incinerators and those living far [59].

The second study reporting significant differences between blood dioxin levels by exposure group was undertaken in Slovakia by Chovancova *et al* 2012. Dioxin serum concentrations among residents of communities near incinerators were substantially higher, 15.4 pg WHO-TEQ/g lipid, n=81, compared with residents in comparator villages, 9.4 pg WHO-TEQ/g lipid, n=45 [60]. This finding was supported by the third study (published within two papers) which reported higher blood dioxin levels for residents near incinerators. Fierens *et al* (2003) and (2007) found 50% higher blood dioxin levels among residents within 2 km of one of the two MSWI studied (MSWI 1: 37.9 pg TEQ/g lipid (n=51)) compared with a reference population of residents in villages within rural areas with no known local sources of pollution (23.9 pg TEQ/g lipid (n=63)) [61, 62].

In Spain the first study to compare blood dioxin levels for residents near an MSWI detected no difference in levels between those living 0.5-1 km from the MSWI (13.5 pg I-TEQ/g lipid (n=104)) and those 4 km (13.4 pg I-TEQ/g lipid (n=97)) in 1995 (16.7 pg I-TEQ/g lipid (n=96) and 1999 (16.7 pg I-TEQ/g lipid (n=91)) [63]. Zubero *et al* 2009 and 2011 supported these findings, reporting residents in zones near the MSWI in 2006 and 2008 (26.88 pg WHO-TEQ ,20.83 pg WHO-TEQ/g lipid respectively) had no significant differences in blood dioxin levels for

residents far from the MSWI (20.02 pg WHO-TEQ/g lipid in 2006 and 26.36 pg WHO-TEQ/g lipid in 2008) [64, 65]. The most recent study also defined exposure based on distance to the plant and supported previous findings. Parera *et al* 2013 found no difference in blood dioxin levels in 2008 for residents living within 1 km of the plant (14.6 pg I-TEQ/g lipid (n=68)) compared with residents greater than 3 km from the plant (12.6 pg I-TEQ/g lipid (n=94)) and residents approximately 11 km from the plant (14.5 pg I-TEQ/g lipid (n=86)) [66].

Temporal changes in blood dioxin levels

Another common study design was to compare blood levels of dioxins over time, usually before and after an incinerator became operational.

Four of the five studies with this design were included in the above section thus providing a comparison of dioxin blood levels between exposed and unexposed populations. Evans *et al* (2000) conducted a temporal analysis of dioxin blood levels across three blood samples, one prior to the HWI operating (11.8 pg TEQ/g lipid (n=67) or 10.82 pg TEQ/g lipid (n=61)), one five months later (9.61 pg TEQ/g lipid (n=67) or 11.63 pg TEQ/g lipid (n=61)) and one six months following the previous sample collection (8.21 pg TEQ/g lipid (n=67) or 9.05 pg TEQ/g lipid (n=61)). Significantly lower blood dioxin levels were observed after the HWI became operational for both study and comparison groups [55]. A decrease was not detected in a second study by Zubero *et al* (2009) and (2011) in which blood dioxin levels were compared 1 year (23.45 pg WHO-TEQ/g lipid (n=322)) and 4 years (overall 23.60 pg WHO-TEQ/g lipid(n=326)) after a MSWI was commissioned [64, 65]. Further Gonzalez *et al* (2000) and (2001) reported contradictory results to the two previous studies with an increase in blood dioxin levels over three blood samples 2 years apart for both exposure groups. Blood dioxin levels among residents between 0.5-1.5 km from the MSWI were measured in 1995 (13.5 pg I-TEQ/g lipid (n=104)), in 1997 (16.7 pg I-TEQ/g lipid (n=93)) and finally in 1999 (19.4 pg I-TEQ/g lipid) compared with residents 3-4 km from the plant in 1995 (13.4 pg I-TEQ/g lipid (n=97)), in 1997(16.7 pg I-TEQ/g lipid (n=91)) and 1999 (19.2 pg I-TEQ/g lipid) [63, 67]. Parera *et al* (2013) also included a temporal analysis of blood dioxin levels between 1995-2012, obtaining 7 samples for subjects in both the exposed (residents within 1 km from the MSWI) and control groups (residents greater than 3 km from the MSWI or in a village ~11 km from the MSWI). In all groups blood dioxin levels increased from 1995 to 1999 (1995-exposed: 13.0 pg I-TEQ/g lipid, control: 13.1 pg I-TEQ/g lipid; 1997-exposed: 15.9 pg I-TEQ/g lipid, control: 16.4 pg I-TEQ/g lipid), followed by a slight decrease from 1999 to 2002 (1999-exposed: 17.8 pg I-TEQ/g lipid, control: 18.1 pg I-TEQ/g lipid; 2002-exposed: 15.1 pg I-TEQ/g lipid, control: 18.2

pg I-TEQ/g lipid) and from 2002 to 2008 levels remained stable (2005-exposed: 11.7 pg I-TEQ/g lipid, control: 12.3 pg I-TEQ/g lipid; 2008-exposed: 14.6 pg I-TEQ/g lipid, control: 12.6 pg I-TEQ/g lipid) [66].

One further study explored temporal trends in blood dioxin levels for residents living near the first HWI in Spain. Residents were monitored from 1998 (a year before the HWI was constructed) until 2012 with blood samples taken a year before operation [68], and then at 3 [69], 8 [70]and 13 [71] years after construction. This study found significant reductions in concentrations over this time period, and by 2012 reported a statistically significant 77% reduction in levels from the baseline (1998: 27.0 pg I-TEQ/g lipid (n=20); 2002: 15.7 pg I-TEQ/g lipid (n=20); 2007: 9.36 pg I-TEQ/g lipid (n=20); 2012:6.18 pg I-TEQ/g lipid (n=40)).

Population dioxin levels & all other studies

As shown in table 1.5 there are a wide range of study aims for papers exploring dioxin levels from incinerators in blood. These have included; studies exploring population levels of blood dioxins (53 pg TEQ/g lipid (n=13) [72]; 35.0-42.7 pg WHO-TEQ/g lipid (n=2) [73]; 23.9 pg I-TEQ/g lipid (n=68) [74], 0.81 pg TEQ/g lipid (n=15) [75], 21.52 pg I-TEQ/g lipid (n=22) [76]; 13.7 pg I-TEQ/g lipid (n=16) [77], 53.4 pg I-TEQ/g lipid (n=10) [77]; 6.60 pg TEQ/g lipid (n=75) [78]; 74.6 pg TEQ/g lipid (n=10) [79]), studies comparing blood dioxin levels among residents living near different industries [74, 77], studies comparing blood dioxins in populations and workers [75, 76, 78], studies exploring the relationship blood dioxins have with diet [80, 81], studies investigating associations with biochemical processes [82, 83] and finally studies using biomonitoring as an exposure assessment method [84].

Dioxins in adipose tissue and breast milk

Studies exploring internal doses of dioxin from incinerators in adipose tissue and breast milk were far less frequent. Table 1.6 provides an overview of the 6 studies, reported in 11 papers, which have included either alone or amongst other matrices a measure of dioxin from incinerators in adipose or breast milk.

Overall there was no evidence of differences in breast milk dioxin levels with distance from incinerators. Reis *et al* (2007) found no difference in milk dioxin levels in subjects resident within 5 km from 2 incinerators (9.5 pg WHO-TEQ/g milk fat (n=73)) compared with residents greater than 5 km away (9.1 pg WHO-TEQ/g milk fat (n=108)) in Portugal [85]. Deml *et al* 1996

reported breast milk dioxin levels for residents within a district with a MSWI to be within background levels in Germany (12.4 pg TEQ/g lipid (n=7)) [86]. A much larger study of 240 Japanese women investigated the relationship between breast milk dioxins and distance to public waste incinerators and industrial waste incinerator (IWI). This study reported a mean concentration of 14.9 pg TEQ/g milk fat and found no correlation between milk dioxin levels and distance to plants (correlation coefficient 0.06) [87]. The authors noted that although no correlation was detected the study did not consider four key variables which may contribute to the internal dose of dioxins: wind direction, concentrations of dioxin emissions, additional environmental dioxin sources and short term maternal migration [87].

One study reported dioxin levels in abdominal adipose tissue of autopsied subjects. Three samples were collected between 1998-2007, one during construction of Spain's first HWI, one at 3 and 9 years after the plant became operational. A significant decrease in dioxin levels was observed between the first (40.1 pg WHO-TEQ/g fat (n=15)) and second sample (9.89 pg WHO-TEQ/g fat (n=15)) and then a non-significant increase at the third sample (14.6 pg WHO-TEQ/g fat (n=15)) [88-90].

Parera *et al* (2013) undertook a temporal analysis of blood dioxin levels between 1995-2012 but further collected and measured dioxin levels in breast milk samples in the last two sampling rounds, 2008 and 2012. In 2008 breast milk levels were reported as three times lower than blood levels (4.5 pg WHO-TEQ/g milk fat (n=46)) and four times lower in 2012 (3.1 pg WHO-TEQ/g milk fat (n=45) [66].

Finally Schuhmacher *et al* (1999) (2004) (2009) (2013) undertook a temporal analysis of breast milk dioxin levels in residents near the first HWI in Spain, as per the studies by Schumacher *et al*, Agramunt et al and Nadal *et al* discussed above in which dioxins were measured in blood [68-71]. Samples were collected during construction and then 3, 8 and 13 years after operation. Compared with levels during construction, at each time point breast milk dioxin levels were significantly reduced, all in accordance to the reductions seen in blood dioxin levels (1998:12.2 pg WHO-TEQ/g milk fat (n=15); 2002: 10.6 pg WHO-TEQ/g milk fat (n=15); 2007: 7.6 pg WHO-TEQ/g milk fat (n=15); 2012: 4.8 pg WHO-TEQ/g milk fat (n=20)) [91-94].

Summary and implications

The body of evidence in which dioxins from incinerators are biologically monitored in blood is much greater than in adipose tissue or breast milk. Overall there is limited evidence for a

relationship between blood dioxin levels and residential distance to an incinerator, conflicting findings on temporal trends in these levels and large variation in dioxins levels between areas and countries.

Although the evidence for dioxin exposure near incinerators is weak, this evidence is heavily weighted by studies in blood and by those in non-European countries with limited numbers of participants. With the number of incinerators in Europe likely to increase, and the toxicity of dioxins clearly established, there is a clear need for multi-site European studies exploring dioxin levels within adipose tissue around modern incinerators. Thereby broadening the limited body of evidence applicable to current European incinerators, within a biological material that can be collected uninvasively and in which dioxins can be detected at lower concentrations.

1.6 EPIDEMIOLOGICAL STUDIES INVESTIGATING HEALTH EFFECTS ASSOCIATED WITH INCINERATION

1.6.1 An overview of the evidence – Incineration and all non-birth related health outcomes

The body of epidemiological studies exploring adverse health effects associated with waste incineration has been reviewed a number of times [2, 4, 18, 19, 95-101]. The health outcomes explored include cancers, respiratory problems and illnesses, skin diseases and reproductive and birth outcomes. Mostly these reviews provided an overview of all health effects [2, 95-98, 100, 101], whereas the supporting reviews for the COC and Health Protection Agency (HPA) statements are limited to cancer alone [18, 19, 99].

Studies exploring the risk of "all cancers" among residents living near incinerators have produced conflicting results [102, 103]. The larger of the two studies by Elliott *et al* (1996) explored the incidence of cancer for over 14 million UK residents near 72 incinerators and found a statistically significant increase in risk of cases of "all cancers" associated with proximity to a MSWI. However, they reported that socioeconomic factors among residents living near incinerators needed to be taken into account and suggested that residual confounding could not be excluded as an explanation for study findings. Elliott *et al* (1996) additionally reported excess risks of lung, colorectal, stomach and liver cancer. These results were not supported by a more recent Italian study which explored all cancer risk [103]. For lung cancer these findings have been supported [104] and contradicted [103, 105]. Similarly liver cancer

risk has shown conflicting results [102, 103, 106, 107], with fewer studies exploring colorectal and stomach incidence. Cancer of the larynx also showed conflicting results [105, 107], whereas childhood cancer patients were found to be more likely to migrate away from incinerators suggesting the possibility of carcinogenic risks near incinerators [108]. Both differences in risk with distance and clustering around incinerators have been found for soft tissue sarcoma [109] [110] [111] and non-Hodgkin's lymphoma risk [109] [112] [113], with no risk evident for breast cancer [114]. The findings for soft tissue sarcomas are of particular interest because increased risk has been associated with dioxin exposure for example following the Seveso accident (chemical factory incident which occurred in Italy in 1976).

Additionally, for respiratory health, three studies have reported no association for residence near incinerators [115-118], whereas two studies have reported a positive association [119, 120].

Overall, the current weight of evidence does not support any clear relationships between exposure to incinerator emissions and all non-birth related health outcomes, with large inconsistencies in study findings and positive associations additionally showing small increases in risk related to older generation incinerators.

1.6.2 A systematic review – Incineration and birth & neonatal outcomes

Aim and rationale of this review

As outlined above, the association between incineration and cancer has been widely studied and reviewed. However questions on the potential risk of adverse birth outcomes associated with incineration are largely unaddressed, despite having the advantage of 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.

The aim of this systematic review is to summarise and critically examine the current evidence base on the association between incineration and birth and neonatal outcomes, thus providing an up to date overview of current knowledge at the same time as identifying any short-comings in the literature in order to identify recommendations for future work. The findings of this review have been published in Environment International [4] **(Appendix A).**

Search strategy and inclusion criteria

Peer reviewed papers were searched for in the MEDLINE database through PubMed and Ovid interfaces using the search strategy outlined in Figure 1.8 until 6th June 2014. Searches were conducted using both key words and MESH terms and identified papers screened twice; first based on title and abstract and second on the full text. Figure 1.8 also outlines the inclusion criteria by which papers were included in the review. Included papers were: (1) human studies (2) written in English (3) examining birth or neonatal outcomes and (4) incineration (all types) defined as the exposure source. Additionally, references of selected articles and existing reviews were screened for inclusion.

Included papers were grouped according to birth outcome and information on the study design, exposure assessment method alongside study findings extracted. In order to assess the quality of the identified papers a checklist was developed. This included items reported in the Strengthening the Reporting of Observational Studies in Epidemiology statement (a criteria developed to assess the reporting and general standard of studies) [121, 122] and was divided into four items reflecting what was deemed most important for study quality i.e. areas with greatest potential for uncertainty. The maximum score achievable was 17, split into the items; study design (5 points), quality of health data (2 points), control for potential confounding (3 points) and exposure assessment (7 points) (often referred to as the 'Achilles heel' of environmental epidemiology [123, 124]).

Included studies

A total of 16 papers met the inclusion criteria, which were selected from the initially identified 205 papers (Figure 1.8).

These papers are described in tables 1.7 and 1.8, of which table 1.7 provides an overview of the health outcomes investigated, study design, participants, exposure assessment methods and adjustment for confounders and table 1.8 the main findings. The quality scores assigned to each study are presented in table 1.9.

Birth outcomes

Of the 16 included studies, eight examined congenital anomalies [125-132] of which one additional included spontaneous abortions [132] and one stillbirths and neonatal deaths [128];

three examined twinning [133-135]; four examined fetal growth [136-139] as well as multiple births [136], neonatal, infant and spontaneous deaths [139], sex ratio at birth [136, 138, 139], preterm delivery [136-138]; and one examined sex ratio only [140].

Congenital anomalies

Of the five studies examining the association between all congenital anomalies and incineration [125, 127, 128, 131, 132] only one, Dummer *et al* (2003), reported a significant association.

Two of the five studies were published by the same first author in two consecutive years. Both studies were undertaken around one MSWI in Northern Italy and defined areas of increasing exposure according to dispersion modelled concentrations of dioxins [131, 132]. The first study by Vinceti *et al* (2008) was a cohort (Quality=8) that found no excess risk of births with major congenital anomalies for mothers resident in areas near the incinerator classified as high/ intermediate exposure compared with those resident in the municipal (Relative risk [RR] 0.64; 95% Confidence Interval 0.20-1.55) [132]. Vinceti *et al* (2008) additionally investigated the risk of major congenital anomalies for mothers working near the incinerator and based on 3 cases, found a large excess risk (RR 2.26; 0.57-6.14). The very small number of cases of both residents (n=4) and workers (n=3) is reflected in the wide confidence interval for both risk estimates (table 1.5). The second study, a population based case-control (Quality=11) by Vinceti *et al* (2009), reported a non-significant excess risk of major congenital anomalies for mothers living in areas classified as medium/high exposure (RR 1.11; 0.60-2.04) [131].

One of the remaining three studies identified reported findings consistent with Vinceti *et al* (2008 and 2009). Cordier *et al* (2004) undertook a multi-site geographic study around 70 MSWIs in South Eastern France (Quality=10). The exposure status of 2,872 communities (<50,000 inhabitants) was defined by "immission" scores calculated using dispersion modelled ambient concentrations of pollutants multiplied by the number of years the MSWI was in operation. Cordier *et al* (2004) found no difference in the rate of all major congenital anomalies for those in the exposed communities compared with unexposed communities.

The remaining two studies were both UK based and used distance to incinerators as a proxy for exposure [127, 128]. Dummer *et al* (2003) conducted a retrospective cohort study (Quality=9) and reported a continuous odds ratio [OR] of 1.10 (1.03-1.19) for lethal congenital anomalies for mothers resident near four industrial and domestic incinerators compared with the odds of living 3 km or further (continuous OR calculated as $OR^{1/(D+0.1)^2-1/3.1^2}$, where D is the distance

from the incinerator). Therefore the risk of lethal congenital anomalies for mothers' resident at 500 m from any of the four incinerators compared with that at 3 km or further would be 1.3, i.e. 30% increased risk. The second, a geographic study by Cresswell *et al* (2003) (Quality=6) found no significant association between risk of major congenital anomalies (RR 1.11; 0.96-1.28) 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.

Three of these five studies additionally investigating broad groups of anomalies [125, 128, 131], within which two reported significant increased risks [125, 128]. While Cordier *et al* (2004) (Quality=10) reported no increase in risk of all anomalies, for specific congenital anomalies exposed communities were found to be at greater risk of facial clefts (RR 1.30; 1.06-1.59) and renal dysplasia (RR 1.55; 1.10-2.20) compared with unexposed communities. Additionally, within the exposed communities a dose response trend in risk of obstructive uropathies was found. Dummer *et al* (2003) (Quality=9) subcategorised lethal congenital anomalies into congenital heart defects and neural tube defects and reported significant continuous odds ratios for neural tube defects (OR 1.13; 1.04-1.23, OR 1.39 at 0.5 km compared to 3km or further), spina bifida (OR 1.17; 1.07-1.28, OR 1.52 at 0.5 km compared to 3km or further) and congenital heart defects (OR 1.12; 1.03-1.22, OR 1.35 at 0.5 km compared to 3km or further). However, 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 (although only a small numbers of cases were included for these rare defects) (table 1.5).

Another three studies focused on single anomalies [126, 129, 130], two of which reported significant increased risk [126, 130]. Two studies investigated the association between refuse and chemical incinerator emissions and orofacial clefts with conflicting results [129, 130]. 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 [130]. 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, with the birth prevalence never exceeding 2.3 per 1000 births and an average of 1.2 per 1000 births. The second study was undertaken in response to a cluster of orofacial clefts at a maternity clinic in the county of Skaraborg in Sweden (Quality=2). Jansson and Voog (1998) found no increase in the rate of orofacial clefts after a refuse incinerator was commissioned within the study area investigated [129]. The third

study substantially improved on all preceding studies in terms of its study design, exposure assessment and adjustment for potential confounders. Cordier *et al* (2010) undertook a population based case-control (Quality=14) study surround 21 MSWIs in the Rhone-Alpes region in southeastern France. Cordier *et al* (2010) assigned individual level exposure estimated using a combination of dispersion modelled concentrations of pollutants and information on individual risk factors collected during interviews of 62% of the participants. Cordier *et al* (2010) 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 [126].

Fetal growth and preterm birth

Three studies examined the relationship between incineration and birth weight [137-139], with two of the three reporting no association [138, 139]. The first study by Tango *et al* (2004) (Quality=7) was a multi-site study in which distance, in 1 km concentric rings, was used as a proxy for dioxin exposure. The 63 "high dioxin emitting" MSWIs included in this study were selected because high soil dioxin measurements, above 80ng TEQ/m^3, where taken 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 its 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) during two periods, one year before the incinerator began operating and six years following. No increased risks were reported by either Tango *et al* (2004) or Lin *et al* (2006). However, the third study by Castello *et al* (2013), an ecological study in Spain, found that mothers resident in municipalities within 3.5 km radius of the industrial activity named "non-hazardous waste" (installations for the incineration of non-hazardous waste) compared with mother resident in municipalities with no industries had significant higher risk of very low birth weight (LBW) (RR 1.13; 1.01-1.25) and moderate LBW (RR 1.05; 1.00-1.10) [137].

An additional measure of fetal growth small for gestational age (SGA) - was explored in two studies [136, 137] in which both defined SGA as babies with birth weights below the 10^{th} percentile for their given gestation week and sex. Castello *et al* (2013) reported a 6% increase in risk of SGA (RR 1.06; 1.02-1.11) based on mothers residence near a "non hazardous waste" installation at birth. Whereas the study by Candela *et al* (2013) in which particulate matter was modelled from 8 incinerators in northern Italy and individual mothers assigned exposure

quintiles based on their residency during pregnancy, reported no association was reported [136].

Lin *et al* (2006), Candela *et al* (2013) and Castello *et al* (2013) also investigated the risk of preterm delivery (PTD). Lin *et al* (2006) found a non-significant increase in the risk for mothers' resident in areas of highest exposure (estimated from modelling) to dioxins and furans concentrations, >0.05pg 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. Castello *et al* (2013) found no excess risk PTD, whereas Candela *et al* (2013) reported a significant increase in risk with increasing modelled exposures for both PTD (OR 1.30; 1.08-1.57) and very PTD (OR 2.19; 1.24-3.85).

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

No associations were reported between incineration and stillbirths [128] or neonatal deaths [128, 139] although the evidence base remains very sparse. Tango *et al* (2007) (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 at 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 [132, 139].

Twinning

The frequency of human twinning in areas potentially exposed to incinerator emissions was explored within three geographic studies, one in central Scotland [133] (Quality=6), one in Hesse Germany [141] (Quality=6) and one in Emilia-Romagna Region of Italy (Quality= 12). Two studies reported that areas with a 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). The third study found an increase in risk of multiple births for mothers resident in areas with high modelled exposure to incinerator emissions [136]. A fourth study (Quality=6) explored spatial and temporal clustering of twins near 14 refuse incinerators in Sweden [135], found no clustering of twinning overall, although there was a significantly higher rate of twin deliveries surrounding one incinerator and a lower rate around another.

Sex ratio at birth

Four studies included an analysis of sex ratio at birth [136, 138-140]. 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 [140].

Study design

Within the 16 included studies there was a great variety in study design. Two studies were case-control [126, 132], three cohort [128, 130, 131], of which one was a hospital based retrospective cohort [130], and eleven geographic [125, 127, 129, 133-140].

Health data

With one exception [130], all studies examining congenital anomalies used data from national birth registries or birth defects registries. As the quality and completeness of nationally collected birth data is often poor this provides a potential source of bias, particularly because incomplete data is unlikely to be randomly distributed, e.g. certain hospitals/registries collect more detail on certain anomalies. Of the studies examining congenital anomalies all included cases among live and stillbirths, however only five [125, 126, 131, 132, 142] incorporated information on cases from medical terminations or abortions. Without terminations an additional source of bias is included. This is because the decision to have a medical termination is heavily dependent on the presence, type and severity of congenital anomalies. Of the 189,100 legal medical terminations in England and Wales in 2009, 2,085 (1%) were justified under grounds E ("*there is substantial risk that if the child were born it would suffer from such physical or mental abnormalities as to be seriously handicapped* [143]*).* Under this ground, 86% of the terminations performed were justified due to the diagnosis of congenital malformation, deformations or chromosomal abnormalities.

Confounding

Potential confounders most commonly accounted for within the identified studies were maternal age [125, 131, 134-136, 138, 139] and surrogate measures of socio-economic status

(SES) [125, 127-131, 136-139] including; educational attainment, family income and parental occupation. Some of these measures will reflect SES better than others.

None of the reviewed studies explained how these confounders were related to exposure. Without this relationship these cannot be construed as true confounders but merely consititute additional risk factors for the birth outcomes. It is however known that the population living near incinerators tends to be more deprived than the general population.

As teratogenic effects associated with environmental exposures tend to be small, it is essential that all possible confounders are taken into account.

Exposure assessment

Cordioli *et al* (2013) provides a comprehensive overview of the exposure assessment methods used within all epidemiological studies on incineration [144], whereas the section below focuses on studies on birth and neonatal outcomes only. The included studies varied in the; (1) number of incinerators included: six single site [127, 130-132, 134, 138] and nine multi-site [125, 126, 128, 129, 133, 135, 136, 139, 140] ranging from two to 70 incinerators; (2) the type of incinerators, including; refuse, chemical, toxic waste and MSWI, with some studies not specifying type; (3) the time period within which the study occurs; 1956-2010; (4) Exposure assessment methods, ranging from those using distance to the incinerator as a proxy for ambient exposure to incinerator emissions in eight studies [127-130, 134, 135, 137, 139] to modelling exposures in six studies [125, 126, 131, 132, 136, 138] (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, distance is highly correlated with modelled exposure estimates [145]. Any inaccuracy and imprecision of such methods and resultant exposure misclassification would most likely lead to the attenuation of any present associations. None of the reviewed studies included measured exposure levels or biomonitoring data as a method of exposure assessment or additionally validated exposure models.

As well as exposure assessment methods there are a number of additional considerations to take into account when assessing exposure from incinerators. Overall these were not well addressed within the epidemiological evidence. These include consideration of: multiple sources − six studies acknowledged and discussed the issue of multiple exposure sources [125, 126, 131, 136, 138, 140], but only Cordier *et al* (2004) and (2010) identified and assessed

exposure to other sources of dioxins within their study population; multiple pollutants – eight studies used aggregate exposure measures, e.g. distance from source [127-130, 134, 135, 137, 139], two other studies used distance with additional information such as wind direction and dioxin soil concentrations [133, 140]and six studies modelled incinerator emissions [125, 126, 131, 132, 136, 138]; different routes of exposure – only one study accounted for dietary intake [126] which is the main route of dioxin exposure exposure period – three studies [126, 131, 136] 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 [146]; and maternal migration – three studies [126, 132] considered residential history during the study period, thereby taking into account changes in exposure status, and only one study [131] 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.

Quality assessment

Using the quality checklist (table 1.9), the studies' overall quality scores ranged from 2 to 14, with a mean of 7.75. The seven studies scoring above the mean [125, 126, 128, 131, 132, 136, 138] reported incineration to be significantly associated with facial clefts [125], urinary tract anomalies [125, 126], lethal neural tube [128], lethal heart defects [128] and PTD [136]. These studies found no associations with all congenital anomalies combined, stillbirths and neonatal deaths, spontaneous abortions, LBW, SGA, multiple births and sex ratio [125, 128, 131, 132, 136, 138]. 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 [126].

Summary and implications

Review of the epidemiological literature found that evidence for an association between incineration and adverse birth outcomes as a whole appears to be limited. Specifically there is no evidence of a relationship with twinning, LBW, stillbirths, sex ratio and all major congenital anomalies combined. However a few of the better quality studies have pointed towards weak

associations with neural tube and heart defects, with stronger associations for facial clefts and urinary tract defects and PTD.

The inconsistent findings of this limited pool of studies with considerable variability in design and outcomes explored and with much of the evidence based on crude exposure assessment methods, means that attempting to draw firm conclusions is difficult. The main gaps in the current body of literature relate to the use of poor exposure assessment methods and there is a distinct need for more sophisticated exposure models and, preferably, individual level biomontoring of exposure to help better understand this field of research.

With the number of incinerators likely to increase and growing potential population exposure to MSWI emissions the evidence needs to be clearer.

1.7 TOXICOLOGICAL EVIDENCE – DIOXINS

This section reviews what is known from human studies, and in more detail from animal studies, on ability of dioxins to induce adverse reproductive effects. This is followed by a short summary of the potential biological mechanisms by which dioxins might cause toxicity.

1.7.1 Introduction

The distribution and number of chlorine atoms within the dioxin congener 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) characterises it as the most toxic and consequently it has been most comprehensively studied [147]. In 2001, a joint report from the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT), the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment and the COC reported that 2,3,7,8-TCDD "*should be regarded as a probable human carcinogen*"[148]. Evidence exploring the toxicological profile of all dioxins remains focused on this congener assuming other less toxic congeners show similar toxicity at higher doses. Dioxins have been evaluated and their Tolerable Daily Intake (TDI) assessed on a number of occasions, most recently by COT [148] but additionally by the WHO [149], the Scientific Committee on Food (SCF) [150] and the US Environmental Protection Agency (EPA) [151]. These international evaluations are constantly revised in order to account for newly published studies, which more recently have investigated the effects of dioxin exposure on the developing fetus (animal studies).

Scientific literature on the toxicity of dioxins is largely focused on the health effects seen in adults exposed to high doses. More recently, animal studies have begun to explore the vulnerability and sensitivity of the developing fetus to exposure. This has led to the re-evaluation of TDIs based on the level at which no adverse effects were observed and the lowest level at which these effects were observed. For example, WHO's assessment of human TDI was lowered from 10 pg WHO-TEQ/kg bw to 1-4 pg WHO-TEQ/kg bw [35]. Other recommending bodies have specified similar TDI for example the SCF established a tolerable weekly intake (TWI) of 14 pg WHO-TEQ/kg bw [150] and the COT recommended a TDI of 2 pg WHO-TEQ/kg bw per day [36].

1.7.2 Human studies

The toxicity of dioxins to humans is not well characterised in epidemiological studies. To date these have been restricted to studies of health effects seen in adults exposed to high doses occurring primarily from occupational exposure or exposure to contamination incidents. Well known contamination incidents include the chemical factory incident in Seveso, Italy in 1976, and contamination of rice oil in both Yusho, Japan (1968) and Yu-Cheng, Taiwan(1979) [35, 37]. Related to these incidents human studies have shown reductions in birth weight among children exposed to contaminated cooking oil in Yu-Cheng [152], changes in sex ratio, with statistically significant excess of female offspring (48 females compared to 26 males, low sex ratio) for births occurring in an area with high concentrations of 2,3,7,8-TCDD in soils after Seveso, between 1977 (9 months following the incident) and 1984 [153]; parental and paternal dioxin serum levels were significantly associated with low sex ratio [154] indicating that if both parents or a father were exposed to 2,3,7,8-TCDD, they had a significant excess of female offspring (low sex ratio).

Due to the lack of evidence of dioxin toxicity in human studies, animal studies have been reviewed in detail. Animal studies were used for a number of reasons; firstly, exposure to dioxins in human studies tended to occur via a single high dose exposure to a mixture of pollutants. This type of exposure does not represent the long term low level exposure that would be experienced from incineration. Secondly, exposure assessment within these studies was consistently poor, with the specific effect of dioxins impossible to distinguish from other pollutants. Thirdly, the most sensitive population and health endpoints, such as fetal effects, are not represented within these studies. Finally, in general human studies lacked information on

the design, confounders and potential sources of bias. Most of these issues can be addressed in animal studies [36].

Although human studies were not reviewed in depth, it was noted that a number of studies supported the association between dioxin exposure and changes in sex ratio [153, 154] and risk of retarded fetal growth [152, 155]. These reproductive endpoints were of particular interest as they were not clearly reflected in animal studies [156-158].

1.7.3 Animal studies

The limitations of human studies, have led to a much wider body of animal research providing a comprehensive overview of how dioxin exposure affects fetal health. Table 1.10 provides an overview of the animal toxicological studies exploring the relationship between 2,3,7,8-TCDD exposure and the following reproductive endpoints: fetal growth, structural malformations and permanent effects on the male and female reproductive system. Papers were selected from international reviews[36, 159, 160], the Agency for Toxic Substances and Disease Registry; Toxicological profile for dioxins[161] and additionally from PubMed and Embase databases, using the MeSH terms “tetrachlorodiobenzo/toxicity” and “prenatal exposure delayed effects”.

Structural malformations

In mice, exposure to 2,3,7,8-TCDD has been shown to induce a number of teratogenic responses. The structural abnormalities most commonly observed are cleft palate and hydronephrosis [162]. These sensitive indicators of toxicity are shown at doses lower than doses capable of maternal and fetal toxicity [163-174]. Similar studies on other laboratory animals rarely show these abnormalities and when seen, only occur at doses sufficiently high that overt signs of maternal and fetal toxicity are evident. As shown in table 1.10, Olson and McGarrigle demonstrated that at sufficiently high doses, Syrian Hampsters and Holtzman Rats show an increase in incidence of cleft palate for both species and hydronephrosis for hampsters. Fetal toxicity was clearly observed at high dose, with 58-72% fetal mortality, reduced thymus and spleen weights and rats showing gastrointestinal haemorrhaging [175]. These findings support the hypothesis that fetuses are highly sensitive to dioxin toxicity, with palatal and kidney tissue being particularly sensitive. This is clear from toxicological studies on mice while the relatively insensitive hampsters also display substantial signs of fetal toxicity.

Note that the induction of terata from 2,3,7,8-TCDD exposure, occurs when only a very small fraction of the maternally administered dose can be detected in the kidney and palate tissue in mice and rats. Three days post exposure, Abbott *et al* reported approximately 0.02-0.03% of the total dose detected in the fetus [176, 177] and between 0.002-0.003% in the palate and kidney fetal tissue [177].

Hydronephrosis is repeatedly reported at lower doses of dioxin exposures than those sufficient to induce cleft palate. This indicates that the kidneys of mice, rat and hampsters are more susceptible to dioxin toxicity than the palatal shelves. This is clearly demonstrated by Birnbaum *et al*, when the offspring of pregnant C57BL/6N mice showed significantly increased incidence of hydronephrosis at and above a dose of 6μg/kg, whereas cleft palate required 9-12μg/kg [164]. At the same dose, incidences were much greater for hydronephrosis, 92%, compared to cleft palate, 21%. The heightened sensitivity of the urinary tract compared to the palate was further explored by Couture *et al.* Their results further supported previous findings, revealing hydronephrosis presenting at a dose as low as 3μg/kg, whereas cleft palate required a dose of 12μg/kg for a significant increase in incidence [178].

Cross fostering studies (offspring transferred after birth to surrogate parent) show hydronephrosis can be induced when exposed prenatally (*in utero*) and postnatally (lactational) [169, 179]. The incidence and severity of hydronephrosis occurs preferentially in the right kidney [165, 169, 171, 173, 174, 179], with better recovery post exposure in the left kidney [179].

The toxicological evidence indicates that cleft palate has a clear dose-response relationship with 2,3,7,8-TCDD exposure [164-166, 169-173]. It is additionally shown that this relationship exists between gestational day (GD) 6-12 (when palatal shelves are fusing), whereas no increase incidence is observed after GD 14. This steep dose response relationship means that a small change in dose could potentially alter the incidence of cleft palate enormously. Weber *et al* shows that increasing the dose of 2,3,7,8-TCDD by 1.8 times, increases the incidence of cleft palate approximately nine fold in mice [173]. This critical window of exposure for cleft palate, with a peak sensitivity at GD 12, was not observed for hydronephrosis [178], as the amount of kidney damage and the extent of the lesion did not alter with dose. The authors suggested that this may be indicative of a saturation effect for hydronephrosis in response to 2,3,7,8-TCDD exposure.

The pathogenesis of 2,3,7,8-TCDD induced hydronephrosis was first investigated by Abbott *et al* using C57BL/6N fetal mice. They concluded that 2,3,7,8-TCDD exposure induced hyperplasia of epithelial cells, blocking the ureteric lumina, leading to the build-up of urine in the kidney, defined as hydronephrosis [180]. Subsequently, the mechanism by which 2,3,7,8-TCDD induces cleft palate in mice was investigated. Abbott and Birnhaum found exposure to 2,3,7,8-TCDD changed the course of differentiation of medial epithelial cells, resulting in fully grown palatial shelves which fail to fuse [181].

It is clear that 2,3,7,8-TCDD exposure interferes with the normal development of organs, however, these effects are both tissue and species specific. Amongst mice, Silkworth *et al* demonstrated that the dose required to induce cleft palate among DBA/2J is twice that required for C57BL/6J and further for a similar incidence of hydronephrosis, DBA/2J mice require 8 times this dose [171]. Although the biological response of the palatal shelf does not vary between species, the dose at which these alterations are seen is very variable. The susceptibility of palatal shelves of humans is thought to be similar to the rat and therefore the dose required to initiate these malformations are approximately 200 times greater than for the mouse. At this dose, human maternal and fetal toxicity would be evident [182].

Six studies [166, 167, 169, 175, 183, 184] have shown, in addition to hydronephrosis, standalone increases in other kidney malformations. Four [166, 169, 183, 184] early studies did not define the observed kidney anomalies as hydronephrosis, although descriptions of the anomalies are similar. Olson *et al* reported that Syrian Hampsters exposed to 2,3,7,8-TCDD had increased kidney abnormities in addition to hydronephrosis [175]. One study showed exposed CD-1 mice had increases in the incidence of cleft palate, kidney anomalies and club foot [166].

Reproductive system

There is a growing body of literature exploring the relationship between animals exposed to low levels of dioxins and adverse effects on the function of the reproductive system.

Male reproductive system

In 2001 the COT statement on dioxins concluded "*the most sensitive indicators of TCDD toxicity were the effects on the developing reproductive systems of male rat foetuses exposed in utero*", and "*the effects on sperm production and morphology represented the most sensitive effects*"[36]. It was stated that these findings are relevant to humans, as their sperm reserve is less than that of a rat. Although these functional effects are indicative of dioxin toxicity, these outcomes can only

be measured in sexually mature offspring and so their relevance for birth outcomes is somewhat minimal, and therefore are not included in table 1.10. The following section provides a brief overview of the main literature reports and their findings.

The Petersons group were first to study how exposure to 2,3,7,8-TCDD effects the male reproductive system. Males rats born to Holtzman dams treated with single doses of 2,3,7,8-TCDD on GD 15 were examined for effects on growth, androgenic status, sexual behaviour, spermatogenesis and reproductive capability. The results were published in three papers [185-187]. *In utero* and lactational exposure to 2,3,7,8-TCDD at low levels reduced anogenital distance, delayed puberty [187], reduced weight of accessory sexual organs (testis, prostate [187], epididymis and cauda epididymis), reduced spermatogenesis-measured by a reduction in daily sperm production and cauda epididymal sperm reserve [185] and demasculinised sexual behaviour[186].

The EPA group, broadened these finding by investigating the reproductive effects of *in utero* exposure to a single dose of 2,3,7,8-TCDD in a different strain of rat, the Long Evans (LE) hooded rat, and an additional species, the Syrian Hampster [188, 189]. The effects on the reproductive system seen in LE rats were consistent with Peterson's group [188, 189]. With the exception of alterations in sexual behaviour and anogenital distance, these effects were demonstrated across the different species [188]. Repeat studies have shown similar adverse effects for the same species [190] and different species, Wister rats, when administered 2,3,7,8-TCDD subcutaneously[191]. The results from a cross-fostering study further reveal that most of these reproductive affects require *in utero* exposure; however, to induce alterations in sexual behaviour it is lactational exposure that is critical [190]. Alterations in sperm quality have more recently been found in male of spring of rhesus monkeys [192].

A dose as low as 0.064μgTCDD/kg was sufficient to significantly reduce spermatogenesis in the offspring of Holzman rats [185] , with additional alterations ocurring at 0.1 μg TCDD/kg [185-187]. For LE rats a dose of 0.05 μg TCDD/kg resulted in a non-significant reduction in ejaculated sperm counts and accelerated eye opening [189]. At these low doses, the human maternal body burden would be similar to if one was residing in an industrial country.

Female reproductive system

Five studies have demonstrated the sensitivity of the female external genitalia to 2,3,7,8-TCDD exposure [193-197]. Exposure has shown to induce delays in vaginal opening, vaginal threads

and clefting of phallus (a mild form of female hypospadias) in female Holtzman, LE rats and the Syrian hampster.

Gray and Ostby [195] were first to investigate this relationship in LE hooded rats and Hotzman rats. The female offspring of both strains of rat, following gestational administration of a single dose of 2,3,7,8-TCDD, displayed cleft phallus and the presence of a "*permanent "thread" of tissue across the opening of the vagina*" [195]. A fundamental limitation of this initial study was the timing of the examinations. Examinations were conducted after puberty, and thus the authors were unable to determine if the thread was occurring at puberty during vaginal opening or during fetal development. Flaws *et al* addressed this issue and found vaginal threads at birth and before the opening of the vagina in pre-pubescent female rats and additionally noted their persistence until 195-204 days old. It was therefore suggested that 2,3,7,8-TCDD permanently alters the function of normal prenatal development [194]. Histological examination of these threads, defined them as a cord of mescenchyme bordered by epithelium [194]. Dienhart *et al* explored the timing and mechanism of action for these threads and detected vaginal morphologensis four days after gestational exposure. It was found that 2,3,7,8-TCDD exposure prevented Wolffian ducts from regressing, increasing the thickness of mesenchymal tissue and preventing the fusion of the Mullerian ducts which resulted in the occurrence of these threads [193].

The relative importance of pre and post natal exposure of 2,3,7,8-TCDD for the formation of malformations of the external genitalia, was explored in a cross fostering study using pregnant LE hooded rat administered with a single dose of 2,3,7,8-TCDD. The results revealed *in utero* exposure was required to induce these malformations, with no such abnormalities observed in lactationally exposed offspring [196]. This study further investigated the relationship between dose of 2,3,7,8-TCDD administered on GD 15 and morphological alterations in the fetus. At 0.2 μgTCDD/kg a significant increase in the proportion of fetuses with temporary and/or permanent vaginal thread were observed along with alterations in morphometric measure, whereas cleft phallus required a higher dose of 0.8 μg TCDD/kg. The presentation of cleft phallus and alterations in urogenital morphometry (increased length of urethral slit and distance from tip of phallus to urethral opening and a decrease in distance from urethral opening to vaginal opening) are characteristics of mild hypospadias.

Two studies [194, 195] looked at how the time of exposure influenced the outcome observed. The first study found LE hooded rats exposed to 2,3,7,8-TCDD on GD 15 had much higher incidences of both cleft phallus and vaginal threads when compared to GD 8 [195]. When the

same dose of 2,3,7,8-TCDD was administered on GD 15, 65% of female offspring displayed complete to partial clefting of phallus and 80% displayed vaginal thread, compared to 25% and 14% respectfully for those administered on GD 8. The second study [194], used a different strain of rat, and supported the sensitivity of these malformations to day of exposure. Exposure to 2,3,7,8-TCDD on GD 11 displayed much higher incidences of cleft phallus than on GD 5 and 18. For vaginal threads this sensitivity was not evident. This shows that there is a critical window of dioxin exposure for the induction of cleft phallus.

Only one study found 2,3,7,8-TCDD exposure too induce these malformations in another laboratory animal. Wolf *et al* found Syrian Hampsters exposed to 2,3,7,8-TCDD had increased incidence of cleft phallus along with delays in vaginal opening and alterations in morphometric measure, indicative of mild hypospadias. No vaginal threads were observed [197]. These malformations were not observed in the ICR mice [174].

To date, vaginal threads have not been induced from exposure to any other chemical. However, cleft phallus and mild hypospadias, have been induced by gestational exposure to higher doses of other chemicals, synthetic oestrogen (RU 2858), high levels of oestradiol and diethylstilbestrol [198, 199]. This would support 2,3,7,8-TCDD acting as an oestrogen antagonist, however, the mechanism of action remains largely unknown.

Fetal growth

Ten studies have explored the relationship between exposure to 2,3,7,8-TCDD and its influence on fetal growth, measured as a comparison of fetal body weight on the day of sacrifice for exposed and unexposed foetuses [168, 171, 183, 184, 190, 195-197, 200, 201]. Two studies noted an increase in fetal weight of mice [168, 171] and the remaining eight, a decrease in fetal weight in five strains of rat [183, 184, 190, 195, 196, 200, 201] and a hamster [197]. A cross-fostering study by Bjerke and Peterson [190] measured fetal growth using body weight and crown-rump length. A reduction in crown-rump length and body weight at 1 day after exposure was observed for both *in utero* exposure and a combination of *in utero* and lactational exposure. On days 4, 21 and 63, exposure via all routes (only *in utero,* only lactational and both) reduced body weight and crown rump length. By day 133 neither *in utero* or lactional exposure found a reduction in these measures of fetal growth.

1.7.4 Interpretation of the toxicological studies on dioxins

Overall the toxicological literature supports the hypothesis that exposure to 2,3,7,8-TCDD is associated with a number of teratogenic responses, resulting in a wide array of adverse reproductive effects. Exposed fetuses have shown similar adverse health endpoints in a variety of species and strains, all displaying the sensitivity of fetus to dioxin toxicity. Discussed below are a number of issues which complicate the interpretation and applicability of the findings from the toxicological evidence.

Firstly, the animal studies reviewed were all exposed to 2,3,7,8-TCDD in a single dose by oral gavage. This does not represent the likely pathway of human exposure to dioxins from MSWI, which would most likely occur at low concentrations over long periods of time. At a given maternal toxicity, fetal body burden is largely dependent on the exposure pathway. In 2001, the SCF [202] used data from two studies by Hurst *et al* [176, 203] to relate maternal and fetal body burden to two types of administration of 2,3,7,8-TCDD: a single acute dose and a sub-chronic dose. As one would predict, for a given maternal body burden, corresponding fetal body burdens were much higher for those administered 2,3,7,8-TCDD with an acute dose. It was calculated that for the same fetal body burden, sub-chronic exposure would require over two and a half times greater maternal body burden. In addition, bioavailability of toxin to the fetus is influenced by the method of exposure. Animals given a single oral dose of 2,3,7,8-TCDD experience an initial peak in serum 2,3,7,8-TCDD levels, which over time subsides as the toxin disperses into the adipose tissue. For chronic exposure a peak exposure would not occur. This peak in serum levels is relevant for 2,3,7,8-TCDD exposure as toxins are transferred from mother to fetus within the blood via the placenta.

Secondly, the timing of exposure greatly influences the health outcome observed. Within the animal studies reviewed, 2,3,7,8-TCDD was generally administered during the critical exposure window for the outcome of interest. For example, those studies interested in male reproductive endpoints in rats most commonly administered 2,3,7,8-TCDD on GD 15. This corresponds to a period when the developing fetus has completed organogenesis and sexual differentiation has been initiated [187]. Gray and Ostby [195] showed an increase in toxic endpoints observed when administered on GD 8 compared to GD 15. Supporting this finding was Hurst *et al* [176] measured mean fetal TCDD concentrations on GD 16 and used response data from four studies [188, 189, 195, 196] to find that administrating 0.2µg TCDD/kg on GD 15 had similar fetal concentrations and adverse health effects as 1µgTCDD/kg administered on GD 8. Therefore, a single dose administered during this critical period is more likely to induce adverse health effects, than the lower continuous exposures that might occur from incineration.

The applicability of the findings from animal studies, to humans is continually questioned. Differences in susceptibility, absorption, transformation, accumulation, elimination and mechanisms of transfer of these toxins from mother to fetus all contribute to the health endpoints observed. Because human studies have not shown increases in mortality after dioxin exposure, it is hypothesized that humans are particularly insensitive to dioxin toxicity [162]. However, this does not reflect the sensitivity of a fetus to dioxin toxicity, which is demonstrated in animal studies. Even hampsters, which are thought to be insensitive to 2,3,7,8-TCDD, showed signs of terogenicity and rat fetuses have been found to be 100 times more sensitive to 2,3,7,8-TCDD exposure than adults rats. It is evident from the toxicological evidence presented, that the developing fetus is particularly sensitive to dioxin exposure, even in the most resistant species.

One must further consider that the congener of dioxin used in the animal studies was limited to 2,3,7,8-TCDD. In spite of this, compounds chemically and structurally related to 2,3,7,8-TCDD have been shown to produce similar adverse health effects at sufficiently high doses [173, 204-206]. Weber *et al* found that to induce a similar spectrum of reproductive endpoints when exposed to 2,3,7,8-tetrachlorodibenzofuran (TCDF) a dose 30 times that of 2,3,7,8-TCDD would be required [173]. Other dioxins have displayed similar dose-response curves to 2,3,7,8-TCDD, which may be indicative of a common mechanism [173, 206]. In the natural environment, humans are more commonly exposed to an array of different potential toxins- this is also true for incineration by-products. Six studies investigated the relationship between co-administration of different dioxins and other chemicals with health outcomes [163-165, 168, 173, 206]. Those administering a combination of congeners of dioxins [165, 173, 206] displayed additive or synergistic effects. When 2,3,7,8-TCDD was administered with other chemicals such as hydrocortisone and retinoic acid, these also showed synergism [163, 164]. An exception to this was findings reported by Haake *et al,* who found Aroclor 1254, a PCB mixture, acted as an antagonist for 2,3,7,8-TCDD toxicity [168].

1.7.5 Biological mechanisms

The mechanisms by which dioxins affect the biological system are thought to be mediated by the ligand activated aryl hydrocarbon receptor (AHR). The binding of dioxins to the AHR and subsequent responses, including changes in gene expression and the cell function, are probably responsible for their toxicity. A detailed understanding of this process remains unknown [36, 160]. However studies of animals without AHR show reduction in toxic effects [160] which would tend to support this theory.

Dioxins are partly absorbed into the gastrointestinal wall. The degree of absorption is dependent on a number of factors including method of exposure, lipophilicity of congeners and the digestion of food. Evidence to date has shown that the size and solubility of molecules are the key limiting factors for the absorption into the gastrointestinal wall [207]. These factors are hypothesised to be partly responsible for the poor absorption of hepta and octa chlorinated congeners [207]. Tissue concentrations of 2,3,7,8-TCDD in pregnant LE rats one day following administration of a single oral dose, revealed that approximately 60% of the total dose was absorbed [176].

After a single oral dose of 2,3,7,8-TCDD in rodents, serum levels of 2,3,7,8-TCDD peak after which levels of 2,3,7,8-TCDD distribute rapidly, primarily in liver and adipose tissue and some into skin and muscle tissue. The lipophilic properties mean approximately 30-47% of the total dose can be found in maternal liver and 6-10% in adipose tissue, a day after administration. By contrast as little as 0.25% is found in the blood [176]. Metabolism is required for dioxin elimination. Dioxin's persistent nature means metabolism is often slow, thereby regulating the rate of elimination.

1.8 OVERALL SUMMARY

This chapter has provided an overview of incineration as a waste management method, including exposure assessment methods in the epidemiological evidence in addition to providing a review of; the epidemiological evidence investigating associations between incineration and birth and neonatal outcomes, individual level exposure to dioxins from incinerators and a toxicological review of dioxins. This chapter has highlighted the gaps in the literature as well as the numerous unanswered questions with regards to; (a) poor exposure assessment methods used in previous epidemiological studies (b) the lack of individual level uptake assessment of dioxins from incinerators (c) the small number of birth outcomes explored within the epidemiological evidence thereby limiting the power of these studies to detect an effect of incinerators if present.

The work undertaken within this thesis will fill these identified gaps, and in turn contribute to the design and conduct, but not the completion, of the UK Small Area Health Statistics Unit (SAHSU) study on MSWI emissions and birth outcomes. SAHSU has received funding from Public Health England (PHE Q formerly HPA) and the Environment Agency (EA) to undertake a study to address the questions *"Do the emissions from modern WID operating incinerators pose a*

risk to reproductive and infant health?" and "*Does living near a municipal solid waste incinerator pose a risk to reproductive and infant health?" (*EA grants permits for MSWIs and PHE has a statutory responsibility to advise government and local authorities on possible health impacts of air pollution). Specifically the SAHSU incinerators study will be an individual-level population based birth cohort study with the aim to investigate the association between dispersion modeled ground level concentrations of particulates emissions from modern MSWIs (those operating under the WID) and the risk of adverse birth and neonatal outcomes in GB. The health endpoints to be investigated are twinning, sex ratio, stillbirths, infant mortality, birth weight (continuous and term low birth weight), small for gestational age, preterm delivery and congenital anomalies (all and selected groups). Additional details of SAHSU's study are provided in **Appendix B.**

The work presented in this thesis provides proof of concept to support the aims and objectives of the SASHU incinerators study. The work within the thesis demonstrates and pilots the feasibility of different methodological principles to be used in the larger SASHU study, but does not aim to undertake the entire SAHSU study.

The thesis aims to develop a dispersion model framework to estimate population exposure to emissions from MSWIs operating under current legislation (the WID). The framework developed and all model outputs presented within the thesis will be used in the SAHSU study. Delays in obtaining emissions data from the Environment Agency for all MSWIs has led to significant delay in the progress of the SAHSU incinerators study (the study remains in the preliminary stages of epidemiological analysis*)*, however these delays had no affect on the specific goals of this thesis.

The thesis additionally aims to pilot a biomonitoring study to estimate individual level dioxin exposure of pregnant women living within the vicinity of two modern MSWIs. The study design and development in addition to pilot data acquisition are included in the aims of this thesis however the full completion and data analysis of milk samples were not amongst the thesis aims. The full expanded biomonitoring study, including data acquisition and milk sample analysis, is still ongoing 5 years after its initiation through this thesis pilot study.

Finally the thesis aims to make recommendations to researchers on the most appropriate national births dataset to use in epidemiological studies of birth outcomes in England, as a basis for informing the SAHSU study on incineration and birth outcomes. Additional details of the thesis aims and specific objectives are provided in chapter 2.

Figure 1.1 The Waste Hierarchy. Diagram duplicated from the Department for Environment, Food and Rural Affairs 2011 report *"Government Review of Waste Policy in England 2011"* [6]

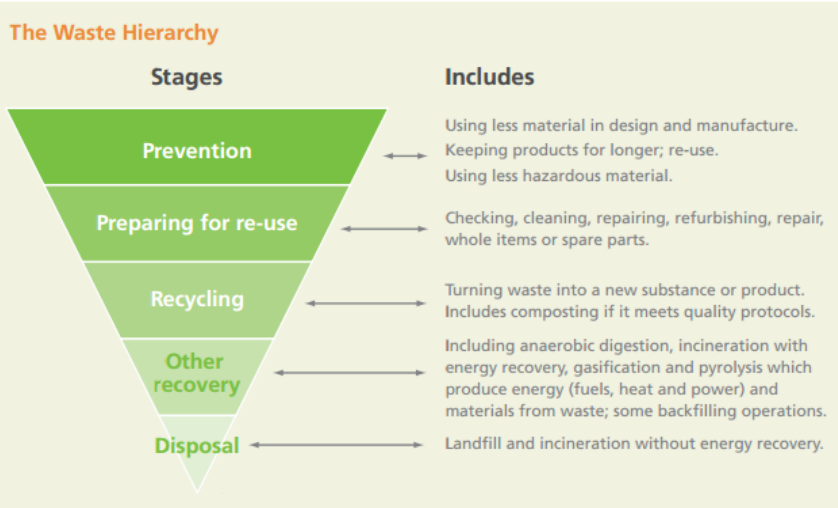
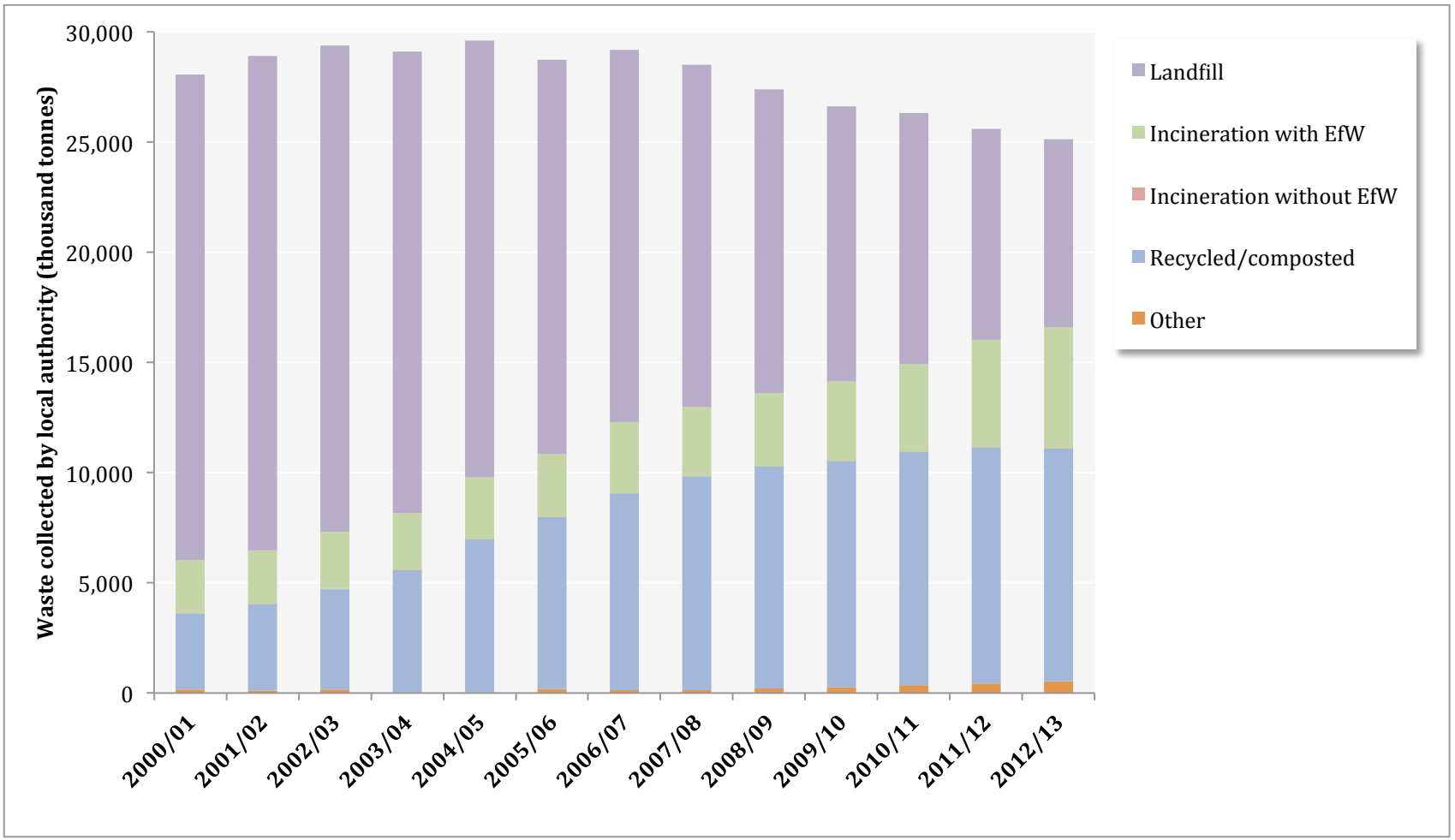
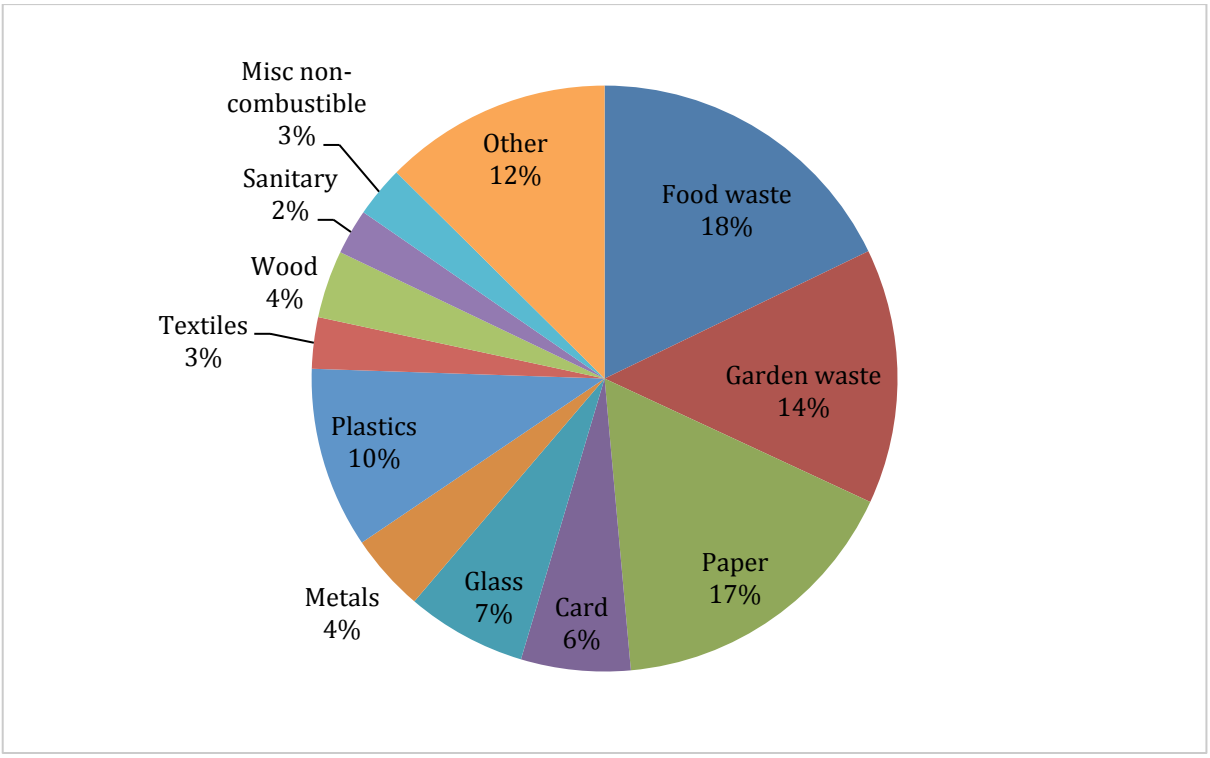


Figure 1.2 Temporal trends in waste management methods



Data extracted from the Department for Environment, Food and Rural Affairs 2013 report "*Statistics on waste managed by local authorities in England in 2012/13*" [3].

Figure 1.3 Composition of municipal waste (2006/07)



Data extracted from the Department for Environment, Food and Rural Affairs 2009 report "*Municipal Waste Composition: A Review of Municipal Waste Component Analyses*" [11].

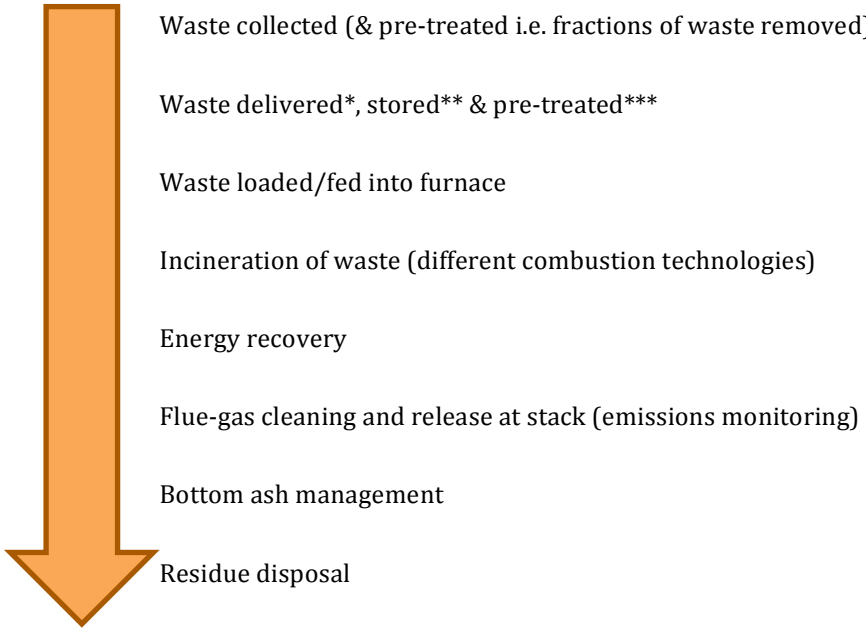
Table 1.1 Characteristics and energy recovery for all MSWIs in the UK

MSWI	Region of UK	Operator	Year established	Number of flues	Licensed throughput (tonnes/year)	Waste incinerated in 2009 (tonnes/year)	Energy recovery	Energy recovery - type
Allington/Maidstone	South East (Kent)	Kent Enviropower Ltd	2008	3	500,000	405,615	ü	Electricity
Bolton	North West (Greater Manchester)	Greater Manchester Waste Ltd	1971	1	130,000	84939	ü	Electricity
Chineham/Basingstoke	South East (Hampshire)	Veolia ES Hampshire Ltd	2003	1	102,000	101,754	ü	Electricity
Coventry	West Midlands (West Midlands Met Districts)	The Coventry & Solihull Waste Disposal Co Ltd	1975	3	240,000	245,187	ü	Electricity & Heat
Crymlyn Burrows	Wales (South West Wales)	Neath Port Talbot Recycling Ltd	2003	1	166,000	10,483		-
Dudley	West Midlands (West Midlands Met Districts)	MES Environmental Ltd	1998	2	105,000	93,445	ü	Electricity
Dundee	Scotland (Dundee)	Dundee Energy Recycling Ltd (DERL)	2000	2	120,000	-	ü	Electricity
Eastcroft/Nottingham	East Midlands (Nottinghamshire)	WasteNotts (Reclamation) Ltd	1973	2	160,000	114,920	ü	Electricity & Heat
Edmonton	London (North London)	London waste Ltd	1975	2	675,000	383,153	ü	Electricity
Grundon/Slough	South East (Berkshire)	Lakeside Energy from Waste Limited	2010	2	410,000	75,000	ü	Electricity
Isle of Wight	South East (Isle of Wight)	Waste Gas Technology Ltd	2009	1	38,000	12,420		-
Kirklees/Huddersfield	Yorkshire and the Humber (West Yorkshire)	SITA (Kirklees) Waste Services Ltd	2002	1	136,000	125,693	ü	Electricity
Marchwood	South East (Hampshire)	Veolia ES Hampshire Ltd	2004	2	165,000	188,244	ü	Electricity
Newlincs/Grimsby	Yorkshire and the Humber (Former Humberside)	Newlincs development Ltd	2004	1	56,000	53,728	ü	Electricity & Heat

Porthmellon	South West (Cornwall)	Council of the Isles of Scilly	1987	1	3,700	2,000	No energy recovery	
Portsmouth	South East (Hampshire)	Veolia ES Hampshire Ltd	2005	2	165,000	196,789	ü	Electricity
SELCHP/Lewisham	London (South East London)	Southern East London Combined Heat and Power Limited	1994	2	420,000	395,641	ü	Electricity
Sheffield	Yorkshire and the Humber (South Yorkshire)	Veolia ES Sheffield Ltd	2006	2	225,000	219,976	ü	Electricity & Heat
Stockton-on-Tees/Billingham/Teeside	North East (Tees Valley Unitary Authorities)	SITA Tees Valley Limited	1998	3	390,000	256,609	ü	Electricity
Stoke-on-Trent/Stoke	West Midlands (Staffordshire)	MES Environmental Ltd	1997	2	200,000	181,339	ü	Electricity
Tyseley/Birmingham	West Midlands (West Midlands Met Districts)	Tyseley Waste Disposal Ltd	1996	2	350,000	342,048	ü	Electricity
Wolverhampton	West Midlands (West Midlands Met Districts)	MES Environmental Ltd	1998	2	110,000	109,991	ü	Electricity

Data obtained directly from communications with the EA and extracted from the Department for Environment, Food and Rural Affairs 2013 report "*Incineration of Municipal Solid Waste*" [13].

Figure 1.4 Incinerator combustion technology



* Delivery of waste by trucks, trains or containers
**Waste stored within a bunker (concrete bed) with the capacity to store approximately 3-5 days of waste
*** Pre-treatment of waste usually occurs within the bunker and involves mixing, crushing and shredding of large waste

Figure based on European Commissions 200 report "*Integrated Pollution Prevention and Control. Reference Document on the Best Available Techniques for Waste Incineration*" [15].

Figure 1.5 Incineration process. Diagram duplicated from the European Environment Agencys book entitled "*EMEP/EEA air pollutant emission inventory guidebook — 2009", Chapter 6.C.c "Municipal waste incineration"*, 2009 [14].

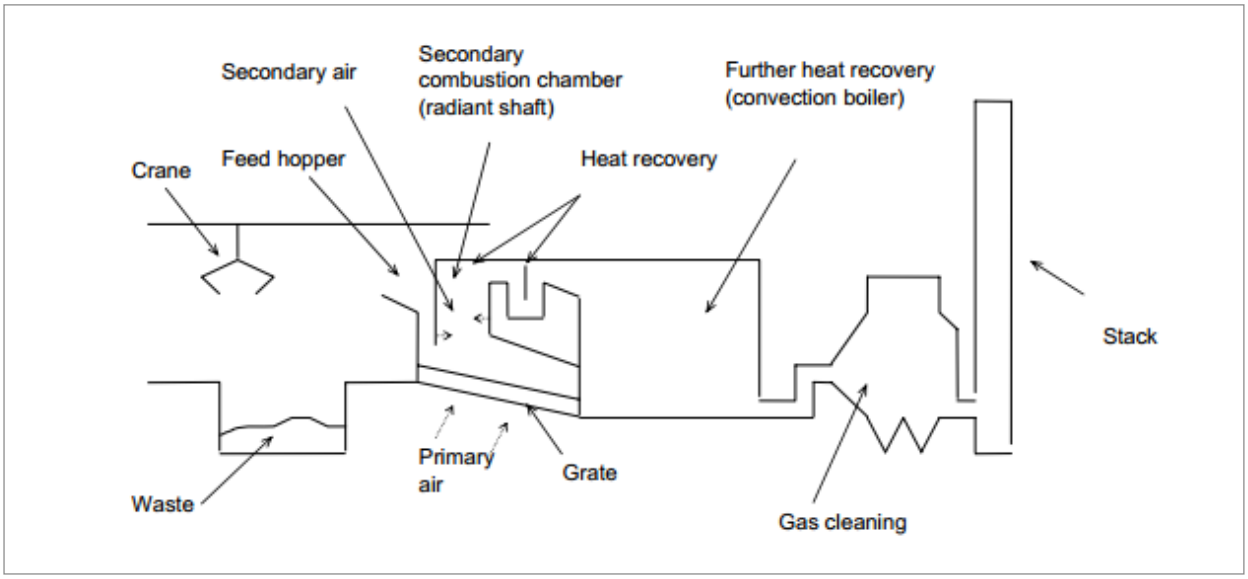


Table 1.2 Abatement methods for incinerator emissions

Product	Abatement method
Particulates	Fabric filters - semi-permeable material used to trap particulates Electrostatic precipitators - discharge electrodes used to generate electrostatic attraction and remove particulates
Acid gas	Wet scrubbers - flue gases cooled by water sprays and then alkali use Spray absorber systems - alkaline reagent slurry spray Dry injection systems – injection of alkaline reagent power
Dioxins* and mercury**	Adsorption using activated carbon inject into gas stream

*Although dioxins have abatement method the greatest influence of dioxins emissions is in control of combustion conditions. This includes gas residence time, temperature and oxygen, cooling of exit gases and limiting the amount of chlorine introduced.
**Dental amalgam is a major source of mercury and therefore often segregated.

Information extracted from the Environment Agencys 2009 report "*How to comply with your environmental permit. Additional guidance for:The Incineration of Waste (EPR 5.01)"* [7].

Table 1.3 WID emission limits

Product	Emission limit	Measurement frequency
24 hour average of ½ hour measurements		
Total dust/ Particulate matter	10 mg/m^3	CEM & twice a year
Total Organic Carbon	10 mg/m^3	CEM & twice a year
Hydrogen chloride	10 mg/m^3	CEM & twice a year
Hydrogen fluoride	1 mg/m^3	CEM & twice a year (if complainant for hydrogen chloride or 6 month sampling/ 3 months within first year of operation)
Sulphur dioxide	50 mg/m^3	CEM & twice a year
Nitrogen monoxide and nitrogen dioxide	200 mg/m^3	CEM & twice a year
>6 tonnes per hour or new	400 mg/m^3	
≤6 tonnes per hour		
Carbon monoxide	50 mg/m^3	CEM & twice a year
Average over sample period (min 30 minutes, max 8 hours)		
Cadmium	0.05 mg/m^3	6 month sampling/ 3 months within first year of operation
Thallium		
Mercury	0.05 mg/m^3	6 month sampling/ 3 months within first year of operation
Antimony, Arsenic, Lead, Chromium, Colbalt, Copper, Manganese, Nickel and Vanadium	0.5 mg/m^3	6 month sampling/ 3 months within first year of operation
Average over sample period (min 60 minutes, max 8 hours)		
Dioxins + Furans	0.1 ng/m^3	6 month sampling/ 3 months within first year of operation

CEM=Continuous Emission Monitoring

Information extracted from the Environment Agencys 2009 report "*How to comply with your environmental permit. Additional guidance for:The Incineration of Waste (EPR 5.01)"* [7].

Table 1.4 Comparing dioxin analysis in blood and breast milk.

Indicator field	Blood	Breast milk
Population	All men and women	Women who initiate breastfeeding, which is a continuously diminishing population (social bias in that deprivation is positively related to breastfeeding uptake)
Best overall indicator of body burden?	✓	
Timing of sample provision	Antenatally	Postnatally
Quantity	~50mL	~20mL
Invasiveness	Moderate	None
Collection	Required a trained medical staff member to collect sample, within a prearranged additional appointment during pregnancy	Self-collection
Staff needed for sampling	Yes	No
Sample representativeness	N/A	Issues arising with the timing of the sample within feed and also within the postnatal period- both of which influence milk fat content
Preparation	Serum extraction- immediately following collection	None
Storage	Deep freeze serum	Short term storage of whole sample in domestic freezer Long term storage in deep freeze
Percentage of lipid	0.6%	3-4%
Lower detection limit?		✓

Data obtained directly from communications with the Centers for Disease Control and Prevention.

Figure 1.6 Pathways of human exposure from incinertors. Diagram duplicated "*Evaluation the health impacts of incinerator emissions*", Journal of Hazardous Materials 47 (1996) 205-227 [34]

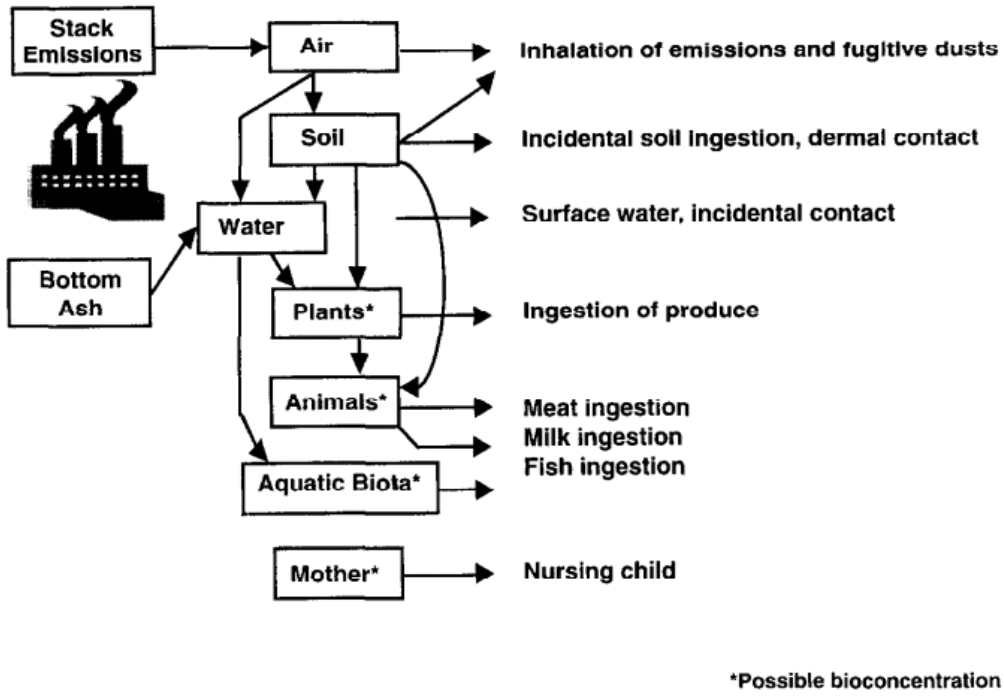


Figure 1.7 Search strategy for all identified studies

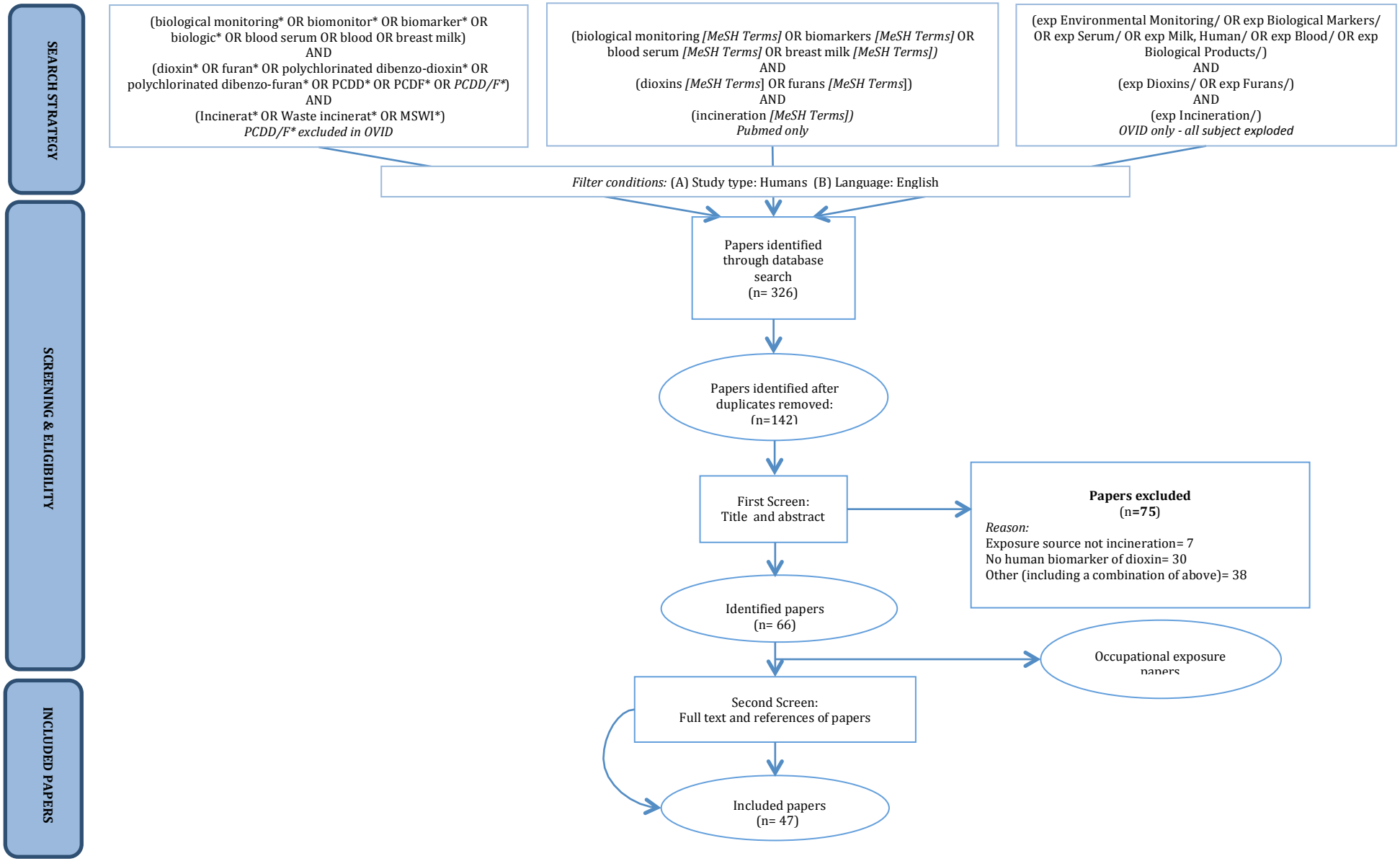


Table 1.5 Summary of biomonitoring studies of blood dioxin levels from incinerators

Author(s) and location of study	Study design				Study period	Incinerator: number and type	Study population	Biological matrix	Biomarker(s) measured	Study aim	PCDD/F levels & Study conclusions (R: Range, SD: standard deviation, CI: confidence interval)
	Timing	*Population levels*	*Distance/ Exposed vs Unexposed*	*Other*							
1998: Schuhmacher *et al* 1999[68] *2002:* Agramunt *et al* 2005 [69] *2007:* Nadal *et al* 2008 [70] *2012:* Nadal *et al* 2013 [71] Spain	✓				1998; 2002; 2007 and 2012 Plant constructed in 1999	1 HWI (a petrol chemical complex, a MSWI & 2 oil refineries)	*1998*: 20 residents (13 males, 7 females), aged 28-62 years *2002:* 20 residents (10 males, 10 females), between 19-62 years *2007:* 20 residents (10 males, 10 females) between 17-61 years *2012*: 40 residents (20 males, 20 females) between 22-67 years Residents who have lived for ≥10 years in study area with no know occupation exposure to PCDD/Fs	Blood (250ml)-plasma	17 congeners (7 PCDDs and 10 PCDFs)	To assess the health risks for the population living in the area under potential influence of the HWI and determine temporal trends of serum exposure before construction (1998), compared with 3, 8 and 13 years after construction	***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** *1998:* 27.0 (R: 14.8-48.9) *2002:* 15.7 (R 4.7-29.2) *2007*: 9.36 (R: 1.76-23.44) *2012*: 6.18 (R: 2.03-18.) Significant reductions in dioxin exposure 3,8 and 13 years after construction of a HWI
Aozasa *et al* 2002 [72] Japan	✓			✓	*Phase 1:* October 2000-February 2001 *Phase 2 (subsample if phase 1):* July 2001-January 2002	1 incinerator facility (type not specified)	*Phase 1:* 13 (7 males, 6 females), between 60-80 years *Phase 2 (subsample of phase 1):* 3 (subjects with highest dioxin levels) Residents near the incinerator facility	Blood (100 ml)-serum	17 congeners (7 PCDDs and 10 PCDFs) 12 PCBs	To evaluate monthly variations of blood dioxin concentrations and composition in subjects with higher dioxin level exposure (7 month monthly monitoring of 3 subjects with high dioxin levels)	*Phase 1:* ***Toxic equivalent levels of PCDD/F/DL-PCBs (pg TEQ/g lipid)*** 53 (R: 27-87) *Phase 2:* ***Toxic equivalent levels of PCDD/F/DL-PCBs (pg TEQ/g lipid)*** Participant A: 91 (R: 69-106)

										Participant B: 69 (R: 46-113) Participant C: 79 (R: 53-100)
2003: Chen *et al* 2003 [80] *2004:* Chen *et al* 2004 [52] *2005:* Lee *et al* 2005 [54] *2006a:* Chen *et al* 2006 [82] *2006b:* Chen *et al* 2006 [83] *2006c:* Chen *et al* 2006 [81] Huang *et al* 2007 [53] Taiwan		✓	✓	*2003:* April-August 2000 *2004:* 2000 *2005:* Not stated *2006a*: 2000-2001 *2006b:* 2000 *2006c:* 2000-2004 *2007:* 1999-2003	*2003:* 3 MSWIs *2004:* 1 MSWI *2005:* 1 MSWI *2006:* 12 MSWIs *2006b:* 19 MSWIs *2006c:* 19 MSWIs *2007:* 19 MWIs	*2003*: 341 residents (171 males, 170 females) *2004:* 95 residents (47 males, 48 females) Residents selected within 4 zones characterised by modelled ambient dioxin levels- in decreasing order of exposure A-D (A: 24; B: 19; C: 33; D: 19) *2005:* 89 residents (45 males, 44 females) Residents selected within 4 zones characterised by modelled ambient dioxin levels using ambient measures- in decreasing order of exposure A-D (A: 23; B: 19; C: 28; D: 19) *2006a:* 1034 residents (525 male, 509 female) *2006b:* 225 residents (106 male, 117 female) *2006c:* 1708 residents (850 males, 858 females) *2007:* 1658 residents Residents selected within 4 zones characterised by modelled ambient dioxin levels- in decreasing order of	Blood (60mL)–serum	17 congeners (7 PCDDs and 10 PCDFs)	*2003:* To compare the consumption frequency of different food groups of residents living in the vicinity of incinerators and to examine how dietary patterns were associated with their serum PCDD/F concentrations *2004:* *T*o evaluate the serum PCDD/F concentration distribution in residents living in the vicinity of an incinerator and its association with annual ambient dioxin exposure predicted by an atmospheric dispersion model *2005:* To measure the PCDD/Fs patterns emitted based on data information generated from ambient air measurements and serum samples of the neighbour residents from the incinerator *2006a*: To establish background levels of serum PCDD/Fs and biochemistry of residents living near municipal waste incinerators (MWIs) and also to examine the association between the serum PCDD/Fs levels and health outcomes of interest *2006b:* To examine the interactive influence of CYP1A1 genotypes and PCDD/Fs exposure on liver function profile	*2003:* ***Toxic equivalent levels of PCDD/F (pg I- TEQ/g lipid)*** 15.1 (R: 14.0-16.2) The frequency of fish consumption may be the most significant contributor to serum PCDD/F levels *2004:* ***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** Overall: 14.1 (SD: 8.9) A: 12.3 (SD: 8.7) B: 14.8 (SD: 10.2) C: 15.6 (SD: 9.0) D: 13.6 (SD: 7.7) No significant correlation between serum and ambient (based on atmospheric dispersion modelled) dioxin concentrations *2005:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** 14.14 (SD: 8.87) The levels of PCDD/Fs did not show the statistical relationship between ambient air and serum except for congener Average PCDD/F levels significantly reduced, 10 fold, when the incinerator was shut down in one of sampling periods. Ambient air exposure was the most important contributor to PCDD/Fs levels in ambient air but not the single in serum *2006a:* ***Toxic equivalent levels of PCDD/F (pg TEQ/g***

	exposure A-D (A: 270; B: 380; C: 563; D: 445) Resident within 5 km from one of the MWI for ≥ 5 years with no occupational exposure, between 18-65 years	*2006c:* To examine how the dietary habits, including a vegetarian regimen and the consumption of locally grown foods of residents living near the incinerators are associated to their serum PCDD/F levels *2007:* To measure dioxin exposure and the body burden for residents living in the vicinity of 19MWIs	***lipid)*** Males: 15.8 (SD: 8.3) Females: 17.6 (SD: 7.8) Human body's biochemistry functions such as liver and glucose modulation were affected by PCDD/Fs Exposure *2006b:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid)*** 20.1 (SD: 10.6) A significant interaction was observed between PCDD/Fs exposures and genetic polymorphisms on elevation of glutamate pyruvate transaminase and glutamyl oxaloacetic transaminase activities but not γ-glutamyl transpeptidase activity levels *2006c:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid)*** 19.65 Significant associations reported for being vegetarian (negative association) and consumption of locally grown food (positively associated) with concentration of dioxins. *2007:* ***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** Overall: 19.6 (SD: 4.2; R:10.6-25.7) A: 18.7 (SD: 3.83: R: 10.6-25.7) B: 19.4 (SD: 4.69; R: 14.3-32.0) C: 20.8 (SD: 5.75; R: 14.8-36.0) D: 19.6 (SD: 4.26; R: 10.7-24.1)) Serum concentrations in zone A was not distinct from that in zone D. No association between serum PCDD/Fs concentrations and ambient levels, the

									distance between residential houses and the incinerator, or years living in any of the zones
Chen *et al* 2010 [74] Taiwan		✓	Not stated	1 MSWI & 1 steel manufacturing company (3 electric arc furnace)	68 residents (44 males, 24 females) within 4 km from the MSWI or 3 electric arc furnaces, between 25-90 years	Blood	17 congeners (7 PCDDs and 10 PCDFs) Heavy metals (potassium, aluminium, serum iron, lead, zinc, cadmium, mercury & copper)	To characterize levels of PCDD/Fs and trace metals in the blood of the no occupationally exposed residents in the vicinity of an MSWI and electric arc furnaces	***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** 23.9 (R: 6.17–70) Mean levels of flue exit total PCDD/Fs in the electric arc furnaces were approximately 2.5 times those found in the MSWI. However the characteristics of the blood were more similar to the characteristics of the stack flux gas in MSWIs than those in electric arc furnaces
Chovancova *et al* 2012 [60] Slovakia	✓		September 2006-March 2007	Not stated	81 residents (40 males, 40 females) within four areas (Krompachy (20), Kosice (20), Nemecka (20), Sala(21)) close to municipal and waste incinerators 45 residents (25 males, 20 females) from 11 comparative villages All over 18 in good health and resident in areas for a minimum of 5 years	Blood (90mL)–serum	17 congeners (7 PCDDs and 10 PCDFs) 12 PCBs & 7 polybrominated diphenylethers	To assess PCDD/F, PCB and polybrominated diphenylethers levels in human specimens of the Slovak population and compare levels of these pollution amongst exposed adults residing in four areas close to municipal and waste incinerators as well as metallurgical industry plant and subjects coming from control area of Slovakia	***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid)*** Overall exposed: 15.4 Krompachy: 19.2 (R: 9.1-88.1) Kosice: 14.8 (R: 4.9-29.2) Nemecka: 10.7 (R: 2.4-20.4 Sala: 13.5 (R: 3.7-42.5) Control: 9.4 (R: 2.4-26.6) Significantly higher serum dioxin levels in donors from areas where known sources causing dioxin contamination than in control group of donors
Crimele *et al* 2005 [73] France		✓	Not stated	1 SWI	2 deceased women, 67 and 70 years, from generalized cancer Autopsies revealed that their bodies showed no signs of violence and manner of death (cancer) was confirmed	Blood (50mL)	17 congeners (7 PCDDs and 10 PCDFs)	To evaluate dioxin levels in two deceased women and provide an analytical method for this using gas chromatography coupled to high-resolution mass spectrometry	***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid)*** Women 1: 35.0 Women 2: 42.7 Dioxin body burden of the two women deceased appear in the range of the one observed in the general European population. It was not possible to correlate dioxin body burden of the two women as a potential contributor of their cancer pathology

					74 residents within 5 study areas with differing distances from the 2 incinerators *MSWI 1:* Study area (V) 8 residents near the plant; Study area (M) 20 residents far from the plant *MSWI 2:* Study area (S) 8 residents near the plant; Study area (FL) 19 residents far from the plant; Study area (F) 9 residents at intermediate distance (between 3-5km) from the plant Resident for ≥ 20 years within the area, women had not breast fed in last 20 years, all residents had no occupation exposure and aged between 27-67 years				***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid)*** *MSWI 1:* Study area (V): 9.3 Study area (M): 9.1 & 8.5 *MS WI 2:* Study area (S): 8.6 & 11 (> mean age) Study area (FL): 8.0 & 11 ((> mean age) Study area (F): 7.7 No significant differences in PCDD/F levels for subjects living in areas under potential impact of 2 incinerators compared to subjects in unexposed areas
De Felip *et al* 2008 [58] Italy	✓	✓	May 2005-December 2006	2 incinerator plants *MSWI:* MSW & sanitary waste *MSWI 2*: MSW & waste wood		Blood (30ml)-serum	17 congeners (7 PCDDs and 10 PCDFs) 26 PCBs	To conduct a pilot to provide preliminary information on the concentrations PCDD/Fs and PCBs in groups of subjects living in the vicinity of two incineration plants		
Deml *et al* 1996 [86] Germany		✓	July 1993	1 MWI	39 residents in the district of Schwandorf (19 males, 20 females)	Blood (50 ml)	17 congeners (7 PCDDs and 10 PCDFs)	To determine the PCDD/F content in blood and human milk of non-occupationally exposed persons living in the vicinity of the MWI in Schwandorf to check the possibility of enhanced body burdens due to immissions originating from the MWl	***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** 17.0 (R: 5.2-34.5) The mean body burden of the group living in the main wind direction related to the MWl was not different from the group living in other areas. As compared to background levels in the general population in Germany the results give no indication of an enhanced body burden of PCDD/F
Evans *et al* 2000 [55] USA	✓		✓	Not stated	1 HWI	*Study group:* 76 residents within a 4 km radius of the HWI (67 providing 3 samples) *Comparison group*: 74 residents of Manchester community (selection based on similarities of	Blood (500ml)-serum	18 congeners (8 PCDDs and 10 PCDFs) 4 PCBs	To determine whether living in the vicinity of a hazardous waste incinerator that was burning material contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) increased TCDD and toxicity equivalencies (TEQ) in individuals living near the incinerator	***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** *Study group:* 9.89 (R: 2.2-25.0) Prior to incineration: 11.8 (SD: 4.8) Four months into incineration: 9.61 (SD: 4.38) Eleven months later immediately after the incineration process was completed: 8.21 (SD: 3.73)

						demographics and socioeconomic factors with study area; ≥15 km from HWI, absence of other dioxin sources, no travel routes through study area) (61 providing 3 samples) Residents has never lived at HWI site, been resident for ≥1 year, had no occupation exposure to PCDD/Fs and were not likely to be pregnant/breastfeeding during the study period				*Comparison group*: 10.29 (R: 1.2-38.9) Prior to incineration: 10.82 (SD: 6.11) Four months into incineration: 11.63 (SD: 6.24) Eleven months later immediately after the incineration process was completed: 9.05 (SD: 5.66) No significant differences in PCDD/F levels between study and comparison areas but a significant decrease in levels from pre incineration to post was observed
Fierens *et a*l 2003/2007 [61, 62] Belgium		✓		✓	Not stated	2 MSWI	*MSWI 1:* 51 residents within 2km from the incinerator (25 male, 26 female)- in a rural area *MSWI 2:* 33 residents within 2km from the incinerator (10 male, 20 female)- in an industrial area *Reference:* 63 residents in 3 villages situated in rural areas with no known local sources of pollution	Blood (200ml)	17 congeners (7 PCDDs and 10 PCDFs) 15 PCBs Lead; Cadmium (in urine) & Mercury (in urine)	Assess the human exposure impact of MSWIs on subjects living in the vicinity two MSWIs (2007- included a steel and iron facility)	***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** *MSWI 1:* 37.9 (R: 32.8–43.8) *MSWI 2*: 24.1 (R: 20.2–28.9) *Reference:* 23.9 (R: 21.4–26.6) Significant increase in PCDD/F serum levels for subjects living in the rural area around MSWI 1 compared with the reference population
Frery *et al* 2012 [59] France			✓	✓	March 2005-July 2005	3 MSWI	1,030 residents from 8 areas around the MSWIs Resident for ≥ 10 years in the study area with no occupational exposure	Blood	17 congeners (7 PCDDs and 10 PCDFs) 12 dioxin like PCBs and 3 non dioxin like PCBs	Its main objective was to know if people living around municipal solid waste incinerators (MSWI) had higher serum dioxin levels than those who lived far from a MSWI, and to assess the contribution of locally produced food to this exposure	***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid)*** 13.7 No difference was observed in geometric mean serum dioxin levels between residents living near incinerators and those far from any known source of dioxins. An increase in serum dioxin levels was seen with consumption of local products of animal origin such as dairy products, eggs and, more generally, lipids
Gonzalez *et al* 2000 [63]	✓		✓		*Phase 1:* March-June 1995	1 MSWI	*Phase 1:* 104 residents near plant (49 males, 55 females)	Blood (50ml)	17 congeners (7 PCDDs and 10 PCDFs)	To evaluate the body burden of PCDDs/PCDFs, PCBs, and heavy	*1995:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)***

Gonzalez *et al* 2001 [67] Spain			*Phase 2:* April-June 1997 *Phase 3:* 1999		97 residents far from plant (51 males, 46 females), between 18-69 years *Phase 2:* 93 near residents near plant (42 males, 51 females) 91 far from plant (47 males, 44 females) *Phase 3:* Residents living in another city 20 km from the plant Near= 0.5-1.5 km from the plant Far= 3-4 km from plant	(Urine-50ml)	*Phase 1 & 2:* 6 PCBs & heavy metals (chromium, lead, cadmium & mercury)	metals in individuals exposed to emissions from a new large MSWl in the city of Matarb, Spain and compare the levels of these compounds in residents who lived far from the plant, and in workers at the plant; individuals were studied both before, 2 years and 4 years after the incinerator began functioning	Near: 13.5 (R: 10.2-17.5) Far: 13.4 (R: 9.8-17.9) *1997:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Near: 16.7 Far: 16.7 Dioxin levels had increased in both groups of residents by approximately 25% and 12% (about 10% when account the mean of two repeated quality-control analyses) Blood dioxin levels did not depend on distance of residence from the incinerator, it would appear unlikely that the small increase in dioxin blood levels resulted from the incinerator's emissions *1999:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Near: 19.4 Far: 19.2 Far 2: 20.0 The observed increasing trend of dioxins blood levels in the Spanish population could reflect a recent increase of exposure to dioxins from foods or other unidentified sources
Kim *et al* 2001 [75] Korea		✓	Not stated	1 waste incinerator	15 residents near incinerator (1 male, 14 female) between 23-47 years	Blood	17 congeners (7 PCDDs and 10 PCDFs)	To compare blood dioxin level levels between workers and non-exposed controls	***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** 0.81 Levels of serum dioxin increased for workers compared with residents
Kim *et al* 2005 [76] Korea	✓		2001	2 MSWI	22 residents (10 males, 12 females) within 5 km of the plants, between 21-63 years Resident for ≥ 5 years with no occupational exposure	Blood	17 congeners (7 PCDDs and 10 PCDFs) 16 PCBs and 7 polybrominated diphenyl	To identify the levels of PBDEs along with PCDD/Fs and PCBs, in Korean blood samples	***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Overall: 21.52 Men: 23.48 (R: 8.06-53.65) Women: 19.89 (R: 3.14-44.28)

							ethers		Levels were similar to the average human exposure to PCDD/Fs in Korean. Levels in the residents were significantly higher than the workers
Kitamura *et al* 2001 [56] Japan	✓	✓	Not stated	Not stated	225 resident *A:* 80 (44 males and 36 female) >5 km from incinerators *B:* 95 (53 males, 42 females) ≤ 2 km from incinerators (emitting slightly higher than allowed dioxins) *C:* 50 (23 males, 27 females) ≤ 2 km from incinerators (emitting high levels of dioxins)	Blood	17 congeners (7 PCDDs and 10 PCDFs) 3 PCBs	To justify reduction from 20 to 8 congeners of dioxin to be analysed in biomonitoring studies of dioxins	***Toxic equivalent levels of PCDD/F/3-DL-PCBs (pg TEQ/g lipid)*** A: 23.8 (SD: 12.3) *B:* 25.6 (SD: 11.6) C: 39.1 (SD: 18.8) The levels of dioxins were approximately equal in groups A and B, however group C levels were 1.5 times higher. Dioxin levels in workers were more than 4 times higher than groups A-C. More than 90% of total TEQs accounted for by 8 congeners
Leem *et al* 2006 [48] South Korea	✓		Not stated	1 IWI	*Near zone:* 40 residents within 5 km from incinerator (20 males, 20 females) *Far zone:* 20 residents 20 km from the incinerator (6 males, 14 females) *Control zone:* 5 residents in agricultural area with no industrial activity	Blood (150 ml)-plasma	17 congeners (7 PCDDs and 10 PCDFs)	To estimate whether the blood levels of PCDD/DFs in residents living near an incinerator were affected by presence of the incinerator and investigated factors that characterize the risk of high exposure to dioxin in the area	***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** *Near zone:* 11.9 (R: 3-26.3) *Far zone:* 11.2 (R: 4.3-21.7) *Control zone*: R: 1.0-6.3 No significant difference in PCDD/F serum concentrations found between the two groups
Leem *et al* 2003 [77] South Korea		✓	Not stated	2 MSWI; 1 IWI	*MSWI:* 16 residents *IWI:* 10 residents Resident within 1.5 Km from the incinerators for more than 1 year	Blood (150 ml)-plasma	17 congeners (7 PCDDs and 10 PCDFs)	To estimate exposure status of these hazardous substances and their heath effects in workers and residents near the MSW incinerators and residents near the industrial waste incinerators	***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** *MSWI:* 13.7 (SD: 8.4) *IWI:* 53.4 (SD: 24.0) Difference in PCDD/F concentrations found between the two groups
Moon *et al* 2005 [78] Korea		✓	2001-2002	4 MSWIs	75 residents (21 males, 54 females) within 300 m of 4 incinerators Resident for ≥ 3 years prior to 2002 with no previous	Blood (150ml)-serum	17 congeners (7 PCDDs and 10 PCDFs)	To evaluate the congeners PCDD/Fs in Korean serum samples as biological markers	***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)*** All: 6.60 Male: 8.04 Female: 6.12

					occupational exposure				The GM PCDD/PCDF level in the serum of workers was not significantly different from the values for residents near MSWIs and overall were lower than those in other countries *1995:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Exposed: 13.0 Non-exposed: 13.1 *1997:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Exposed: 15.9 Non-exposed: 16.4 *1999:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Exposed: 17.8 Non-exposed: 18.1 Non-exposed 2: 18.7 *2002:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Exposed: 15.1 Non-exposed: 18.2 Non-exposed 2: 16.0 *2005:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Exposed: 11.7 Non-exposed: 12.3 Non-exposed 2: 17.9 *2008:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Exposed: 14.6
Parera *et al* 2013 [66] Spain	✓	✓	1995-2008	1 SWI	*1995:* 104 residents (49 males, 55 females)- "*exposed*"- living <1 km from the plant 97 residents (51 males, 46 females)- "*non-exposed*"- living >3 km from the plant Blood samples collected in 1995, 1997, 1999, 2002, 2005, 2008 & 2012 Added subjects: *1999:* 100 residents (48 males, 52 females)-"*non-exposed 2*"- living in the nearby City of Arenys de Mar ~11 km from plant *2008:* 30 residents (14 males, 16 females)-"*exposed*" 39 residents (19/20 males, 19/20 females)- "*non-exposed*" 38 residents (22 males, 16 females)- *"non-exposed 2"*	Blood	17 congeners (7 PCDDs and 10 PCDFs) 3 PCBs	To monitor and compare PCDD/Fs and PCBs levels in blood samples from general populations considered exposed and non-exposed to a SWI in the City of Mataró	

									Non-exposed: 12.6 Non-exposed 2: 14.5 *2012:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** Exposed: 12.9 Non-exposed: 13.9 Non-exposed 2: 12.5 No differences in levels of PCDD/Fs for exposed and control zones. In both exposed and non-exposed groups, PCDD/Fs concentrations experienced a slight increase from 1995 to 1999, followed by a slight decrease from 1999 to 2002 and stabilization afterwards ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** *R group:* 12.9 *B group:* 12.6 Blood levels of PCDD/Fs in two groups were not significantly different, however works at the MSWI had significantly lower blood dioxin levels than all residents. Low chlorinated DD/Fs should be studied extensively until they have been elucidated for their toxicities ***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid)***
Park *et al* 2013[51] Korea	✓	✓	2006	1 MSWI	49 residents ≤ 300m from plant- *R group* 11 residents >10 km from the plant- *B group*	Blood (100ml)-serum	17 congeners (7 PCDDs and 10 PCDFs) Mono- to octa-chlorinated dibenzo-p-dioxin/dibenzo furans	To evaluated for the first time mono- to octa-chlorinated dibenzo-p-dioxin/dibenzofurans (DD/Fs) from individuals working in an MSWI, residents living near the facility, and the general population	
Park *et al* 2009 [50] Korea		✓	2000-2002	2 MSWI (1 industrial complex)	28 residents (9 males, 19 females) near the plants- *MR group* 7 residents (4 males, 3 females) > 10 km away from any incinerator facilities- *BR group*	Blood (100ml)-serum	25 congeners 12 PCBs	To evaluate potential occupational exposure of the workers and rationalize the related health risk assessment.	*MR group:* 13.63 *BR group*: 6.91 No significant difference in PCDD/F levels in these groups or with MSWI workers. In the industrial complex workers had double PCDD/Fs levels as residents. ***Toxic equivalent levels of PCDD/F (pg I- TEQ/g lipid)***
Park *et al* 2004 [49] South Korea	✓		2002-2003	1 IWI	*Near site:* 40 residents within 5 km of the incinerator *Far site:* 20 residents between 7-12 km *Control site:* 5 samples in agricultural site with no	Blood-serum	17 congeners (7 PCDDs and 10 PCDFs)	Influence of an industrial waste incinerator as assessed by the levels and congener patterns of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans. Furthermore, to evaluate the influence of the incinerator on the residents near the	*Near site:* 12.2 (R: 3.0-26.3) *Far site:* 11.0 (R: 4.3-21.7) *Control site:* 4

						industrial activity			incinerator, the levels and congener patterns of PCDD/Fs in human blood samples were also studied	No statistically significant difference in the PCDD/F serum concentrations between near and far zones. However, both were statistically higher than the control area
Pirard *et al* 2005 [79] France			✓	February-April 2003	1 MSWI	10 residents (8 males, 2 females) between 51-75 years No-occupational exposure, resident within 2 km radius of the incinerator for at ≥ 25 years 65 "exposed" residents	Blood (100ml)	17 congeners (7 PCDDs and 10 PCDFs) 15 PCBs	To assess the impact of an old French incinerator on dioxin and PCB levels in soil, in locally produced animal food and in resident serum	***Toxic equivalent levels of PCDD/F (pg TEQ/g lipid*** 74.6 (R: 59.8-86.6) Blood levels were higher than general European populations and comparable to a similarly exposed Belgian population
Reis *et al* 2007 [57] Portugal		✓		1999; 2002	Not stated	51 "control" residents Resident in area for ≥1 year with no known occupational exposure between 18-65 years	Blood (80ml)	17 congeners (7 PCDDs and 10 PCDFs)	To investigate potential determinants of dioxin levels in the studied populations	***Toxic equivalent levels of PCDD/F (pg WHO TEQ/g lipid)*** Exposed: 15.8 (SD: 6.2; R 4.0-34.3) Control: 15.3 (SD: 5.8; R: 5.3-32.3) No significant differences between PCDD/F levels in exposed and control individuals
Viel *et al* 2011 [84] France			✓	2003-2005	1 MSWI	34 newly diagnosed NHL *cases* (15 males, 19 females) 34 *controls* (15 males, 19 females) Residents in the 3 electrical wards containing or surrounding the MSWI	Blood (150ml) - serum	17 congeners (7 PCDDs and 10 PCDFs) 10 pesticides & 18 PCBs	To investigate organochlorines and the risk of NHL among neighbours of a French MSWI with high levels of dioxin emissions, using serum concentrations to assess exposure	***Toxic equivalent levels of PCDD/F/DL-PCBs (pg WHO TEQ/g lipid)*** *Cases:* 55.96 *Controls:* 35.10 ***Odds ratio*** *PCDD:* 1.12 (CI: 1.03-1.26) *PCDF*: 1.16 (CI: 1.03-1.35) *PCDD/DFs/DL-PCBs:* 1.04 (CI: 1.01-1.05) Strong evidence of increased NHL risk associated with dioxins and furans and all PCDD/Fs/DL-PCBs
2006: Zubero *et al* 2009 [65] *2008:* Zubero *et al* 2011[64] Spain	✓	✓	✓	*2009:* 2006 *2011:* 2008	1 MSWI	*2006:* 322 residents (159 males; 163 females) from 4 zones 2008: 326 residents (162 males, 164 females) from near and far zones *Near zones:* Zone E1: metropolitan area <	Blood (20 ml)-Serum	17 congeners (7 PCDDs and 10 PCDFs) *2009:* 19 PCBs *2011:* 12 PCBs	*2006:* (1) To evaluate exposure to PCDD/Fs by an urban waste treatment plant to trace any changes following plant start up (2) to analyse the relationship between exposure biomarker markers and the main variables: sex, age and area of residence; (3) to investigate the links between PCBs and other variables	*2006:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid*** Overall: 23.45 (SD: 8.51) *Near zone:* 26.88 (SD: 9.79) Zone E1: 24.47 (SD: 8.79) Zone E2: 29.29 (SD: 11.43) *Far zones:* 20.02 (SD: 5.69) Zone C1: 21.36 (SD: 8.15)

		2km from plant & high traffic density Zone E1: metropolitan area < 2km from plant & high traffic density *Far zones:* Zone C1: urban area 5 km from plant & high traffic density Zone C2: municipality 20km from plant with minimal industrial activity and low traffic density Residents lived in the zone for ≥ 5 years and had no occupational exposure	of interest *2008:* To assess serum levels of PCDD/Fs and PCBs after commissioning of an MSWI plant (2005). Blood samples were obtained in 2006 and 2008	Zone C2: 18.68 (SD: 2.11) No statistically significant differences in levels of PCDD/Fs, between the various zones *2008:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g lipid*** Overall: 23.60 (SD: 12.86) *Near zone:* 20.83 (SD: 10.08) *Far zones:* 26.36 (SD: 15.35) No significant differences were observed in PCDD/Fs as a function of area of residence or proximity to the plant over the time of the study

Abbreviations: HWI (hazardous waste incinerator); IWI (industrial waste incinerator); MSWI (municipal solid waste incinerator); PCDD (Polychlorinated dibenzo-p-dioxins); PCDF (Diobenzofurans); PCBs (polychlorinated biphenyls); DL-PCBs (dioxin-like polychlorinated biphenyls)

Table 1.6 Summary of biomonitoring studies of adipose dioxin levels from incinerators

Author(s) and location of study	Study design				Study period	Incinerator: number and type	Study population	Biological matrix	Biomarker(s) measured	Study aim	PCDD/F levels & Study conclusions (R: Range, SD: standard deviation, CI: confidence interval)
	Timing	*Population levels*	*Distance/ Exposed vs Unexposed*	*Other*							
1998: Schuhmacher *et al* 1999 [90] *2002:* Schuhmacher *et al* 2004 [89] *2007:* Nadal *et al* 2009 [88] Spain	✓	✓			*1998:* during construction of the HWI *2002:* 3 years after regular operation of HWI *2007:* 9 years after regular operation of HWI	1 HWI (a petrol chemical complex, a MSWI & 2 oil refineries)	*1998:* 15 autopsied subjects (10 males, 5 females) (3 subjects- < 1 km from MSWI-"*near*"; 12- 3-5 km from the plant-"*far*") between 30-83 years *2002:* 15 autopsied subjects (11 males, 4 females) between 19-94 years *2007:* 15 autopsied subjects (11 males, 4 females) between 19-94 years At time of death and for the last 10 years lived in the city of Tarragona or surrounding area	Adipose tissue	17 congeners (7 PCDDs and 10 PCDFs) 3 PCBs	To assess the influence of a new hazardous waste incinerator on public health. A biomonitoring study was established during construction of the HWI, with adipose tissue sampled at this time, 3 years after regular operation and 9 years after regular operation	*1998:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** *All:* 30.98 (SD: 15.38; R: 13.37-69.37) *Near:* 24.96 (R: 13.37-43.12) *Far:* 32.49 (R: 13.49-69.37) No significant difference between near and far adipose PCDD/F levels and levels were in the same order of magnitude than those reported for most industrialized countries *2002:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g lipid)*** *All:* 9.22 (SD: 8.74) Significant reduction in PCDD/F levels, 70% reduction. The results indicate that there is not any additional significant exposure to PCDD/Fs for this population

									2007: ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g fat)*** *1998:* 40.1 (SD: 12.7) *2002:* 9.89 (SD: 9.27) *2007:* 14.6 (SD: 14.2) A significant reduction of 64% from 1998-2002 and A non-significant increase of 47% from 2002-2007. The increase is thought not to be attributable to the HWI, as other biological monitors such as human plasma and milk decreased ***Toxic equivalent levels of PCDD/F (pg TEQ/g milk fat)*** 12.4 (R: 6-19) No correlation between PCDD/F in milk fat, length of lactation period, and number of children could be detected. Compared to background levels in the general population the results give no indication of an enhanced body burden of PCDD/F
Deml *et al* 1996 [86] Germany	✓		July 1993	1 MWI	7 women resident in the district of Schwandorf, between 25-32 years	Breast milk (200 ml)	17 congeners (7 PCDDs and 10 PCDFs)	To determine the PCDD/F content in blood and human milk of non-occupationally exposed persons living in the vicinity of the MWI in Schwandorf to check the possibility of enhanced body burdens due to immissions originating from the MWI	
Parera *et al* 2013 [66] Spain	✓		2008; 2012	1 SWI	46 women residents in the city of Mataró (1 km from the plant), between 18-40 years	Breast milk (10ml)	17 congeners (7 PCDDs and 10 PCDFs) 3 PCBs	To monitor and compare PCDD/Fs and PCBs levels in blood samples from general populations considered exposed and non-exposed to a SWI in the City of Mataró	*2008:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g milk fat)*** 4.5 R: (3.2-6.6) *2012:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g milk fat)*** 3.1 R: (2.3-3.8) Levels of PCDD/Fs were in accordance or lower than previous studies
Reis *et al* 2007 [85] Portugal	✓	✓	1999-2003	2 waste incinerators	181 women 73- ≤5 km from a plant-*"exposed"* 108-live or work > 5 km from plant-*"control"*	Breast milk (40ml)	17 congeners (7 PCDDs and 10 PCDFs)	To investigate the difference between exposed and non-exposed dioxin levels in human milk	***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g milk fat)*** Exposed: 9.5 (SD: 3.9; R: 2.8-20.9) Control: 9.1 (SD: 3.3; R: 3.0-19.9)

1996/1998: Schuhmacher *et al* 1999 [92] *2002:* Schuhmacher *et al* 2004 [91] *2007:* Schuhmacher *et al* 2009 [93] *2012:* Schuhmacher *et al* 2013 [94] Spain	✓	✓	1996: 2002; 2007; 2012	1 HWI	Healthy pregnant women, with no known occupational exposure, primiparous or breast feeding first child or 3 years after breast feeding & resident for > 1 year *1998*: 15 women, between 25-35 years *2002:* 15 women, between 25-35 years *2007:* 15 women, between 25-35 years *2012*: 20 women, between 22-44 years Women resident in zones under potential influence of HWI for ≥ 5 years and were healthy and primiparous	Breast milk	17 congeners (7 PCDDs and 10 PCDFs) 37 PBCs & 15 polybrominated diphenyl ethers (not measured in 1998)	To determine the levels of PCDD/Fs, PCBs, and PBDEs in breast milk of primiparae mothers living in the area under direct influence of the HWI. Evaluate levels of breast milk dioxins during construction of the HWI, 3 years after regular operation, 8 years after regular operation and 13 years after regular operation	Not significant difference of PCDD/F levels in exposed and control women, however significant differences by community of residence were observed. Emissions from both incinerators appear to be well controlled as there is no increase of human body burden of dioxins as measured in human milk of individuals living near these facilities *1998:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g milk fat)*** 11.82 (SD: 2.71; R: 5.93-17.10) PCDD/F levels were similar or lower than those previously reported for most industrialized countries *2002:* ***Toxic equivalent levels of PCDD/F (pg I-TEQ/g milk fat)*** 10.0 (4.3-39.9) Significant 34.2% decrease in median levels from 1998. In WHO TEQ, significant 13% decrease *2007:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g milk fat)*** 7.6 (SD: 2.4; R: 2.8-11.2) A general decrease of the concentrations for PCDD/Fs *2012:* ***Toxic equivalent levels of PCDD/F (pg WHO-TEQ/g milk fat)*** *1998:* 12.2 (SD: 2.8) *2002:* 10.6 (SD: 9.6) *2007:* 7.6 (SD: 2.4) *2012:* 4.8 (SD: 2.8; R: 1.06-12.3) Significant 61% decrease from 1998.

								Non-significant 37% decrease from 2007. A general decrease of the concentrations in breast milk for PCDD/Fs which were in accordance with the reduction in the dietary intake of these pollutants found in recent studies carried out in the same area of study. Living in the vicinity of the new HWI should not mean additional exposure to PCDD/PCDFs for the general population of the area ***Toxic equivalent levels of PCDD/F (pg TEQ/g milk fat)*** 14.9 (SD: 6.0; R: 2.8-37.2) The distances to the nearest waste incinerators bore no apparent correlations with the congeners of PCDD/Fs or levels.
Tajimi *et al* 2005 [87] Japan	✓	June-September 1999; 2000	1 public waste incinerator & 1 IWI	240 mothers residing in Tokyo, between 25-35 years Resident in Tokyo for > 5 years	Breast milk (50ml)	29 congeners (14 PCDDs and 15 PCDFs) 12 PCBs	To examine the relationship between the PCDD/F and Co-PCB levels in samples of human breast milk and nearby waste incinerators in Tokyo, Japan	

Abbreviations: HWI (hazardous waste incinerator); IWI (industrial waste incinerator); MSWI (municipal solid waste incinerator); PCDD (Polychlorinated dibenzo-p-dioxins); PCDF (Diobenzofurans); PCBs (polychlorinated biphenyl

Figure 1.8 Selection of all epidemiological studies investigating the association between incineration and birth outcomes

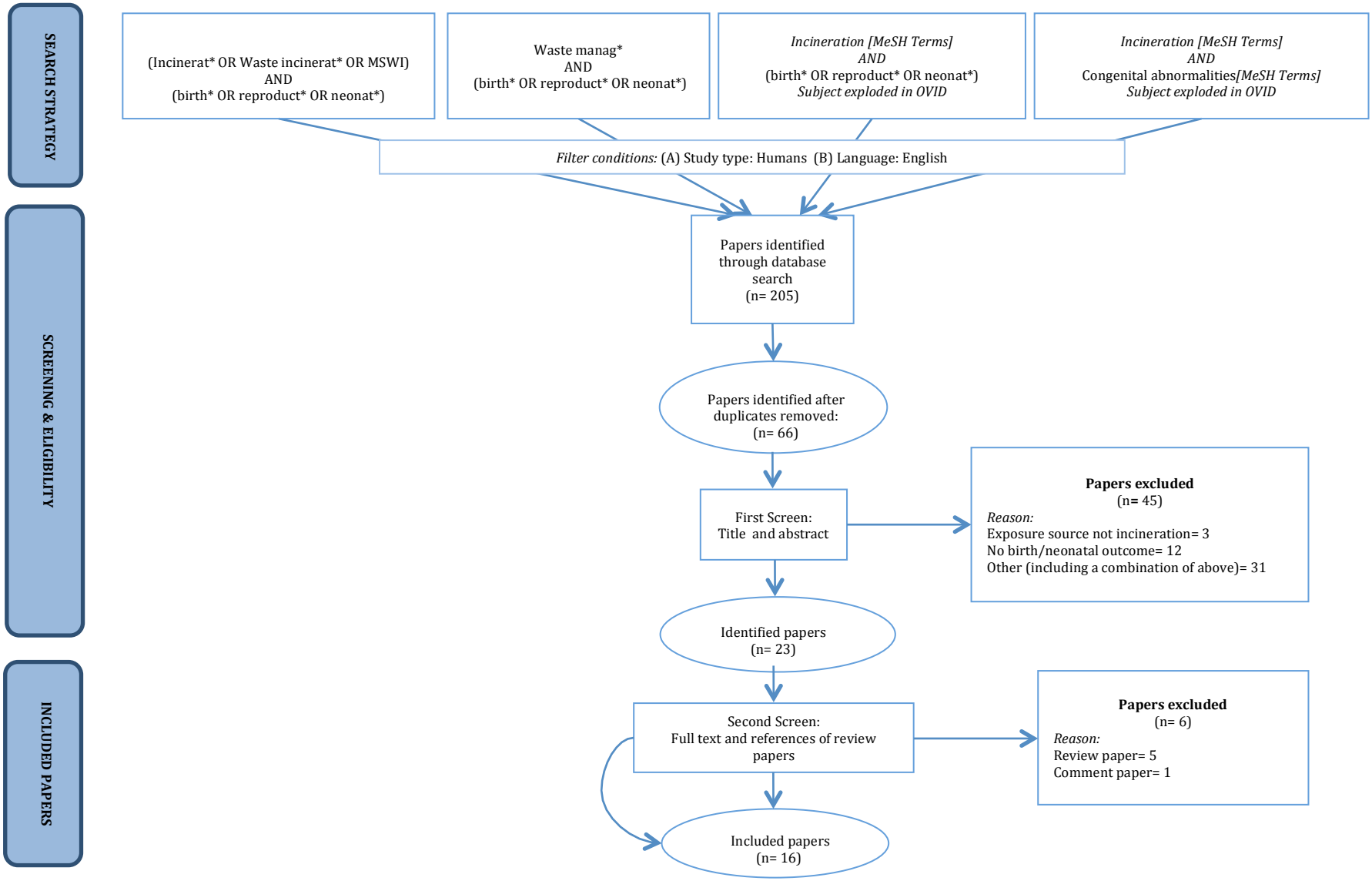


Table 1.7 Summary of epidemiological design on incineration and risk of birth outcomes by group of outcome

Birth outcomes investigated	Author(s) and location of study	Study design	Study period	Study participants	Exposure source	Exposure assessment	Confounders
Sex ratio Multiple births PTD SGA	Candela *et al* 2013, Italy	Geographic study	2003-2010	All births within the study area (4km around the 8 inclusive incinerators)= 21,517 Girls births= 10,227 Multiple births= 260 PTD= 1,316 SGA=2,278	8 incinerators	Modelled exposure to particulate matter (PM_{10}) - used as a tracer for all air pollution from incinerators Exposure assessment based on maternal residence during 9 months of pregnancy Quintiles of exposure from incineration (PM_{10}) and quartiles of exposure to other sources (NO_x)	*For entire study period (2003-2010):* Exposure to other pollution sources, maternal age, maternal educational level, maternal country of origin, birth order and sex of the baby *For subset of study period (2007-2010):* Exposure to other pollution sources, maternal age, maternal educational level, maternal country of origin, birth order, sex of the baby, maternal smoking during pregnancy, deprivation index and maternal hospitalizations 3 years before conception

PTD LBW SGA	Castello *et al* 2013, Spain	Geographic (ecological) study	2004-2008	Municipalities within 3.5km of industrial activity group "Non-hazardous waste" (installations for the incineration of non-hazardous waste)= 114 Singleton live births in 8,098 municipalities= 2,319,555 *Observed births within municipalities within 3.5km radius of activity group "Non-hazardous waste"* Very PTD= 626 Moderate PTD=3307 Very LBW= 472 Moderate LBW=3688 SGA=6633	Not stated	Exposure assessment based on maternal municipality of residence at birth-distance from administrative centre of municipality of residence to installation A "near vs far" analysis (3.5km threshold)	Proportion of adolescent mothers, proportion of mature mothers, proportion of immigrant mothers coming from countries with low income, proportion of mothers who were illiterate or did not complete primary school education, proportion of mothers developing manual work, population size, habitability index, unemployment rate, average socioeconomic level, percentage of mono-parental families and number of vehicles per household
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	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)	Year of birth, maternal age, department of birth, population density, average family income *Exposed communities only; o*ther sources of dioxin exposure, local road traffic

				Congenital anomalies=6730		Three classes of exposure	
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 (10km 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; 3km from the plant, Outer zone, 3-7km 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 PTD Sex ratio	Lin *et al* 2006, Taiwan	Geographic study (ecological study- before and after the introduction of an incinerator)	1991 & 1997	Births in 1991 (1 year before incinerator opened) =6,697 neonates 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	1 MSWI	Modelled dioxin concentrations as a proxy for ambient dioxin exposure 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	Gender, birth order, maternal age, maternal education level

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 10km) MSWIs selected for inclusion were those reported by the Ministry of Health and Welfare of Japan as high dioxin emitting (>80ng 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 clefts=25 Wilhelmina clinic syndromal orofacial clefts=10	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 Wilhelmina Gasthuis maternity clinic (located12km from the incinerator)	Smoking, socioeconomic status, genetic encaves, anti-epileptic medication use, alcohol consumption
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	1 MSWI	Modelled dioxin concentrations Exposure assessment based on females residing or working in areas defined as	Socio-economic status

				All cases of birth defects and spontaneous abortions in Modena municipal population Spontaneous abortions=28 Birth defects=7		"exposed" to incinerator dioxins (based on modelled dioxin concentrations) Three classes of exposure- Exposed areas had annual average modelled concentrations ≥0.5*10^{-9} µg/m^3 Two classes of increasing exposure: Intermediate = 0.5-1*10^{-9} µg/m^3 & High= ≥1*10^{-9} µg/m^3	
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 ≥0.5*10^{-9} µg/m^3 Two classes of increasing exposure: Intermediate = 0.5-1*10^{-9} µg/m^3 & High= ≥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); SGA (small for gestational age

Table 1.8 Summary of findings for epidemiological studies on incineration and risk of adverse birth and neonatal outcome

Author(s)	Birth outcomes	Summary estimate: Risk estimates for significant findings (95% CI)	Number of cases
Candela *et al* 2013	1. Sex ratio 2. Multiple births 3. PTD 4 SGA	1,2,4 No association reported between modelled incinerator emissions and sex ratio, multiple birth or frequency of SGA births 3 Significant increase in PTD with increasing exposure *Odds ratio at highest exposure quintile (entire study period)* PTD 1.30 (1.08-1.57) Very PTD 2.19 (1.24-3.85) *Odds ratio at highest exposure quintile (subset of study period-2007-2010)* PTD 1.44 (1.11-1.85) Very PTD 2.27 (1.08-4.76)	1. Number of girls= 10,227 2. Multiple births= 260 3. PTD= 1,316 4. Small for gestational age=2,278
Castello *et al* 2013	1. PTD 2. LBW 3. SGA	1 No excess risk of PTD observed for mothers living in municipalities within a 3.5km radius of the activity type "non hazardous waste" compared with mothers resident in municipalities with no industries 2,3 Significant excess risk of LBW and SGA for mothers living in municipalities within a 3.5km radius of the activity type "non hazardous waste" compared with mothers resident in municipalities with no industries *Relative risk* Very LBW 1.13 (1.01-1.25) Moderate LBW 1.05 (1.00-1.10) SGA 1.06 (1.02-1.11)	1. Very PTD= 626 Moderate PTD=3307 2. Very LBW= 472 Moderate LBW=3688 SGA=6633

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* 1.04 (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*	1. 304 2. 187

		Dioxin deposits: Exposed 2.05 (0.92- 4.57)	
Cresswell *et al* 2003	Major congenital anomalies	No increases in risk of congenital anomalies for residents living within 3km 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 (<2500g) 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) Small significant decrease in gestational weeks, in exposed districts compared to unexposed districts following the introduction of the	1991 1. 247 2. 562 3. 3092/3604 1997 1. 237 2. 753 3. 3002/3280

		incinerator (-0.09 weeks)	
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 2km from the incinerators *Ratio of observed divided by expected rates at 0-1km* 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 <u>Zeeburg clinic:</u> 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 <u>Wilhelmina clinic:</u> 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	Zeeburg 24 Wilhelmina clinic 35

		per 1000 births)	
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. 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)	1. 28 2. 7
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. 16

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); SGA (small for gestational age)

Table 1.9 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)
Candela *et al* 2013	3	1	5	3	12
Castello *et al* 2013	1	1	2	2	6
Cordeir *et al* 2004	3	1	4	2	10
Cordeir *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	2	1	1	-2	2

1998					
	2	1	4	2	9
Lin *et al* 2006					
	2	1	2	1	6
Lloyd *et al* 1988					
	1	2	1	2	6
Obi-Osius *et al* 2004					
	3	1	1	1	6
Rydhstroem 1998					
	3	2	1	1	7
Tango *et al* 2004					
	3	1	1	2	7
ten Tusscher *et al* 2000					
	3	1	3	1	8
Vinceti *et al* 2008					
	2	2	5	2	11
Vinceti *et al* 2009					
	3	1	3	-2	5
Williams *et al* 1992					

Table 1.10 Summary of main animal toxicology studies of the reproductive effects of 2,3,7,8-TCDD exposure

Fetal effect	Ref	Dioxin	Animal (strain)	Method of exposure	Dose (μg/kg)	Day(s) of administration; Sacrifice day (GD)	Relationship	Maternal toxicity/effect	Additional fetal effects	Note
Fetal growth										
Increase in body weight	Haake *et al*., 1987	2,3,7,8-TCDD	Mice(C57BL/6J)	Oral gavage	20	10; 17	N/A	Increased in liver/body weight	Increased cleft palate and hydrophrosis	
	Silkworth *et al* 1989†	2,3,7,8-TCDD	Mice(C57BL/6J)	Oral gavage	0, 0.5,1,2,4	6-15; 18	Dose response	Increase in liver/body weight and decrease in thymus/body weight	Increased cleft palate and hydrophrosis	
Decrease in body weight	Giavini *et al*., 1983*	2,3,7,8-TCDD	Rat(CRCD)	Oral gavage	0, 0.125, 0.5, 2	14 days before mating; 21	No clear dose reponse	Less active females at high doses/reduced weight gain, pre/post implantation loss	Increased fetal mortality and malformations	
	Giavini *et al*., 1982*	2,3,7,8-TCDD	Rat(Sprague-Dawley)	Oral gavage	0, 0.125, 0.5, 2	1-3;21	Dose response	Reduced maternal weight gain (days 1-6)	Increased in malformations	
	Khera and Ruddick, 1973*	2,3,7,8-TCDD	Rat(Wister)	Oral gavage	0, 0.125, 0.25, 0.5, 1, 2, 4, 8, 16	6-15;22	Dose response	Maternal toxicity	Visceral anomalies:edema and haemorrhage, increased fetal mortality	
	Gray and Ostby	2,3,7,8-TCDD	Rat (LE Hooded)	Oral gavange	1	8 and 15; NR	N/A	None	Vaginal threads, cleft phallus, AGD reduced,	Postnatal observations

	,1995							reduced fertility, increase in cystic hyperplasia	
	Gray et al., 1997	2,3,7,8-TCDD	Rat (LE Hooded)	Oral gavage	0, 1	15; PND 80	N/A	NR	Reduced ovarian and pituitary weights, increased cleft phallus	Postnatal observations
	Huuskonen *et al.*, 1994**	2,3,7,8-TCDD	Rat(LE Hooded)	Oral gavage	0,1,5	8;20	No clear dose reponse- as effect only seen at 5ug/kg	Reduced body weight gain and thymus weight, increased liver weight	Increased late fetal deaths, cleft palate and placental wights	
	Bjerke and Peterson, 1994**	2,3,7,8-TCDD	Rat(Holtzman)	Oral gavage	0,1	15; NR	N/A	None	Delayed puberty, reduced accessory sex organ weight, sperm production and reserve and feminisation of sexual behaviour	Reduced crown-rump length and body weight
	Wolf *et al.*, 1999	2,3,7,8-TCDD	Hampsters (Syrian)	Oral gavage	2	11.5; PND 25, 234-397	N/A	None	Cleft phallus, delayed vaginal opening, delayed puberty, reduced fertility, reduced litter size, maternal death, decreased survival of the next generation, decreased weight of liver,	Postnatal observations

									reproductive tract, ovaries, decreased urethal-vaginal distance, altered vaginal estrous cycles	
Structural malformations										
Increase in malformations	Courtney, 1976†	2,3,7,8-TCDD	Mice(CD-1)	Orally and subcutaneously	0, 25, 50, 100, 200, 400	7-16;18	Dose-response for oral administration	Increased liver/body weight	Increased fetal mortality, increase cleft palate and kidney defects	Club foot
Increase in cleft palate	Moore *et al*., 1973	2,3,7,8-TCDD	Mice(C57B1/6)	Oral gavage	0, 1, 3	10 and 10-13;18	Dose response	Not reported	Increase in kidney anomalies	Incidence of cleft plate greater for same dose administered on GD10-13 compared to 10GD
	Weber *et al*., 1985	2,3,7,8-TCDD	Mice(C57BL/6N)	Oral gavage	0,12,17,22	10;18	Dose response	Increased liver/body weight	Increase in hydrophrosis	
	Birnbaum *et al*., 1985	2,3,7,8-TCDD	Mice(C57BL/6N)	Oral gavage	0, 3, 12	11 and 10-13;18	Dose response	Increased liver/body weight	Increase in hydrophrosis	
	Birnbaum *et*	2,3,7,8-	Mice(C57BL/6N)	Oral gavage	0, 6, 9, 12, 15,	10 and 12;18	Dose response-≥9	Increased liver/body weight,	Increase in hydrophrosis	

al., 1989	TCDD			18		the increase in incidence was statistically different from control	reduced weight gain	
Haake *et al*., 1987	2,3,7,8-TCDD	Mice(C57BL/6J)	Oral gavage	20	10; 17	N/A	Increased in liver/body weight	Increased fetal weight and hydrophrosis
Silkworth *et al* 1989†	2,3,7,8-TCDD	Mice(C57BL/6J)	Oral gavage	0, 0.5,1,2,4	6-15; 18	Dose response	Increase in liver/body weight and decrease in thymus/body weight	Increase in body weight and hydrophrosis
Courtney and Moore, 1971‡	2,3,7,8-TCDD	Mice(C57BL/6J)	Injected for subcutaneous exposure	0, 3	6-15;18	N/A	Increased liver/body weight	Increase in kidney anomalies
Courtney and Moore, 1971‡	2,3,7,8-TCDD	Mice(DBA/2J)	Injected for subcutaneous exposure	0, 3	6-15;18	N/A	Increased liver/body weight	Increase in kidney anomalies
Silkworth *et al* 1989†	2,3,7,8-TCDD	Mice (DBA/2J)	Oral gavage	0, 0.5, 2, 4, 8	6-15; 18	Dose response	Increase in liver/body weight and decrease in thymus/body weight	Increase in hydrophrosis
Neubert and Dilman	2,3,7,8-TCDD	Mice(NMRI)	Oral	0.3, 3, 4.5, 9 and 9	6-15 and 9-13; 18	Dose response	Not reported	Increased fetal mortality

1972								
Courtney, 1976†	2,3,7,8-TCDD	Mice(CD-1)	Orally and subcutaneously	0, 25, 50, 100, 200, 400	7-16;18	Dose response	Increased liver/body weight	Increased fetal mortality, increase club foot and kidney defect
Courtney and Moore, 1971‡	2,3,7,8-TCDD	Mice(CD1)	Injected for subcutaneous exposure	0,1,3	6-15;17	No clear dose reponse	None	Increase in kidney anomalies
Smith *et al*., 1976	2,3,7,8-TCDD	Mice(CF-1)	Oral gavage	0, 0.001, 0.01, 0.1, 1, 3	6-15;NR	Dose response	None	Increase in hydrophrosis
Olson and McGarrigle, 1990	2,3,7,8-TCDD	Rat(Holtzman)	Oral gavage	0, 1.5, 3, 6, 18	10;20	NR- only after 18µg/kg	Reduced weight gain	Increase in late fetal deaths: gastrointestinal haemorrhaging. Decreased thymus and spleen weight
Huuskonen *et al*., 1994	2,3,7,8-TCDD	Rat(LE)	Oral gavage	0,1,5	8;20	No clear dose reponse- as effect only seen at 5µg/kg	Reduced bosy weiught gain and thymus weight, increased liver weight	Increased late fetal deaths, reduced fetal weights and placental weights
Olson and McGarrigle, 1990	2,3,7,8-TCDD	Hampsters (Golden Syrian)	Oral gavage	0, 1.5, 3, 6, 18	9;15	NR- only after 18µg/kg	None	Increase in late fetal deaths: gastrointestinal haemorrhaging, edema, renal congestion.

									Decreased developed glomeruli. Decreased thymus and spleen weight, kidney defects and hydophrensis	
Increase in hydrophrosis	Weber *et al*., 1985	2,3,7,8-TCDD	Mice(C57BL/6N)	Oral gavage	0,12,17,22	10;18	No clear dose response	Increased liver/body weight	Increase in cleft palate	Kidney lesions later characterised as hydrophrosis; dose too high to show dose response
	Birnbaum *et al*., 1985	2,3,7,8-TCDD	Mice(C57BL/6N)	Oral gavage	0, 3, 12	11 and 10-13;18	No clear dose response	Increased liver/body weight	Increase in cleft palate	
	Birnbaum *et al*., 1986	2,3,7,8-TCDD	Mice(C57BL/6N)	Oral gavage	0, 3	10-13;18	N/A- at 3µg/kg the incindence was significantly higher than the control	Increased liver/body weight	None	
	Birnbaum *et al*.,	2,3,7,8-TCDD	Mice(C57BL/6N)	Oral gavage	0, 6, 9, 12, 15, 18	10 and 12;18	dose response-≥6 the increase	Increased liver/body weight, reduced weight	Increase in cleft palate	

	1989						in incidence was statistically different from control	gain	
	Haake *et al*., 1987	2,3,7,8-TCDD	Mice(C57BL/6J)	Oral gavage	20	10; 17	N/A	Increased in liver/body weight	Increase in fetal weight and cleft palate
	Silkworth *et al* 1989†	2,3,7,8-TCDD	Mice(C57BL/6J)	Oral gavage	0, 0.5,1,2,4	6-15; 18	Dose response	Increase in liver/body weight and decrease thymus/body weight	Increase in total, moderate and severe hydronphronsis and increase in cleft plate and body weight
	Silkworth *et al* 1989†	2,3,7,8-TCDD	Mice (DBA/2J)	Oral gavage	0, 0.5, 2, 4, 8	6-15; 18	Dose response	Increase in liver/body weight and decrease in thymus/body weight	Increase in total and moderate hydronphronsis and cleft plate
	Smith *et al*., 1976	2,3,7,8-TCDD	Mice(CF-1)	Oral gavage	0, 0.001, 0.01, 0.1, 1, 3	6-15;NR	Dose response	None	Increase in cleft palate	Reported as dilated renal pelvis
	Theobald and Peterson 1997	2,3,7,8-TCDD	Mice (ICR)	Oral intubation	15, 30, 60	14;PND 23-142	No clears dose resposne	None	Decrease in weight of thymus, prostate and coagulating gland, pituitary gald, uterus weights .	Only significant in males.
	Huuskonen *et al*.,	2,3,7,8-TCDD	Rat(Han/Wister)	Oral gavage	0,1,10	8 or 12;20	Dose response	Reduced thymus weight, increased liver weight	Dilation of renal pelvis, thymus size, edemas and

	1994**								gastrointestional haemorrhaging	
	Olson and McGarrigle, 1990	2,3,7,8-TCDD	Hampsters (Golden Syrian)	Oral gavage	0, 1.5, 3, 6, 18	9;15	NR- over 1.5µg/kg	None	Increase in late fetal deaths: gastrointestinal haemorrhaging, edema, renal congestion. Decreased developed glomeruli. Decreased thymus and spleen weight, cleft palate	
Increase in kidney defects	Moore *et al*., 1973	2,3,7,8-TCDD	Mice(B57 B1/6)	Oral gavage	0, 1, 3	10 and 10-13;18	Dose response	Not reported	Increase in cleft palate	Kidney anomalies(including bilateral anomalies): renal papilla and early stage hydrophrosis; incidence of kidney anomalies greater for same dose administe

										red at GD10-13 compared to 10GD
	Courtney and Moore, 1971‡	2,3,7,8-TCDD	Mice(C57BL/6J)	Injected for subcutaneous exposure	0, 3	6-15;18	N/A	Increased liver/body weight	Increase in cleft palate	Unilocular cystinephrotic kidney and hydrophrosis
	Courtney and Moore, 1971‡	2,3,7,8-TCDD	Mice(DBA/2J)	Injected for subcutaneous exposure	0, 3	6-15;18	N/A	Increased liver/body weight	Increase in cleft palate	Unilocular cystinephrotic kidney and hydrophrosis
	Courtney and Moore, 1971‡	2,3,7,8-TCDD	Mice(CD1)	Injected for subcutaneous exposure	0,1,3	6-15;17	Dose response	None	Increase in cleft palate	Unilocular cystinephrotic kidney and hydrophrosis
	Courtney, 1976†	2,3,7,8-TCDD	Mice(CD-1)	Orally and subcutaneously	0, 25, 50, 100, 200, 400	7-16;18	Dose response for oral administration	Increased liver/body weight	Increased fetal mortality, cleft palate and club foot	
	Courtn	2,3,7,	Rat(CD)	Injected	0, 0.5	6-15;20	N/A	None	None	Unilocula

	ey and Moore, 1971‡	8-TCDD		for subcutaneous exposure						r cystinephrotic kidney and hydrophrosis
	Giavini *et al*., 1983*	2,3,7,8-TCDD	Rat(CRCD)	Oral gavage	0, 0.125, 0.5, 2	14 days before mating; 21	Dose response	Less active feamls at high doses/reduced weight gain, pre/post implantation loss	Increased fetal mortality, decreased weight	In all malformed fetuses exp (cystic kidney, subcutaneous edema, gastrointestional hemorrhage)
	Giavini *et al*., 1982*	2,3,7,8-TCDD	Rat(Sprague-Dawley)	Oral gavage	0, 0.125, 0.5, 2	1-3;21	Dose response	Reduced maternal weight gain (days 1-6)	Decrease in fetal weight	Not statistically significant, cystic kidney
	Olson and McGarrigle, 1990	2,3,7,8-TCDD	Hampsters (Golden Syrian)	Oral gavage	0, 1.5, 3, 6, 18	9;15	NR- over 1.5µg/kg	None	Increase in late fetal deaths: gastrointestinal haemorrhaging, edema, renal congestion. Decreased developed	Congestion

									glomeruli. Decreased thymus and spleen weight, cleft palate and hydropronesis	
Reproductive malformations										
Female clefting of phallus	Gray and Ostby,1995**	2,3,7,8-TCDD	Rat (Holtzman)	Oral gavange	1	15; NR	N/A	None	Delayed vaginal opening, vaginal threads, decreased fetal viability, decreased AGD, increase in cystic hyperplasia	100% clefting
	Flaws et al., 1997	2,3,7,8-TCDD	Rat (Holtzman)	Oral gavage	1	11,15 and 18; PND 2,21, 42 or 195-205	N/A	NR	Decreased pup mortality, irregular invagination of the canal and hyperkeratinization, vaginal thread	55-96%, increased frequency when administered on GD 11. Permanent as seen when observed at 195-204 PND.
	Gray et al., 1997	2,3,7,8-TCDD	Rat (LE Hooded)	Oral gavage	0, 0.05, 0.20, 0.80	15;PND 70 and 20 months	Dose reponse	NR	Delayed vaginal opening, increase size of urethral slit and distance from tip	

								of phallus to urethral opening and decreased distance from urethral opening to vagina, increased age at vaginal opening, delayed time-to-pregnancy,ovrai n neoplasms, ovarian interstitial hyperplasia, vaginal thread	
	Gray et al., 1997	2,3,7, 8-TCDD	Rat (LE Hooded)	Oral gavage	0, 1	15; PND 80	N/A	NR	Reduced ovarian and pituitary weights, decreased body weight	
	Gray and Ostby,1 995**	2,3,7, 8-TCDD	Rat (LE Hooded)	Oral gavange	1	8 and 15; NR	N/A	None	Delayed vaginal opening, vaginal threads, AGD reduced, reduced fertility, increase in cystic hyperplasia	Those administe red at GD15, 65% had complete to partial clefting of phallus, GD8 25% partially cleft phallus

	Wolf *et al.*, 1999	2,3,7,8-TCDD	Hampsters (Syrian)	Oral gavage	2	11.5; PND 25, 234-397	N/A	None	Reduced body weight, delayed vaginal opening, delayed puberty, reduced fertility, reduced litter size, maternal death, decreased survival of the next generation, decreased weight of liver, reproductive tract, ovaries, decreased urethal-vaginal distance, altered vaginal estrous cycles	
Vaginal threads	Gray and Ostby,1995**	2,3,7,8-TCDD	Rat (Holtzman)	Oral gavange	1	15; NR	N/A	None	Delayed vaginal opening, cleft phallus, decreased fetal viability, decreased AGD, increase in cystic hyperplasia	83% vaginal thread
	Flaws et al., 1997	2,3,7,8-TCDD	Rat (Holtzman)	Oral gavage	1	11,15 and 18; PND 2,21, 42 or 195-205	N/A	NR	Decreased pup mortality, irregular invagination of the canal and hyperkeratinization, cleft clitoris	36-44%. Permanent as seen when observed at 195-204

	Dienhart *et al*., 2000*	2,3,7,8-TCDD	Rat (Holtzman)	Oral gavage	1	15; 17, 18, 19, 20, 21	N/A	NR	None	
	Gray and Ostby,1995**	2,3,7,8-TCDD	Rat (LE Hooded)	Oral gavange	1	8 and 15; NR	N/A	None	Delayed vaginal opening, cleft phallus, AGD reduced, reduced body weights, reduced fertility, increase in cystic hyperplasia	At GD 15, 80% vaginal thread, at GD 8 14%
	Gray et al., 1997	2,3,7,8-TCDD	Rat (LE Hooded)	Oral gavage	0, 0.05, 0.20, 0.80	15;PND 70 and 20 months	Dose reponse	NR	Delayed vaginal opening,increase size of urethral slit and distance from tip of phallus to urethral opening and decreased distance from urethral opening to vagina, increased age at vaginal opening, delayed time-to-pregnancy, ovrain neoplasms, ovarian interstitial hyperplasia, cleft phallus	Permanent and temporary

GD based on presence of vaginal plug= GD0: * Positive vaginal smear= GD 1; †Vaginal plug= GD1; ‡Vaginal plus and positive smear =GD0; **Positive vaginal sperm =GD0; Wolf et al defined successful mating verified by absence of lordosis behaviour on next proestrus. GD 0

CHAPTER 2: AIMS & OBJECTIVES

The overall aim for this thesis is to address a number of the gaps identified in the literature with regards to estimating population and individual level exposure to modern MSWI emissions in GB, in addition to the use of birth datasets for epidemiological studies on birth outcomes in England.

The work presented in this thesis provides proof of concept in support of SAHSU's national study investigating the association between MSWI emissions and adverse birth and neonatal health outcomes in GB. Although the methodologies developed and detailed in the thesis alongside all results will be used in the SASHU study the thesis did not aim to accomplish all of SASHUs study goals.

The specific aims and sub aims of this thesis are:

1. To develop a dispersion model framework to estimate population exposure to emissions from a subset of MSWIs operating under current legislation (the WID). The framework developed and all model outputs presented within the thesis will be used in the SAHSU study investigating the relationship between incineration and birth outcomes.

- To use atmospheric dispersion modelling to best estimate exposure to particulates emitted by modern day MSWIs (as a proxy for exposure to all emitted pollutants from MSWIs) at a small area level.
    - To describe the spatial variability in modelled estimates and locate areas of contrasting exposure.
    - To predict ground level concentrations of particulates within the vicinity of MSWIs.
    - To investigate the distance from MSWIs at which the ground level concentrations of pollutants from the MSWIs are negligible.
    - To assess the sensitivity of the atmospheric dispersion model to input data.
- To compare modelled exposure estimates with distance as a proxy for exposure to incineration by-products and explore issues of exposure misclassification.

2. To design, develop and undertake pilot data collection, including breast milk sample collection, for a biomonitoring study which aims to estimate individual level dioxin exposure of pregnant women living within the vicinity of two modern MSWIs.

- To design a pilot epidemiological biomonitoring study to answer the study aim.
- Design study materials to be dispatched to participants.
- Acquire ethical permissions to undertake the study.
- Recruit participants to the study and establish a study database of approximately 100 participants.
- Undertake data collection, including breast milk sample collection, for all study participants residing around two MSWIs.
- Undertake a descriptive analysis of the characteristics of the study participants.

3. To make recommendations to researchers on the most appropriate national births dataset to use in epidemiological studies of birth outcomes in England. These recommendations will be used to inform the choice of data source for birth outcomes without complete single dataset sources within the SASHU study on incineration and birth outcomes,.

   For each national birth dataset to;

- Explore methodological issues during data extraction and cleaning.
- Investigate the availability of data relevant for birth outcomes.
- Evaluate the quality of the data.
- Update the descriptive epidemiology on the following birth outcomes: low birth weight, very low birth weight, term low birth weight, stillbirths, preterm delivery and very preterm delivery.
- Explore temporal and spatial variability in reporting of these birth outcomes.
- Undertake a small area level analysis of live births, stillbirths and birth weight in the areas surrounding two MSWIs.

CHAPTER 3: METHODS

This chapter describes the methods used to investigate the three aims of this thesis, namely: small area level exposure assessment of MSWI emissions; biological monitoring of dioxins; and the use of national birth data in epidemiological studies of birth outcomes. As discussed in chapter 1, Section 1.4 there is a variety of different techniques for assessing exposure to MSWI emissions each of which hold advantages and disadvantages. In order to give a comprehensive assessment of exposure both at population and individual level, within the financial constraints of the study, the decision to undertake dispersion modelling and biological monitoring was made.

3.1 SMALL AREA LEVEL EXPOSURE ASSESSMENT OF MUNICIPAL SOLID WASTE INCINERATOR EMISSIONS

This section describes the methodology developed to assess exposure to MSWIs emissions at small area level. As part of this thesis, the dispersion model developed was applied to four MSWI sites, with contrasting topography and population density. The model that was built (including all coding) was subsequently rolled out to all 22 MSWIs in GB by Maria Leal Sanchez for use in SAHSU's national study investigating the associations between MSWI emissions and adverse birth and neonatal health outcomes in GB [208]. Some of the methods presented in this chapter were published in the Journal of Environmental and Public Health in 2013 **(Appendix C)** [145, 209, 210].

3.1.1 Methods

Epidemiological context-Study design, area and population

SAHSU's incinerator study is the first to investigate the association between modelled ground level concentrations of stack emissions from modern MSWIs (those operating under new legislation), and the risk of adverse birth and neonatal outcomes in GB. This study includes all operational MSWIs in GB from the implementation of the WID [211] on the 28th December 2002, with a study period from 1st January 2003 until 31st December 2010 (20 in England, 1 in Wales and 1 in Scotland-locations depicted in Figure 3.1). Twelve MSWIs came into operation

following the implementation of the WID [211]. The remaining ten were in operation beforehand and were therefore required to adhere to the WID [211] from December 2005.

The study area was defined as a 10 km radius around each MSWI. This area was selected in co-ordination with the UK EA's Horizontal Guidance (H1) [212] which outlines the environmental risk assessment procedures required during permit application (under the Environmental Permit Regulations [213]). Annex F of the H1 [214] specifies the need for an air quality assessment at all European conservation sites within a 10 km radius of permitted installations.

The study population comprised of postcodes and therefore residents, within the study area. On average one UK postcode represents 12-15 households and 40-45 people.

3.1.1.2 Atmospheric dispersion modelling

As discussed in chapter 1 the majority of previous epidemiological studies investigating population exposure to incineration have used distance as a proxy for exposure. This method does not consider the individual properties of the incinerator, the magnitude of emissions or local meteorology and topography, all of which can significantly influence the propagation of emitted pollutants and ground level concentrations. ADMS–Urban version 3.1 [215] software was used to undertake the atmospheric dispersion modelling presented in this section. ADMS-Urban has been extensively validated [29-32] and is used widely in the UK for regulatory purposes and policy support. This 'new generation' Gaussian-based plume air dispersion model has improved from older generation models both in its rendition of turbulence and of atmospheric boundary layer structure [216] (using the Monin-Obukhov length to simulate dispersion in the atmospheric boundary layer, instead of the outdated Pasquill stability classes, as outlined in chapter 1). ADMS-Urban is capable of incorporating multiple sources within complex terrain and can be used in conjunction with Geographic Information System (GIS) [216].

Exposure to particulates from MSWIs is most likely via inhalation, so this was the route considered within our model. Figure 3.2 provides a schematic overview of the exposure modelling methodology.

Model input data and sensitivity analysis

Point source

Municipal Solid Waste Incinerators

All MSWIs operating in England and Wales are regulated by the UK EA. The EA provided general information on each operating MSWI, including; location, commissioning date and the amount of waste licensed to incinerate annually (Table 3.1). The exact locations of the MSWI stacks were verified through checks of site addresses against six-figure grid references (geo-referenced location of the stack in the British National Grid projection) and satellite map searches in Google maps. The locations of the four contrasting MSWIs sites described within this section are highlighted in Figure 3.1.

The MSWIs included were selected in order to illustrate variability in sites across GB, with regard to;

- The operational standards to which they were built (Edmonton and Stockton-on-Tees operated before the implementation of the WID [211], whereas Marchwood and Sheffield have only ever operated to the WID [211])
- Their capacity (ranging from 165,000 tonnes a year to 750,000 tonnes a year)
- The number of flues they have (Stockton on Tees commissioned a third flue in May 2009, whereas the other three sites have two flues each)
- Their location (Marchwood and Stockton-on-Tees are located on the coast with Marchwood within a particularly rural area, whereas Sheffield and Edmonton are both inland located within urban areas)
- The surrounding terrain (Sheffield is surrounded by hills whereas the other three MSWIs are located on predominantly flat land)

Stack characteristics

The EA additionally provided stack characteristics per MSWI and per flue. Stack characteristics were extracted from environmental risk assessment reports submitted to support MSWI permit applications. Characteristics included; stack height (m), stack diameter (m), exit velocity (m/s), exit flow (m^3/s), and exit temperature (°C). Table 3.1 details the stack characteristics for the four included MSWIs in this section-Edmonton, Marchwood, Stockton-on-Tees and Sheffield. All flues were modelled as individual point sources.

Emissions data

As detailed in chapter 1, table 1.3, WID compliance reporting requires dioxins to be monitored biannually, or every 3 months within the first year of operation. In order to generate time sensitive models that will enable trimester weighting particulate data which is monitored continuously was used as a proxy for all MSWI emissions. Daily mean particulate concentrations (total dust) at the flue exit were provided by the EA for each flue from 1st January 2003 (if the MSWI was operational) until 31st December 2010. As bag-filtered stack emissions from the MSWIs do not contain a significant number of particulates greater than 10 μm diameter, emitted particulates were modelled as those with a diameter less than 10μm (PM_{10}). To support the use of particulate emissions data as a proxy for all MSWI emissions including dioxins a correlation analysis was conducted between dioxins and particulates for all 22 MSWIs in the UK. The results revealed a coefficient of 0.213. However when using a multiple linear regression model, adjusted for MSWI, flue and year, a 0.108 coefficient was achieved. These weak correlations are likely due to the scarcity of the dioxin data.

Emissions data – Sensitivity analysis

All emissions data underwent thorough checking, with all coding issues identified and clarified with the EA. This checking was particularly important when identifying periods in which a plant was non-operational, i.e. down time, and when it was operating but no emissions data were recorded or available, i.e. missing data. A variety of methods were explored to address periods with missing data on emissions. Multiple imputation [217] is a highly validated method for addressing missing data was explored first. However as the performance of the bag filter is the biggest predictor of particulate emissions followed by the incinerator load, neither of which are routinely documented, this sophisticated statistical imputation was not possible. Therefore a sensitivity analysis was undertaken using four different methods to provide values for the missing data. This analysis was undertaken for Stockton-on-Tees MSWI because over 70% of the total number of missing days across all four MSWIs occurred at that site (on average there were between 15-19 days per year per flue with missing daily concentrations). This analysis was conducted for 2004, as this was the year with the greatest proportion of missing data (25%). These methods included:

1) Annual mean concentration of particulates during operational days per flue per year
2) Annual median concentration of particulates during operational days per flue per year
3) Annual maximum daily concentration of particulates during operational days per flue per year

4) Two day average concentration of particulates either side of the missing period – named "day average"

Daily models using each method were run within ADMS-Urban at postcode level. The correlation of model outputs was explored and outputs plotted and compared. Additionally model outputs were aggregated to trimester specific exposures, calculated as the 90 day period before the day of interest i.e. date of birth, and compared in order to assess which method bore the highest level of suitability for filling in the missing data.

Dispersion site characteristics -Study Area

A number of dispersion site characteristics were considered within the model. These include the type and shape of the surrounding terrain as well as the local meteorological conditions.

Site characteristics

The Monin-Obukhov (MO) length is an indicator of atmospheric stability calculated using the frictional velocity and heat flux at Earth's surface [216]. The magnitude of the MO length indicates the height above which turbulent flows are generated by thermal convection rather than friction at ground level [216].

ADMS-Urban requires a MO length representative of the site location to be entered. The default length is set at 30m, as the model assumes an urban site and accounts for the heat island effect of major cities and prevents the atmosphere from stablising [216].

The dispersion pattern of pollutants is also highly influenced by the type of terrain surrounding the site location. Surface roughness length is a model parameter ADMS-Urban requires to be entered to provide an indicator of how much drag the wind experiences from the ground.

Site characteristics – Sensitivity analysis

In order to select the most representative values for both minimum MO length and the surface roughness length a sensitivity analysis was conducted. Sensitivity analysis involved extracting land cover data for the fetch of each MSWI (fetch defined by the US Environmental Protection Agency as 1 km surrounding the MSWI [218]) and selecting a number of appropriate values to compare. Land cover data were extracted from the Co-ordination of Information on the Environment (CORINE) land cover map 2000 [219]. CORINE is a European land use database that uses satellite images to provide geographical information on the observed physical cover.

CORINE was initiated by the European Commission in 1985 and is compiled by the European EA. The updated CORINE land cover dataset, CLC2000, includes three levels of data with the most detailed level made up of 44 classes of which 11 relate to urban land cover [219].

Local meteorology

Four climatic variables are required as a minimum input into ADMS-Urban: land surface air temperature, wind speed, wind direction and cloud cover. These meteorological data are processed through a meteorological pre-processor which calculates atmospheric boundary layer parameters [216].

All meteorological data and the locations of UK Met Office stations were obtained from the British Atmospheric Data Centre (BADC) [220]. All unique Met office stations were mapped in GIS ArcMap version 10 and information on the annual completeness of hourly land surface observations between 2003 and 2010 calculated. Due to changes in availability of station locations data, any stations without XY coordinates were individually obtained from the BADC website [220].

Local meteorology– Sensitivity analysis

Inputting meteorological data is critical for dispersion modelling and was therefore extensively explored at each MSWI site in order to select a meteorology station which best represents the surrounding area of the site location. At each UK Met office station, the following criteria were assessed and prioritised: meteorological variables measured, annual coverage of variables, distance from the incinerator, temporal coverage across the study period and data quality. SPSS version 20 was used to extract, clean and restructure the meteorological data for use in ADMS-Urban. Once a representative station was selected, an Excel VBA macro was generated and used to divide hourly meteorological data into daily .MET files for use in ADMS-Urban.

Local topography

An assessment of the terrain elevation surrounding the study area for each site was conducted to characterise each MSWI location. The local topography of the study area was extracted from the Ordnance Survey PANORAMA™ digital terrain model (DTM), with a 1:50,000 scale and 50m horizontal resolution [221] in a .terr format (a terrain file). Including terrain files within the hill

option in ADMS-Urban allows the model to adjust plume height and spread parameters according to the surrounding terrain [216].

Local topography– Sensitivity analysis

A terrain file was included if 5% of the study area surrounding a MSWI contained a gradient over 10% (as advised by ADMS [216]).

Background levels

No information on background levels of pollutants were input into the dispersion models as the study area was relatively small and it was therefore hypothesised that the background levels for all population exposures were approximately the same and therefore incorporating them into the model was not necessary. Additional information on study confounders are discussed in chapter 5, Section 5.1.

Running ADMS exposure models

In order to calculate daily average ground-level concentrations of PM_{10} per MSWI, daily incinerator specific ADMS-Urban input files were generated (file format UPL). For each MSWI a unique "template file" was created detailing the characteristics of the MSWI and surrounding area that remained fixed throughout the study period. These included point source characteristics, local topography and the surrounding dispersion site characteristics. An Excel VBA macro was then generated and used to create daily ADMS input files with changing meteorological data and emission concentrations (converted from mg/m^3 provided by EA to g/s for ADMS-Urban).

Model output

All residential postcode centroids within the study area were extracted between 1998 and 2010 (to account for changes/terminated postcodes, which can remain in the system for approximately 5 years) and used as model receptors. Daily average ground level concentrations of PM_{10} were calculated by ADMS-Urban at postcode level within the study area. All sensitivity analysis was conducted using a 200m by 200m grid as model receptors. This greatly reduced

the number of receptors and therefore the model run times, whilst at the same time maintaining the spatial accuracy.

Modelling assumptions

A number of assumptions were made when undertaking this modelling, these include:

- The horizontal and vertical distribution of plume concentrations follow a Gaussian distribution [24, 216] .
- The Gaussian plume properties are constant and continuous within a circular cross section [216].
- Particulate emissions rates are constant for every hour of the day.
- Flue characteristics: temperature of release, exit velocity and exit volume remain constant throughout the study period.
- Dispersion site properties (surface roughness and MO length) are uniform across and representative of the study area.
- Meteorological data are representative of the study area.
- PM_{10} incorporates all particulates emitted from a MSWI.
- The spatial distribution of particulates from other sources are significantly different.
- Background particulate levels are constant across the study area.
- Modelled outputs, distribution patterns and relative concentrations of ground level particulates, are representative as a proxy for exposure to all emitted pollutants from MSWIs.

3.1.1.3 Distance to source

All receptors were mapped in ArcMap version 10 and assigned a proximity value based on their distance to the MSWI of interest. Proximity was assigned the greatest value at the edge of the study area (10 km) and lowest at the MSWI site.

3.1.1.4 Exposure assessment comparison: Modelled estimates *vs* proximity

To compare exposure estimates, each residential postcode (model receptor) was assigned a proximity value and an average modelled ground-level concentration of PM_{10} during the period of operation. Postcodes additionally were assigned a headcount value extracted from the 2001 census [222], to represent the number of people residing at each individual postcode. Exposure estimates using each method were then classified into deciles, quintiles and tertiles from high to

low exposures (distance arranged in ascending order, modelled ground-level concentrations of PM_{10} in descending order).

In order to provide a statistical measure of inter-observer agreement, unweighted and population weighted Cohen's kappa coefficients were calculated for deciles, quintiles and tertiles of exposure [223-225]. This was conducted in R version 3.0.2**.** Finally long term average modelled PM_{10} concentrations were plotted against distance.

3.2 BIOLOGICAL MONITORING OF DIOXINS- INCINERATORS BIOMONITORING STUDY

This section documents the study design, materials, permissions required and obtained to undertake the Incinerators Biomonitoring Study, alongside sample and data acquisition as per the aims outlined for the thesis (detailed in chapter 2).

The aim of the Incinerators Biomonitoring Study is to acquire a personal exposure profile to dioxins for a small group of pregnant women resident within the vicinity of MSWIs in the UK. Thereby enabling the investigation of the relationship between individual level dioxin exposure and residential distance to the MSWI alongside dietary habits. The results of laboratory analysis of dioxin concentrations within the breast milk samples will allow congener profiling within the samples and comparisons with fingerprint dioxin emissions from MSWIs and therefore providing potential for source appointment. Although this is a stand-alone study, it is linked to SAHSU's study on MSWIs and adverse birth and neonatal outcomes whereby the results are expected to aid the interpretation and findings from SAHSU's national study. The full completion and data analysis of milk samples were not amongst the thesis aims.

3.2.1 Selected MSWIs

Of the 22 operational MSWI's in GB, 10 were omitted for inclusion in this study. Those excluded were;

- Island MSWI's - due to their relatively small size and issues experienced during their commission (Porthmellon on the Isles of Scilly and the Isle of Wight)
- MSWIs in Wales and Scotland - due to differences in study permissions required to undertake the study (Crymlyn Burrows MSWI and Dundee MSWI)

- "Overlapping" MSWIs i.e. those with intersecting study areas (10 km radius from the plant) - to avoid issues of multiple MSWI exposure (Dudley, Tyseley, Wolverhampton, Edmonton and SELCHP)
- Recently commissioned MSWIs- due to the half-life of dioxins, approximately 7 years (Isle of Wight, commissioned in 2009 (previously excluded), Grudon, commissioned in 2009)

To help increase the probability of dioxin detection from MSWIs in breast milk it was hypothesised that the most important factors for consideration were ambient dioxin concentrations within the study area, and the fewest number of additional industrial dioxin emitting sources. Dioxin data from the National Atmospheric Emissions Inventory [226], indicated that of the five MSWIs with greatest ambient dioxin concentrations within their study area, Dudley, Sheffield and SELCHP had the greatest number of additional dioxin emitting sources. Furthermore as Dudley and SELCHP are both "overlapping" MSWIs, Stockton-on-Tees and Marchwood were selected for inclusion in the Incinerators Biomonitoring Study. Figure 3.1 and Table 3.1 provide the location and characteristics of the two selected MSWIs.

3.2.2 Study design

Power calculations were undertaken in light of one of the study aims, to undertake a correlation analysis of individual milk dioxin levels and modelled ambient particulate exposure as a proxy for dioxin exposure. Given a specified significance level, power and a series of sample sizes (as existing literature did not provide hypothesized correlation coefficients), the effect size (correlation coefficient) the study was powered to detect could be calculated. The null hypothesis detailed no correlation between individual milk dioxin and modelled ambient dioxin. For sample sizes of 25, 50, 100, 150 and 200, at 5% statistical significance (Alpha= 0.05, probability of rejecting the null hypothesis when its true) and 80% power (Beta=0.2, probability of accepting the null hypothesis when its false), the corresponding correlation coefficients could be detected; 0.53, 0.39, 0.28, 0.23 and 0.20. Due to the financial constrains of the study a sample size of 100 was selected where by the study will be able to detect a medium effect size.

Women recruited to the Incinerators Biomonitoring Study were primiparous, between 18 and 36 weeks gestation, over 18 years of age and resident within postcode districts where the population weighted centroid, associated with their address, were located within the study area (10 km radius around Stockton-on-Tees and Marchwood MSWIs). This inclusion criterion was selected in order to maximise the ability to detect dioxins (primiparous women have substantially higher breast milk dioxin levels than multiparous women), reduce the likelihood

of participants experiencing miscarriages (restricting recruitment to women over 18 week's gestation) and avoid issues of consent for women under 18 years of age.

Potential participants were identified from hospitals (maternity wards) within the study area. All hospitals situated within the study area, with greater than 500 births a year, were approached and recruited to the study. The sites included were;

- Princess Anne Hospital in Southampton (5,584 births in 2010, located 4 km North of the Marchwood MSWI)
- James Cook University Hospital in Middlesbrough (4,312 births in 2010, located 5.6 km South East of the Stockton-on-Tees MSWI)
- University Hospital of North Tees in Stockton-on-Tees (3,257 births in 2010, located 5.9 km South West of the Stockton-on-Tees MSWI).

Figure 3.3 provides the location of the included MSWIs and hospitals in addition to the study area and postcode districts recruited from.

Participants were asked to complete a study questionnaire during pregnancy to collect information on their residential history, personal details, lifestyle characteristics, socio-economic indictors and dietary habits. Additionally they were asked to provide a small 20 mL breast milk sample using a breast pump provided within the first six weeks of birth (samples were stored in a bottle provided, within their domestic freezer). Study questionnaires and frozen breast milk samples were collected from participant's home addresses.

Recruitment was conducted antenatally because of the short window postnatally for sample collection, therefore postnatal recruitment would not give new mothers sufficient time to consider whether they wanted to take part in the study. In order to account for participants dropping out of the study, for example, those experiencing adverse pregnancy outcomes and women unable or choosing not to breastfeed following delivery, there was need to over recruit. Figure 3.4 details the stage of pregnancy and the postnatal period in which recruitment, questionnaire completion and sample provision occurred.

3.2.3 Study team – Investigators, sponsor, funder, NHS trusts & local collaborators

Research site: Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London

Study investigators: Chief investigator - Miss Danielle Ashworth; Primary academic supervisor - Dr Mireille B Toledano; Secondary academic supervisor - Professor Paul Elliott; Co-investigator - Dr Rebecca Ghosh

Study sponsor: Joint Research Compliance Office, Imperial College London and Imperial College Healthcare NHS trust. Sponsor contact- Christine Buicke, Research Governance Manager.

Study funding: Funding was received from the Medical Research Council (MRC) within the Centenary Award by the MRC-PHE Centre for Environment and Health. Additionally this study was adopted into the National Institute for Health Research (NIHR) Clinical Research Network (CRN) portfolio and was eligible for CRN support. As the Marchwood MSWI falls within the Hamphire and Isle of Wight (HIOW) Comprehensive Local Research Networks (CLRN) (now Wessex CLRN), they were confirmed as the lead CLRN on this study and all associated service support costs were covered by HIOW CLRN.

Participant Identification Centres (PICs): The identification of participants and study invitation packs were sent from the recruited hospitals or participant identification centres (PICs), namely;

- Princess Anne Hospital- University Hospital Southampton NHS foundation trust
- James Cook University Hospital- South Tees Hospitals NHS foundation trust
- University Hospital of North Tees- North Tees & Hartlepool NHS foundation trust

In Cleveland, where hospitals were smaller, two PICs were recruited to ensure that a sufficient number of potential participants were approached.

Local collaborators (LCs): LCs at each PIC were identified by HIOW CLRN, with the responsibility of acting as the contact and through whom all liaison was conducted. Many changes in the LCs throughout the study occurred. The final LCs were;

- Jane Forbes-Senior Research Midwife - Princess Anne Hospital
- Hazel Alexander-Research Midwife- James Cook University Hospital
- Anne-Marie Jones- Research Midwife- University Hospital of North Tees

Liaison with local collaborators (LCs)

As detailed above, LCs were identified by the lead CLRN and following their agreement to take part in the study and once all study permissions were in place, these LCs where provided with

all the study materials, briefed on the phone and provided with "Sampling and Mailing Strategy" documents further detailing the inclusion criteria.

Weekly excel spreadsheets of consenting women at each trust were exchanged by the LC and chief investigator via secure NHS.net email accounts in order to ensure that women, who were dispatched study packs, were still known to be pregnant and during reminder calls i.e. following delivery, that the mother and baby were well. This ensured that any participants experiencing adverse outcomes were not approached.

3.2.4 Study materials

The Incinerators Biomonitoring Study requested two items from study participants: completion of a study questionnaire and the provision of a breast milk sample. Study materials required for this study included: study invitation letters, participant information sheets (PIS), consent/recruitment forms, study questionnaires (including occupational questionnaires), breast milk sample, FAQs sheets and a breast milk document to record the date and time of sample collection. All final versions of the study materials, including the study protocol are provided in **Appendix D.**

Study invitation packs

Study invitation letters were addressed by LCs at the PIC (hospital at which women attended their booking appointment at) to women who met the study inclusion criteria. All additional forms within the study invitation pack (PIS, consent/recruitment form and addressed return envelopes) were prepared (printed and folded) at Imperial College, with postage stamps included. LCs were then responsible for dispatching these packs by post.

Invitation letter (Appendix D)

All women invited to take part in the study were provided with an invitation letter detailing what the study proposed to accomplish alongside who was undertaking the study and why this letter was being sent from their hospital and not by the study team (i.e. to protect their confidentiality). Invitation letters emphasised that participation was voluntary and detailed what would be involved should one decide to take part.

Participant information sheet (PIS) (Appendix D)

Alongside invitation letters prospective participants were sent clear and concise PIS's which was designed in a question and answer format. The PIS summarised the study design and included information on why participants had been invited, what taking part involved and what would be the next steps should they decide to take part. Emphasis was given to three particular questions in order to not to cause unnecessary concern to prospective participants; "*Should I be worried about living near an incinerator?", "Should I worry about incinerator pollutants in my breast milk?"* and *"What if I can't breastfeed?".*

Consent/recruitment forms (Appendix D)

Consent/recruitment forms were designed to be a formal record of a women's consent to take part in the Incinerators Biomonitoring Study at the same time as providing contact information, residential address, expected delivery date, confirmation of eligibility (maternal age, previous live births, gestational age) and practical details relevant for study pack dispatch and sample storage (requirement of breast pump and access to a freezer). Consent forms required a written signature from participants.

Women consenting to take part in the study were advised to complete the study consent/recruitment form and place it in the prepaid envelope provided. Return envelopes were arranged as part of the royal mail response service ensuring that only posted envelopes were paid for.

Study packs

All recruited participants progressing in their pregnancy were sent a study pack to their home address approximately 6 weeks before their expected delivery date. The study pack included:

- A study questionnaire.
- A manual breast pump.
- A bottle for milk storage.
- Instructions on how and when to take the breast milk sample.
- A form for the participants to fill in about when the breast milk sample was taken.

Following a substantial amendment an occupational questionnaire was additionally incorporated.

Study questionnaire & occupational questionnaire (Appendix D)

The study questionnaire included 24 questions of varied length in an 8 sided A4 document. The questionnaire required participants to fill this in by hand. By contrast the occupational questionnaire made up of four questions, was filled out by the study team on collection. These questionnaires recorded a plethora of information: residential (both within pregnancy and within the past 5 years), personal (age, height, weight, ethnicity, marital status), lifestyle (smoking status and dietary) and socio-economic (educational level and current occupation).

In order to reduce the time it took to complete the questionnaire, wherever possible, questions had tick boxes answers. The questionnaire therefore took approximately 20 minutes to complete.

As the questionnaire was limited to primiparous (first time mothers) women, parity was not a key consideration for capturing dioxin body burden. However, of particular importance for dioxin exposure, information was collected on: age, residence, tobacco use, occupation and diet. Dietary information included a 24 hour dietary recall alongside questions on their consumption of animal products, any dietary restrictions, avoidances and type of milk consumed. Current diets were assumed to provide the best inductor of dietary history and also acted to reduce recall bias; however, it is noted that diet in pregnancy often changes and consequently questions on any change were included.

Breast milk sample

Expressing breast milk for first time mothers soon after birth, when women are inexperienced and unfamiliar with handling their breasts, was deemed to be challenging. In order to limit any burden to participants and to help with sample collection, consenting participants were offered and sent a manual breast pump. Accompanying the breast pump was a breast milk storage bottle and documentation explaining how to take the breast milk sample. Also included was a document for the participants to complete to log when their sample was taken. All study documentation emphasized that only participants who were able and willing to provide a sample were being asked to do so and that participation was entirely voluntary.

As the composition of breast milk changes dramatically over time, both from birth and most considerably during a feed, it was critical to know the precise time and date each sample was collected. For approximately one week after birth breast milk is known as colostrum, milk that is high in protein (10%) and low in fat (1%). Following this milk is produced which is lower in

protein (1%) and higher in fat (4%) [227]. Additionally the amount of fat in breast milk increases over each feed, starting with the most watery thirst quenching milk then becoming fattier milk towards the later part of the feed [227]. The number of infant's breastfeeding dramatically decreases after 6 weeks following birth, with breastfeeding initiation rates in England in 2012/13 at 73.9% reducing to a prevalence of 47.2% at 6-8 weeks. Studies collecting breast milk in the USA, have collected a complete milk expression, which means infants are required to miss a feed. To collect a representative, high fat sample from as many participants as possible without unduly burdening the participants, a small (20 mL) breast milk sample at the end of a feed between 1-6 weeks after birth was requested.

A. Breast pump

Recommendations for breast pump providers were sought from staff at the postnatal ward at St Mary´s Hospital Paddington, the National Childbirth Trust, collaborating research midwives (LCs), Dr Mike Woolridge (principal investigator of the SUREmilk study) and the breast milk bank. Within hospitals, breast pumps were hospital grade electric pumps and at St Mary´s were manufactured by Medela. The brands mentioned included Avent, Ameda (used by SUREmilk) and Ardo. Price quotes were obtained for each of these brands with Ardo providing the most competitive price. That brand was therefore selected. Breast pumps used within the study were Amaryll Start manual breast pumps.

B. Breast milk storage bottles

Pre-cleaned Qorpak, 30mL (1 oz.) glass bottles with Teflon lined screw-caps bottles were provided for participants to store their breast milk sample. These bottles were pre-labelled with unique samples IDs on labels manufactured to be able to withstand extremely low temperatures.

C. Documentation (Appendix D)

Alongside the breast pump two study documents were provided to participants. The first was a breast milk sample FAQ which provided instructions on how to take the sample, when, how much and where to store the sample; the second was a form for participants to complete about when their breast milk was taken, including information on whether the requested 20 mL was collected and also if the participant was able to get the sample into the freezer within 30 minutes to prevent the sample from spoiling.

3.2.5 Ethical consideration & study permissions

Permissions to undertake this study were sought from the NHS Research Ethics Committee (REC) committee and the NHS Research and Development (R&D) for PIC approval. These applications alongside the NIHR CRN portfolio were all submitted within the Integrated Research Application System.

As chief investigator I attended the REC meeting. One iteration of study materials was required. The areas of ethical considerations for this study are detailed in the study protocol **(Appendix D),** but include issues of informed consent, data storage and confidentiality, feedback to participants on milk dioxin levels and adverse birth outcomes. All hardcopies of study documents were agreed to be kept in locked cabinets at the Department of Epidemiology and Biostatistics, Imperial College London, in a locked room on a floor that can only be accessed via security card. With the exception of the consent form, participants' names were not on study documents and only identified by a unique patient identifier, the study ID. All electronic data were stored securely on a password protected private computer network (an airgapped network that is not connected to any other network) at Imperial College London and individual records were only accessible to the study team.

Ethical approval was obtained from the National Research Ethics Service Committee North West-Preston (13/NW /0202) and R&D approval for all three NHS trusts. All documents are provided in **Appendix D.**

Two substantial amendments were successfully submitted to REC, the first detailed the occupational questionnaire and the second for a reminder letter which was dispatched to eligible participants not recruited in the first round of invitations.

3.2.6 Participants – Invited, recruited & completed

As documented in sections 3.2.2, 3.2.3 and 3.2.4 above, participants meeting the study inclusion criteria were mailed invitation packs addressed and dispatched by the LC from the participating hospital/PIC. Anonymised information on the invited participants' age, ethnicity and occupation was requested from the LCs. Participants recruited to the study were those who completed, signed and returned their consent forms. Upon receipt of the consent forms, all data were entered into a study database on the private network. Participants completing the study were

those able and willing to provide a breast milk sample, determined through direct contact with the participants. All contact with the participants, reminder calls, emails, texts, were documented on the private network.

3.2.7 Breast milk sample & document collection

Frozen breast milk samples, study questionnaires, study occupational questionnaires and breast milk collection sheets were collected from the participants' homes (prearranged with participants) within 6 months of sample collection. This enabled samples to be kept frozen and the cost of transportation reduced compared with temperature controlled postage. All samples were stored in the deep freezer at -80°C at the Queen Elizabeth and Queen Mother building of St Mary's Hospital under permissions of the Imperial College Human Tissue Bank.

3.2.8 Data analysis

Consent form data

Information extracted from participants' study consent forms were analysed in Excel 2010 for each NHS trust. Participants' home addresses provided on their consent form were additionally mapped within ArcGIS 10 using a current address point database and their location from the MSWI of interest determined. Information on expected delivery dates obtained from the study consent form and actual delivery date provided by the LC were compared.

Study questionnaire/Occupational questionnaire data

Anonymised paper copies of study questionnaires and occupational questionnaires for participants completing the study (those able to provide a breast milk sample) were converted to an electronic dataset by double entry at Data Image Limited. The study questionnaire analysis was split into two; the first was a descriptive analysis of personal, residential and occupational data and the second, a dietary analysis including estimates of daily intake of dioxins.

Personal, residential, educational and occupational data descriptive analysis

Participants' responses to Questions 4 to 18 in the study questionnaire and Question 1 of the occupational questionnaire were analysed by MSWI site and categorised into resident "near" a MSWI site (within 3000m from the MSWIs) or "far" from the MSWI (at or greater than 3000m

from the MSWI). All analyses categorised by distance were undertaken across both MSWIs due to the small sample size surrounding the Stockton-on-Tees MSWI. All analyses were performed in Excel 2010 and included information on age, height, weight and body mass index (BMI), residential history, marital status, ethnicity, educational achievement, occupation and current and historical smoking status.

Height and weight were converted into metric units and BMI calculated (weight (kg)/ height^2 (m^2)) and categorised into underweight (<18.5 kg/m^2), normal weight (18.5- 25 kg/m^2), overweight (25-30 kg/m^2), obese (>30 kg/m^2) according to established criteria. Residential history was analysed at postcode area level. Ethnicity categories were collapsed due to the small numbers of women. Categories were collapsed as follows: White (British/Irish and Other White background); Black (Caribbean, African, Other Black background); Asian (Indian, Pakistani, Bangladeshi, Chinese and Other Asian background); Mixed (White and Black, White and Asian, Black and Asian and Other Mixed background) and Other (Other ethnic group). Finally job titles were used within the Computer Assisted Structural Coding Tool to provide four digit Standard Occupational Classification (SOC) 2010 codes for each participant. All other variables were categories within the study questionnaire and therefore analysed as is.

Descriptive analysis of women within the Incinerators Biomonitoring Study were analysed within the context of population data extracted from the NOMIS website [228]. This included data from the 2011 Census for all women between the ages 21 and 43 (age categories of the Census data provided meant all age groups which included women aged 21 and 43 were included within the comparative analysis), resident within all middle layer super output areas (MSOA) within the study areas around both MSWIs.

Dietary analysis

Participants' responses to Questions 19-23 in the study questionnaire were additionally analysed by MSWI site and categorised into "Near" and "Far" from the MSWIs. All analyses were performed in Excel 2010 and included two themes, the first, dietary restrictions, avoidances, milk consumption, locally sourced food and diet during pregnancy and the second, daily dietary intake of dioxins.

Calculating daily intake of dioxins for the study participants from dietary sources required information on fat intake by food group, dioxin concentrations of these food groups and dietary information.

Estimates of dietary intake of dioxins from food in the UK have been undertaken previously, both by MAFF and the FSA using food samples from the Total Diet Study (TDS). Estimates of dietary intake of both dioxins and PCBs for adults and children between 1982 and 2012 were calculated using TDS concentrations measured within 11- 19 food group samples and dietary information from the National Food Survey. Food samples within TDS are selected across 24 locations in the UK. These studies have enabled the evaluation of temporal changes in dioxin levels in food alongside providing population exposure estimates. In addition, they allow an assessment of pollution control effectiveness, with sampling periods overlapping the implementation of the EU Integrated Pollution Control Regulations (implemented in 1992 for industrial process including MSWIs) and EU limits to dioxins in foods and animal feed (introduced in 2002). Figure 3.5 displays the temporal change in upper bound concentrations of dioxins found in TDS food samples (only food groups with measurements over the entire time period were included) [229] [230]. Figure 3.5 shows a decline in dioxin levels within all food groups, with the greatest reduction in concentrations between 1982 and 2012 found within poultry and eggs and the smallest in bread and fish.

Using the most recent dioxin concentrations, 2012, [230] and the dietary data collected within the study questionnaire (extracted from the 24 hour recall question, question 24 in the study questionnaire), dietary intake of dioxins for five food groups with high fat content (meat products, poultry, fish, eggs and milk and dairy) was calculated. Daily dietary intake of dioxin was calculated as the sum of [daily consumption of fat from each of the five food groups food group (g)] * [upper bound mean concentrations from the TDS of the food group]. Exposure estimates were calculated as both (A) pg WHO-TEQ/ day (B) pg WHO-TEQ/ kg bodyweight/ day.

3.3 USING NATIONAL BIRTH DATA WITHIN EPIDEMIOLOGICAL STUDIES OF BIRTH OUTCOMES

This section describes the methodology used to make recommendations to researchers on the most appropriate births dataset to use in epidemiological studies on birth outcomes, motivated by the SAHSU study of MSWIs.

The methods presented in this chapter have been accepted for publication in the Archives of Disease in Childhood **(Appendix E).** It is noted that all birth outcomes to be investigated in the

SASHU study were not investigated here. The birth outcomes excluded were those with single dataset sources and therefore no comparison analysis was relevant or applicable.

3.3.1 Methods

National birth data

In England information on births can be sourced from two routinely collected databases: Registrar data within the Office for National Statistics (ONS) dataset and hospital data within the Hospital Episode Statistics (HES) dataset.

Birth and stillbirth registration: ONS births

All live births in England and Wales are required by law to be registered at a local Registrar of births and deaths within 42 days of birth [231-233]. This information is usually provided by the parents of the child but can also be provided by anyone present at the birth, the person in charge of the child born or the person living in the house where the birth occurred [234]. This information is verified monthly by the Clinical Commissioning Group (CCG), previously primary care trust (PCT), within which the birth took place. CCG´s are provided with births data by the hospital or by the attending doctor or midwife under the National Health Service Act (1977 and 2006) [232].

The information required to be collected by the Registrar is prescribed by the Births and Deaths Registration Act 1953 [231] and includes registration district, child's place and date of birth, sex and since 1975 birth weight. Alongside birth data details of both parents are also documented, including occupation, place of birth, date of birth and previous marriages. All details are entered in a draft entry form 3.9 [234].

Stillbirths, defined as a child which shows no signs of life after the 24th week of pregnancy [235], are also required to be registered with the additional requirement of a medical certificate of stillbirth (introduced in 1986). This certificate is completed by the attending member of staff and provides information on place of birth, cause of death (categorised into a. diseases or conditions of the fetus, b. maternal diseases or conditions affecting fetus, c. other relevant causes), weight of fetus, when the fetus died and an estimated duration of pregnancy. All details are entered in draft entry form 3.8 [234].

Registrars send these draft entry forms to the ONS who hold this information in a national dataset of live and stillbirths. ONS births dataset is considered to be a complete record of total births in England.

Hospital maternity data: HES maternity

Since 1989 all admissions, outpatients appointments and accident and emergency attendances into English NHS hospitals and facilities funded by the NHS have formed part of a routinely collected administrative hospital data warehouse [236]- HES. Administrative data are collected primarily for planning health services and facilitating reimbursement of healthcare costs but have more recently been recognised as a rich data resource for research. HES data not only capture a large population and contains extensive clinical information, but are widely available at a low cost. HES is however criticised for data inaccuracies and completeness with variability in data capture and coding across NHS trusts [236].

HES is the largest health dataset in England and details each "episode" of care provided by an individual consultant. A general HES record details information on [236]:

- The patient, including date of birth, ethnicity, unique identification number (NHS number and HES ID), sex, indicators of socio economic status and postcode of residence. Postcode of residence is subsequently used to extract additional geographical information on the patient such as county of residence, electoral ward and primary care trust of residence.
- The patient's admission and discharge, including admission date, admission method, type of episode, discharge date and discharge method.
- The patient's clinical care, including diagnoses, operative procedures, who the care was provided by and where the care was provided.

HES maternity records form part of the admitted patient care dataset, known as the inpatient HES dataset. An inpatient general record is transferred to a maternity record when a birth occurs. For example, even if a heavily pregnant woman is admitted to hospital with signs of labour but does not deliver, her record will remain an inpatient record rather than a maternity record. Within the inpatient HES dataset, maternity records include an additional 19 data fields known as the "baby tail". The additional information within the baby tail provides details on the delivery (including delivery place and delivery method), the baby (including birth weight, gestational age, ethnicity and sex) and the mother (including the number of previous babies

born and number of previous pregnancies) for each baby born. HES maternity records are therefore categorised into two datasets:

- The HES births dataset, which is made up of birth episodes- general inpatient records for each baby born including the information within the "baby tail".
- The HES deliveries dataset made up of delivery episodes- general inpatient records for the mother including the information within the "baby tail" for each baby born at the delivery.

Data extraction

Births occurring in England from the 1st January 2001 until the 31st December 2010 were extracted by Dr Kevin Garwood, a member of the database team at SAHSU, for three birth datasets: ONS births, HES deliveries and HES births.

ONS births

The ONS births dataset was created by merging both the live and stillbirths datasets together for the relevant years. The ONS births dataset was extracted for England only, (government office regions (GORs) indicated in Figure 3.6) A-K , and included twelve data fields. Seven fields were extracted from the live and stillbirths dataset, three were spatial fields generated by SAHSU and two from the stillbirths dataset alone. A total of 6,293,672 live and stillbirths were extracted between 2001-2010.

HES maternity

For both HES datasets (embedded within the larger HES inpatients dataset), a number of extractions were performed and records compared using different extraction methods.

Both HES maternity data extractions were complicated by their defining variables. This was made particularly difficult by the sparsity of published epidemiological studies using the HES maternity dataset and the fact that within these studies the extraction method utilised was seldom documented. Five different dataset extraction methods, selected in accordance to previously published papers [237, 238], reports [239] and personal communication with the HES team [210, 240], were defined and the number of births yielded is presented in table 3.2.

For both HES deliveries and HES births the widest ranging and most inclusive method yielding the most records was undertaken by Northgate solution and used by Dattani *et al* [237]. Northgate solution defined their HES deliveries dataset as records with specified episode types in addition to records with procedure codes R14 to 27 (labour and delivery codes) and diagnoses codes O00-99 (pregnancy, childbirth and puerperium conditions). Between 2001 and 2010 this extraction method yielded over 13 million delivery records (table 3.2). The most restrictive extraction method was the method used from the most recent communication with the HES team, which also defined HES deliveries and birth by episode type, but excluded all births and deliveries occurring at home and within private or other hospitals (HES field "delivery place"). This extraction method yielded just over 6 million deliveries and births (table 3.2).

Although delivery and birth records by definition are unable to occur twice, episode duplication was explored. Note, each baby within a multiple delivery will be assigned a unique HES ID, derived from a number of patient identifiable fields including NHS number. Both HES maternity datasets were de-duplicated using an adapted version of the Dr Foster method [241] (detailed in Figure 3.7) and when records were identified as duplicate, the record with the greatest number of completed data fields was retained. Figure 3.7displays a flow diagram for the final extraction method used for both HES maternity datasets within this chapter.

Data analysis

For each dataset, the following were analysed:

- What data fields are collected?
- How complete are these data fields?
- Are there any spatial (national level and by GOR) and temporal trends in the data?

Descriptive epidemiology of the following birth outcomes, defined in table 3.3 was carried out:

- Low birth weight (LBW),
- Very LBW (vLBW),
- Stillbirths,
- Term LBW,
- Preterm delivery
- Very preterm delivery (v preterm delivery).

Additionally the spatial trend in reporting of these birth outcomes was analysed.

All data handling and analysis was performed in R version 2.14.2 and mapped in ArcGIS version 10.

Small area level analysis

Births occurring within residential postcodes both within 10 km from the two MSWIs, Marchwood in Southampton and Stockton-on-Tees, and the GORs in which these MSWIs fall were extracted for HES deliveries and ONS births at the level of Lower Super Output Areas (LSOAs). LSOAs are built from groups of census output areas with populations between 1,000 to 3,000. Descriptive statistics on numbers and rates of live births, stillbirths and birth weight were extracted and mapped in ArcGIS 10.1. This analysis was undertaken by Dr Rebecca Ghosh and performed in STATA version 13.

Figure 3.1 Location of Municipal Solid Waste Incinerators in Great Britain; 20 in England, 1 in Wales and 1 in Scotland. Four incinerators discussed in this chapter are indicated in blue.

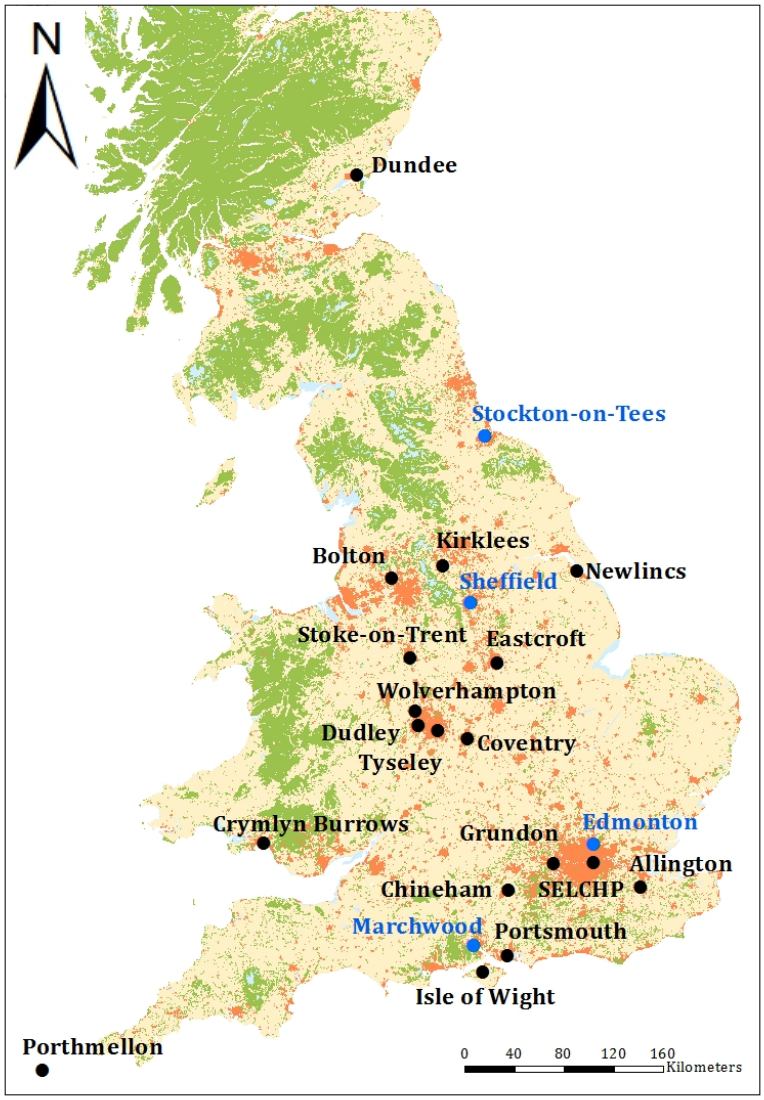


Figure 3.2 Schematic overview of the exposure modelling methodology.

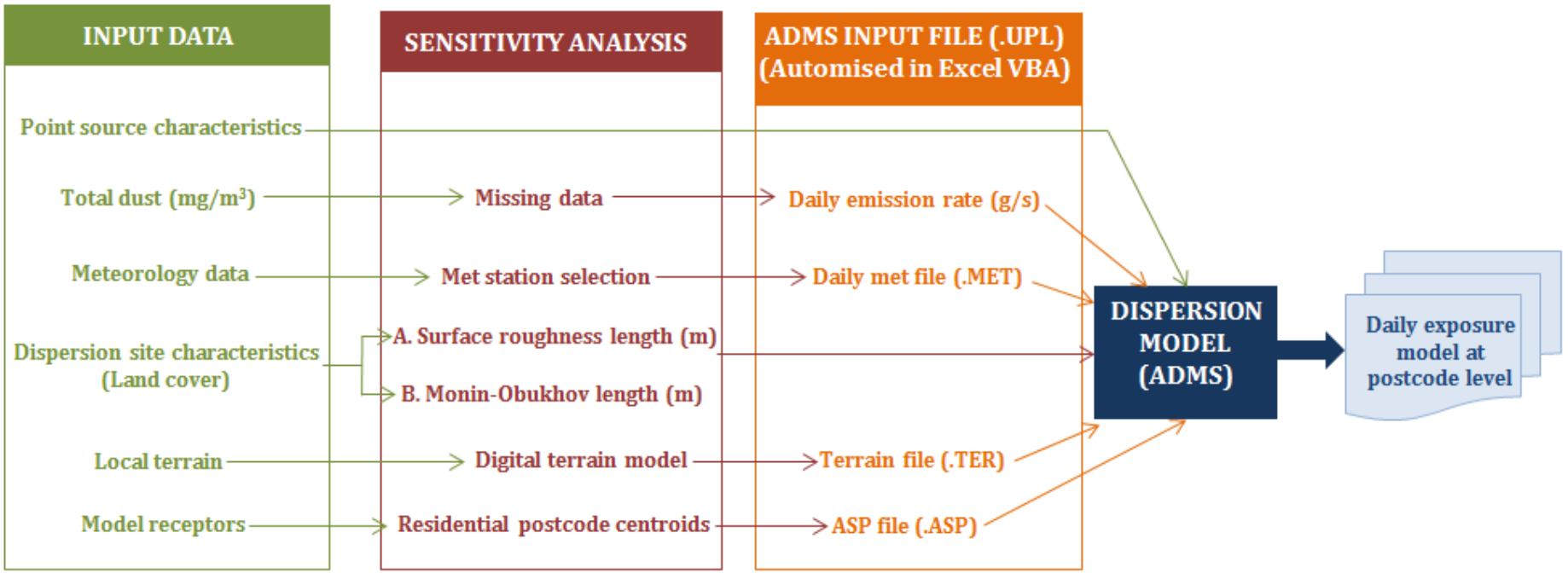


Table 3.1 Source characteristics of the four inclusive municipal solid waste incinerators within this chapter (data provided by Environment Agency).

Incinerator	County of England	Date commissioned	Permitted throughput (tonnes/year)	Flue	Stack height (m)	Stack diameter (m)	Flue exit flow rate (m^3/s)	Flue exit velocity (m/s)	Temperature (°C)
Edmonton	Outer London	1970	750,000	1	100	2.87	72.3	11.2	159
				2	100	2.87	71.9	11.1	150
Marchwood	Hampshire	2006	165,000	1	65	1.25	30.3	24.7	150*
			(later increased to 210,000)	2	65	1.25	30.9	25.2	148*
Sheffield	South Yorkshire	2006	225,000	1	76	1.45	21.1	13.0	146
				2	76	1.45	20.1	12.0	147
Stockton-on-Tees	Cleveland	1998	263,000	1	70	1.65	41.1	19.2	140
				2	70	1.65	39.0	18.2	147
				3	70	1.65	34.2	18.1	147

*Converted from Kelvin

Figure 3.3 Included MSWIs, affiliated hospitals and study area. (A) Map showing both Stockton-on-Tees and Marchwood MSWI (B) Map displaying; Stockton-on-Tees MSWI, the two affiliated hospitals (James Cook University Hospital and University Hospital of North Tees) and the study area in which the study population was identified (C) Map displaying; Marchwood MSWI, the affiliated hospital (Princess Anne Hospital) and the study area in which the study population was identified

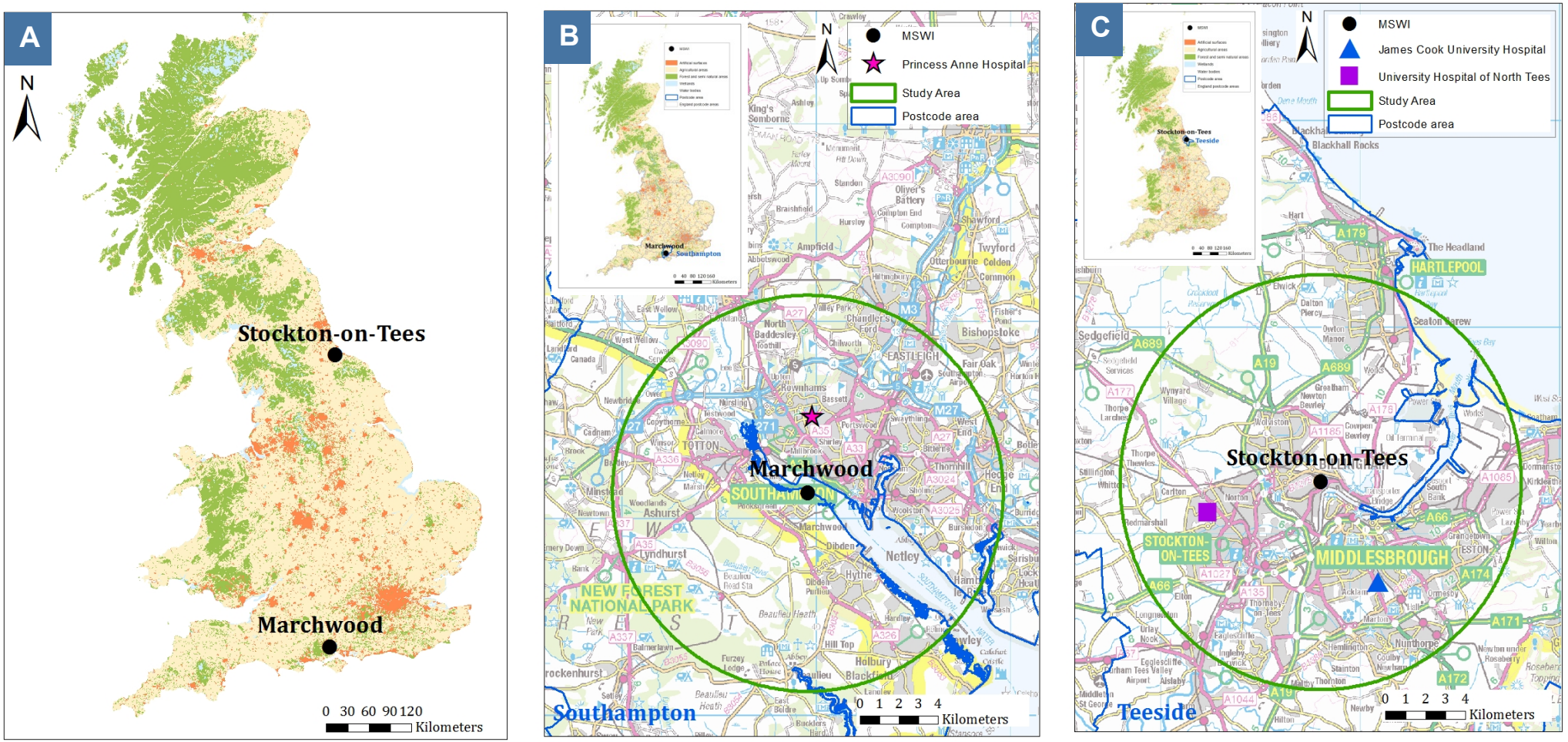


Figure 3.4 Prenatal and postnatal study involvement

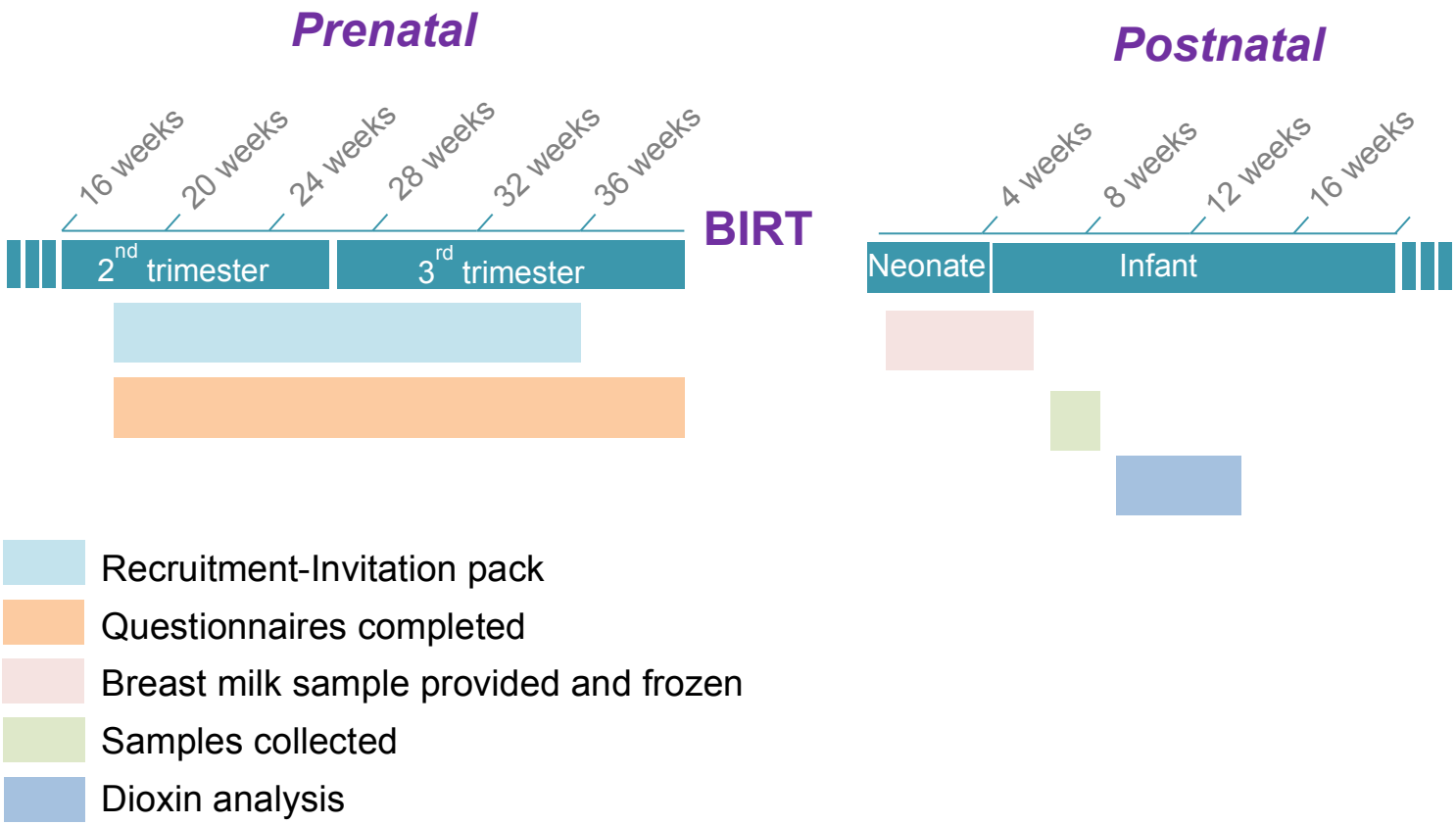


Figure 3.5 Temporal trend in dioxin concentrations in UK food samples, the Total Diet Study

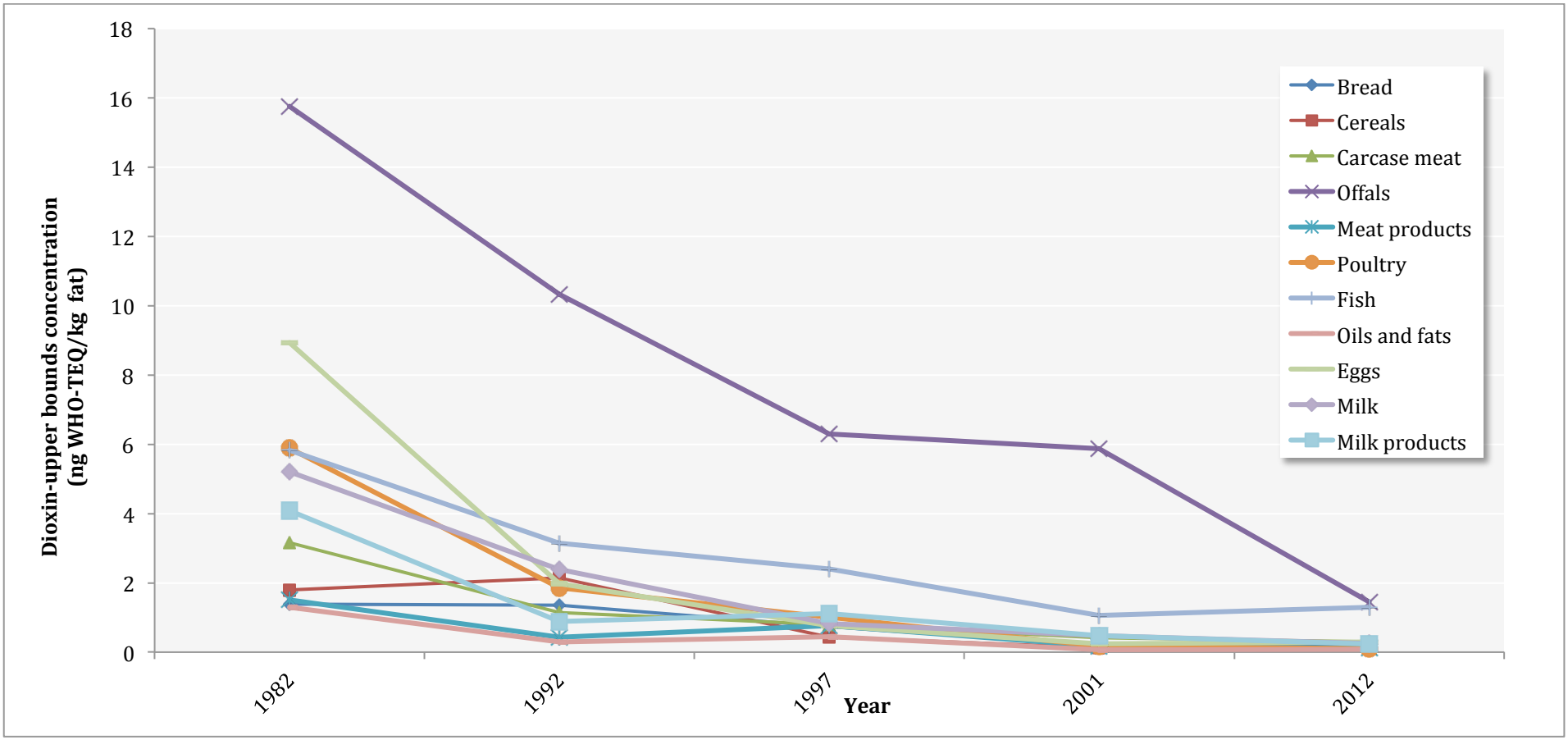


Figure 3.6 Government Office Regions (GORs) in England



Table 3.2 Overview of different extraction methods for both HES maternity databases and the corresponding number of records obtained.

Reference	HES dataset	Extraction method	Number of records (2001-2010)
Northgate solutions[237]	Deliveries	Episode type = 2 OR 5 OR Main procedure code between: R14-R27 OR Main diagnosis codes between: O00-O99	13,333,759
	Births	Episode type = 3 OR 6 OR Well baby flag=Yes OR Neonatal level of care= 0,1,2,3,4,9 OR Main diagnosis codes between: P00-P99 OR Main diagnosis codes between: Q00-Q99	13,565,849
Care Quality Commission[239]	Deliveries	Episode status =3 AND Episode type = 2 AND EXCLUDE if: Procedure codes are Q13 or Q383 Diagnosis code are Z311, Z312 or Z313	6,163,789
	Births	Episode status =3 AND Episode type = 3 AND EXCLUDE if: Procedure codes are Q13 or Q383 Diagnosis code are Z311, Z312 or Z313	6,194,966

Murray *et al[238]*	Deliveries	N/A	
	Births	Method of admission=82 OR 83	6,558,389
First email communication with HES [240]	Deliveries	Episode type = 2 OR 5	6,185,419
	Births	Episode type = 3 or 6	6,213,851
Second email communication with HES [210]	Deliveries	Episode type=2 OR 5 AND EXCLUDE if: Delivery Place=1 OR 5 OR 66,133,126	6,133,126
	Births	Episode type=3 OR 6 AND EXCLUDE if: Delivery Place=1 OR 5 OR 6	6,165,709

Figure 3.7 Flow diagram for the extraction method used to identify both HES maternity datasets.

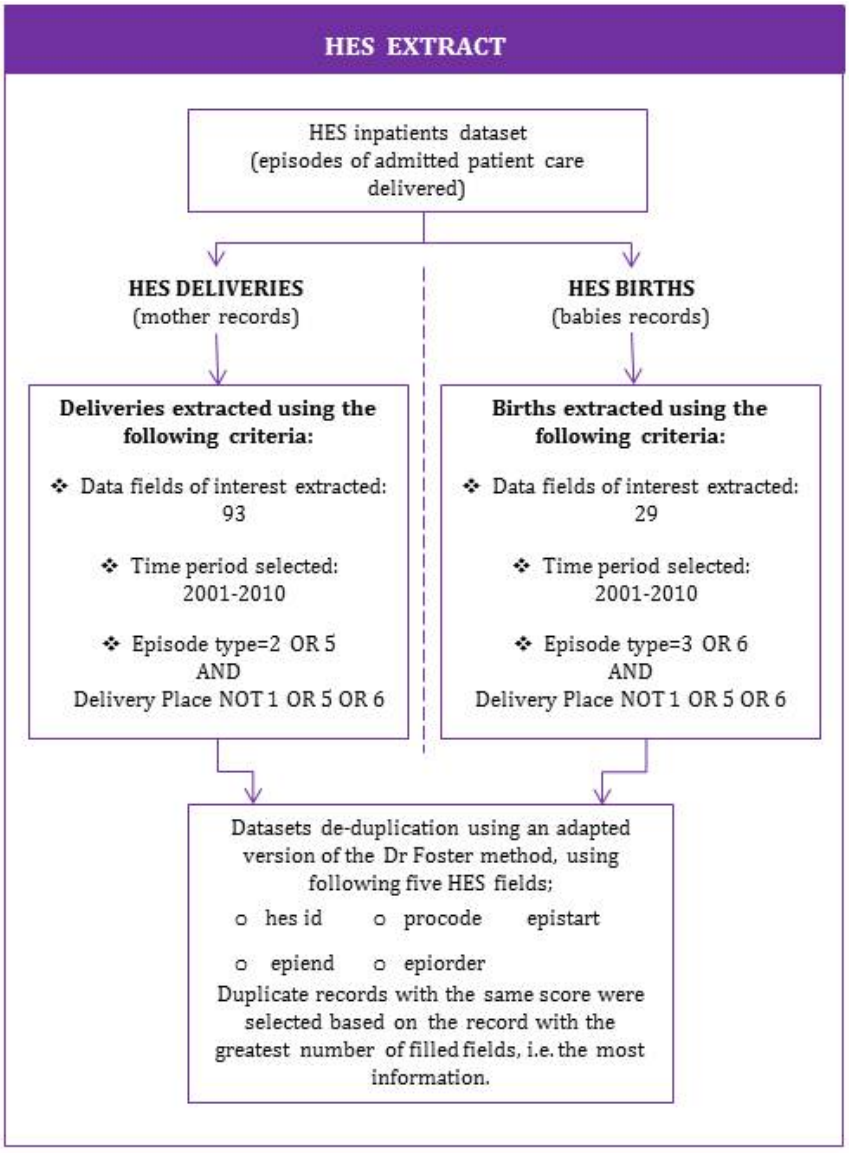


Table 3.3 Definition of birth outcomes investigated

Birth outcome	Definition	Denominator	Datasets	Exclusions
LBW	Weight at birth < 2,500g	Live births	HES deliveries HES births ONS births	Weight at birth <200g and all multiple births
vLBW	Weight at birth <1,500g	Live births	HES deliveries HES births ONS births	Weight at birth <200g and all multiple births
Stillbirth	Fetal death at or after 24 weeks of pregnancy	Live and stillbirths	HES deliveries HES births ONS births	
Term LBW	Weight at birth <2,500g and baby born at or after 37 weeks pregnancy	Live births	HES deliveries HES births ONS births	Weight at birth <200g and multiple births
Preterm delivery	Baby born before 37 weeks pregnancy	Live births	HES deliveries HES births ONS births	Multiple births
Very preterm delivery	Baby born before 34 weeks pregnancy	Live births	HES deliveries HES births ONS births	Multiple births

CHAPTER 4: RESULTS

This chapter presents results of the atmospheric dispersion models built to assess exposure around MSWIs; descriptive analysis of questionnaire data collected within the Incinerators Biomonitoring Study; analysis of national birth data and recommendations for their use in epidemiological studies of birth outcomes.

4.1 SMALL AREA LEVEL EXPOSURE ASSESSMENT OF MUNICIPAL SOLID WASTE INCINERATOR EMISSIONS

4.1.1 Atmospheric dispersion modelling

Model input data and sensitivity analysis

Point source

Particulate emissions data

Daily concentrations of particulate matter measured at the flue exit for each MSWI are presented in Figure 4.1. The WID limit of 10 mg/m^3 per flue is indicated on each graph by the red line. Table 4.1 provides an overview of the operating schedule at each MSWI and summarises measured flue exit concentrations by incinerator, flue and year.

Figure 4.1 and Table 4.1 demonstrate the temporal coverage of the particulate data, the operational patterns of the flues in addition to the variability across flues of individual incinerators and by incinerator.

Edmonton and Stockton-on-Tees had the greatest coverage of particulate data, with daily concentrations provided for the whole study period, 1st January 2003 until 31st December 2010. Sheffield particulate data were available from June 2003 and Marchwood from October 2004, although Marchwood then experienced plant closure for over a third of the year in 2005. Figure 4.1 additionally shows changes in the number of flues commissioned during the study period at two plants, Sheffield and Stockton-on-Tees. Sheffield's second flue ceased operation from the

beginning of December 2005 and Stockton-on-Tees commissioned a third flue in May 2009 which in turn coincides with a period, 2009-2010, in which the plant had a high frequency of closure days (particularly flue 1).

Both Figure 4.1 and Table 4.1 demonstrate the variability in flue exit emissions by MSWIs. Sheffield had the lowest concentration of total particulates over the study period, with a peak in emissions in 2006 which included two days in which the plant reported emissions over the WID limit. Marchwood additionally displayed lower overall concentrations than both Sheffield and Stockton-on-Tees (with the emissions provided by the EA at a lower degree of precision than the other three MSWIs) and no reported WID exceedances. Edmonton and Stockton-on-Tees reported higher concentrations, with Stockton-on-Tees reporting higher average emission concentrations between 2003 and 2005 and thereafter Edmonton exceeding Stockton-on-Tees average levels. Despite this, Stockton-on-Tees showed a much greater number of WID exceedances than all other MSWIs, with 107 reported exceedances across its three flues compared with a cumulative of 5 days of exceedances across the other three incinerators. Stockton-on-Tees additionally reported a maximum particulate matter concentration of 66.2 mg/m^3 in November 2008, which was three times that of the maxima of all the other MSWIs combined for 2008.

Particulate emissions data – Sensitivity analysis

Flue exit particulate matter data additionally provided information on plant down time and missing data (figures provided in Table 4.1). Of the inclusive incinerators, Stockton-on-Tees had both the greatest number of plant down days (followed by Marchwood) and missing days (followed by Edmonton). As Stockton-on-Tees had the greatest number of missing data with variability in their occurrence (as both blocks and single days), this MSWI was selected for sensitivity analysis. Sensitivity analysis was conducted for 2004 and undertaken with the methods described in section 3.3.2.1.1. Within each model the same model parameters were input; the results are shown in Figure 4.2. Figure 4.2 C and D demonstrate the high correlation in model output (annual averages) using each method (≥0.98). However, when daily modelled outputs were compared by method, Figure 4.2 A, a difference can be observed. Figure 4.2 A indicates both when the emissions data are missing (chart below) and the daily model output, with Figure 4.2 D aggregating model output into trimester specific emissions. Using the "maximum concentration" to fill in missing data both within the correlation matrix and the graphs (Figure 4.2 A and C) is least consistent with the other methods. This is particularly apparent when there are larger periods with missing data. Of the remaining three methods the

mean and median concentrations were most highly correlated. In conjunction with the EA, the method agreed upon was to use median concentrations as it was considered to be more appropriate due to the frequency of extreme emission values likely to influence mean concentrations.

Dispersion Site-Study Area

Site characteristics

Site characteristics – Sensitivity analysis

The sensitivity of the model to dispersion site characteristics was investigated by extracting land use data from the CORINE Land Cover map for the incinerator fetch and study site, as well as comparing model outputs using different surface roughness lengths and minimum MO lengths. Land use type at the incinerator site (1 km radius) was predominantly urban for the four sites, with the exception of Marchwood where 38% of the area around the site was categorised as artificial land (Table 4.2a). When expanding the study areas to a 10 km radius, a larger variation in land use type was observed (Table 4.2b). The study area surrounding Edmonton MSWI was the most homogeneous with 77% urban land use. Sheffield was also highly urban (56%), Marchwood more rural with ~60% agricultural and forest land and Stockton-on-Tees split between urban land and rural, agricultural land.

An investigation of the land cover types surrounding each incinerator allowed a range of potentially representative surface roughness lengths and minimum MO lengths to be selected. Models using these different lengths were run and model outputs compared, shown in Table 4.3. Although the modelled annual average concentrations of PM_{10} over the study area showed little absolute difference using these different lengths, a large relative difference was observed when MO lengths of 30 m and 100 m were compared (with over 60% of model receptors showing 25% percentage difference or greater) and surface roughness lengths of 1 m and 1.5 m compared (at the Sheffield site over 50% of the model receptors showed a percentage difference of 25% or greater).

Local meteorology

Local meteorology– Sensitivity analysis

The following quality indicators of Met office stations data were prioritised as follows;

1. Variables collected within the study period (land surface air temperature, wind speed, wind direction and cloud cover).
2. Equal to or greater than 90% annual hourly completeness for land surface air temperature, wind speed and wind direction (although cloud cover was additionally extracted, the Air Quality Modelling Assessment Unit at the EA advised that with all other climatic variables with high completeness, it was appropriate to "borrow" cloud cover information from a nearby station, where possible).
3. Distance to the MSWIs of interest
4. Temporal coverage of each station across the study period

The quality of the meteorology data was additionally explored through wind roses (graphical tool to view the relationship between wind direction and speed at the meteorological station), in addition to visual comparisons of model outputs using all of the same input characteristics with the exception of the meteorological station.

Preliminary models excluded [145, 209, 210] met stations with unexpected wind rose patterns. However, as all met stations included within the study were set up in accordance with the Met Office guidelines/standards and are required to meet quality control requirements, all data were retained unless there was evidence of a fail in Met Office quality control criteria. It was further decided that the distance from a meteorological station to the incinerator site was of greater importance than temporal coverage i.e. the use of one station for the duration of the study. This was because of the 737 unique met stations operating between 2003 and 2010, only 238 had at least 90% coverage and a further 139 only operated throughout the study period (2003-2010) and not all were located near the MSWIs. This criterion meant that for some MSWIs numerous meteorological stations were used within the model. Marchwood model included one meteorological station, Sheffield two, Stockton-on-Tees three and Edmonton four. Of the four stations used within the Edmonton model, none covered the entire study period; only one additional station was found to cover the whole study period, located 26 km away. The sensitivity of the dispersion model to meteorological data is demonstrated for Edmonton in Figure 4.3.

The four selected meteorological stations were all located within 14 km from Edmonton MSWI, ranging from the nearest station at 2.2 km north of Edmonton to 13.3 km south east (see Figure 4.3). Model outputs show different patterns of dispersion and therefore exposed populations, however all showed decreasing exposure with distance from the incinerator.

Local topography

The elevation of the terrain within the study area for each MSWI was explored and the results presented in Table 4.4. The elevation range within study areas varied from 93 m at Marchwood to 400 m at Sheffield. Although all study areas show variability in elevations, with the exception of Sheffield, all were low lying, with mean elevations between 23 m and 37 m. In order to quantify the proportion of mountainous region within the study area, the percentage of the study area with a gradient greater than 10% was calculated. Table 4.4 shows that Edmonton, Marchwood and Stockton-on-Tees study areas are all greater than 97% low lying whereas Sheffield is surrounded by hills, with 28% of the study area showing considerable gradient. It was therefore decided that Sheffield model would require a terrain file.

The sensitivity of the model to the topography data was investigated by running the Sheffield exposure model with and without the terrain file and comparing model outputs (Figure 4.4). Removing the terrain file resulted in a small difference in average concentration of PM_{10} across the model output area (0.000303 $\mu g/m^3$ without terrain and 0.000269 $\mu g/m^3$ with terrain); however, there was a moderate change in the dispersion pattern between the two models, with a larger area of higher exposure identified when no terrain file was included, Figure 4.4 C, compared to the model with a terrain file, Figure 4.4 D.

Model Output

Annual average model outputs are displayed in Figure 4.5 for each of the four MSWIs. The surfaces display areas of higher exposure in black, with modelled PM_{10} concentrations above the median, and areas of lower exposure in grey, defined as those with concentrations below the median. The receptors used in the dispersion model are shown as dots in Figure 4.5, representing the geographic centroid of the postcodes within the study area. All four models resulted in irregular shapes of population exposure, with a higher exposure reaching the north eastern area of the study area and decreasing exposure levels with distance from the source. Areas without model receptors are rural locations where postcodes extend over larger areas due to lower population density (Figure 4.5 b and 4.5 d).

Table 4.5 presents modelled annual mean ground level concentrations of PM_{10} by incinerator for all days in which at least one flue was operational. The table additionally indicates the number of days in which sufficient meteorological data was present for the model to be able to

generate an output. As meteorological stations with less than 90% coverage of the climatic variables were eliminated the maximum number of days any of the models were unable to run for was 19 days at Stockton-on-Tees.

Modelled annual mean ground level concentrations of PM_{10} were extremely low for all MSWIs, with annual mean concentrations ranging from 0.000097 $\mu g/m^3$ for Sheffield in 2004 to 0.0059 $\mu g/m^3$ for Edmonton in 2003.

4.1.2 Distance to source

The population distribution by distance from the incinerator is shown in Table 4.6. The study area surrounding Edmonton was the most densely populated (1,532,124 people live within 10 km) and Marchwood the least (361,005 people within 10 km). The population surrounding Sheffield tended to reside closer to the MSWI (0-2 km) than the other three and residents near Edmonton were more likely to live further from the MSWI comparatively (8-10 km).

4.1.3 Exposure assessment comparison: Modelled estimated and proximity

Figure 4.6 shows modelled long term annual average PM_{10} concentrations against distance from the MSWI for each model receptor. Concentrations towards the edge of the modelling domain fall to extremely low levels, with Edmonton's concentrations between 9-10 km at 0.06% of peak concentrations, Marchwood 5.7%, Sheffield 4.1% and Stockton-on-Tees 3.9%. The influence of stack height is clearly demonstrated in Sheffield, where residents tend to reside close to the MSWI. Here modelled PM_{10} concentrations are very low until approximately 640 m from the MSWI. This pattern is less clear in Marchwood and Stockton-on-Tees where peak mean concentrations are reached at approximately 1,100 m and 800 m respectively. This pattern was not demonstrated in Edmonton, potentially because there were small numbers of postcodes located near the MSWI.

Agreement between PM_{10} exposure estimates and distance was quantified by categorising estimates into deciles, quintiles and tertiles and Cohen's kappa coefficient calculated. Postcode weighted coefficients are shown in Table 4.7a and population weighted estimates in 4.7b. A clear improvement was seen when the number of exposure categories was reduced with tertiles yielding higher coefficients, and therefore greater agreement than deciles reflecting greater exposure misclassifcation. Across all MSWIs the Cohen's kappa coefficient increased by 38% when exposure indices were decreased from deciles to tertiles for postcode weighted estimates

and 62% for population weighted estimates. Overall Marchwood showed the best agreement between the two methods, with tertiles showing a 0.588 coefficient when postcode weighted and 0.548 when population weighted

4.2 BIOLOGICAL MONITORING OF DIOXINS- INCINERATORS BIOMONITORING STUDY

4.2.1 Participants

Invited participants

Overall 1,194 invitation packs where dispatched from the three PICs. The highest proportion were sent by Princess Anne Hospital in Southampton, from now on referred to as Southampton (674 invites sent (56.4%)), followed by James Cook University Hospital, from now on referred to as South Tees (282 invites (23.6%)), and finally University Hospital of North Tees, from now on referred to as North Tees (238 invites (19.9%)). Ethnicity and age of the women invited to the study are shown in table 4.8 for North and South Tees only as these data were not made available by Southampton. The mean age of women invited to the study in these two regions was 26 years old, ranging from 17 (11 women who at booking were 17 but when they received the invitation packs were 18) to 42 years old. Women invited were largely of white ethnicity (86.0%), followed by women of Asian (Pakistani, Indian, Bangladeshi) ethnicity (4.6%). A comparison of ethnicities by trust showed South Tees to have a much higher proportion of women of Asian ethnicity (7.1%) compared with North Tees (1.7%).

Recruited

Figure 4.7 shows a flow diagram of study recruitment and sample collection, further quantified in table 4.9. Of the 1,194 women invited to take part in the study, 160 consented to take part. Six women were subsequently excluded, three without access to a freezer to prevent samples from spoiling and an additional three who did not provide contact details for themselves (additional letters were resent to women if LCs were able to identify women based on their name alone). Therefore, 154 women made up the study database for the Incinerators Biomonitoring Study, a 12.9% recruitment rate was achieved, with highest recruitment occurring in Southampton, with 94 participants recruited (13.9% of total invited), followed by

North Tees, with 29 participants recruited (12.2%) and finally South Tees, with 31 participants recruited (11.0%).

Completed

Of the 154 consenting participants, 98 provided a breast milk sample and completed the study questionnaires (study questionnaire, occupational questionnaire and sample time and date document), a 63.6% completion rate amongst consented individuals. Completion was greatest in Southampton (71.3%) and lowest at South Tees (45.2%) (table 4.9). Of the 56 women who did not provide a breast milk sample, 62.5% were unable to do so, and the remaining 37.5% were lost to follow up.

4.2.3 Data analysis

Consent form data

Participants recruited

Table 4.10 provides a summary of the details collected within the study consent forms for the 154 consenting participants by PIC. On average, age of women consented was 28 years old, with ages ranging from 18 to 42 years. Across all PICs, younger participants were recruited from North Tees (average age 26 years old, ranging from 18 to 37 years old) and older participants from Southampton (average age 31 years old, ranging from 19 to 42 years old). On average participants were recruited during the first two weeks of their third trimester (mean gestation 29.3 weeks), with recruitment occurring earlier than average in North Tees (mean 28.3 weeks) and later in Southampton (mean 30.8 weeks). Across all PIC, over 90% of participants had the intention to initiate breastfeeding.

Although the study inclusion criterion specified that participants invited should be primiparous and between 18-36 weeks gestation, one participant had previously delivered twins and documented their gestation at 13 weeks. With the exception of gestation weeks, missing fields occurred in less than 1.5% of participant's records. Information on gestation weeks was not documented for four women; one woman consented postnatally (baby was born prematurely) and one was recruited via email but was unable to provide a sample and therefore did not complete a consent form.

Table 4.11 provides a comparison of delivery dates (provided by LCs) with expected delivery date (EDD) (provided on the study consent forms). Overall 52.6% of participants delivered within a week of their EDD, with 22.1% delivering over a week late, 14.3% under a week early and 9.7% on their EDD.

Residential distance of participants from the MSWI of interest varied from 578 m to 10,510 m, with most participants' resident between 4-5 km from the MSWI (16.9%) (average distance of 5,497m (Tables 4.12 A and 4.12 B)). A comparison of distances by PIC (table 4.12 A) shows that participants tended to live closer to the MSWI in Southampton (4,648 m), where the greatest range in distances was additionally observed (578 m to 10,510 m). The direction of participants relative to the MSWI (table 4.12 B) in North Tees was predominately in the South West, in South Tees to the South East and in Southampton to the North East, reflecting the geography of these regions.

Participants completing the study

Compared with women recruited to the study, those able to complete the study were marginally older, with a mean age at consent of 29 years old (minimum 21-42 maximum) compared with 28 years old (minimum 18-42 maximum) for all women recruited. Additionally they were slightly further along in their pregnancy, average gestation at 30.4 weeks, ranging from 20-38 weeks, compared with a mean of 29.3 weeks, ranging from 13-38 weeks (table 4.13 and table 4.10). Women completing the study showed no divergence in trends of delivery dates compared with their EDD in comparison with consenting women. Finally, participants completing the study were located on average 337 m closer to the MSWI of interest compared with consenting participants; average distance from MSWI for consenting participants 5,479 m and 5,142 m for participants completing the study (table 4.15 A and B).

Study questionnaire/Occupational questionnaire

As detailed above, 98 participants were able to provide a breast milk sample, of these, 97 samples were collected (one participant was not available during both collection trips). The section below gives a descriptive analysis of the details captured within the study questionnaire and the occupational questionnaire, grouped by MSWI site: Stockton (North Tees and South Tees combined due to the small number of participants) and Southampton.

Descriptive analysis of personal, residential and occupational data

A descriptive analysis of the answers to Questions 4 to 18 in the study questionnaire and Question 1 of the occupational questionnaire is provided in table 4.16. A number of these questions were additionally analysed by residential proximity to the MSWIs, defined as participants "near" the MSWIs (23% of participants resident within 3km) and those "far" from the MSWIs (77% of participants resident further than 3km), table 4.19.

Age, Height, Weight & Body Mass Index (BMI)

The mean age of participants was 30.5 years, ranging from 18 to 43 years. As noted above mean ages were higher in Southampton (31.7 years) compared with Stockton (29.9 years). Mean height of participants was 164 cm with a 2 cm difference in mean heights between Southampton and Stockton. Weight was similar across the sites with a mean weight of 68 kg. Participant's height and weight were used to calculate BMI, reported both as a continuous variable and stratified according to underweight, normal weight, overweight and obese categories. The greatest proportion of participants fell within the normal BMI range (63.3%), followed by overweight (17.7%) and obese (17.7%).

Participants resident near the MSWIs were found on average to be older (mean age 31.5 years old, compared with 30.2 years old) with a greater proportion of women falling within the normal BMI range compared with participants living further from the MSWIs.

Residential history

Changes in address both during pregnancy and within the last five years were captured with the study questionnaire. In pregnancy, on average, over 85% of participants remained at the same address, with a slightly larger proportion of participants moving address in Stockton 19.4% compared with 10.6% in Southampton. However, of the 13.4% participants moving residence during pregnancy, 85% remained within the same postcode area. The figures for five year residency were somewhat different, with 72% of participants reporting a change in address within this period, although 83% of participants changing address had their previous address within the same postcode area. Although no significant differences for participants near and far from the MSWIs were observed for residence during pregnancy, residents near the MSWIs were more likely to have changed address in the last five years, 82%, compared with residents further from the MSWIs, 69%.

Marital status

Large disparities in marital status were seen between the two sites. In Southampton 69.7% of participants reported they were married compared with 58.1% in Stockton.

The proportion of births reported in marriage for both sites was significantly greater than that reported in the 2011 Census, where 37.3% of women between 20 and 44 reported they were married (40.9% including those legally married but separated).

Ethnicity

Across both sites, the large majority of participants, 89 of the 97 participants (92%), reported their ethnic group as white. Only one other ethnic group was reported for participants, with 8% reporting their ethnicity to be Asian (includes Indian, Pakistani, Bangladeshi, Chinese and Other Asian groups). No participants reported themselves as belonging to Black, Mixed or Other ethnic groups.

Compared with information extracted from 2011 Census (women between 20-44 years old), the proportion of White participants was similar, 91.8% compared with 91.1%. However there was a greater proportion of Asian participants within the study, 8.2% compared with 5.7%. No participants reported Mixed, Black or Other ethnicities which, although they account for a small proportion of the population in the area (1.4% Mixed, 1.1% Black and 0.6% Other), where represented within the study population.

Educational achievement

A large proportion of participants were educated to a degree level or above, 71.1% (40% with a first degree and ~30% with higher than a first degree). This proportion was found to be higher in Southampton, 72.7%, compared to Stockton, 67.8%.

These proportions are over three times greater than reported in the 2011 Census where 20.8% of women between the ages of 16 to 49 had a degree level or above. When comparing participants' resident near and far from the MSWIs there was little difference in educational achievement, both with greater than 70% obtaining a degree level or above.

Occupation

Over 90% of participants worked during their pregnancy. None reported this work to be in industrial production or within the chemical and textile industry. The greatest proportion of participants, 56.7%, were categorised within the SOC group "Professional occupations". The two most common occupations both fell within the "Professional occupations" categories, with the most common job title "Nursing and Midwifery Professional" and the second most common "Secondary educational teaching professional". Together these two occupations made up a quarter of the participants within the "Professional occupations" group.

A comparison between participants resident near and far from the MSWIs indicated that those resident further away were more likely to be categorised as "Manager, director and senior officials", "Professional occupations" and "Associate professional and technical occupations", with all three making up 68.1% of participants resident far from the MSWIs compared with 59.1% of participants resident near the MSWIs.

Smoking

One participant reported that they currently smoked and one additional participant reported that they had smoked during pregnancy; 20% of participants had previously smoked within the last 10 years, with a greater proportion of participants in Southampton, 23%, compared with Stockton, 13%. Of those who previously smoked the greatest proportion, 37%, smoked fewer than 5 cigarettes a day.

No difference in smoking status, current or previous, was observed for participants living near and far from a MSWI.

Dietary analysis

A descriptive analysis of the answers to Questions 19-23 of the study questionnaire is provided in table 4.17 and table 4.20.

Dietary restrictions, avoidances, milk consumption, locally sources food & diet during pregnancy

Most study participants, 84.5%, reported that they had no dietary restrictions (86.4% in Southampton and 80.6% in Stockton). Of the 14 participants reporting dietary restrictions, 11

(78.6%) were vegetarian, with the remaining three reporting "Other dietary restrictions" (two were pescetarians and one had food restrictions due to medication). The proportion of participants with food avoidances was greater, with 23.7% declaring that they avoided certain food groups at both sites (Southampton, 25.8% and Stockton, 19.4%). Among the 23 participants with avoidances, most avoided seafood (47.8%), followed by those who avoided both seafood and meat (34.8%).

Only one participant reported they did not consume milk. Of the remaining 96, 94.8% consumed cow's milk, followed by soya milk, 3.1% (all in Southampton). Most participants consumed semi-skimmed milk, 81.3%, with a fat content of ~1.7%. The second most common was skimmed milk, 12.1% (fat content 0.1%), followed by whole milk 9.9% (fat content 3.5%).

Participants' consumption of locally sourced foods showed that 8-18% of participants consumed meat, poultry, fish, eggs and dairy from local sources. Eggs were most likely to be sourced locally, 18%, and all dairy products the least likely, 7.9%. A comparison between the two sites revealed that within each food group, with the exception of dairy products, participants from Stockton were more likely to consume products from local sources than those from Southampton. Further when comparing particpants by distance to the MSWIs, with the exception of meat, participants resident near to the MSWIs were more likely to consume locally sourced foods.

When asked about changes to diet during pregnancy, over 50% of participants reported that their diet had changed. However, in Stockton the proportion of women reporting dietary changes was much higher, over 60%, than in Southampton where most reported that their diet had not changed.

Daily dietary intake of dioxins

Table 4.18 and Table 2.21 provide an overview of estimated daily dioxin intake from foods. Amounts ranged from 1.1- 61.7 pg WHO-TEQ/day with an average concentration of 27.5 pg WHO-TEQ/day. Mean concentrations for participant's resident near the MSWIs were 28.5 pg WHO-TEQ/day compared with 27.2 pg WHO-TEQ/day for those further from the MSWIs. A comparison of daily dioxin intake estimates between participants with and without reported dietary restrictions indicated that dioxin intakes were lower for participants with dietary restrictions, 21.5 pg WHO-TEQ/day compared to participants with no restrictions, 28.5 pg WHO-TEQ/day. This difference was apparent at both sites, both for participants near and far

from the MSWIs (table 4.20). Among participants with dietary restrictions, lower dioxin intake was primarily among vegetarians who had a mean dioxin intake of 20.2 pg WHO-TEQ/day. A comparison of daily dioxin exposure estimates between participants with and without reported food avoidances indicated that participants with avoidances had lower dioxin intake levels 24.4 pg WHO-TEQ day compared to participants with no avoidances, 26.0 pg WHO-TEQ/day. This was particularly evident for participants avoiding both meat and seafood, 15.9 pg WHO-TEQ/day. All calculated levels were found to be higher among participants resident nearer to the MSWIs with the exception of participants avoiding seafood, possibly reflecting the small sample size, 3 participants (table 4.21).

Daily dioxin intake estimates were further analysed per kilogram of bodyweight. Concentrations ranging from 0.02-1.10 pg WHO-TEQ/kg body weight/day with an average of 0.42 pg WHO-TEQ/kg body weight/day. This mean dioxin intake was equivalent to that reported by the Food Standard Agency in 2001, calculated at 0.4 pg WHO-TEQ/kg body weight/day [229].

Future dioxin analysis

The laboratory analysis of dioxins within frozen breast milk samples, by high-resolution gas chromatography/mass spectrometry, was not undertaken within the time frame of the PhD due to the study expansion (additional information provided in chapter 5, Section 5.2). Additional funds have been awarded to the study, which has allowed an increase in both in the number of samples to be collected, including those from an additional MSWI, and also the number of biomarkers to be measured. For reasons of quality control all samples will be analysed in one batch. At present breast milk samples are still being collected.

4.3 USING NATIONAL BIRTH DATA WITHIN EPIDEMIOLOGICAL STUDIES OF BIRTH OUTCOMES

This analysis was motivated by the SAHSU study of reproductive health effects associated with MSWIs.

4.3.2 Temporal and spatial variability in births

Throughout the ten-year study period, 2001-2010, the number of births was consistently higher in the ONS births dataset compared with both HES datasets (Figure 4.8). Overall the HES

deliveries dataset captured 94.7% of ONS births and 94.6% for HES births, with a vast improvement in capture over time, ranging from 73.0% in 2001 to 96.4% in 2010 for HES deliveries and 73.6% to 96.7% for HES births. All three datasets showed an increasing trend in the number of births and deliveries between 2001 and 2010 (Figure 4.8). This increase was greatest for both HES datasets, where HES deliveries increased by 60.9% and HES births by 60.1%, compared with ONS births, which showed an increase of 21.9%. For both HES datasets this increase was mainly driven by the large increase in births and deliveries recorded between 2001 and 2002, with HES deliveries increasing by 31.7% and HES births by 32.5%. Excluding 2001 the increase in births and deliveries was similar across all datasets, ONS 21.4%, HES deliveries 22.2% and 20.8% for HES births.

In addition to an overall increasing trend, there was a year on year increase in births for all years except 2008 to 2009, when all three datasets showed a decrease in births, 1.6% decrease in HES deliveries, 0.1% in HES births and 0.2% in ONS births. Excluding 2001, overall the annual increase in births and deliveries was 18,801 (3.2%) in HES deliveries, 16,483 in HES births (2.8%) and 17, 587 ONS births (2.8%), reflecting the improvements in their total capture of births each year.

The spatial distribution of births across England was similar within HES deliveries and ONS births datasets (73% of HES births had no information on GOR at birth) (Figure 4.9a & b). The proportion of births occurring within each GOR within the HES deliveries and ONS births datasets was similar with a maximum difference of 0.4% births in Yorkshire and Humber. A comparison of births by GOR within HES births was limited due to the vast proportion of births with missing information of GOR of residence (extracted from home address); 72.9% of births had missing GOR. Both HES deliveries and ONS births reported the highest proportion of births in England between 2001-2010 occurred in London (18.64% in HES deliveries and 18.96% in ONS births) and the lowest in the North East (4.64% in HES deliveries and 4.55% in ONS births).

4.3.3 Data analysis

Data collected

As an administrative dataset, the data items collected in HES are different to those of ONS (table 4.22). They have a number of data fields in common, but many are unique to the HES datasets. Of particular interest for epidemiological studies on birth outcomes is the inclusion of

information on ethnic origin of the mother/baby, previous pregnancies and gestational age, all of which are not recorded in ONS births (table 4.22).

Completeness of the data fields

A comparison of the completeness of the data showed the ONS births datasets to be far superior to HES. Between the two HES datasets, the HES deliveries dataset was found to be more completed than HES births (table 4.23). For a number of common variables, such as maternal age, residential postcode and birth weight, ONS had near 100% completeness, compared with HES deliveries, in which 99.7% of deliveries recorded maternal age, 99.4% residential postcode and 76.1% birth weight. The corresponding figures for HES births were much lower with 61.6% complete for maternal age, 27.1% residential postcode and 62.2% birth weight.

Two data fields within the ONS dataset with poor annual and overall completeness were parity and gestational age (table 4.23). Note all births in 2001 were excluded from comparisons due to the low completeness within both HES datasets. This can be explained because parity is only collected for births occurring within marriage, thereby considerably restricting its overall completeness. For gestational age, this field is only collected for stillbirths, making up less than 1% of all births.

The completeness of deliveries and births within HES varied, showing significant improvements for a number of fields over the study period. HES deliveries improved completeness in the fields of; birth weight (71.3% in 2002 and 89.4% in 2010), birth status (65.3% of deliveries had birth status recorded in 2002, increasing to 88.3% in 2010), mothers ethnicity (68.4% in 2002 and 92.3% in 2010), delivery place (59.4% in 2002 and 87.0% in 2010) and the greatest improvement found for gestational age in which 54.6% of records were complete in 2002 increasing to 83.8% in 2010. Completeness of fields in HES births showed greater variability over the study period, with a number of variables showing significant improvements in their completeness: babies ethnicity (48.7% of births had ethnicity recorded in 2002, increasing to 90.5% in 2010), delivery place (55.5% in 2002 and 81.9% in 2010), gestational age (54.3% in 2002 and 79.9% in 2010), birth weight (58.6% in 2002 and 82.1% in 2010), and birth status (58.6% in 2001 and 83.0% in 2010). However for HES births there were decreases in completeness for a number of fields including residential postcode (29.5% of births had postcode recorded in 2002, decreasing to 7.3% in 2010)- thereby influencing other spatially derived variables such as Carstairs score, and sex of baby which has not been documented since 2002.

In addition to completeness, the number and proportion of births and deliveries with medically unrealistic values was compared (table 4.24). This included a comparison of the proportion of multiple births (triplets or greater), young and older mothers, high and low birth weights and high and low gestational ages. Overall the proportions of these records were small, less than 1% of the total births, however they did occur more frequently in both HES datasets compared with ONS. For example between 2002 and 2010, 18,871 live singleton births with a birth weight below 500 grams were recorded in HES births, in HES deliveries there were 6,171 records and 4,855 in ONS.

Data trends

Overall when the information was present, in both HES datasets there was good agreement with ONS data (table 4.25), showing similar proportions of births by GOR, socio-economic sector, plurality (single and multiple), status (live and stillbirths), birth weight distributions and sex. GOR of residence and socio-economic sector within 0.5% of ONS births distribution for HES deliveries, while for HES births there was a maximum difference of 4.4% for GOR of residence compared with ONS. The proportion of single births, live births and female births within the HES births matched more closely to ONS births than HES deliveries, whereas mean birth weight was most similar between ONS births and HES deliveries, where mean birth weight of 3,319 g and 3,329 g were recorded respectively.

Descriptive epidemiology, spatial and temporal trends of birth outcomes in England

The birth outcomes investigated within this section are defined in chapter 3 and the datasets in which these outcomes were explored indicated. With the exception of the analysis for stillbirths, all multiple births and stillbirths were excluded from the analysis and birth weight restricted to greater than 200 g.

The percentages of births by birth outcome were in high agreement across the datasets (table 4.26). The most common birth outcome investigated was preterm delivery, occurring in 7.5% of births in the HES deliveries and HES births datasets. Stillbirths were the least common birth outcome, occurring in 0.6% of births in the HES deliveries dataset, 0.5% in HES births and 0.5% in ONS births. The frequency of birth outcomes comparable across all three datasets (LBW, vLBW and stillbirths), were similar within each dataset with marginally lower percentages found within the ONS dataset compared with both HES datasets. The frequency of LBW births

was most similar between HES deliveries and ONS births, with 6.0% and 5.9% of births documented as LBW respectively and 1.0% and 0.9% vLBW.

Defining birth outcomes

In order to explore the birth outcomes information on birth status, plurality, birth weight and gestational age was required. The completeness of these data fields varied both temporally within the datasets and across the three datasets.

As the ONS births dataset was constructed by joining together live and stillbirth tables, the completeness of birth status (live or still) was 100%. Birth status within both HES datasets was poorly documented, with an average of 27.8% records within HES deliveries with no status recorded and 37.4% for HES births (table 4.23). Although the overall completeness was poor, both dataset have shown considerable improvement over the study period, increasing by over 20% in both datasets.

Plurality within the ONS dataset is further considered to be 100% complete as this field is only marked when a birth is a multiple (table 4.23). Compared with ONS HES deliveries captured 83.7% of records with plurality, improving from 81.8% in 2002 to 91.6% in 2010, and HES births captured 71.7% of births with plurality, increasing from 66.3% in 2002 to 86.2% in 2010.

The birth weight data field was better completed in the ONS births dataset than in either HES datasets. For the total births recorded by ONS between 2002 and 2010, 99.4% of the records included birth weight information (table 4.23). Missing birth weights within the ONS datset were defined as births where weights were recorded as 0 g or 9998 g; however, no records were present without birth weight documented. HES births had the largest number of records that were missing birth weight information, on average only 62.3% of births had birth weight recorded rising to 76.6% for HES deliveries. Although the overall completeness for birth weight was lower within the HES datasets, there have been significant improvements in its completeness, with HES deliveries increasing from 71.3% of records with birth weight information in 2002 to 89.4% in 2010 and for HES births increasing from 58.6% to 83.0% respectively.

Gestational age at pregnancy was recorded in 60.3% of births in the HES deliveries dataset, 59.7% in the HES births dataset (table 4.23) and for all stillbirths in the ONS dataset. Again improvements can be seen over the time period with HES deliveries, improving from 54.6% of

records with gestational age recorded in 2002 to 83.8% in 2010 and HES births improving from 54.8% to 79.9%.

LBW and very LBW

Descriptive epidemiology

The characteristics of LBW babies are described in table 4.27. Compared with all births in England (table 4.25), all three datasets showed that LBW babies occur more frequently in the most deprived quintile of the population (HES deliveries – 40.1% of LBW babies compared with 29.2% of all births; ONS births – 38.5% of LBW babies compared with 28.7% of all births). Both HES datasets demonstrated that LBW babies occur less frequently in the white population (mothers and babies ethnicity), more frequently in the Asian population (HES deliveries – 18.4% of LBW babies compared with 11.5% of all births) and are delivered more often by caesarean section (HES deliveries – 36.6% of LBW babies compared with 22.6% of all births). ONS data additionally showed LBW babies to occur more frequently in first time mothers (ONS births – 50.9% of LBW babies compared with 42.0% of all births).

The most prominently observed difference with LBW babies was their tendency to be born preterm (gestational age not available in ONS). For all HES deliveries only 7.5% were born preterm and 3.2% very preterm, compared to LBW babies where 58.4% births were preterm and 28.3% very preterm.

Temporal & spatial trends

The overall proportion of babies born LBW and vLBW was lower in the ONS dataset compared with both HES deliveries and HES births (6.0% LBW and 1.0% vLBW for HES deliveries, 6.3% and 1.2% for HES births and 5.9% and 0.9% in ONS births) (table 4.26). Although differences in overall rates were observed amongst the datasets, all three showed a decreasing trend over the study period (Figures 4.10 ai & b). The sharpest decrease in rates was observed for HES births and in vLBW babies, with LBW babies displaying a 28.4% decline in LBW rates and 88.1% in vLBW rates from 2002 to 2010, compared with 15.8% and 37.2% for HES deliveries and a more stable 14.7% and 14.9% for ONS births. By 2010 all three datasets showed similar rates of LBW births (560 per 10,000 - HES births; 551 per 10,000 - HES deliveries; 541 per 10,000 – ONS;) and vLBW births (82 per 10,000 - HES births; 81 per 10,000 - HES deliveries; 84 per 10,000 – ONS).

An overview of the spatial distribution of LBW births across England for HES deliveries and ONS births was similar (Figure 4.10 aii). Both datasets showed the highest proportion of LBW birth occurring in London (19.19% in HES deliveries and 19.69% in ONS births) and lowest occurring in the North East (6.02% in HES deliveries and 4.76% in ONS births). The greatest difference in the proportion of LBW births between datasets was observed in the North East and South East, in which the percentage difference was 1.26% and 1.33% respectively.

Stillbirths

Descriptive epidemiology

All three datasets found that stillbirths tended to be LBW (66.1% LBW and 43.3% vLBW compared with approximately 6% and 1% in the general population based on ONS data) (table 4.27 and table 4.26). Both HES datasets showed that stillbirths occurred less frequently in the white population, more frequently in the Asian population (HES deliveries – 19.1% of stillbirths compared with 11.5% of all births) and were less often delivered by caesarean section when compared to all births (HES deliveries – 15.4% of stillbirths compared with 22.6% of all births) (table 4.27 and table 4.25). ONS data also indicated that stillbirths occurred more frequently in women who have had more than one child previously (ONS births – 26.4% of stillbirths compared with 22.3% of all births). Both HES deliveries and ONS data indicated that stillbirths occurred more frequently in the more deprived areas, a finding which was not supported by the HES births dataset (HES deliveries – 36.3% of stillbirths compared with 29.2% of all births; ONS births – 36.8% of stllbirths compared with 28.7% of all births). However this may be partly due to the fact that the HES births deprivation score was calculated at small area level, and also that information on residence for stillbirths was missing in 71.2% of HES birth records.

Temporal & spatial trends

Overall the percentage stillbirths were highest in the HES deliveries dataset, 0.6% of births. Both HES births and ONS births documented the same occurrence at 0.5% of births (table 4.26). The trend for stillbirth rates within the ONS births dataset showed a stable pattern over the study period, ranging from a minimum of 51 per 10,000 births in 2007 to a maximum of 57 per 10,000 births in 2003 (Figure 4.10 c). The pattern for both HES datasets was unstable, with HES deliveries reporting a decrease in stillbirth rates from 113 per 10,000 in 2002 to 51 per 10,000

in 2003. A distinct peak in stillbirth rates was seen in 2007 in both HES datasets but this was not reflected in ONS births (Figure 4.11 c).

Consequently the spatial distribution of stillbirths across England between 2002-2010 within the HES deliveries and ONS births were different (Figure 4.10 cii). The greatest difference was found in the South East (29.8% for HES deliveries and 13.7% for ONS births) and Yorkshire and The Humber (17.0% in HES deliveries and 10.7% in ONS births), with the proportion of stillbirths occurring in these GORs substantially higher in HES deliveries compared with ONS births.

Term LBW

Descriptive epidemiology

An extraction and analysis of term LBW allowed examination of LBW babies occuring due to restrictions in their intrauterine growth as distinct from babies that are low weight because they have been born preterm. As expected term LBW babies had similar characteristics to LBW babies in their ethnicity (more frequent in the Asian population), deprivation score (more frequently occurring in the deprived population) and method of delivery (more frequently delivered by caesarean section) (table 4.28).

There was a tendency for term LBW to occur in the female population (HES deliveries data: 49.6% - all births; 53.4%- LBW babies; 59.7%– term LBW) (table 4.28 and table 4.27).

Temporal & spatial trends

Overall the percentage of births occurring at term and defined as LBW was 2.7% for the HES births dataset and 2.5% for HES deliveries (table 4.26). The trend for term LBW was found to be more stable than LBW and for HES deliveries compared with HES births (Figure 4.11ai). The two datesets show similar patterns after 2004, before which HES births are distinctly higher than HES deliveries.

The spatial distribution of term LBW births across England between 2002 and 2010 are mapped for HES deliveries in Figure 4.11 aii. The highest proportion of term LBW births occurred in London (21.6% in HES deliveries) and the lowest in the North East (4.84 in HES deliveries).

Preterm and v preterm delivery

Descriptive epidemiology

Preterm births were explored for both HES datasets (table 4.28). Preterm births occurred more frequently in the East of England (HES deliveries: 21.5% and all births – 10.4%), in the most deprived (HES deliveries: 36.3% and all births – 29.2%) and born by caesarean section (HES deliveries: 33.5% and all births – 22.6%). Additionally preterm deliveries occurred less frequently in the white population (HES deliveries: 72.5% and all births – 78.3%). The largest difference observed was the proportion of preterm births that were LBW, with 46.8%, 47.3% LBW compared with 6.0%, 6.3% in all births for HES deliveries and HES births respectively (table 4.26).

Temporal & spatial trends

The overall proportion of babies born preterm and v preterm were comparable (7.5% preterm and 3.2% v preterm for HES deliveries and 7.5% and 3.1% for HES births) (table 4.26). Although the difference in overall rates was negligible between the datasets, both showed an unstable trend over the study period (figure 4.11 bi & c). This unstable pattern was particularly evident for HES births where rates ranged from a minimum of 691 preterm births per 10,000 births in 2003 to a maximum of 826 preterm births per 10,000 births in 2007. For v preterm births these rates ranged from a minimum of 237 v preterm births per 10,000 births in 2002 to a maximum of 400 v preterm births per 10,000 births in 2007.

The spatial distribution of preterm births across England between 2002 and 2010 are mapped for HES deliveries in Figure 4.11 bii. The highest proportion of preterm term births occurred in the East of England (22.6%) and the lowest in the North East (4.5%).

Small area level analysis

Table 4.29 and table 4.30, display the small area level analysis of HES deliveries and ONS data by GOR and around two MSWIs. A review of national birth weight data in HES and ONS at SOA revealed good agreement in mean and median birth weights (within 10 g) of one another. However differences were observed in their variability, reflected in the standard deviations (ONS 94.9g; HES 122.8g) and in the minimum and maximum weights (ONS 2956-3729g; HES

606-4600g). For the North East and South East GOR the variability in HES was less apparent with mean and median weights differing by a maximum of only 2g.

Live births counts were additionally compared at SOA level. This analysis revealed lower counts of live births within the HES deliveries dataset compared with ONS. This is reflected at a national level and also within North East and South East GORs with mean, median and maximum numbers consistently falling below those reported in ONS. Compared with the differences observed at a national level (Mean: ONS 112; HES 158, Median: ONS 99; HES 144) live birth counts in the North East (Mean: ONS 125; HES 140, Median: ONS 116; HES 130) were much closely matched between the two datasets. However in the South East agreement was found to be poor (Mean: ONS 95; HES 149, Median ONS 84; HES 138).

This analysis was further conducted at SOA level around the Stockton-on-tees and Marchwood MSWIs. The underreporting in HES live births captured at GOR level was reflected around the Stockton-on-Tees MSWI. However for Marchwood the poor agreement between HES and ONS at GOR level was found to be more apparent, with mean, median and maximum counts in HES less than half of those reported in ONS.

Stillbirth counts at SOA level at a national level were found to be on average lower in HES compared with ONS. The underreporting in stillbirth numbers within the HES dataset is reflected in the North East; however, counts in the South East for HES were over two times that reported in ONS (Mean: ONS 0.71; HES 1.43). At MSWI level these differences become more apparent. This is particularly evident for Marchwood where at GOR level stillbirth counts are twice those in ONS and the MSWI level reported counts for HES are 7% of ONS counts.

Figure 4.12 and 4.13 show rates of live birth, stillbirths and mean birth weight for all SOAs within 10 km from Marchwood and Stockton-on-Tees MSWIs. Due to data governance reasons scale bars for live and stillbirth rates were removed, however the spatial patterns can still be observed. In Figure 4.13 shows similar spatial variability between the two datasets for live births, stillbirth rates and birth weight at the Stockton-on-Tees site. Although this variability is similar between the datasets, rates are consistently lower in the HES dataset. Figure 4.12 demonstrates the influence of administrative boundaries on small area level analysis, with one SOA geographically dominating the entire study area due to the small population. For the Marchwood site spatial patterns appear to be different between the datasets for both live birth rates and in particular stillbirth rates, with HES capturing almost none of the variability captured in ONS.

Figure 4.1. Daily particulate concentrations measured at flue exit for; (A) Edmonton between 2003 and 2010 (B) Marchwood between 2004 and 2010 (C) Sheffield between 2003 and 2010 (D) Stockton-on-Tees between 2003 and 2010

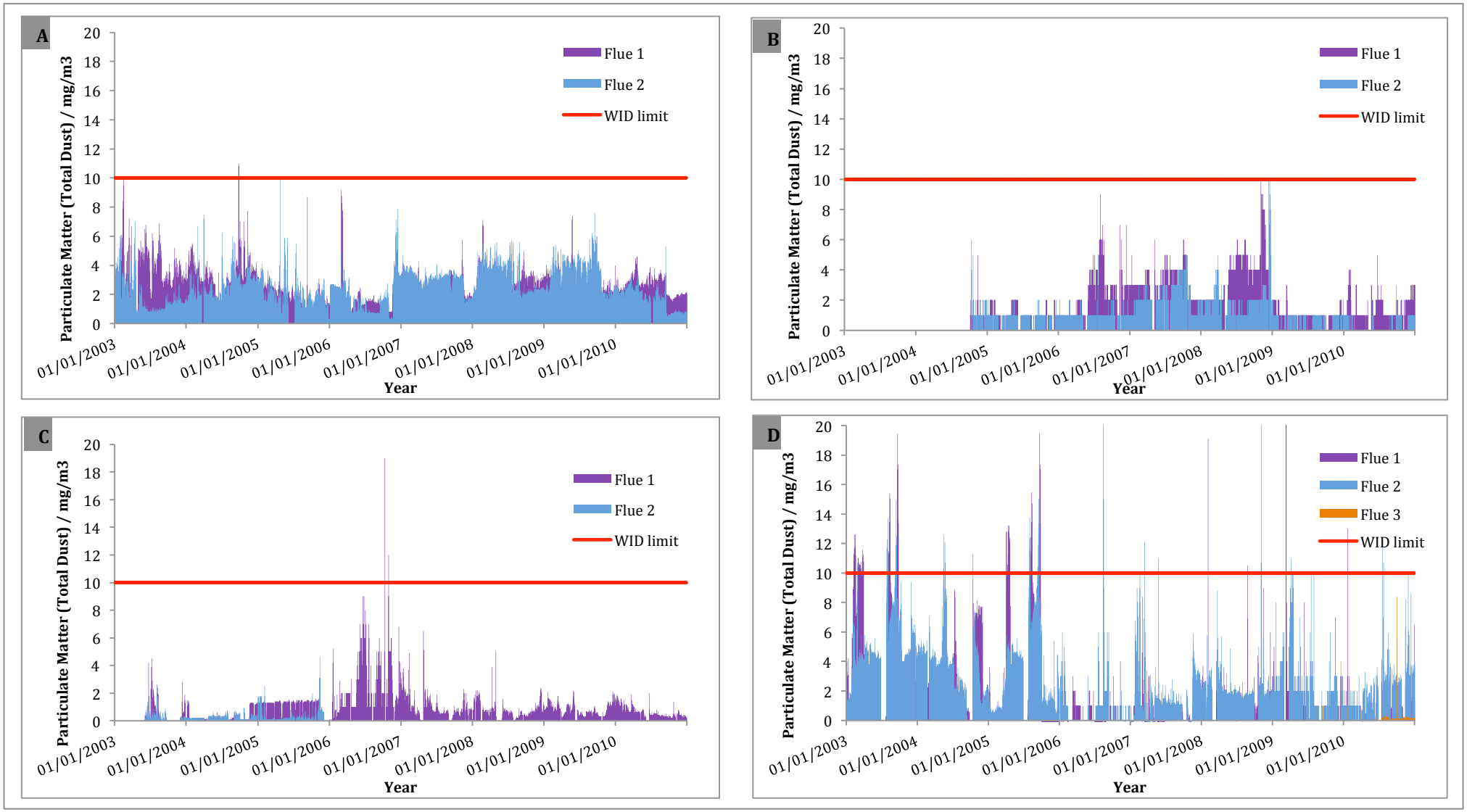


Table 4.1. Summary table of concentrations of particulate matter (total dust) measured at stack for four operating MSWIs by year (2003-10)

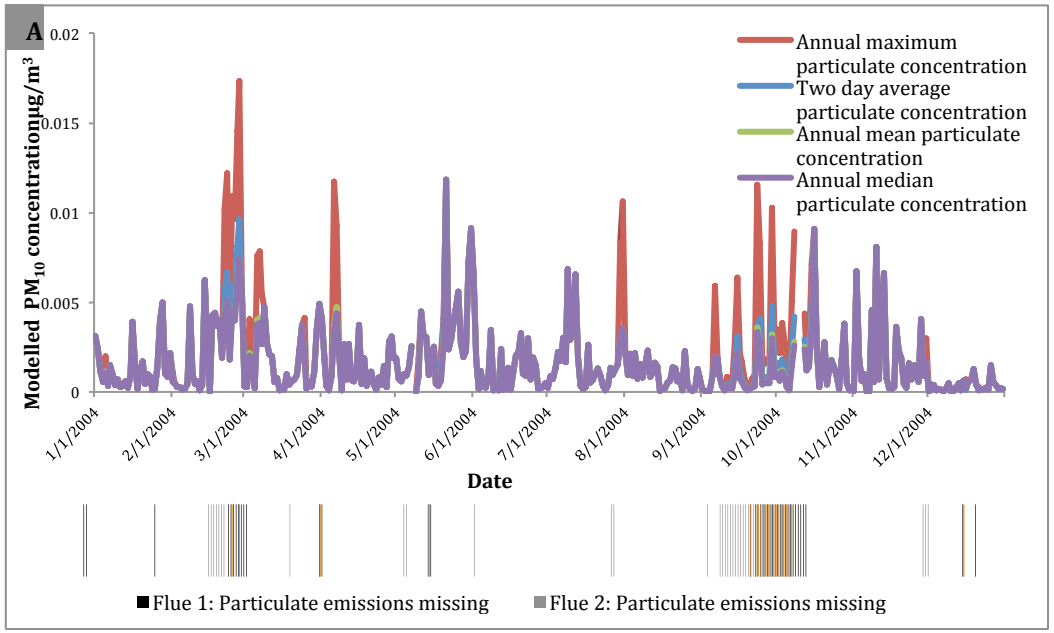
Incinerator(s)		Plant operation					Particulate Matter (Total Dust) for operational days			
		Days not in operation	Days with missing emission values	Days in operation (includes 0 mg/m^3)	Days in operation	Days with at least one flue operational	Mean (mg/m^3)	Median (mg/m^3)	Minimum (mg/m^3)	Maximum (mg/m^3)
2003										
Edmonton	Flue 1	0	30	335	335	365	3.61	3.4	0.8	9.9
	Flue 2	0	0	365	365		1.77	1.4	0.7	7
Marchwood	Flue 1					N/A				
	Flue 2									
Sheffield (June-December)	Flue 1	151 (0)	0	365 (214)	87	365 (214)	0.24	0	0	4.5
	Flue 2	151 (0)	0	365 (214)	100		0.13	0	0	2.5
Stockton-on-Tees	Flue 1	0	51	314	308	365	4.78	3	0	19.44
	Flue 2	0	35	330	326		5.14	4.62	0	14.94
	Flue 3									
2004										
Edmonton	Flue 1	0	30	336	336	366	3.41	3.2	0.7	11
	Flue 2	0	11	355	355		2.62	2.4	1.1	7.7
Marchwood (October-December)	Flue 1	305 (31)	0	61	58	65	1.08	1	0	5
	Flue 2	312 (38)	0	54	54		1.48	1	1	6
Sheffield	Flue 1	0	0	366	265	366	0.24	0.1	0	1.5

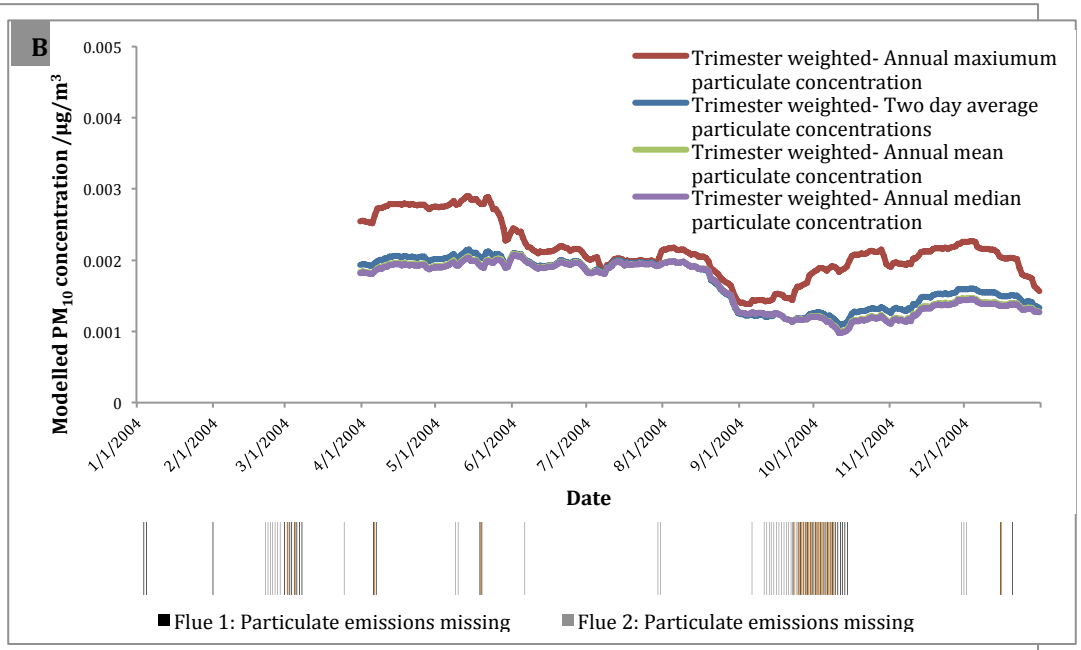
	Flue 2	0	0	366	271		0.21	0.2	0	1
Stockton-on-Tees	Flue 1	0	39	327	326	366	2.81	2.36	0.32	8.88
	Flue 2	0	51	315	313		3.85	3.85	0	12.52
	Flue 3					N/A				
2005										
Edmonton	Flue 1	28	0	337	337	365	1.88	1.8	0.9	8.7
	Flue 2	31	3	331	331		1.92	1.8	0.3	10
Marchwood	Flue 1	121	0	244	244	282	1.23	1	1	2
	Flue 2	125	0	240	240		1.03	1	1	2
Sheffield	Flue 1	75	0	290	285	335	1.24	1.3	0	2.7
	Flue 2	77	0	288	277		0.40	0.2	0	4.6
Stockton-on-Tees	Flue 1	0	42	233	230	365	3.91	2.58	0	19.49
	Flue 2	8	31	326	324		3.48	2.4	0	15.05
	Flue 3					N/A				
2006										
Edmonton	Flue 1	0	0	365	365	365	1.50	1.34	0.43	9.15
	Flue 2	0	0	365	365		1.73	1.6	0.09	7.91
Marchwood	Flue 1	55	0	310	308	334	2.38	2	0	9
	Flue 2	62	0	303	302		1.08	1	0	5
Sheffield	Flue 1	25	0	340	313	340	2.24	1.8	0	19
	Flue 2					N/A				
Stockton-on-Tees	Flue 1	35	16	267	77	350	0.37	0	0	4
	Flue 2	50	1	313	128		0.94	0	0	35
	Flue 3					N/A				

2007										
Edmonton	Flue 1	0	0	365	364	365	2.03	1.87	0	5.73
	Flue 2	0	0	365	364		2.97	3.13	0	4.73
Marchwood	Flue 1	40	0	325	325	344	3.06	3	1	6
	Flue 2	38	0	327	327		2.23	2	1	5
Sheffield	Flue 1	52	0	313	312	313	1.01	0.7	0	6.5
	Flue 2					N/A				
Stockton-on-Tees	Flue 1	60	0	262	188	343	0.40	0.2	0	8.4
	Flue 2	43	1	276	263		2.08	1.4	0	12.1
	Flue 3					N/A				
2008										
Edmonton	Flue 1	0	31	335	333	365	2.94	2.77	0	7.1
	Flue 2	0	0	366	364		3.12	2.88	0	5.71
Marchwood	Flue 1	26	0	340	340	358	3.53	4	1	10
	Flue 2	38	0	328	325		1.95	2	0	10
Sheffield	Flue 1	74	0	292	289	292	0.75	0.6	0	5
	Flue 2					N/A				
Stockton-on-Tees	Flue 1	78	2	285	255	338	0.84	0.5	0	19.1
	Flue 2	54	0	312	308		2.39	1.9	0	66.2
	Flue 3					N/A				
2009										
Edmonton	Flue 1	0	1	364	364	365	2.37	2.2	1.04	7.38
	Flue 2	0	0	365	365		3.38	3.57	1.26	7.6
Marchwood	Flue 1	24	0	341	296	357	0.98	1	0	3

	Flue 2	33	2	330	192		0.59	1	0	2
Sheffield	Flue 1	28	0	337	337	337	0.78	0.7	0.1	2.2
	Flue 2					N/A				
Stockton-on-Tees	Flue 1	135	2	228	141	346	1.25	1	0	44
	Flue 2	99	3	263	251		2.61	2	0	11
	Flue 3	178	10	177	7		0.04	0	0	4
2010										
Edmonton	Flue 1	0	0	365	365	365	2.53	2.5	1.5	4.6
	Flue 2	0	0	365	354		1.62	1.8	0	5.3
Marchwood	Flue 1	36	0	329	323	356	1.45	1	0	5
	Flue 2	23	0	342	104		0.31	0	0	3
Sheffield	Flue 1	39	0	326	325	326	0.59	0.5	0	2
	Flue 2					N/A				
Stockton-on-Tees	Flue 1	116	1	247	204	344	0.95	0.90	0	13
	Flue 2	94	0	271	267		2.31	2.3	0	12.4
	Flue 3	69	0	296	159		0.11	0.1	0	8.4

Figure 4.2. Comparing methods of "filling in" missing particulate emissions data-Stockon-on-Tees 2004 (A) Mean daily modelled PM_{10} across all postcodes within the study area by method (B) Trimester weighted mean daily modelled PM_{10} across all postcodes within the study area by method (C) Correlation matrix of annual mean modelled PM_{10} by postcode by method (D) Correlation matrix of annual median modelled PM_{10} by postcode by method





C

A. Two day average particulate concentrations-Annual mean
B. Annual maximum particulate concentration-Annual mean
C. Annual mean particulate concentration- Annual mean
D. Annual median particulate concentration- Annual mean

	A	B	C	D
A				
B	0.992			
C	0.999	0.989		
D	0.999	0.989	1.00	

D

A. Two day average particulate concentrations-Annual median
B. Annual maximum particulate concentration-Annual median
C. Annual mean particulate concentration- Annual median
D. Annual median particulate concentration- Annual median

	A	B	C	D
A				
B	0.999			
C	0.999	0.998		
D	0.999	0.998	1.00	

Table 4.2a. Land cover data from CORINE-Land 2001 1km around the four inclusive municipal solid waste incinerators within this chapter.

Incinerator(s)	CORINE Land Cover				
	Artificial surfaces (%)	Agricultural areas (%)	Forest and semi natural areas (%)	Wetlands (%)	Water bodies (%)
All incinerators*	68.6	24.1	2.9	1.8	2.6
Edmonton	95.5				4.5
Marchwood	37.6	24.2		0.1	38.1
Sheffield	100.0				
Stockton-on-Tees	70.4	24.6			5.1

*Porthmellon MSWI not included in total as CORINE-Land map indicates no land is present

Table 4.2b. Land cover data from CORINE-Land 2001 10km around the four inclusive municipal solid waste incinerators within this chapter.

Incinerator(s)	CORINE Land Cover				
	Artificial surfaces (%)	Agricultural areas (%)	Forest and semi natural areas (%)	Wetlands (%)	Water bodies (%)
All incinerators*	42.2	42.0	7.3	1.6	6.9
Edmonton	77.0	14.5	6.4		2.1
Marchwood	33.0	29.2	30.1	1.6	6.1
Sheffield	56.3	34.4	9.1		0.2
Stockton-on-Tees	44.7	46.5	2.7	1.7	4.4

*Porthmellon MSWI not included in total as CORINE-Land map indicates no land is present

Table 4.3. Model **s**ensitivity to dispersion site characteristics; surface roughness length and minimum Monin-Obukhov length. Median particulate emission concentrations and meteorological station data were input onto the model for 2005.

Incinerator(s)	**Dispersion site characteristics**					
	Surface roughness length (m)*			**Minimum Monin-Obukhov length (m)****		
	Selected length A (m)	Selected length B (m)	Model receptors with >25% percentage difference between selected lengths A and B (%)ǂ	Selected length A (m)	Selected length B (m)	Model receptors with >25% percentage difference between selected lengths A and B (%)ǂ
Edmonton	1.5	1	0	30	100	0
Marchwood	0.5	0.2	5.2	30	10	65.9
Sheffield	1.5	1	54.5	30	100	0
Stockton-on-	0.75	1	0	30	10	64.4

* Default minimum Monin-Obukhov length at site (30m) was used when surface roughness lengths compared
** Default surface roughness length at site (0.5m) was used when Minimum Monin-Obukhov lengths compared
ǂ Model receptors defined within a 200 by 200m grid within a 10km from the incinerator of interest (dispersion site)

Figure 4.3. Selected meteorological stations for Edmonton. Maps B-F use the same site surface roughness length and minimum Monin-Obukhov length. Median particulate emission concentration were input onto the model for the year of interest. (A) Map showing Edmonton MSWI and meteorological stations surrounding this point source (B) Model output and wind rose using meteorology data from Enfield station for 2003 (C) Model output and wind rose using meteorology data from London Weather Centre station for 2004 (D) Model output and wind rose using meteorology data from London Weather Centre station for 2005 with different cloud cover (E) Model output and wind rose using meteorology data from London city station for 2006-2009 (F) Model output and wind rose using meteorology data from London Olympic Park North station for 2010

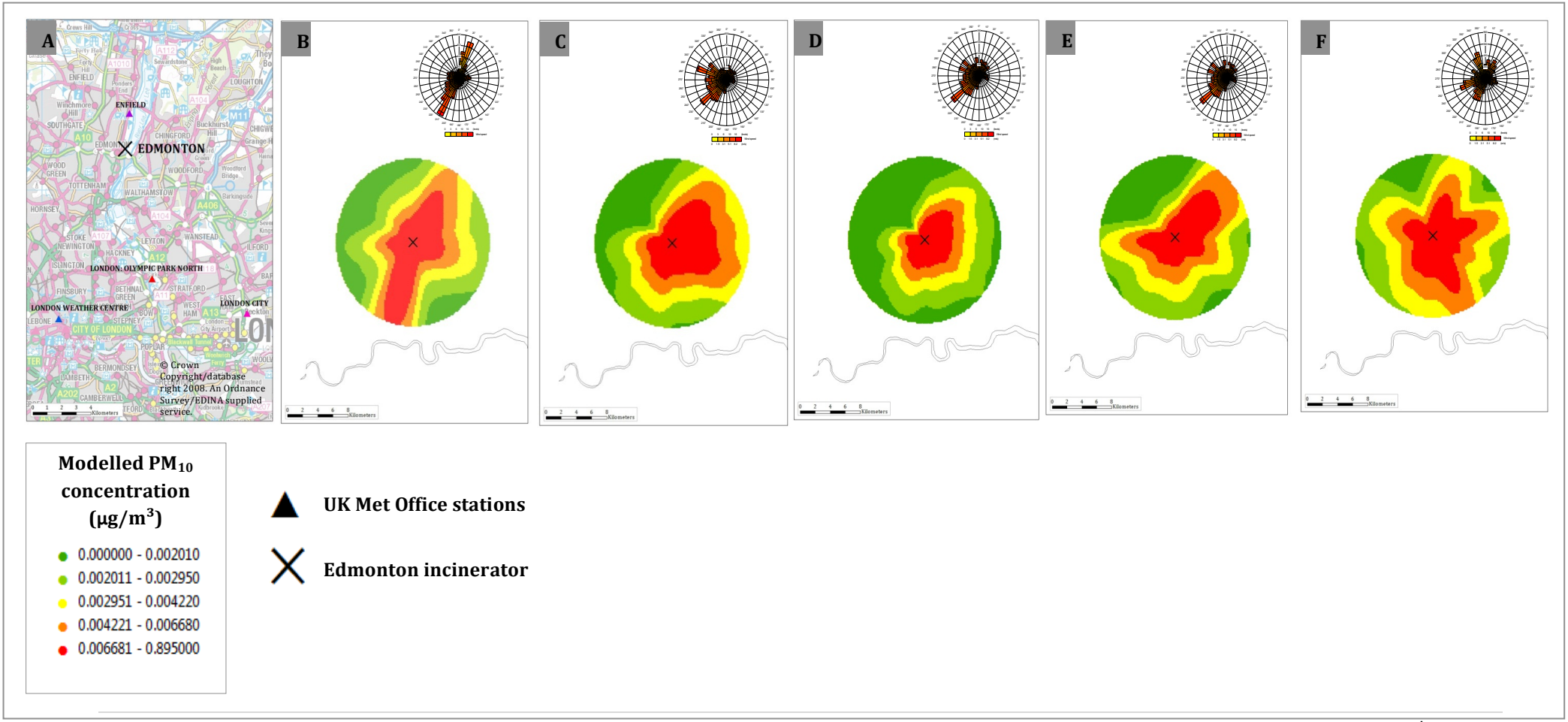


Table 4.4. Summary table of the surface elevation of the study area by incinerator in order to quantify the need for a terrain file in the exposure model.

Incinerator(s)	Elevation of terrain within dispersion site			Criteria for use of terrain file	
	Range (m)	Mean (m)	Median (m)	Percentage of dispersion site with terrain gradients >10% (%)	Need for terrain file
Edmonton	125	36.7	30	2.1	×
Marchwood	93	22.7	20	1.8	×
Sheffield	400	133.0	118	28.0	✓
Stockton-on-Tees	242	26.2	17	2.3	×

Figure 4.4. Exploration of the terrain surrounding the Sheffield incinerator. Maps C and D use the same site surface roughness length, minimum Monin-Obukhov length, meteorological data and median particulate emission concentration for 2005. (A) Map showing Sheffield MSWI location and model receptors within the output area (dispersion site) (B) Surface elevation extracted from Ordnance Survey PANORAMA™ digital terrain model (DTM), with a horizontal resolution of 50 m (C) Model output and wind rose when no terrain file is included in the exposure model (D) Model output and wind rose when a terrain file is included within the exposure model.

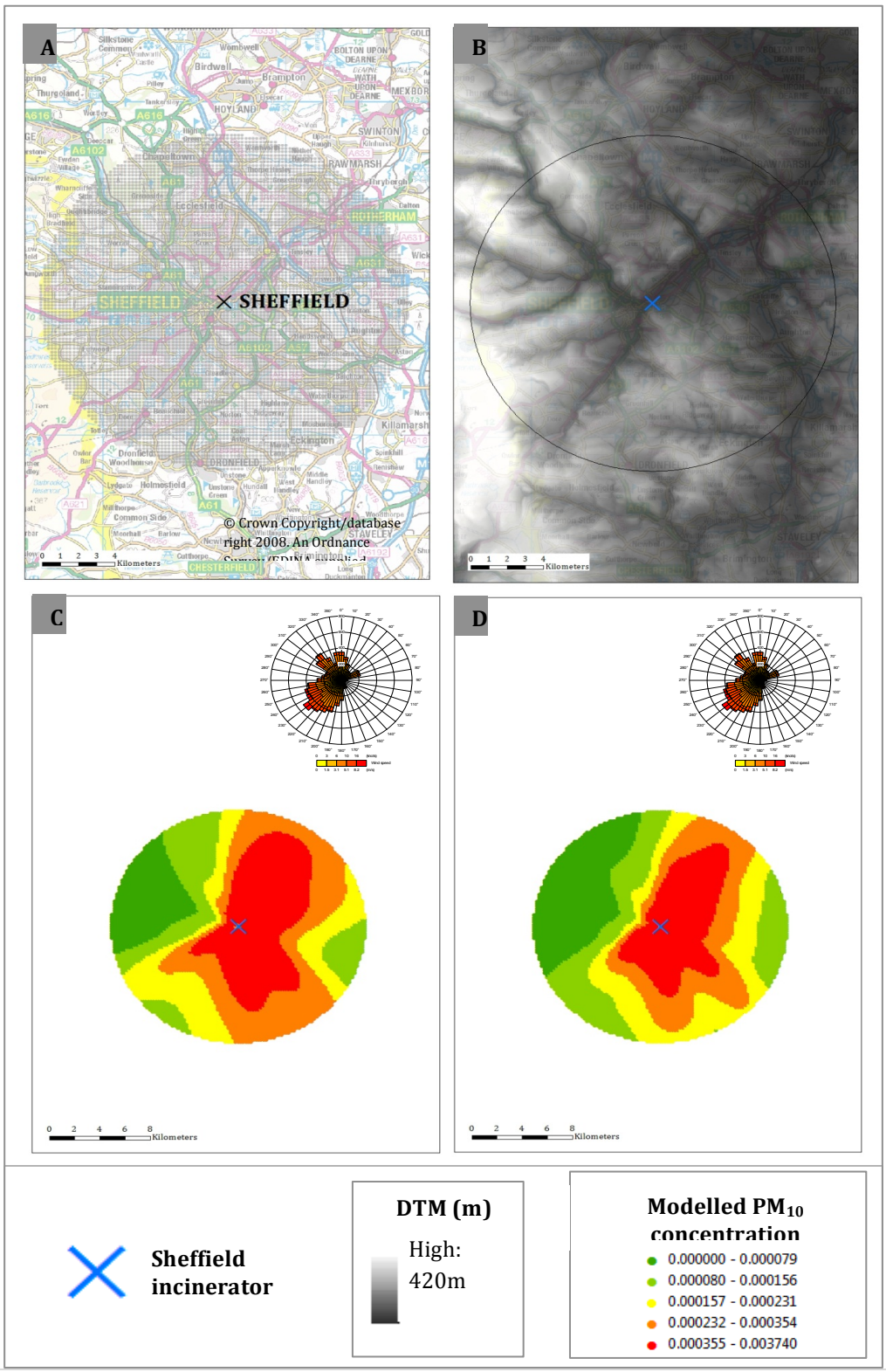
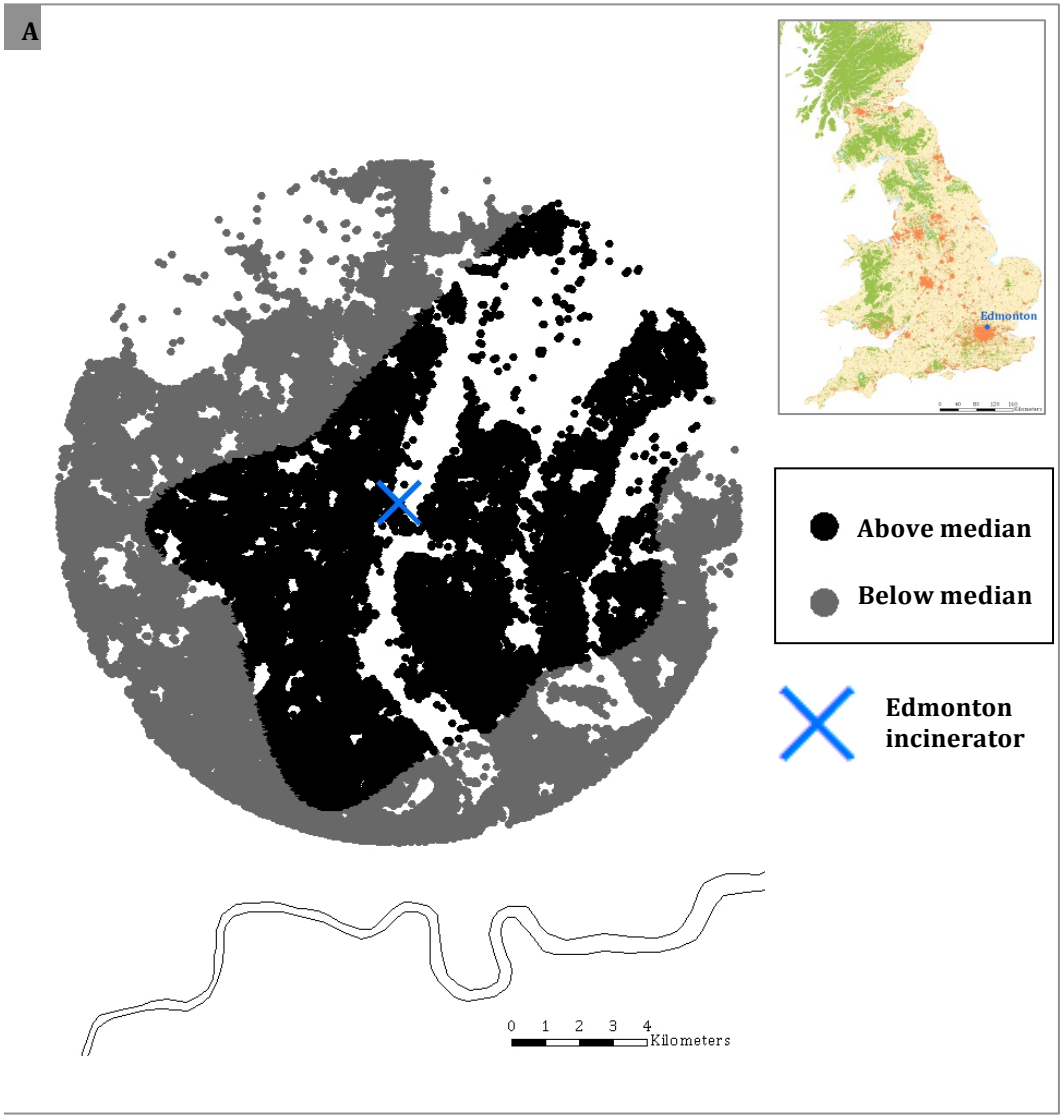
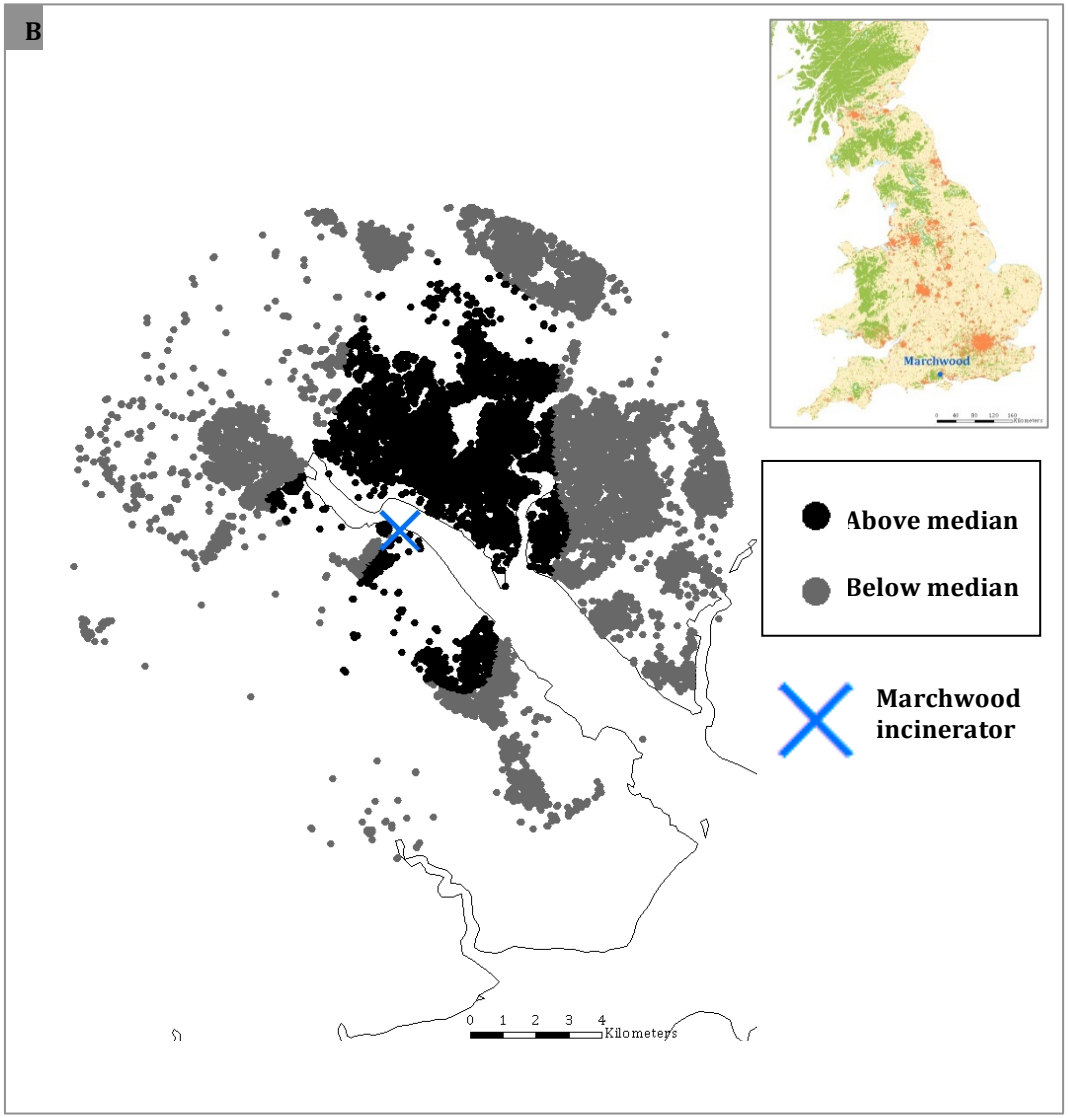
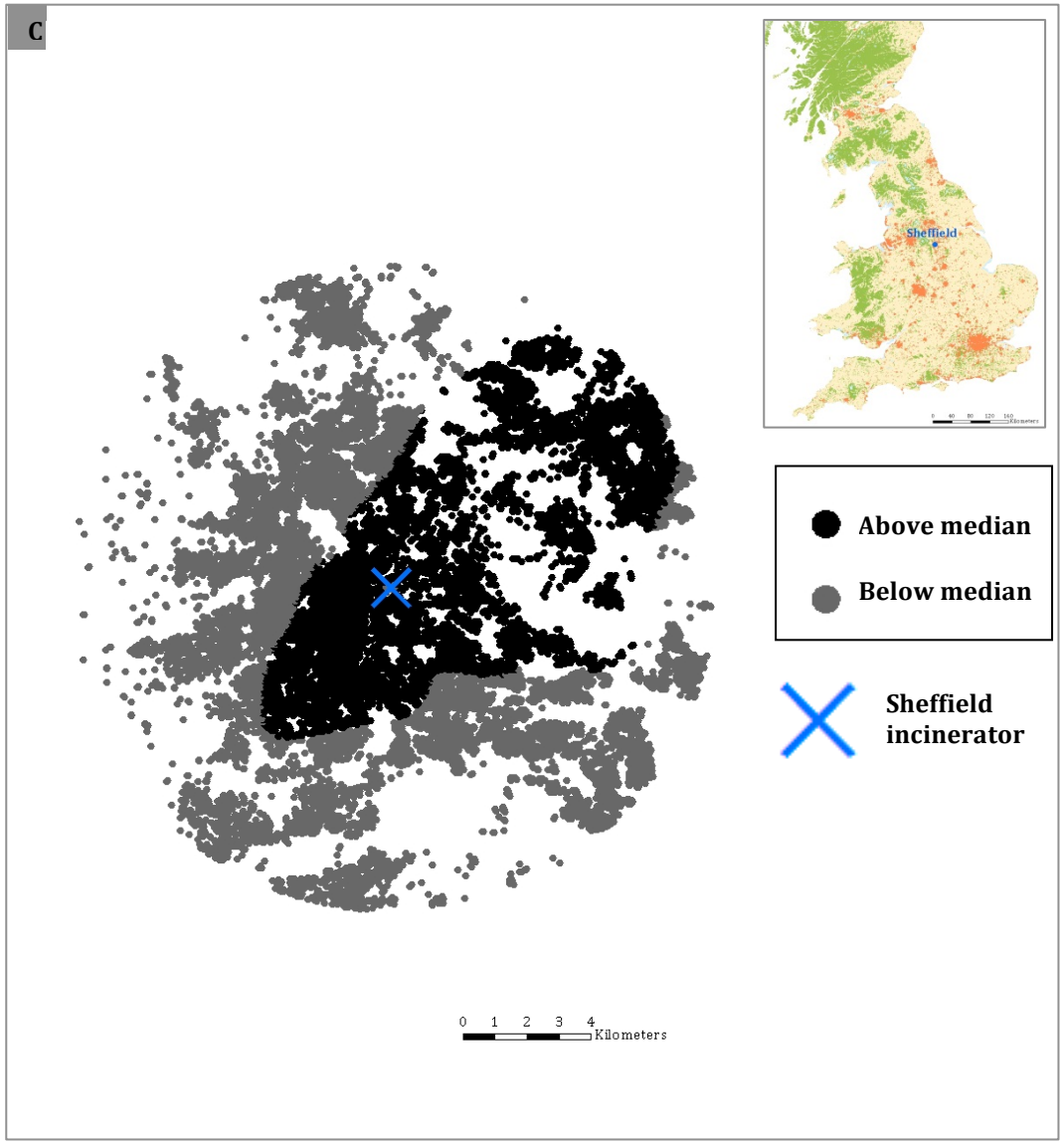


Figure 4.5. Average annual exposure model output at postcode level for (A) Edmonton between 2003 and 2010 (B) Marchwood between 2005 and 2010 (c) Sheffield between 2004 and 2010 (d) Stockton-on-Tees between 2003 and 2010






C
Sheffield
Above median
Below median
Sheffield incinerator
0 1 2 3 4
Kilometers

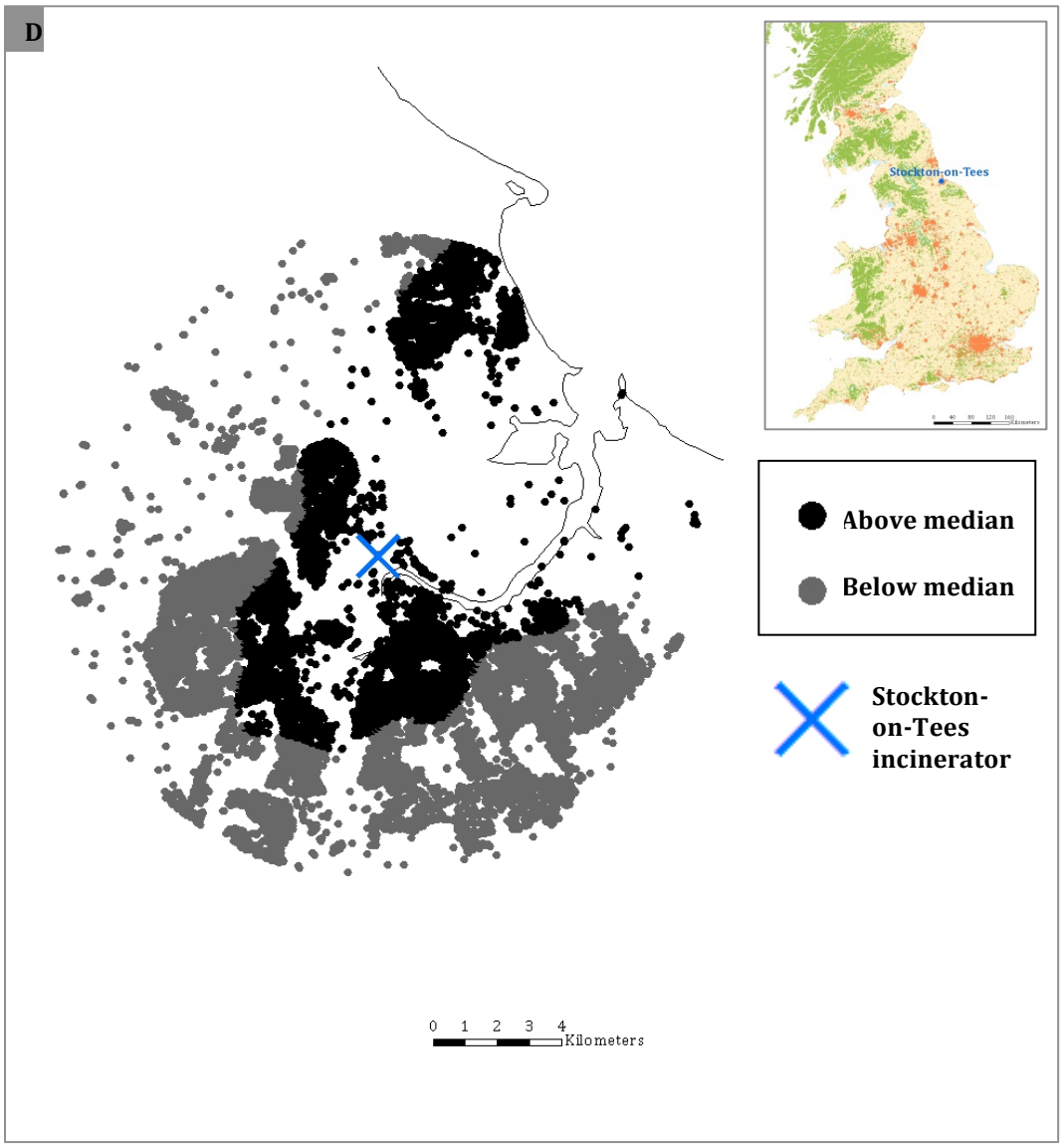

D
Stockton-on-Tees
Above median
Below median
Stockton-on-Tees incinerator
0 1 2 3 4
Kilometers

Table 4.5. Annual mean, median and range of modelled PM_{10} concentration in the 10km surrounding each incinerator weighted by postcode for days in which at least one flue was operational.

Incinerator(s)	Plant operation	Meteorological data	Modelled PM_{10} concentration for days in with at least one flue operational ($\mu g/m^3$)			
	Days with at least one flue operational	Days with sufficient meteorological data to model in ADMS	Mean ($x10^{-4}$ $\mu g/m^3$)	Median ($\mu g/m^3$)	Minimum ($\mu g/m^3$)	Maximum ($x10^{-2}$ $\mu g/m^3$)
2003						
Edmonton	365	365	59.28	3.44E-06	0	3003.20
Marchwood				N/A		
Sheffield	214	365	1.81	0.00E+00	0	10.29
Stockton-on-Tees	365	365	20.79	4.38E-29	0	44.26
2004						
Edmonton	366	366	54.72	2.01E-09	0	3288.61
Marchwood	65	366	7.40	3.17E-12	0	20.74
Sheffield	366	362	0.97	2.16E-24	0	2.76
Stockton-on-Tees	366	362	15.35	3.39E-21	0	48.99
2005						
Edmonton	365	365	33.24	4.53E-09	0	2651.97
Marchwood	282	361	8.26	2.67E-08	0	12.10
Sheffield	335	363	3.66	1.20E-14	0	8.39
Stockton-on-Tees	365	346	14.68	1.39E-28	0	78.93
2006						

Edmonton	365	365	30.12	7.67E-15	0	5363.86
Marchwood	334	365	13.93	2.36E-08	0	24.65
Sheffield	340	363	6.45	1.72E-28	0	19.64
Stockton-on-Tees	350	364	3.57	0.00E+00	0	113.42
2007						
Edmonton	365	363	50.99	2.26E-13	0	3969.18
Marchwood	344	365	22.85	6.78E-06	0	17.29
Sheffield	313	363	2.95	9.76E-19	0	13.67
Stockton-on-Tees	343	363	4.65	0.00E+00	0	19.19
2008						
Edmonton	365	366	55.88	2.83E-21	0	4201.50
Marchwood	358	366	24.99	7.23E-07	0	30.01
Sheffield	292	364	1.79	7.69E-25	0	5.60
Stockton-on-Tees	338	361	8.01	4.22E-30	0	96.24
2009						
Edmonton	365	365	56.69	7.97E-14	0	3820.17
Marchwood	357	365	6.22	1.29E-11	0	8.12
Sheffield	337	365	2.08	3.52E-22	0	4.53
Stockton-on-Tees	346	364	6.27	0.00E+00	0	103.66
2010						
Edmonton	365	365	50.96	7.50E-07	0	2472.93
Marchwood	356	364	5.56	1.06E-13	0	6.82
Sheffield	326	365	1.61	5.44E-20	0	4.32
Stockton-on-Tees	344	363	9.77	8.24E-20	0	29.67

Table 4.6. Distance of the study population (all residents within 10 km) to the incinerators

Distance to source (km)		**0-<1**	**1-<2**	**2-<3**	**3-<4**	**4-<5**	**5-<6**	**6-<7**	**7-<8**	**8-<9**	**9- 10**	**Total**
Edmonton	Number of modelled PCs*	313	2042	2991	4695	5654	7597	7516	8626	10299	12883	63231†
	(%)	*0.5*	*3.3*	*4.8*	*7.5*	*9.0*	*12.1*	*12.0*	*13.8*	*16.4*	*20.6*	*100*
	Number of PCs with population data *(%)*	70	841	1315	2049	2419	3201	3265	3644	4104	5273	26181
		0.3	*3.2*	*5.0*	*7.8*	*9.2*	*12.2*	*12.5*	*13.9*	*15.7*	*20.1*	*100*
	Population count	5193	53210	88174	129050	141450	187273	188807	215264	227803	295900	1532124
	(%)	*0.3*	*3.5*	*5.8*	*8.4*	*9.2*	*12.2*	*12.3*	*14.1*	*14.9*	*19.3*	*100*
Marchwood	Number of modelled PCs*	87	813	2363	2720	2969	2999	2171	1378	1611	2055	19299†
	(%)	*0.5*	*4.2*	*12.3*	*14.2*	*15.5*	*15.6*	*11.3*	*7.2*	*8.4*	*10.7*	*100*
	Number of PCs with population data *(%)*	42	307	765	1076	1303	1433	1043	655	717	761	8102
		0.5	*3.8*	*9.4*	*13.3*	*16.1*	*17.7*	*12.9*	*8.1*	*8.8*	*9.4*	*100*
	Population count	1677	12829	31729	46690	59070	69784	48832	25298	32654	32442	361005
	(%)	*0.5*	*3.6*	*8.8*	*12.9*	*16.4*	*19.3*	*13.5*	*7.0*	*9.0*	*9.0*	*100*
Sheffield	Number of modelled PCs*	595	2399	3173	4012	3804	3424	2602	2477	2920	2728	28261†
	(%)	*2.1*	*8.5*	*11.3*	*14.3*	*13.5*	*12.2*	*9.2*	*8.8*	*10.4*	*9.7*	*100*
	Number of PCs with population data *(%)*	123	497	1047	1636	1663	1580	1171	1022	1299	1199	11237
		1.1	*4.4*	*9.3*	*14.6*	*14.8*	*14.1*	*10.4*	*9.1*	*11.6*	*10.7*	*100*
	Population count	5444	22998	55727	93939	100800	92016	61268	49427	66184	62811	610614
	(%)	*0.9*	*3.8*	*9.1*	*15.4*	*16.5*	*15.1*	*10.0*	*8.1*	*10.8*	*10.3*	*100*
Stockton-on-Tees	Number of modelled PCs*	47	449	1675	2531	2754	3630	2911	2984	2444	1547	21052†
	(%)	*0.2*	*2.1*	*8.0*	*12.1*	*13.1*	*17.3*	*13.9*	*14.2*	*11.7*	*7.4*	*100*
	Number of PCs with population data *(%)*	3	122	535	1138	1099	1510	1385	1434	1141	686	9053
		0.0	*1.3*	*5.9*	*12.6*	*12.1*	*16.7*	*15.3*	*15.8*	*12.6*	*7.6*	*100*
	Population count	16	4935	20677	49580	42185	57502	57386	60837	51202	32586	376906
	(%)	*0.0*	*1.3*	*5.5*	*13.2*	*11.2*	*15.3*	*15.2*	*16.1*	*13.6*	*8.6*	*100*

PC=postcodes
*All postcodes between 1998-2010 were used as model receptors
† PC were modelled 50m beyond the study area (10,050m radius around each incinerator) and therefore total numbers are greater than the sum of the PCs within 10km

Figure 4.6a. Modelled long term mean annual PM_{10} concentrations (µg/m3) between 2003 and 2010, plotted against distance to the MSWI stack (m) at postcode centroid for Edmonton.

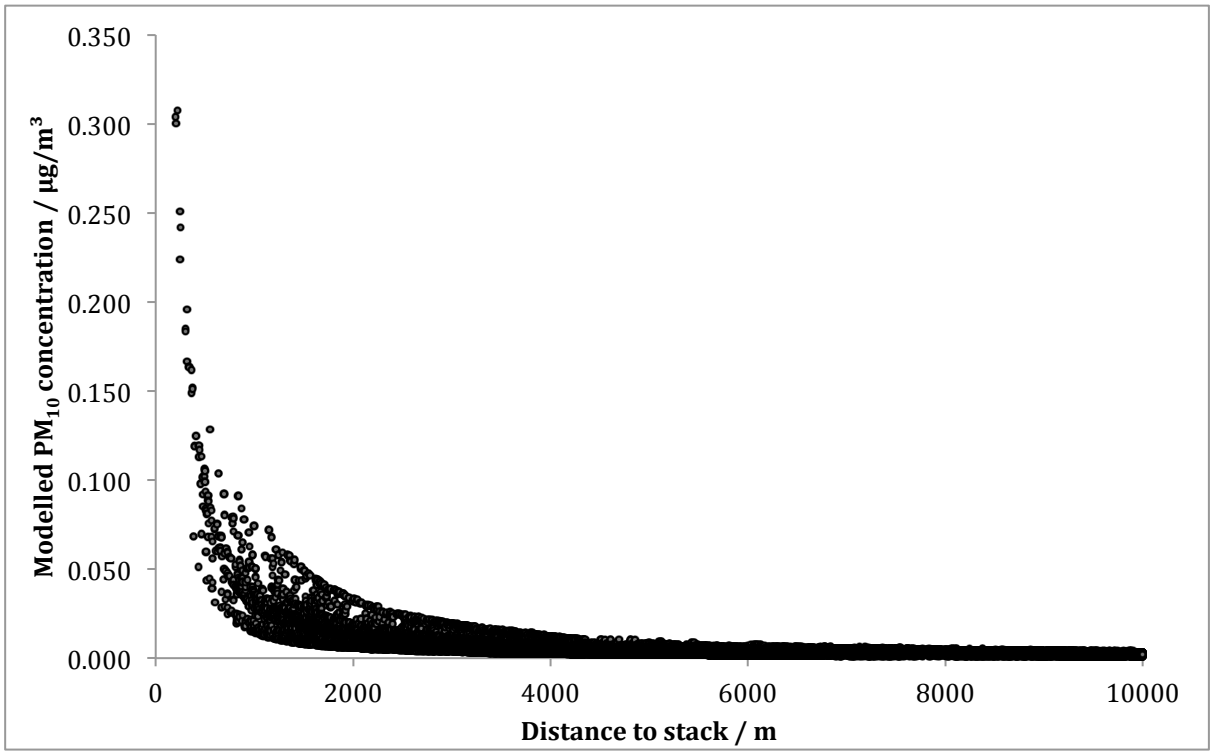


Figure 4.6b. Modelled long term mean annual PM_{10} concentrations (µg/m3) between 2005 and 2010, plotted against distance to the MSWI stack (m) at postcode centroid for Marchwood.

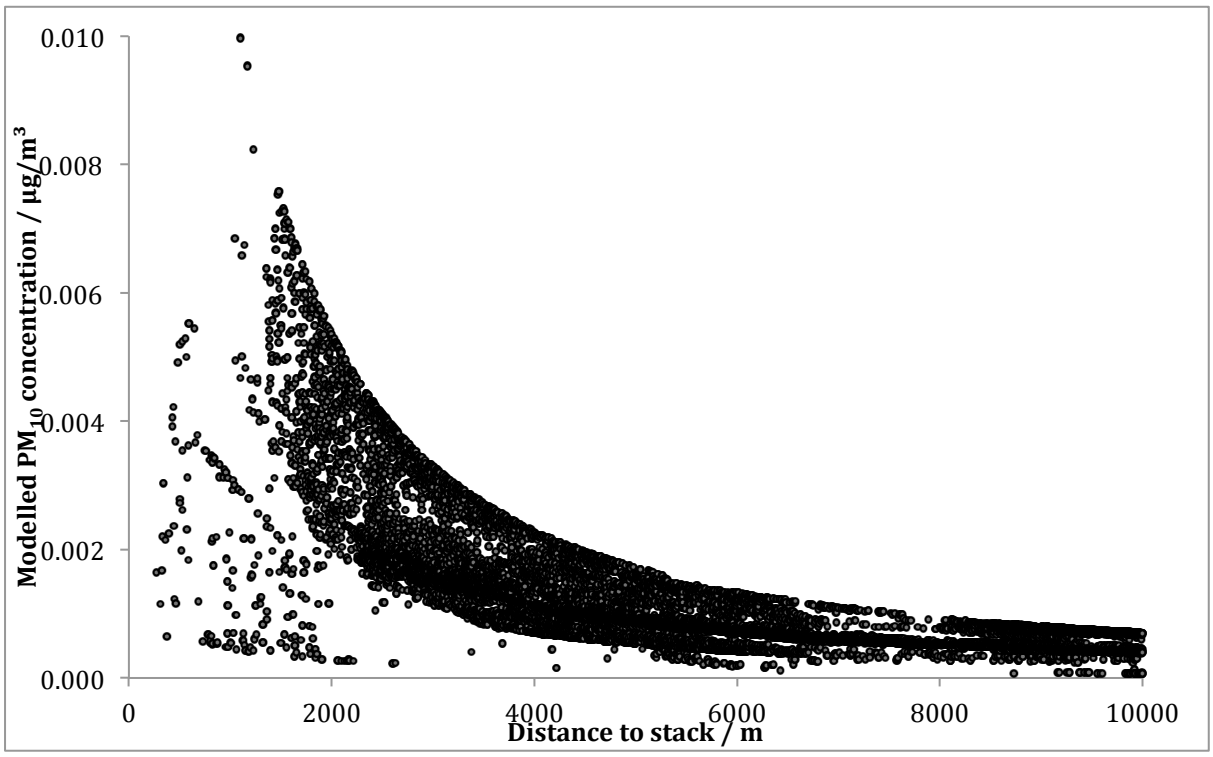


Figure 4.6c. Modelled long term mean annual PM_{10} concentrations (µg/m3) between 2004 and 2010, plotted against distance to the MSWI stack (m) at postcode centroid for Sheffield.

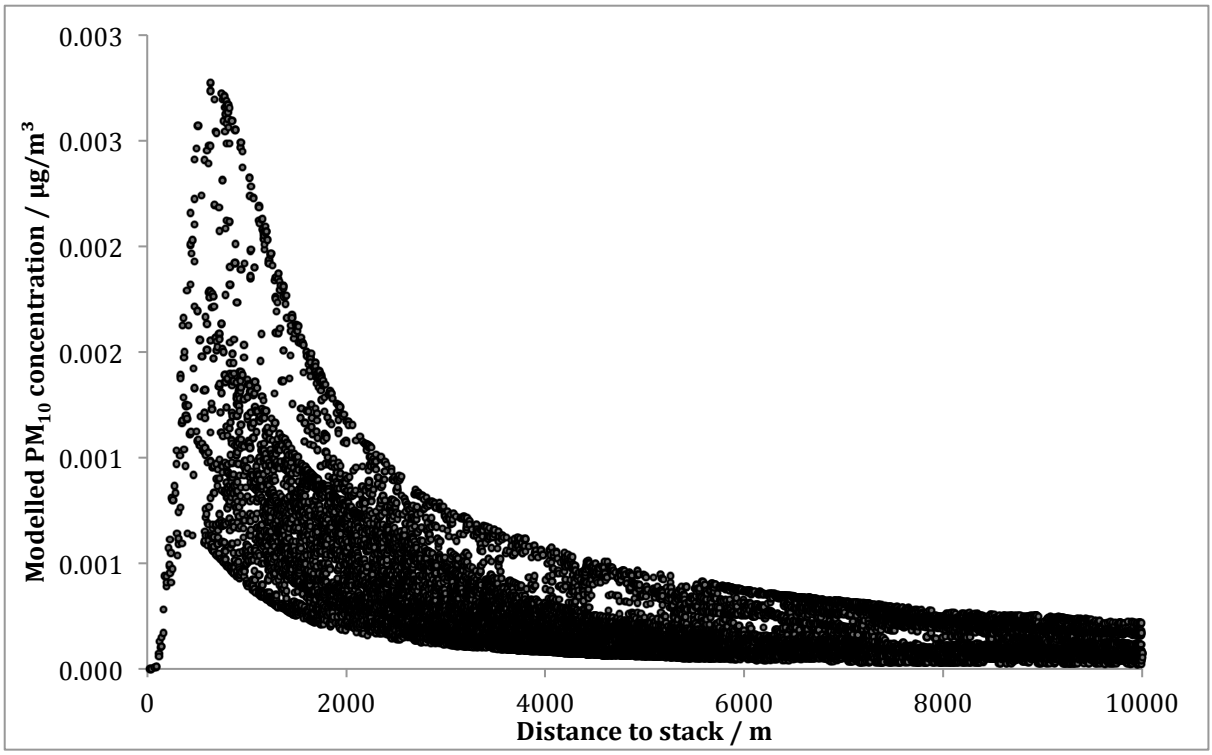


Figure 4.6d. Modelled long term mean annual PM_{10} concentrations (µg/m3) between 2003 and 2010, plotted against distance to the MSWI stack (m) at postcode centroid for Stockton-on-Tees.

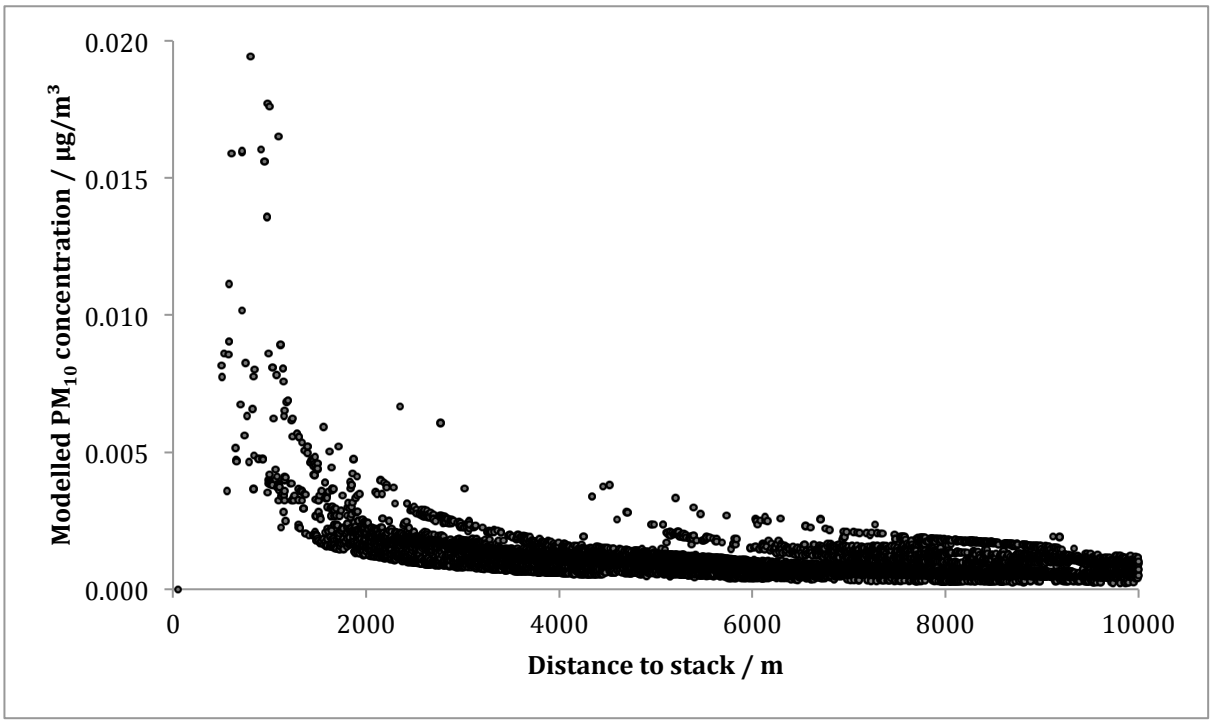


Table 4.7a. Measure of agreement, Kappa coefficient (0 = no agreement; 1 = perfect agreement), between modelled long term PM_{10} concentrations and distance to incinerator stack categorised in deciles, quintiles and tertiles at postcode level.

Incinerator(s)	N	Type of Kappa	Deciles	Quintiles	Tertiles
Edmonton	63231	Unweighted	0.222	0.366	0.472
		Weighted –Equal	0.389	0.560	0.565
Marchwood	19299	Unweighted	0.296	0.416	0.588
		Weighted –Equal	0.514	0.647	0.684
Sheffield	28261	Unweighted	0.138	0.232	0.305
		Weighted –Equal	0.235	0.402	0.407
Stockton-on-Tees	21052	Unweighted	0.190	0.356	0.433
		Weighted –Equal	0.367	0.505	0.493

Table 4.7b. Measure of agreement, Kappa coefficient (0 = no agreement; 1 = perfect agreement), between population weighted modelled long term PM_{10} concentrations and distance to incinerator stack categorised in deciles, quintiles and tertiles at postcode level

Incinerator(s)	N	Type of Kappa	Deciles	Quintiles	Tertiles
Edmonton	26181	Unweighted	0.220	0.373	0.473
		Weighted –Equal	0.383	0.566	0.569
Marchwood	8102	Unweighted	0.320	0.436	0.548
		Weighted –Equal	0.529	0.644	0.649
Sheffield	11237	Unweighted	0.122	0.204	0.274
		Weighted –Equal	0.190	0.343	0.347
Stockton-on-Tees	9053	Unweighted	0.183	0.324	0.398
		Weighted –Equal	0.348	0.466	0.461

Table 4.8. Descriptive analysis of data for women invited to the Incinerators Biomonitoring Study in North and South Tees

	North Tees		South Tees		Total	
	n	%	n	%	n	%
Invited	238		282		520	
Age*						
Mean	26.3		25.0		25.6	
Median	25.9		25.0		25.2	
Min	18.0		17.0		17.0	
Max	41.7		38.0		41.7	
Range	23.6		21.0		24.7	
Ethnicity						
White	207	87.0	240	85.1	447	86.0
Asian	4	1.7	20	7.1	24	4.6
Asian	1	0.4	1	0.4	2	0.4
Asian	2	0.8	6	2.1	8	1.5
Black	2	0.8	2	0.7	4	0.8
Mixed	1	0.4	6	2.1	7	1.3
Other	3	1.3	5	1.8	8	1.5
Not stated	18	7.6	2	0.7	20	3.8

*North Tees: Age defined on the day database search performed; South Tees: Age at booking and then search for 17 year olds at booking who are now 18

Figure 4.7. Recruitment to the Incinerators Biomonitoring Study

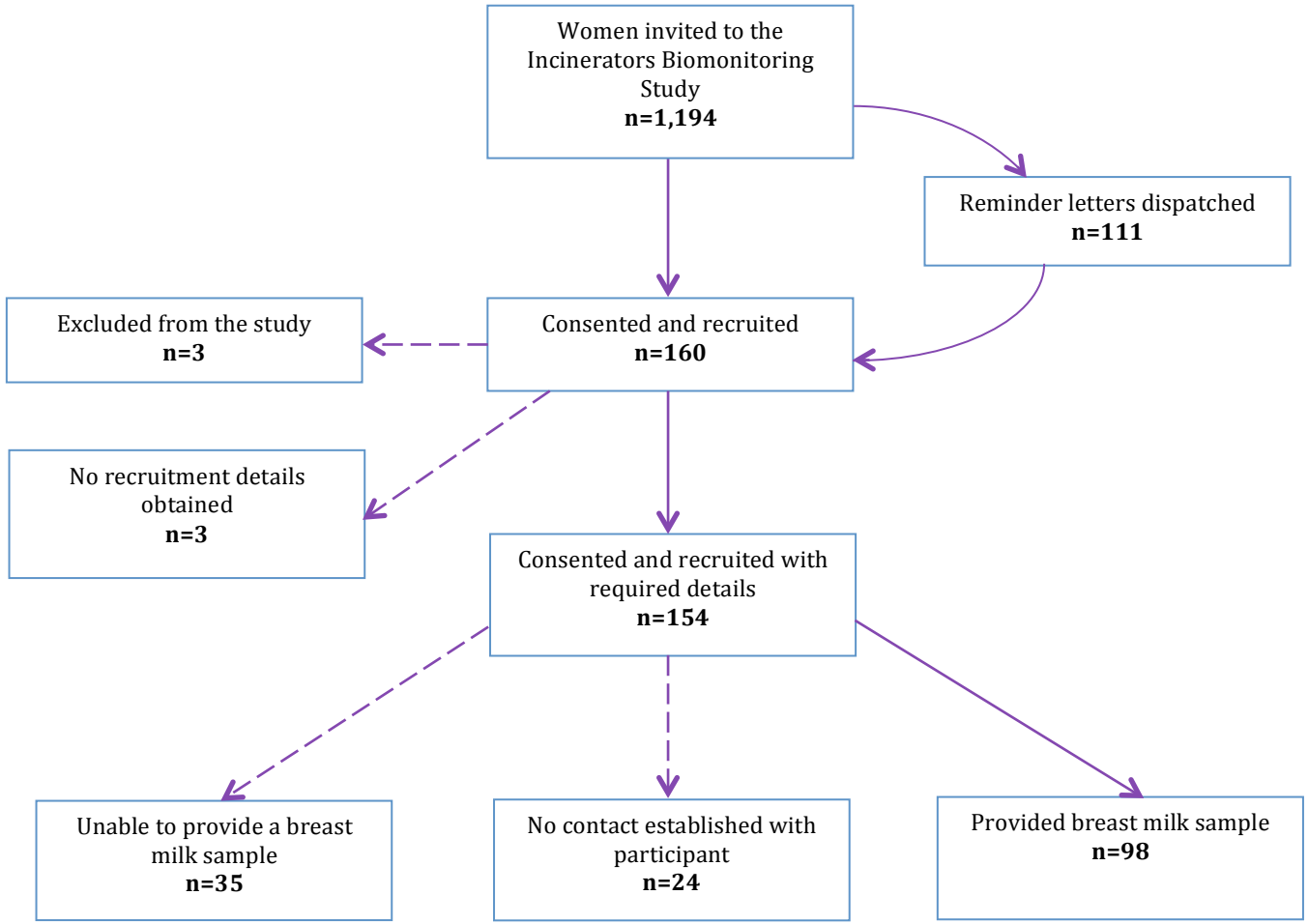


Table 4.9. Recruitment to the Incinerators Biomonitoring Study by Participant Identification Centre (PIC)

	North Tees		South Tees		Southampton		Total	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Invited	238		282		674		1194	
Recruited¥	29	12.2	31	11.0	94	13.9	154	12.9
Provided a breast milk sample	17	58.6	14	45.2	67	71.3	98	63.6
Did not provide a breast milk sample	12	41.4	17	54.8	27	28.7	56	36.4

¥Excludes 3 women with no recruitment data and 3 excluded women

Table 4.10. Overview of consent form details for the 154 participants consenting to take part in the Incinerators Biomonitoring Study

Details from consent form	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
Total recruited¥	**29**		**31**		**94**		**154**	
Age at consent								
Mean	26.9		27.1		31.1		28.4	
Median	26.9		26.4		30.8		N/A	
Min	18.1		19.5		19.5		18.1	
Max	37.5		39.3		42.9		42.9	
Range	19.4		19.8		23.4		N/A	
Missing∫	0	0.0	2	6.5	0	0.0	2	1.3
Previous live births								
None	28	96.6	30	96.8	94	100.0	152	98.7
>1	0	0.0	0	0.0	0	0.0	0	0.0
>1	1	3.4	0	0.0	0	0.0	1	0.6
Missing∫	0	0.0	1	3.2	0	0.0	1	0.6
Gestational age								
Mean	28.3		28.8		30.8		29.3	
Median	29.5		30.0		32.0		N/A	
Min	13.0		19.0		21.0		13.0	
Max	37.0		38.0		38.0		38.0	
Range	24.0		19.0		17.0		N/A	
Missing∫*	1	3.4	1	3.2	2	2.1	4	2.6
Intention to initiate breastfeeding								
Yes	28	96.6	28	90.3	94	100.0	150	97.4
No	1	3.4	1	3.2	0	0.0	2	1.3
Free text	0	0.0	1	3.2	0	0.0	1	0.6
Missing∫	0	0.0	1	3.2	0	0.0	1	0.6

Access to a freezer								
Yes	29	100.0	30	96.8	94	100.0	153	99.4
No	0	0.0	0	0.0	0	0.0	0	0.0
Missing∫	0	0.0	1	3.2	0	0.0	1	0.6
Breast pump								
Yes	27	93.1	30	96.8	92	97.9	149	96.8
No	2	6.9	0	0.0	2	2.1	4	2.6
Missing∫	0	0.0	1	3.2	0	0.0	1	0.6

¥Excludes 3 women with no recruitment data and 3 excluded women

∫Missing data occurring because consent/recruitment forms with missing data or absent (women recruited via email) but did not provide sample

*Baby delivered before consent forms completed

Table 4.11. A comparison of delivery dates and expected delivery dates (EDD) for the 154 participants consenting to take part in the Incinerators Biomonitoring Study

Delivery dates	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
Delivered on EDD	1	3.4	3	9.7	11	11.7	15	9.7
Delivered within 7 days of EDD	18	62.1	15	48.4	48	51.1	81	52.6
Delivered more than 7 days early	6	20.7	6	19.4	10	10.6	22	14.3
Delivered more than 7 days late	4	13.8	7	22.6	23	24.5	34	22.1
Missing either EDD or delivery date*	0	0.0	0	0.0	2	2.1	2	1.3

¥Excludes 3 women with no recruitment data and 3 excluded women

*Women with missing EDD were those unable to identify or a participant who has their study pack returned and unabel to contact

Table 4.12a. Distance of the 154 participants consenting to take part in the Incinerators Biomonitoring Study to the included MSWIs

Distance to MSWI (m)	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
Mean	5736.7		6052.7		4647.9		5479.1	
Median	5845.7		6001.6		4403.2		N/A	
Min	1233.0		2525.4		578.4		578.4	
Max	9260.5		9486.2		10510.3		10510.3	
Range	8027.5		6960.9		9931.9		N/A	
0-1,000	0	0.0	0	0.0	2	2.1	2	1.3
1,000-2,000	2	6.9	0	0.0	12	12.8	14	9.1
2,000-3,000	2	6.9	3	9.7	8	8.5	13	8.4
3,000-4,000	3	10.3	4	12.9	17	18.1	24	15.6
4,000-5,000	3	10.3	4	12.9	19	20.2	26	16.9
5,000-6,000	5	17.2	4	12.9	15	16.0	24	15.6
6,000-7,000	5	17.2	4	12.9	10	10.6	19	12.3
7,000-8,000	4	13.8	3	9.7	0	0.0	7	4.5
8,000-9,000	2	6.9	6	19.4	3	3.2	11	7.1
9,000-10,000	3	10.3	3	9.7	4	4.3	10	6.5
10,000+	0	0.0	0	0.0	4	4.3	4	2.6

Table 4.12b. Direction of the 154 participants consenting to take part in the Incinerators Biomonitoring Study from the included MSWIs

Direction of participant from MSWI	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
N-NE	6	20.7	0	0.0	23	24.5	29	18.8
NE-E	0	0.0	0	0.0	37	39.4	37	24.0
SE-E	0	0.0	5	16.1	7	7.4	12	7.8
S-SE	0	0.0	19	61.3	4	4.3	23	14.9
S-SW	8	27.6	4	12.9	1	1.1	13	8.4
SW-W	11	37.9	1	3.2	4	4.3	16	10.4
NW-W	3	10.3	1	3.2	9	9.6	13	8.4
N-NW	1	3.4	1	3.2	9	9.6	11	7.1

Table 4.13. Overview of consent form details for the 98 participants completing the Incinerators Biomonitoring Study

Details from consent form	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
Total providing a breast milk sample	**17**		**14**		**67**		**98**	
Age at consent								
Mean	27.9		28.3		32.0		29.4	
Median	27.7		27.0		32.0		N/A	
Min	21.0		24.4		22.6		21.0	
Max	37.5		37.7		42.9		42.9	
Range	16.5		13.3		20.3		N/A	
Missing	0	0.0	0	0.0	0	0.0	0	0.0
Previous live births								
None	17	100.0	14	100.0	67	100.0	98	100.0
>1	0	0.0	0	0.0	0	0.0	0	0.0
>1	0	0.0	0	0.0	0	0.0	0	0.0
Missing	0	0.0	0	0.0	0	0.0	0	0.0
Gestational age								
Mean	30.4		29.9		31.0		30.4	
Median	31.0		30.5		32.0		N/A	
Min	20.0		22		21.0		20.0	
Max	37.0		38		37.0		38.0	
Range	17.0		16.0		16.0		N/A	
Missing*	1	5.9	0	0.0	1	1.5	2	2.0
Intention to initiate breastfeeding								
Yes	16	94.1	14	100.0	67	100.0	97	99.0
No	1	5.9	0	0.0	0	0.0	1	1.0
Free text	0	0.0	0	0.0	0	0.0	0	0.0
Missing	0	0.0	0	0.0	0	0.0	0	0.0

Access to a freezer								
Yes	17	100.0	14	100.0	67	100.0	98	100.0
No	0	0.0	0	0.0	0	0.0	0	0.0
Missing	0	0.0	0	0.0	0	0.0	0	0.0
Breast pump								
Yes	15	88.2	14	100.0	66	98.5	95	96.9
No	2	11.8	0	0.0	1	1.5	3	3.1
Missing	0	0.0	0	0.0	0	0.0	0	0.0

*Baby delivered before consent forms completed

Table 4.14. A comparison of delivery dates and expected delivery dates (EDD) for the 98 participants completing the Incinerators Biomonitoring Study

Delivery dates	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
Delivered on EDD	1	5.9	2	14.3	6	9.0	9	9.2
Delivered within 7 days of EDD	10	58.8	8	57.1	37	55.2	55	56.1
Delivered more than 7 days early	4	23.5	3	21.4	5	7.5	12	12.2
Delivered more than 7 days late	2	11.8	1	7.1	19	28.4	22	22.4
Missing either EDD or delivery date	0	0.0	0	0.0	0	0.0	0	0.0

Table 4.15a. Distance of the 98 participants completing the Incinerators Biomonitoring Study to the included MSWIs

Distance to MSWI (m)	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
Mean	5137.3		5739.8		4550.0		5142.3	
Median	5300.6		5363.8		4543.2		N/A	
Min	1233.0		2525.4		578.4		578.4	
Max	9148.1		9486.2		10510.3		10510.3	
Range	7915.2		6960.9		9931.9		N/A	
0-1,000	0	0.0	0	0.0	2	3.0	2	2.0
1,000-2,000	2	11.8	0	0.0	11	16.4	13	13.3
2,000-3,000	1	5.9	1	7.1	6	9.0	8	8.2
3,000-4,000	3	17.6	2	14.3	11	16.4	16	16.3
4,000-5,000	2	11.8	2	14.3	11	16.4	15	15.3
5,000-6,000	3	17.6	3	21.4	12	17.9	18	18.4
6,000-7,000	3	17.6	2	14.3	6	9.0	11	11.2
7,000-8,000	1	5.9	2	14.3	0	0.0	3	3.1
8,000-9,000	1	5.9	1	7.1	1	1.5	3	3.1
9,000-10,000	1	5.9	1	7.1	4	6.0	6	6.1
10,000+	0	0.0	0	0.0	3	4.5	3	3.1

Table 4.15b. Direction of 98 participants completing the Incinerators Biomonitoring Study from the included MSWIs

Direction of participant from MSWI	North Tees		South Tees		Southampton		Total	
	n	%	n	%	n	%	n	%
N-NE	3	17.6	0	0.0	17	25.4	20	20.4
NE-E	0	0.0	0	0.0	27	40.3	27	27.6
SE-E	0	0.0	1	7.1	3	4.5	4	4.1
S-SE	0	0.0	9	64.3	3	4.5	12	12.2
S-SW	4	23.5	2	14.3	1	1.5	7	7.1
SW-W	7	41.2	1	7.1	4	6.0	12	12.2
NW-W	3	17.6	0	0.0	7	10.4	10	10.2
N-NW	0	0.0	1	7.1	5	7.5	6	6.1

Table 4.16. Personal, residential and occupational characteristics of the 97 participants who provided a breast milk sample.

Details from study questionnaire	Stockton			Southampton			Total				
	Mean (Min-Max)	**n**	**%**	**Mean (Min-Max)**	**n**	**%**	**Mean (Min-Max)**	**n**	**%**	**Missing**	**%**
Total providing a breast milk sample		31	32.0		66	68.0		97	100		
Age (years)	29.9 (21-37)			31.7 (22-43)			30.5(21-43)			1	1.0
Height (cm)	166 (152-178)			164 (140-182)			164 (140-182)			15	15.5
Weight (kgs)	69 (48-113)			67 (48-105)			68 (48-113)			7	7.2
BMI at beginning of pregnancy (kg/m²)	25 (18-36)			25 (19-40)			25 (18-40)			18	18.6
Underweight (<18.5)		1	3.2 (4.3)		0	0.0		1	1.0 (1.3)		
Normal (18.5 - <25)		14	45.2 (60.9)		36	54.5 (64.3)		50	51.5 (63.3)		
Overweight (25 - <30)		4	12.9 (17.4)		10	15.2 (17.9)		14	14.4 (17.7)		
Obese (≥30)		4	12.9 (17.4)		10	15.2 (17.9)		14	14.4 (17.7)		
Residence during pregnancy											
Change in residence		6	19.4		7	10.6		13	13.4	0	0.0
Same residence		25	80.6		59	89.4		84	86.6		
Change in residence within postcode area		5	83.3		6	85.7		11	84.6		
Five year residence											
Change in residence		21	67.7		49	74.2		70	72.2	1	1.0
Same residence		10	32.3		16	24.2		26	26.8		
Change in residence within postcode area		18	85.7		40	81.6		58	82.9		
Marital status											
Single		10	32.3		8	12.1		18	18.6		
Married		18	58.1		46	69.7		64	66.0	1	1.0
Other		3	9.7		11	16.7		14	14.4		

Parity								
Primiparous	31	100.0	66	100.0	97	100.0		
Multiparous		0.0		0.0				
Ethnicity								
White (British/Irish/other)	28	90.3	61	92.4	89	91.8		
Black (Caribbean, African, Other)	0	0.0	0	0.0	0	0.0		
Asian (Indian, Pakistani, Bangladeshi, Chinese, Other)	3	9.7	5	7.6	8	8.2	0	0.0
Mixed	0	0.0	0	0.0	0	0.0		
Other	0	0.0	0	0.0	0	0.0		
Highest qualification								
University higher degree	10	32.3	19	28.8	29	29.9		
First degree level	11	35.5	29	43.9	40	41.2		
A level or equivalent	7	22.6	10	15.2	17	17.5	1	1.0
GCSE/O level or equivalent	2	6.5	4	6.1	6	6.2		
Other school	0	0.0	2	3.0	2	2.1		
None of the above	1	3.2	1	1.5	2	2.1		
Work during pregnancy								
No	4	12.9	4	6.1	8	8.2	0	0.0
Yes	27	87.1	62	93.9	89	91.8		
Within industrial production								
No	25	92.6	62	100.0	87	97.8	2	2.2
Yes	0	0.0	0	0.0	0	0.0		
Within the chemical or textile industry								
No	25	92.6	62	100.0	87	97.8	2	2.2
Yes	0	0.0	0	0.0	0	0.0		
Ever worked in industrial production								
No	31	100.0	64	97.0	95	97.9	1	1.0
Yes	0	0.0	1	1.5	1	1.0		
Ever worked in the chemical or textile industry								

No	30	96.8	64	97.0	94	96.9	1	1.0
Yes	1	3.2	1	1.5	2	2.1		
Occupation								
Manager, director & senior officials	1	3.2	4	6.1	5	5.2		
Professional occupations	15	48.4	40	60.6	55	56.7		
Associate professional & technical occupations	1	3.2	3	4.5	4	4.1		
Administrative & secretarial occupations	3	9.7	5	7.6	8	8.2		
Skilled trades occupations	1	3.2	1	1.5	2	2.1	1	1.0
Caring, leisure & other service occupations	5	16.1	6	9.1	11	11.3		
Sales & Customer service occupations	0	0.0	1	1.5	1	1.0		
Process, plant and machine operatives	2	6.5	1	1.5	3	3.1		
Elementary occupations	0	0.0	2	3.0	2	2.1		
Unemployed	3	9.7	2	3.0	5	5.2		
Smoking status								
Current smoker								
No	29	93.5	66	100.0	95	97.9	1	1.0
Yes	1	3.2	0	0.0	1	1.0		
<5 cigarettes	0	0.0	N/A		0	0.0		
5-10 cigarettes	0	0.0	N/A		0	0.0	0	0
10-20 cigarettes	1	100.0	N/A		1	100.0		
>20 cigarettes	0	0.0	N/A		0	0.0		
Before becoming pregnant (within the last 10 years)								
No	25	80.6	51	77.3	76	78.4	2	2.1
Yes	4	12.9	15	22.7	19	19.6		
<5 cigarettes	1	25.0	6	40.0	7	36.8		
5-10 cigarettes	1	25.0	5	33.3	6	31.6	1	5.3
10-20 cigarettes	2	50.0	3	20.0	5	26.3		
>20 cigarettes	0	0.0	0	0.0	0	0.0		

During pregnancy								
No	27	87.1	65	98.5	92	94.8	3	3.1
Yes	1	3.2	1	1.5	2	2.1		
<5 cigarettes	0	0.0	0	0.0	0	0.0		
5-10 cigarettes	0	0.0	0	0.0	0	0.0	0	0
10-20 cigarettes	1	100.0	1	100.0	2	100.0		
>20 cigarettes	0	0.0	0	0.0	0	0.0		

Table 4.17. Dietary characteristics of the 97 participants who provided a breast milk sample.

Details from study questionnaire	Stockton		Southampton		Total			
	n	%	n	%	n	%	Missing	%
Total providing a breast milk sample	**31**	**32.0**	**66**	**68.0**	**97**	**100**		
Dietary restrictions								
No restrictions	25	80.6	57	86.4	82	84.5	1	1.0
Restricted	5	16.1	9	13.6	14	14.4		
Vegetarian	4	80.0	7	77.8	11	78.6		
Vegan	0	0.0	0	0.0	0	0.0		
Other	1	20.0	2	22.2	3	21.4		
Avoidances								
No avoidances	24	77.4	48	72.7	72	74.2	2	2.1
Avoid foods	6	19.4	17	25.8	23	23.7		
Avoid Meat	2	33.3	3	17.6	5	21.7		
Avoid Seafood	2	33.3	9	52.9	11	47.8		
Avoid both	2	33.3	6	35.3	8	34.8		
Milk								
Do not consume milk	0	0.0	1	1.5	1	1.0	0	0.0
Consume milk	31	100.0	65	98.5	96	99.0		
Soya	0	0.0	3	4.6	3	3.1		
Goat	0	0.0	1	1.5	1	1.0		
Cow	31	100.0	60	92.3	91	94.8		
Other	0	0.0	1	1.5	1	1.0		
Whole milk	4	12.9	5	8.3	9	9.9		
Semi-skimmed milk	24	77.4	50	83.3	74	81.3		
Skimmed milk	3	9.7	8	13.3	11	12.1		
Long life (UHT)	0	0.0	1	1.7	1	1.1		
Dried milk	0	0.0	0	0.0	0	0.0		
Other	0	0.0	0	0.0	0	0.0		

Local sources of food								
Meat								
No	23	74.2 (85.2)	55	83.3 (85.9)	78	80.4 (85.7)	6	6.2
Yes	4	12.9 (14.8)	9	13.6 (14.0)	13	13.4 (14.3)		
Poultry				0.0				
No	23	74.2 (85.2)	56	84.8 (87.5)	79	81.4 (86.8)	6	6.2
Yes	4	12.9 (14.8)	8	12.1 (12.5)	12	12.4 (13.2)		
Fish								
No	23	74.2 (85.2)	58	87.9 (93.5)	81	83.5 (91.0)	8	8.2
Yes	4	12.9 (14.8)	4	6.1 (6.5)	8	8.2 (9.0)		
Eggs								
No	21	67.7 (80.8)	52	78.8 (82.5)	73	75.3 (82.0)	8	8.2
Yes	5	16.1 (19.2)	11	16.7 (17.5)	16	16.5 (18.0)		
Dairy								
No	26	83.9 (96.3)	56	84.8 (90.3)	82	84.5 (92.1)	8	8.2
Yes	1	3.2 (3.7)	6	9.1 (6.7)	7	7.2 (7.9)		
Diet during pregnancy								
No changes	10	32.3 (34.5)	32	48.5 (51.6)	42	43.3 (46.2)	6	6.2
Diet has changed	19	61.3 (65.5)	30	45.5 (48.4)	49	50.5 (53.8)		

Table 4.18. Estimated daily intake of dioxins calculated from 24 dietary recalls.

24 hour dietary recall	Stockton	Southampton	Total		
	Mean (Min-Max)	Mean (Min-Max)	Mean (Min-Max)	Missing	%
Dioxin intake from 24 hour recall (pg WHO-TEQ/day)	27.0 (2.9-61.7)	27.7 (1.1-60.3)	27.5 (1.1-61.7)	4	4.1
No restrictions	27.0	29.2	28.5		
Restrictions	26.0	18.9	21.5		
Vegetarian	26.3	16.8	20.2		
Other	24.9	26.6	29.0		
No avoidances	24.9	28.7	26.0		
Avoidances	26.2	25.2	24.4		
Avoid meat	36.4	25.1	29.7		
Avoid seafood	26.0	32.3	31.1		
Avoid both	16.1	15.8	15.9		
Dioxin intake from 24 hour recall (pg WHO-TEQ/ kg body weight/ day)	0.39 (0.05-1.08)	0.43 (0.02-1.10)	0.42 (0.02-1.10)	10	10.3
No restrictions	0.38	0.45	0.43		
Restrictions	0.43	0.31	0.35		
Vegetarian	0.43	0.27	0.33		
Other	N/A	0.44	0.44		
No avoidances	0.38	0.44	0.42		
Avoidances	0.42	0.39	0.39		
Avoid meat	0.63	0.41	0.50		
Avoid seafood	0.39	0.49	0.46		
Avoid both	0.23	0.26	0.25		

Table 4.19. Personal, residential and occupational characteristics of the 97 participants who provided a breast milk sample categorised into those resident "near" the MSWI or "far" from the MSWI.

Details from study questionnaire	Near (<3 Km)			Far (≥3 Km)		
	Mean	n	%	Mean	n	%
Total providing a breast milk sample		22			75	
Age (years)	31.5			30.2		
Weight (kgs)	65			69		
BMI at beginning of pregnancy (kg/m²)						
Underweight (<18.5)		0	0.0		1	1.3
Normal (18.5 - <25)		13	59.1		37	49.3
Overweight (25 - <30)		4	18.2		10	13.3
Obese (≥30)		3	13.6		11	14.6
Residence during pregnancy						
Change in residence		3	13.6		10	13.3
Same residence		19	86.4		65	86.7
Change in residence within postcode area		3	100.0		8	80.0
Five year residence						
Change in residence		18	81.8		52	69.3
Same residence		3	13.6		23	30.7
Change in residence within postcode area		15	83.3		45	86.5
Ever worked in industrial production						
No		21	95.5		74	98.7
Yes		1	4.5		0	0.0
Ever worked in the chemical or textile industry						
No		22	100.0		72	96.0
Yes		0	0.0		2	2.7

Highest qualification				
University higher degree	6	27.3	23	30.7
First degree level	10	45.45	30	40.0
A level or equivalent	6	27.3	11	14.7
GCSE/O level or equivalent	0	0.0	6	8.0
Other school	0	0.0	2	2.7
None of the above	0	0.0	2	2.7
Occupation				
Manager, director & senior officials	0	0.0	5	6.7
Professional occupations	11	50.0	44	58.7
Associate professional & technical occupations	2	9.1	2	2.7
Administrative & secretarial occupations	3	13.6	5	6.7
Skilled trades occupations	0	0.0	2	2.7
Caring, leisure & other service occupations	3	13.6	8	10.7
Sales & Customer service occupations	0	0.0	1	1.3
Process, plant and machine operatives	1	4.5	2	2.7
Elementary occupations	1	4.5	1	1.3
Unemployed	1	4.5	3	4.0
Smoking status				
Current smoker				
No	22	100.0	73	97.3
Yes	0	0.0	1	1.3
<5 cigarettes			0	0.0
5-10 cigarettes			0	0.0
10-20 cigarettes			1	100.0
>20 cigarettes			0	0.0
Before becoming pregnant (within the last 10 years)				
No	17	77.3	59	78.7
Yes	5	22.7	14	18.7

<5 cigarettes	3	60.0	4	28.6
5-10 cigarettes	1	20.0	5	35.7
10-20 cigarettes	1	20.0	4	28.6
>20 cigarettes	0	0.0	0	0.0
During pregnancy				
No	20	90.9	72	96.0
Yes	1	4.5	1	1.3
<5 cigarettes	0	0.0	0	0.0
5-10 cigarettes	0	0.0	0	0.0
10-20 cigarettes	1	100.0	1	1.3
>20 cigarettes	0	0.0	0	0.0

Table 4.20. Dietary characteristics of the 97 participants who provided a breast milk sample, categorised into those resident "near" the MSWI or "far" from the MSWI.

Details from study questionnaire	Near (≤ 3km from MSWI)		Far (> 3km from MSWI)	
	n	%	n	%
Total providing a breast milk sample	**22**	**22.7**	**75**	**77.3**
Dietary restrictions				
No restrictions	18	81.8	64	85.3
Restricted	4	18.2	10	13.3
Vegetarian	3	75.0	8	80.0
Vegan	0	0.0	0	0.0
Other	1	25.0	2	20.0
Avoidances				
No avoidances	16	72.7	56	74.6
Avoid foods	6	27.3	17	22.7
Avoid Meat	0	0.0	5	29.4
Avoid Seafood	3	50.0	8	47.1
Avoid both	3	50.0	5	29.4
Milk				
Do not consume milk	1	4.5	0	0.0
Consume milk	21	95.5	75	100.0
Soya	2	9.5	1	1.3
Goat	0	0.0	1	1.3
Cow	18	85.7	73	97.3
Other	1	4.8	0	0.0
Whole milk	1	5.6	8	11.0
Semi-skimmed milk	14	77.8	60	82.2
Skimmed milk	4	22.2	7	9.6
Long life (UHT)	1	5.6	0	0.0
Dried milk	0	0.0	0	0.0

Other	0	0.0	0	0.0
Local sources of food				
Meat				
No	17	77.3	61	81.3
Yes	4	18.2	9	12.0
Poultry				
No	18	81.8	61	81.3
Yes	3	13.6	9	12.0
Fish				
No	21	95.5	60	80.0
Yes	0	0.0	8	10.7
Eggs				
No	17	77.3	56	74.7
Yes	4	18.2	12	16.0
Dairy				
No	19	86.4	63	84.0
Yes	1	4.5	6	8.0

Table 4.21. Daily intake of dioxins calculated from 24 dietary recalls, categorised into those resident "near" the MSWI or "far" from the MSWI.

24 hour dietary recall	Near	Far
	Mean	**Mean**
Dioxin intake from 24 hour recall (pg WHO-TEQ/day)	28.5	27.2
No restrictions	30.0	28.11
Restrictions	22.4	21.1
Vegetarian	21.6	19.7
Other	24.8	26.6
No avoidances	30.5	27.4
Avoidances	22.6	26.3
Avoid meat	0	29.7
Avoid seafood	24.0	32.8
Avoid both	21.6	12.5
Dioxin intake from 24 hour recall (pg WHO-TEQ/ kg body weight/ day)	0.45	0.41
No restrictions	0.47	0.41
Restrictions	0.35	0.35
Vegetarian	0.35	0.32
Other		0.44
No avoidances	0.48	0.40
Avoidances	0.35	0.41
Avoid meat		0.50
Avoid seafood	0.36	0.50
Avoid both	0.35	0.20

Figure 4.8. Number of births/deliveries in England by dataset from 2001 to 2010.

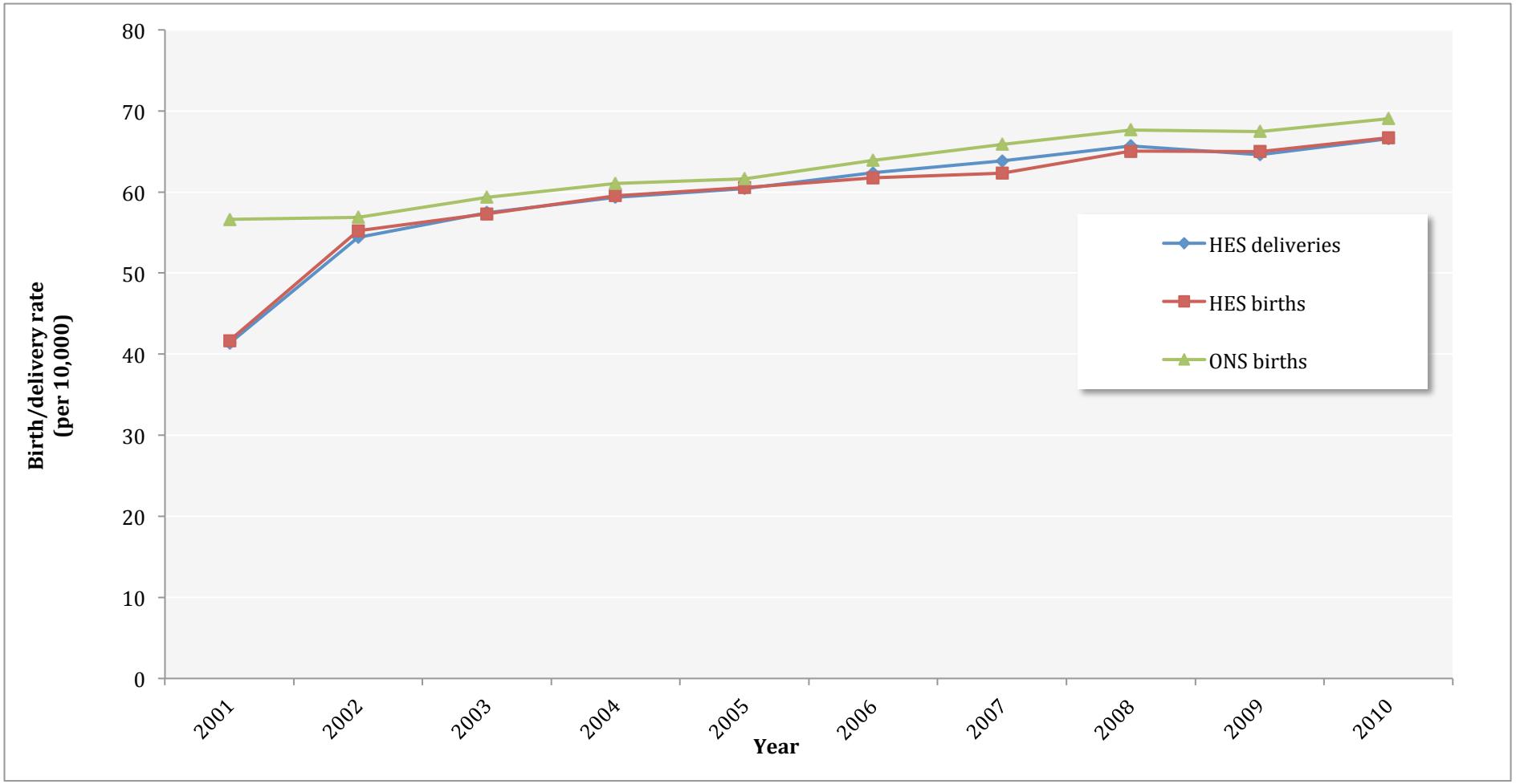
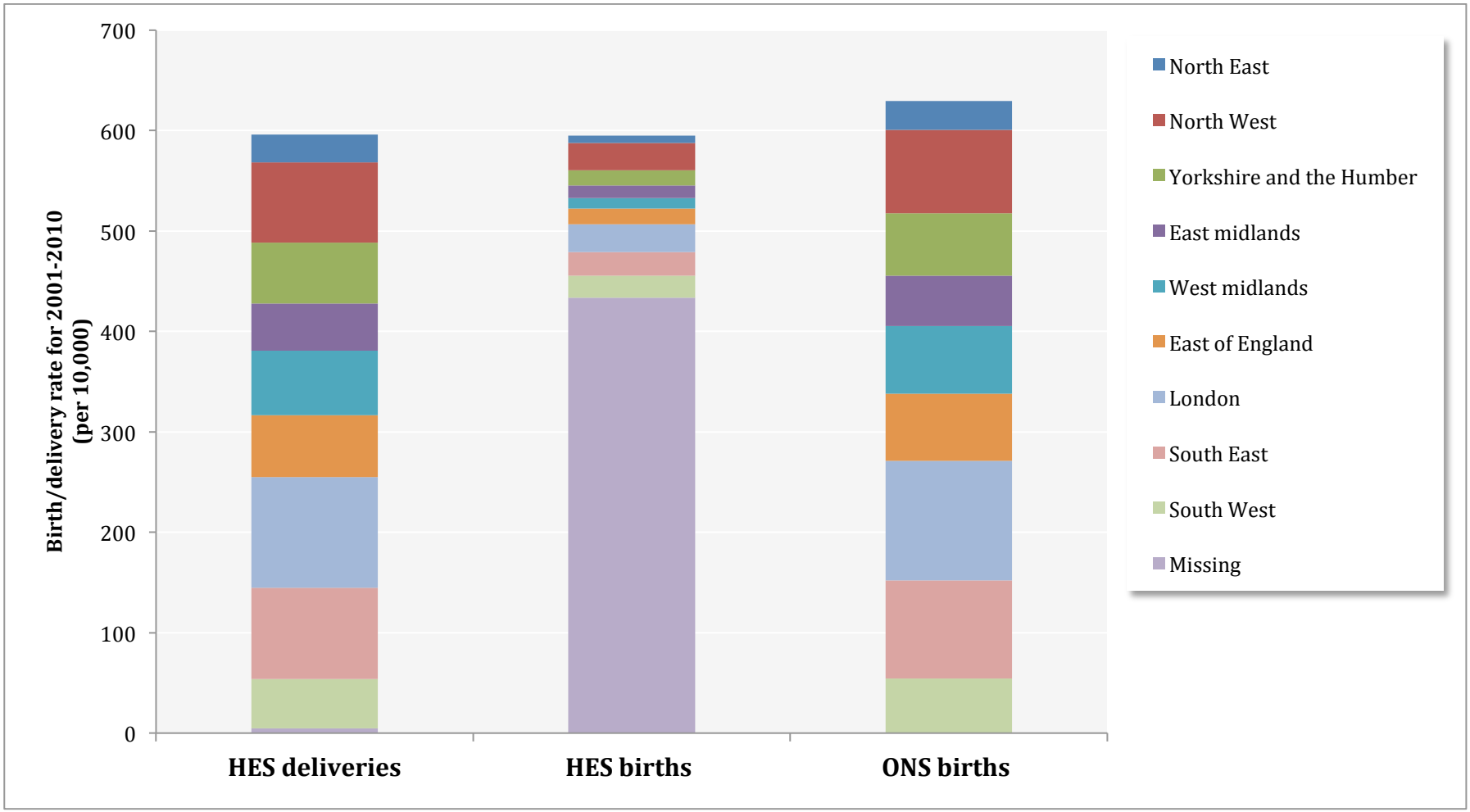


Figure 4.9a. Total births/deliveries in England from 2001 to 2010 by government office region (GOR) by dataset.



Note: ONS births dataset has no missing as the full dataset includes Wales and only births within England (GOR's A-K) were extracted.

Figure 4.9b. Percentage of HES deliveries (A) and ONS births (B) in England from 2001 to 2010 by government office region (GOR)

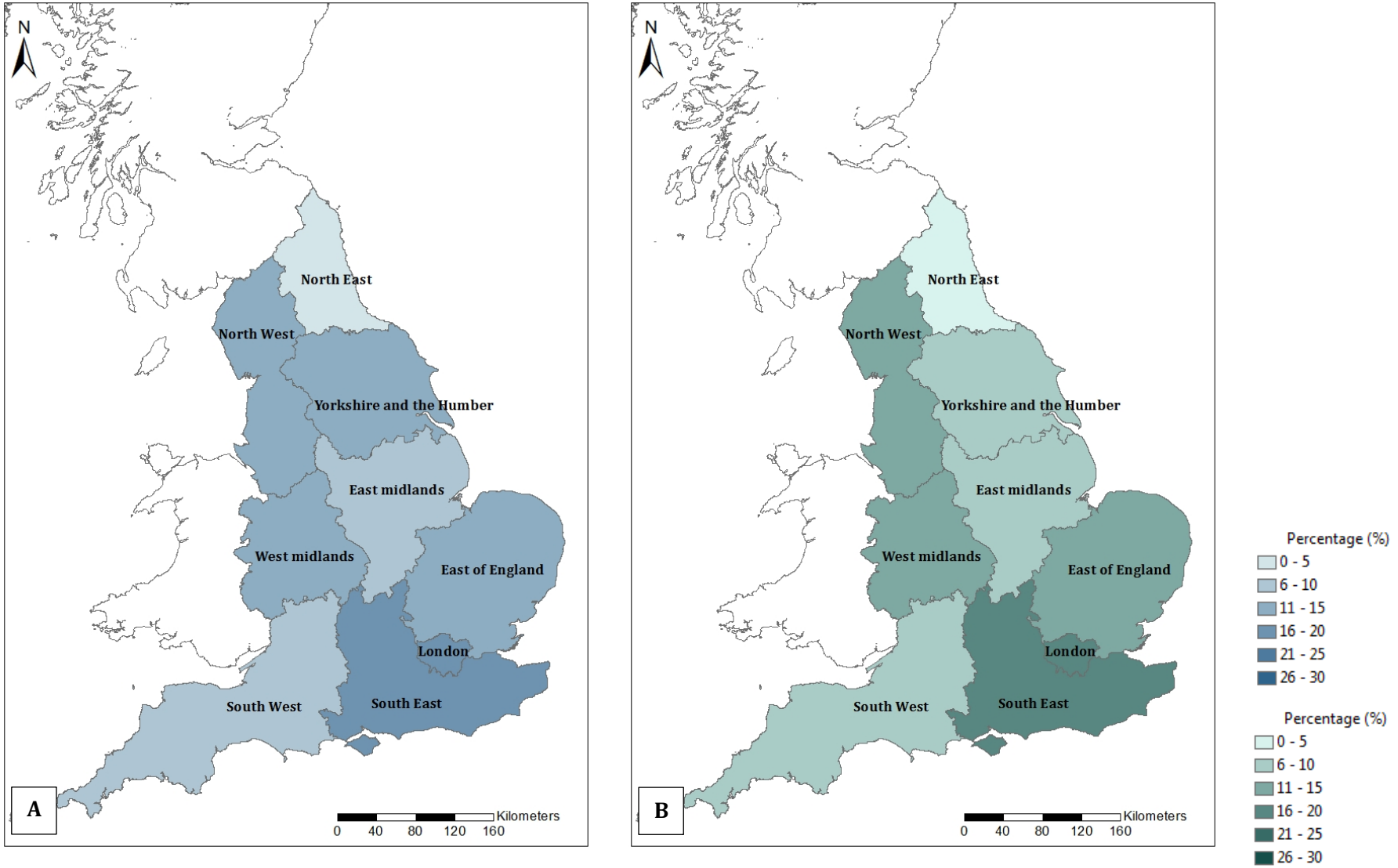


Table 4.22 Information on maternity fields of information collected by HES and ONS datasets

Data fields	HES deliveries	HES births	ONS births
NHS number			
Date of birth of baby			
Residential postcode			
Maternal date of birth			*
Mothers ethnicity			
Babies ethnicity			
Plurality			
Previous pregnancies			
Parity (Previous children)			
Birth status (live/still)			
Birth order			
Birth weight			
Delivery method			
Delivery place			
Gestational age			†
Sex of baby			

* Mothers date of birth is recorded in the ONS births dataset legislation prohibits disclosure of its value and two year maternal age bands provided.
† Gestational age is recorded in the ONS births dataset legislation for stillbirths only.

Table 4.23. Completeness of data fields by dataset (2002-2010)

Data field	Missing											
	HES deliveries				HES births				ONS births			
	n	%	Change in completeness 2002 - 2010 (%)		n	%	Change in completeness 2001 - 2010 (%)		n	%	Change in completeness 2001 - 2010 (%)	
Total births or deliveries	**5545905**				**5534194**				**5727407**			
Region (GOR)	32245	0.6	↓	0	4086574	73.8	↓	22		NA		
Maternal age	14605	0.3	↑	0	2128620	38.5	↑	10	0	0.0	-	-
Residential postcode	36185	0.7	↓	0	4088071	73.9	↓	22	318	0.0	↓	0.0
Mothers ethnicity	943329	17.0	↑	24		NI				NI		
Babies ethnicity		NI			1441154	26.0	↑	42		NI		
Carstairs scoreΩ	49526	1.0	↓	0	3473637	71.4	↓	22	8625	0.2	↑	0.1
Plurality	905313	16.3	↑	10	1563918	28.3	↑	20		N/A*		
Previous pregnancies	2061539	37.2	↑	3	5390377	97.4	↓	4		NI		
Parity (Previous children)†		NI				NI			2480180	43.3	↓	6.1
Birth status (live/still)	1540412	27.8	↑	23	2072393	37.4	↑	24		N/A‡		
Birth Weight¥	1300202	23.4	↑	18	2085549	37.7	↑	24	36224	0.6	↓	0.8
Delivery method	1294750	23.3	↑	14	1742960	31.5	↑	18		NI		
Delivery place	1881901	33.9	↑	28	2213562	40.0	↑	26		NI		
Gestational age	2201195	39.7	↑	29	2227618	40.3	↑	25		N/A		
Sex of baby	1326373	23.9	↑	17	5409048	97.7	↓	23	0	0.0	N/A	

NI: Not included
NA: Not applicable
Ω Not data for 2010, results displayed for years 2002 to 2009
* ONS codes multiple births as 1, all other births are considered singleton. Coverage is therefore 100%
† Applies to live and stillbirths within marriage only
‡ ONS data is sorted as stillbirths and live births tables separately. Coverage is therefore 100%
¥ Valid birth weight range from: HES; 1-7000g and ONS; 1-9997g

Table 4.24. Number of births with "unlikely" or "medically questionable" information by dataset (2002-2010)

Data field	Medically questionable data					
	HES deliveries		HES births		ONS births	
	n	%	n	%	n	%
Total	**5545905**		**5534194**		**5727407**	
Multiple- Total births/deliveries						
Triplets	2356	0.0	2884	0.1		
Quadruplets	730	0.0	335	0.0		
Quintuplets	902	0.0	97	0.0		
Sextuplets	10687	0.2	2998	0.1		
Live singletons	**3898095**		**3113141**		**5524318**	
Maternal Age- Live singletons						
Minimum	2		8		10	
Maximum	115		98		56+	
Under 14 years of age	148	0.0	95	0.0	234	0.0
Under 11 years of age	16	0.0	7	0.0	14*	0.0
Over 44 years of age	6221	0.2	3933	0.1	18462*	0.3
Over 49 years of age	520	0.0	260	0.0	478	0.0
Over 59 years of age	262	0.0	59	0.0	0	0.0
Birth weight- Live singletons						
Minimum	1		10		1	
Maximum	7000		7000		9900	
Under 200 grams	765	0.1	8015	0.3	1043	0.0
Under 500 grams	6171	0.2	18871	0.6	4855	0.1
Over 5000 grams	6573	0.2	5375	0.2	8857	0.2
Over 6000 grams	478	0.0	440	0.0	162	0.0
At or over 7000 grams	310	0.0	312	0.0	52	0.0
Gestational age - Live singletons						
Minimum	10		10			
Maximum	49		49			
Under 23 weeks of pregnancy	11888	0.3	54941	0.2		
Over 42 weeks of pregnancy	19147	0.5	15726	0.5		
Over 44 weeks of pregnancy	3962	0.1	3382	0.1		

*Maternal age within the ONS is required to be reported in 2 year bands. Mothers 11 years of age and mothers 44 years of age therefore included within table above

Table 4.25. Comparison of the number and proportion of all births by key variables of interest for epidemiological studies by dataset (2002-2010)

Data field	HES deliveries			HES births			ONS births		
	n	%	Average	n	%	Average	n	%	Average
Total births or deliveries	5545905			5534194			5727407		
Region (GOR) - Total[£]	5502125			1445504			5727407		
North East	255063	4.6		69247	4.8		260315	4.5	
North West	743847	13.5		240280	16.6		754445	13.2	
Yorkshire and the Humber	562408	10.2		131971	9.1		564384	9.9	
East Midlands	437474	8.0		122778	8.5		457983	8.0	
West Midlands	595646	10.8		91551	6.3		612677	10.7	
East of England	572458	10.4		143341	9.9		606522	10.6	
London	1033349	18.8		245705	17.0		1088634	19.0	
South East	842383	15.3		209160	14.5		885458	15.5	
South West	459497	8.4		191471	13.2		496989	8.7	
Maternal age - Total[£]									
Mean			28.9			28.9			28-30**
Ethnicity - Total[£]	4602576			4093040					
White	3602282	78.3		3159217	77.2		NI		
Mixed	67454	1.5		144991	3.5		NI		
Asian	530416	11.5		427238	10.4		NI		
Black	273350	5.9		244920	6.0		NI		
Other	129074	2.8		116674	2.9		NI		
Carstairs score Ω - Total[£]	4831062			1393402			5028498		
First quintile	883745	18.3		273293	19.6		934170	18.6	
Second quintile	730357	15.1		222353	16.0		767797	15.3	
Third quintile	826675	17.1		239317	17.2		864256	17.2	
Fourth quintile	979373	20.3		279426	20.1		1017755	20.2	
Fifth quintile	1410912	29.2		379013	27.2		1444520	28.7	
Plurality - Total[£]	4640592			3970276			5727407		
Singleton	454585	98.0		3851860	97.0		5552583	96.9	
Multiple	95107	2.0		118416	3.0		174824	3.1	

Previous pregnancies - Total£	3484366			143817					
No previous pregnancies	1430922	41.1		61696	42.9		NI		
1 previous pregnancy	1052018	30.2		41722	29.0		NI		
>1 pregnancies	1001426	28.7		40399	28.1		NI		
Parity (Previous children)† - Total£							3247227		
No previous children	NI			NI			1362486	42.0	
1 previous child	NI			NI			1161957	35.8	
>1 previous children	NI			NI			722784	22.3	
Birth status (live/still) - Total£	3999908			3458345			5727407		
Live	3976707	99.4		3440305	99.5		5696784	99.5	
Still (≥ 24 weeks gestation)	23201	0.6		18040	0.5		30284	0.5	
Birth weight ¥ - Total£									
Mean (grams)			3329.1			3293.7			3318.7
Delivery method - Total£	4251155			43791234					
Vaginal unassisted	2719285	64.0		2377527	62.7		NI		
Vaginal assisted including breech	499424	11.7		436421	11.5		NI		
Caesarean section (elective & emergency)	959361	22.6		881381	23.2		NI		
Other	73085	1.7		95905	2.5		NI		
Delivery place - Total£	3664004			3320632					
Hospital (NHS)	3633489	99.2		3302051	99.4		NI		
Other	30515	0.8		18581	0.6		NI		
Gestational age - Total£									
Mean (weeks)			38.9			38.9			NI
Sex of baby - Total£	4219533			5727407			5727407		
Male	2126953	50.4		63454	50.7		2936278	51.3	
Female	2090631	49.6		61692	49.3		2791129	48.7	
Indeterminate	1948	0.0		0	0.0		0	0.0	

NI: Not included
NA: Not applicable
Ω No data for 2010, results displayed for years 2002 to 2009
† Applies to live and stillbirths within marriage only
¥ Valid birth weight range for HES; 1-7000g and ONS; 1-9997g
** Median
£ Excludes missing values

Table 4.26. Annual average percentage of birth outcomes by dataset (2002-2010)

Birth outcome	Percentage of births (%)		
	HES deliveries	HES births	ONS births
LBW	6.0	6.3	5.9
vLBW	1.0	1.2	0.9
Stillbirth	0.6	0.5	0.5
Term LBW	2.5	2.7	
Preterm delivery	7.5	7.5	
Very preterm delivery	3.2	3.1	

Table 4.27 Descriptive epidemiology for low birth weight babies and stillbirths by dataset (2002-2010)

Variable	Low Birth Weight						Stillbirths					
	HES deliveries		HES births		ONS births		HES deliveries		HES births		ONS births	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Total births or deliveries	**232341**		**191724**		**323306**		**23201**		**18040**		**30284**	
Region (GOR) - Total[£]	**230677**		**26395**		**323306**		**22999**		**5198**		**30284**	
North East	13838	6.0	791	3.0	15391	4.8	650	2.8	28	0.5	1382	4.6
North West	31460	13.9	9258	35.1	44780	13.9	2291	10.0	1252	24.1	4065	13.4
Yorkshire and the Humber	24730	10.7	1813	6.9	34904	10.8	3895	16.9	111	2.1	3247	10.7
East Midlands	20929	9.1	1320	5.0	26716	8.3	1610	7.0	83	1.6	2412	8.0
West Midlands	28671	12.4	2000	7.6	40496	12.5	2005	8.7	151	2.9	3469	11.5
East of England	23557	10.2	2342	8.9	30410	9.4	1386	6.0	165	3.2	2831	9.3
London	44133	19.1	4138	15.7	63668	19.7	2959	12.9	162	3.1	6497	21.5
South East	27512	11.9	4034	15.3	42991	13.3	6843	29.8	3204	61.6	4161	13.7
South West	15096	6.5	593	2.2	23950	7.4	1298	5.6	30	0.6	2220	7.3
Missing∫	1667	0.7	165329	86.2	0	0.0	202	0.9	12842	71.2	0	0.0
Maternal age												
Mean (years)	28.3		28.2		28-30**		28.98		29.06		28-30**	
Missing∫	678	0.3	21361	11.1	0	0.0	85	0.4	1260	7.0	0	0.0
Ethnicity - Total[£]	**199691**		**147535**				**19338**		**9288**			
White	139567	69.9	103127	69.9	NI		13266	68.6	6629	71.4	NI	
Mixed	3420	1.7	5463	3.7	NI		269	1.4	336	3.6	NI	
Asian	36686	18.4	24534	16.6	NI		3687	19.1	1428	15.4	NI	
Black	14646	7.3	10724	7.3	NI		1578	8.2	646	7.0	NI	
Other	5372	2.7	3687	2.5	NI		538	2.8	249	2.7	NI	
Missing∫	326550	14.1	44189	23.0	NI		3863	16.7	8752	48.5	NI	
Carstairs score Ω - Total[£]	**198183**		**26226**		**287027**		**20731**		**5178**		**26702**	
First quintile	24355	12.3	3502	13.4	36854	12.8	3476	16.8	1227	23.7	3727	14.0
Second quintile	23225	11.7	3069	11.7	34187	11.9	2551	12.3	714	13.8	3447	12.9
Third quintile	29937	15.1	3664	14.0	43950	15.3	3362	16.2	872	16.8	4141	15.5
Fourth quintile	41211	20.8	4895	18.7	61534	21.4	3827	18.5	925	17.9	5574	20.9

Fifth quintile	79455	40.1	11096	42.3	110502	38.5	7515	36.3	1440	27.8	9813	36.8
Missing∫	2530	1.3	136855	83.2	612	0.2	272	1.2	11153	61.8	77	0.3
Plurality - Total£							**23191**		**17923**		**30284**	
Singleton	N/A		N/A		N/A		22600	97.5	17015	94.9	27944	92.3
Multiple	N/A		N/A		N/A		591	2.5	908	5.1	2340	7.7
Missing∫	N/A		N/A		N/A		10	0.0	117	0.6	NA	
Previous pregnancies - Total£	**178535**		**4202**				**10992**		**758**			
No previous pregnancies	78278	43.8	2368	56.4	NI		4992	45.4	410	54.1	NI	
1 previous pregnancy	46014	25.8	919	21.9	NI		2663	24.2	193	25.5	NI	
>1 pregnancies	54243	30.4	915	21.8	NI		3337	30.5	155	20.4	NI	
Missing∫	53806	23.2	187522	97.8	NI		12209	52.6	17282	95.8	NI	
Parity (Previous children)† - Total£					**160114**						**16221**	
No previous children	NI		NI		81451	50.9	NI		NI		7113	43.9
1 previous child	NI		NI		43620	27.2	NI		NI		4827	29.8
>1 previous children	NI		NI		35043	21.9	NI		NI		4281	26.4
Missing∫	NI		NI		163192	50.2	NI		NI		14063	46.4
Birth Weigh t¥ - Total£							**22825**		**17763**		**29910**	
Mean (grams)	1992		1940		2004		2277		2218		1849	
>200g & <1500g	38045	16.4	36608	19.1	51241	15.8	6013	26.3	4570	25.7	12964	43.3
>200g & <2500g	N/A		N/A		N/A		9850	43.2	7608	42.8	19783	66.1
Missing∫	N/A		N/A		N/A		376	1.6	277	1.5	374	1.2
Delivery method - Total£	**230822**		**184693**				**23145**		**17853**			
Vaginal unassisted	122333	53.0	99089	53.7	NI		15733	68.0	11650	65.3	NI	
Vaginal assisted	20173	8.7	15900	8.6	NI		3575	15.4	2837	15.9	NI	
Caesarean section (elective & emergency)	84553	36.6	67450	36.4	NI		3559	15.4	3182	17.8	NI	
Other	3763	1.6	2254	1.2	NI		278	1.2	184	1.0	NI	
Missing∫	1519	0.7	7031	3.7	NI		56	0.2	187	1.0	NI	
Delivery place - Total£	**199090**		**160527**				**17794**		**16053**			
Hospital (NHS)	197579	99.2	159743	99.5	NI		17680	99.4	15996	99.6	NI	
Other	1511	0.8	784	0.5	NI		114	0.6	57	0.4	NI	
Missing∫	33251	14.3	31197	16.3	NI		5407	23.3	1987	11.0	NI	
Gestational age - Total£	**187786**		**160362**				**23201**		**18040**		**30284**	

Mean (weeks)	34.88		35.03		NI		34.85		34.41		32.64	
<34 weeks (over 10 weeks)	53077	28.3	43824	27.3	NI		6953	30.0	5661	31.4	15593	51.5
<37 weeks (over 10 weeks)	109481	58.4	91032	56.8	NI		9450	40.7	7858	43.6	20301	67.0
Missing∫	44555	19.2	31362	16.4	NI		0	0.0	0.0	0.0	0	0.0
Sex of baby - Total£	**229213**		**27077**		**323306**		**19812**		**293**		**30284**	
Male	106659	46.5	2325	8.6	153822	47.6	10184	51.8	156	53.2	15934	52.6
Female	122532	53.4	2485	9.2	169484	52.4	9610	48.5	136	46.8	14350	47.4
Indeterminate	22	0.0	22267	82.2	0	0.0	18	0.1	0	0.0	0	0.0
Missing∫	3128	1.3	164647	85.9	0	0.0	3389	14.6	17747	98.4	0	0.0

NI: Not included
NA: Not applicable
Ω No data for 2010, results displayed for years 2002 to 2009
† Applies to live and stillbirths within marriage only
¥ Valid birth weight range for HES; 1-7000g and ONS; 1-9997g
** Median
£ Excludes missing values
∫ Percentages calculated from total births or deliveries

Figure 4.10ai. Low birth weight (LBW) rate per 10,000 live singleton births with birth weight recorded in England by dataset by year from 2002-2010

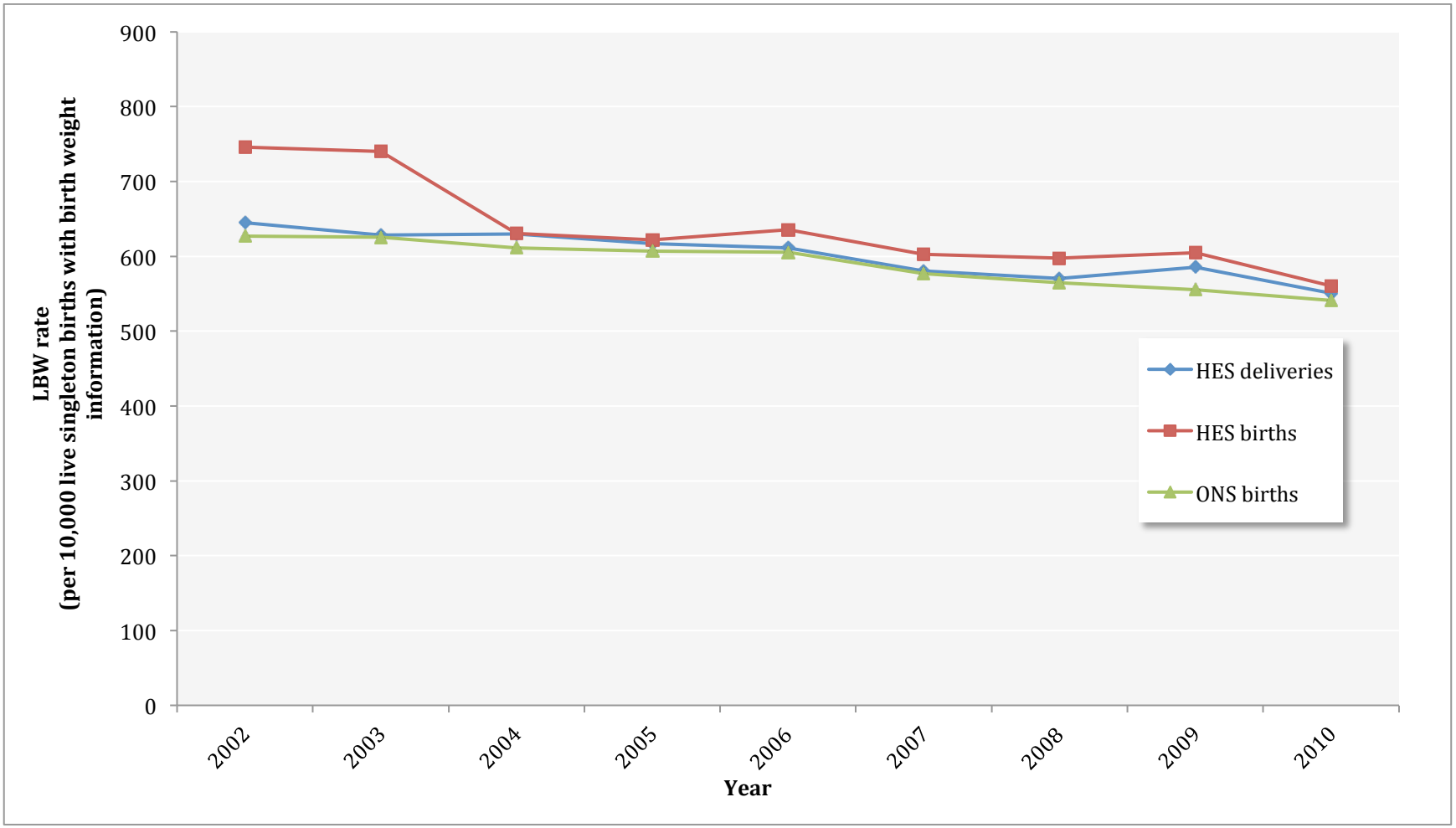


Figure 4.10aii. Proportion of Low birth weight (LBW) live singleton births within the HES deliveries (A) and ONS births (B) dataset by government office region (GOR) 2002-2010

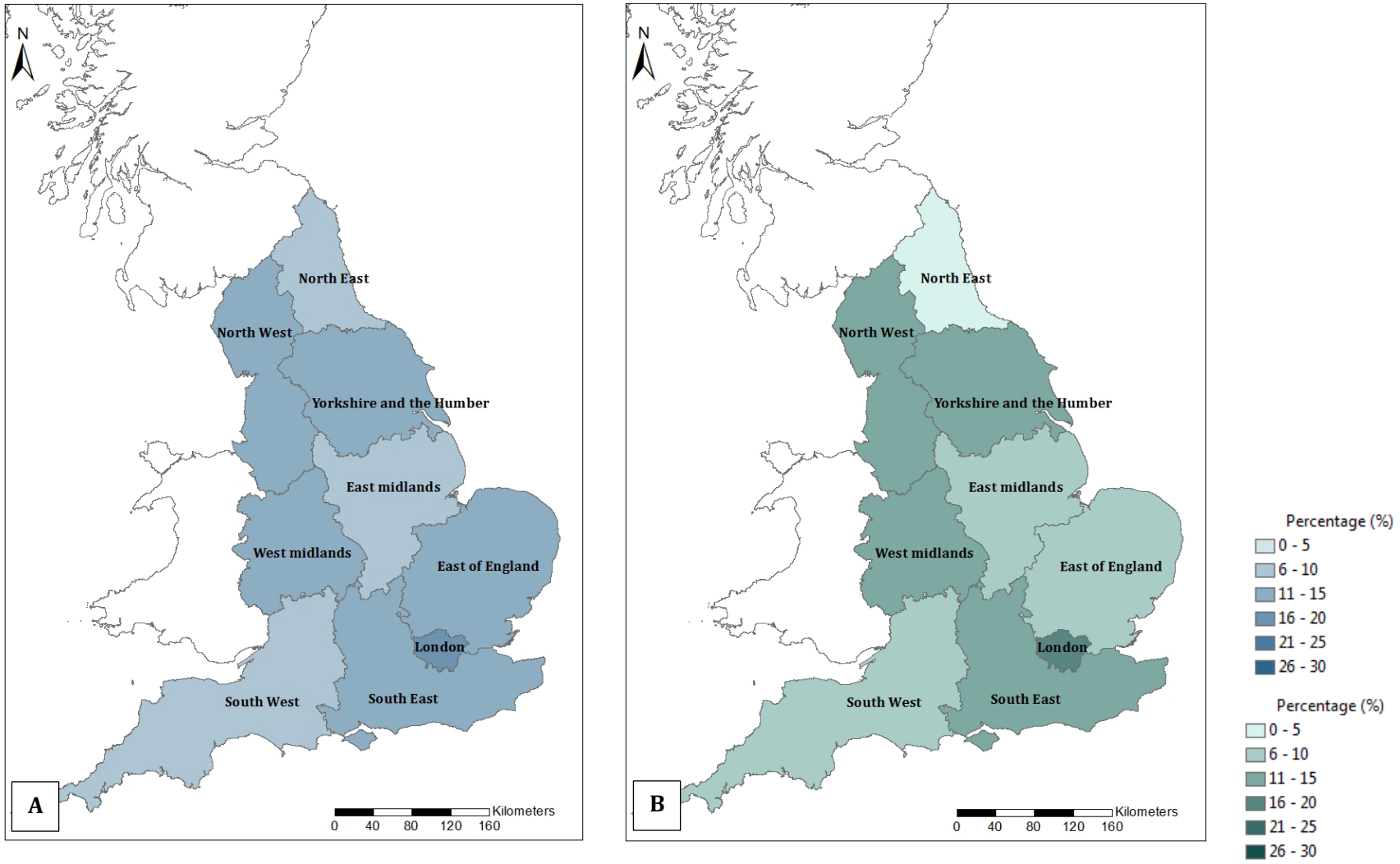


Figure 4.10b. Very low birth weight (vLBW) rate per 10,000 live singleton births with birth weight recorded in England by dataset by year from 2002-2010

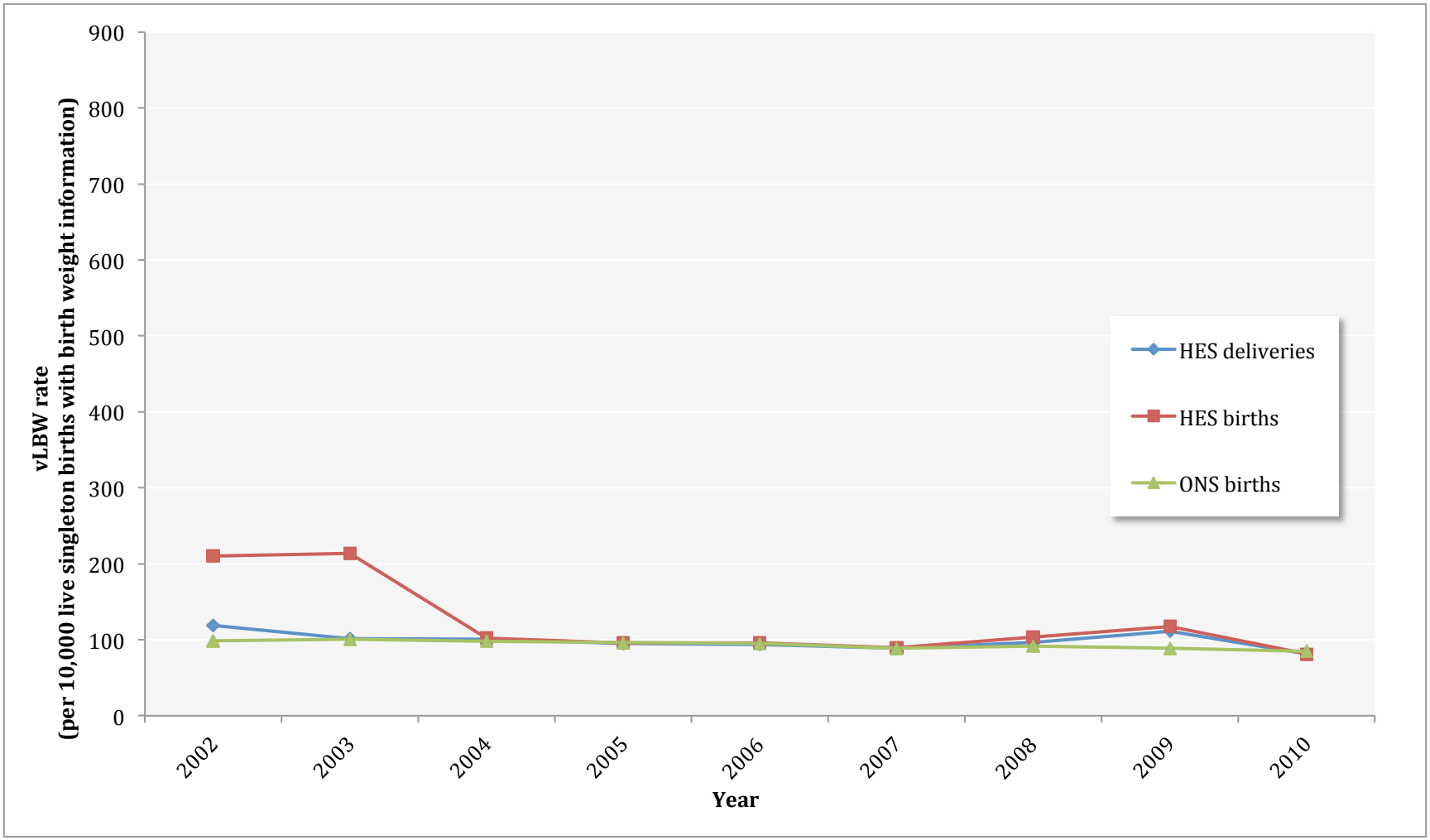


Figure 4.10ci. Stillbirth rate per 10,000 live and stillbirths in England by dataset by year from 2002-2010

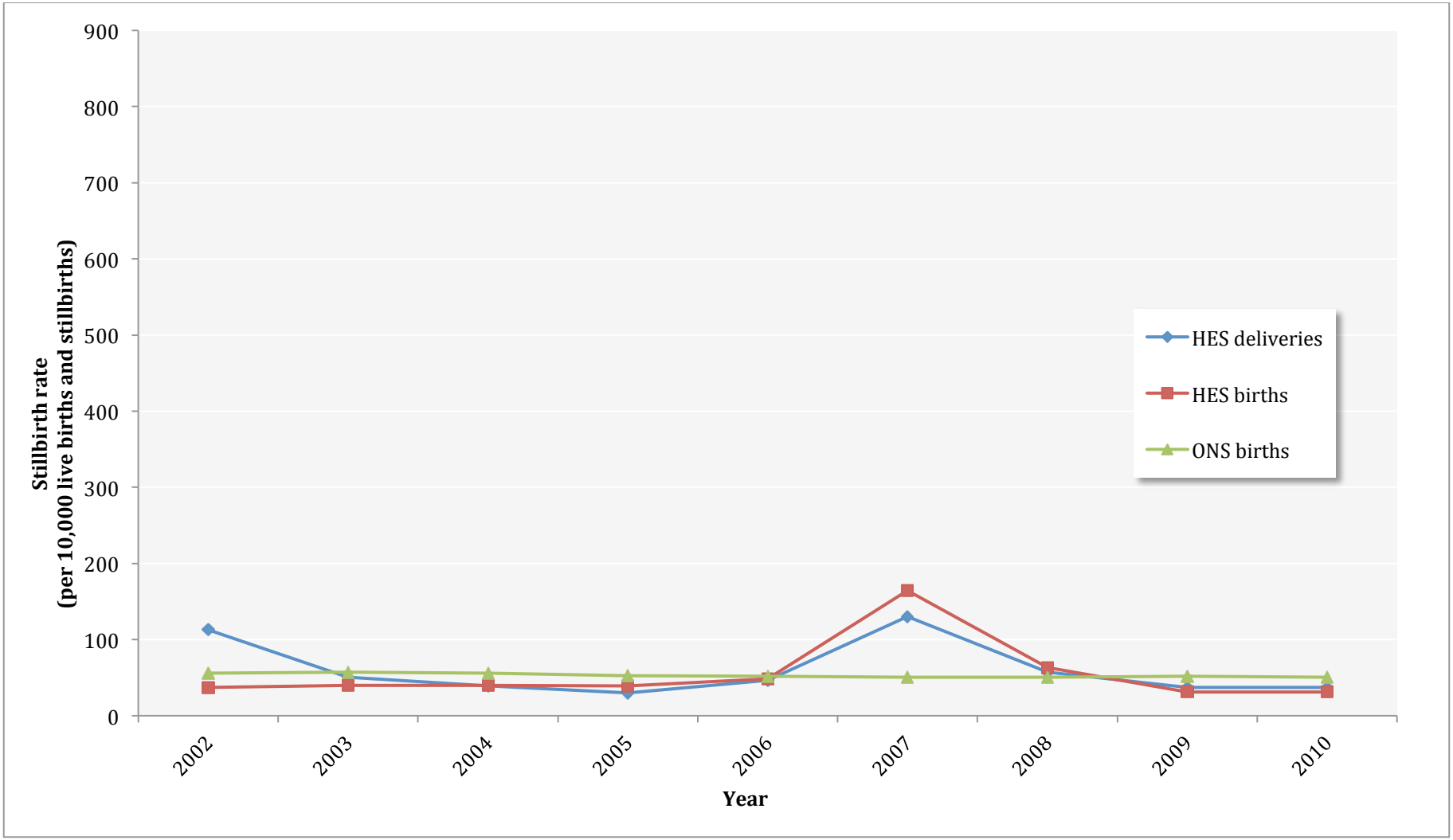


Figure 4.10cii. Proportion of stillbirth singleton births within the HES deliveries (A) and ONS births (B) dataset by government office region (GOR) from 2002-2010

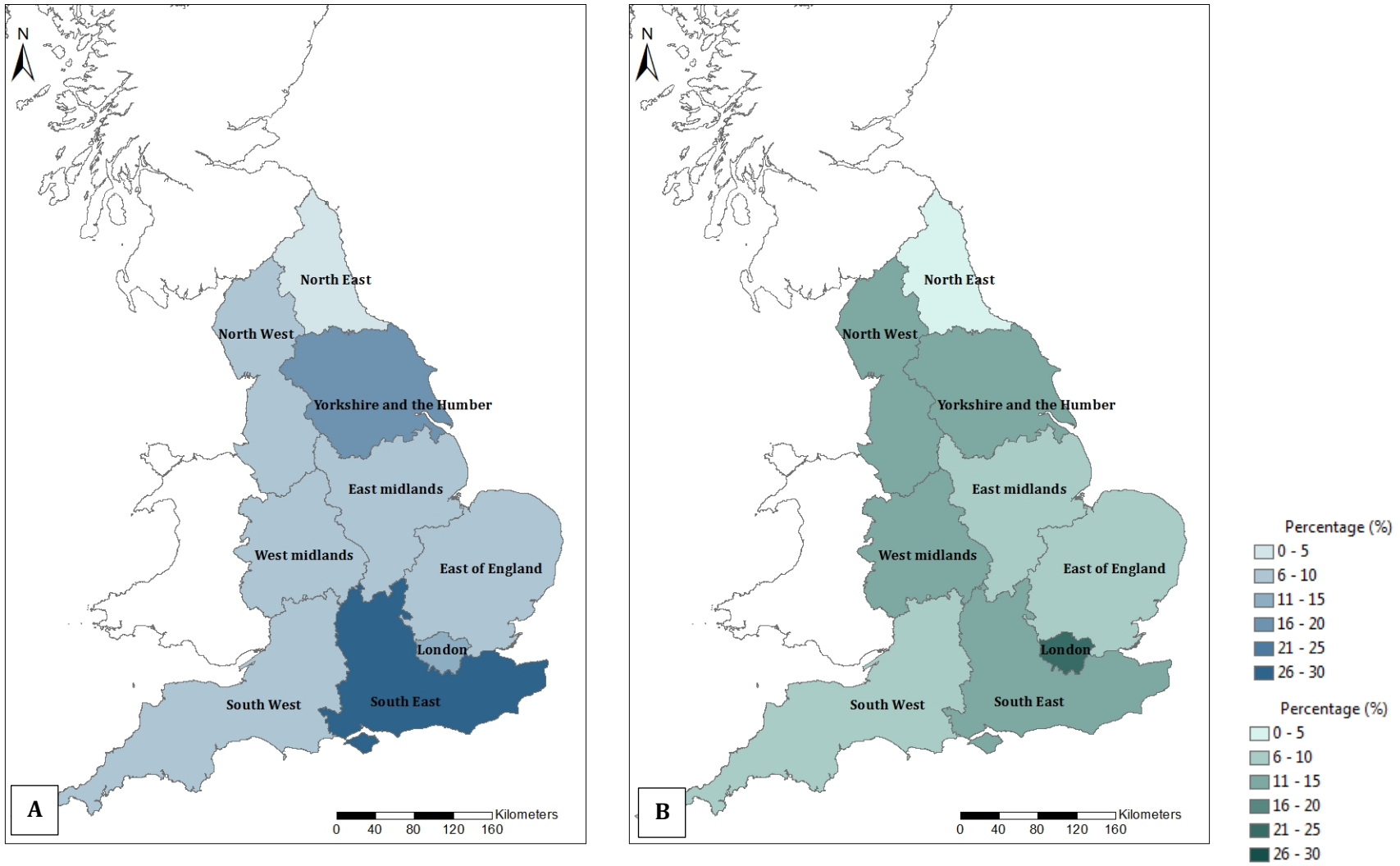


Table 4.28 Descriptive epidemiology for term low birth weight babies and preterm deliveries by dataset (2002-2010)

Variable	Term low birth weight				Preterm delivery			
	HES deliveries		HES births		HES deliveries		HES births	
	n	%	*n*	%	*n*	%	*n*	%
Total births or deliveries	**78305**		**69330**		**234737**		**196141**	
Region (GOR) - Total£	**77757**		**8650**		**232832**		**28010**	
North East	3690	4.7	224	2.6	10444	4.5	499	1.8
North West	10235	13.2	3240	37.5	27594	11.9	8567	30.6
Yorkshire and the Humber	9534	12.3	741	8.6	18193	7.8	1693	6.0
East Midlands	5716	7.4	388	4.5	14613	6.3	1161	4.1
West Midlands	11636	15.0	759	8.8	26829	11.5	1838	6.6
East of England	6858	8.8	703	8.1	50085	21.5	6848	24.4
London	16722	21.5	1098	12.7	43288	18.6	2553	9.1
South East	7722	9.9	1332	15.4	24850	10.7	4208	15.0
South West	5436	7.0	148	1.7	16112	6.9	549	2.0
Missing∫	548	0.7	60680	87.5	1905	0.8	168131	85.7
Maternal age								
Mean (years)	27.96		27.94		28.70		28.61	
Missing∫	189	0.2	9316	13.4	458	0.2	23175	11.8
Ethnicity - Total₤	**67683**		**51405**		**206629**		**161941**	
White	43532	64.3	35076	68.2	149798	72.5	117579	72.6
Mixed	1087	1.6	1845	3.6	3502	1.7	6455	4.0
Asian	16527	24.4	10262	20.0	31798	15.4	22802	14.1
Black	4542	6.7	2953	5.7	16297	7.9	11411	7.0
Other	1995	2.9	1269	2.5	5230	2.5	3694	2.3
Missing∫	10622	13.6	17925	25.9	28108	12.0	34200	17.4
Carstairs score Ω - Total£	**65559**		**8614**		**192167**		**27833**	
First quintile	6720	10.3	1054	12.2	28041	14.6	4768	17.1
Second quintile	6980	10.6	955	11.1	24619	12.8	3684	13.2
Third quintile	9413	14.4	1224	14.2	29958	15.6	3936	14.1
Fourth quintile	13588	20.7	1541	17.9	39754	20.7	5121	18.4

Fifth quintile	28858	44.0	3840	44.6	69795	36.3	10324	37.1
Missing∫	775	1.2	50203	85.4	2806	1.4	135480	83.0
Previous pregnancies - Total£	**60272**		**1750**		**183415**		**4498**	
No previous pregnancies	27219	45.2	977	55.8	71366	38.9	2583	57.4
1 previous pregnancy	15721	26.1	393	22.5	50053	27.3	947	21.1
>1 pregnancies	17332	28.8	380	21.7	61996	33.8	968	21.5
Missing∫	18033	23.0	67580	97.5	51322	21.9	191643	97.7
Birth Weigh t¥ - Total£					**233704**		**192637**	
Mean (grams)	2214		2080		2496		2486	
>200g & <1500g	3868	4.9	9552	13.8	26968	11.5	22313	11.6
>200g & <2500g	N/A		N/A		109481	46.8	91032	47.3
Missing∫	N/A		N/A		1033	0.4	3504	1.8
Delivery method - Total£	**78074**		**67286**		**231632**		**191601**	
Vaginal unassisted	47399	60.7	41177	61.2	126834	54.8	105316	55.0
Vaginal assisted	7447	9.5	6515	9.7	20993	9.1	17708	9.2
Caesarean section (elective & emergency)	22464	28.8	18929	28.1	77711	33.5	62653	32.7
Other	764	1.0	655	1.0	6094	2.6	5924	3.1
Missing∫	231	0.3	2044	2.9	3105	1.3	4540	2.3
Delivery place - Total£	**69543**		**55693**		**211320**		**170827**	
Hospital (NHS)	68876	99.0	53390	99.5	209202	99.0	170089	99.6
Other	667	1.0	303	0.5	2118	1.0	738	0.4
Missing∫	8762	11.2	13637	19.7	23417	10.0	25314	12.9
Gestational age - Total£								
Mean (weeks)	38.36		38.43		32.09		32.34	
<34 weeks (over 10 weeks)	N/A		N/A		99335	42.3	81398	41.5
Sex of baby - Total£	**77615**		**2174**		**232375**		**3734**	
Male	31280	40.3	955	43.9	123109	53.0	2059	55.1
Female	46332	59.7	1219	56.1	109243	47.0	1675	44.9
Indeterminate	3	0.0	0	0.0	23	0.0	0	0.0
Missing∫	690	0.9	67156	96.9	2362	1.0	192407	98.1

NI: Not included
NA: Not applicable
Ω No data for 2010, results displayed for years 2002 to 2009
† Applies to live and stillbirths within marriage only

¥ Valid birth weight range for HES; 1-7000g and ONS; 1-9997g
** Median
₹ Excludes missing values
∫ Percentages calculated from total births or deliveries

Figure 4.11ai. Term low birth weight (Term LBW) rate per 10,000 live, singleton births with birth weight and gestation weeks at birth recorded in England by dataset by year from 2002-2010

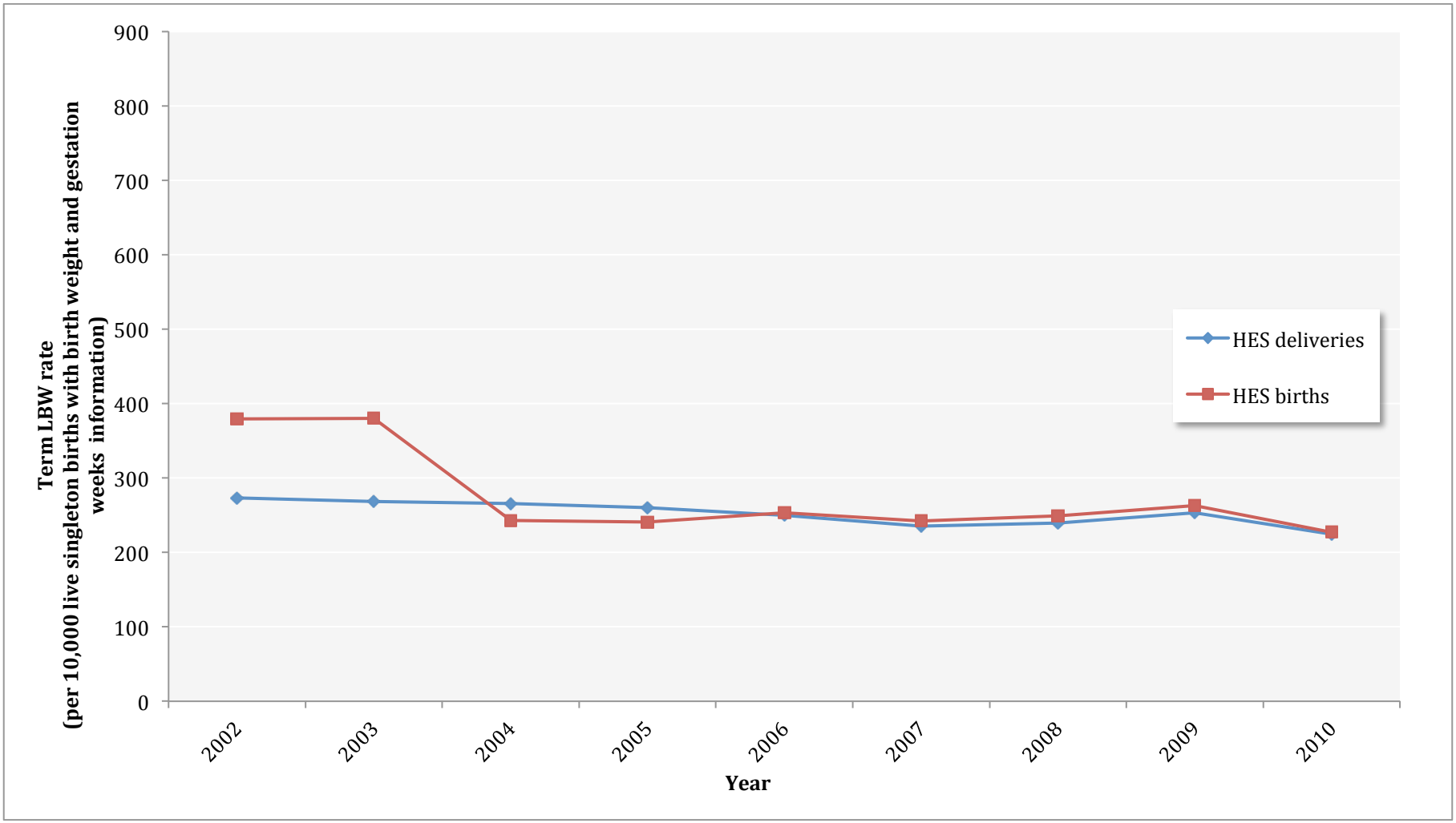


Figure 4.11aii. Proportion of term Low birth weight (LBW) live singleton HES deliveries by government office region (GOR) from 2002-2010

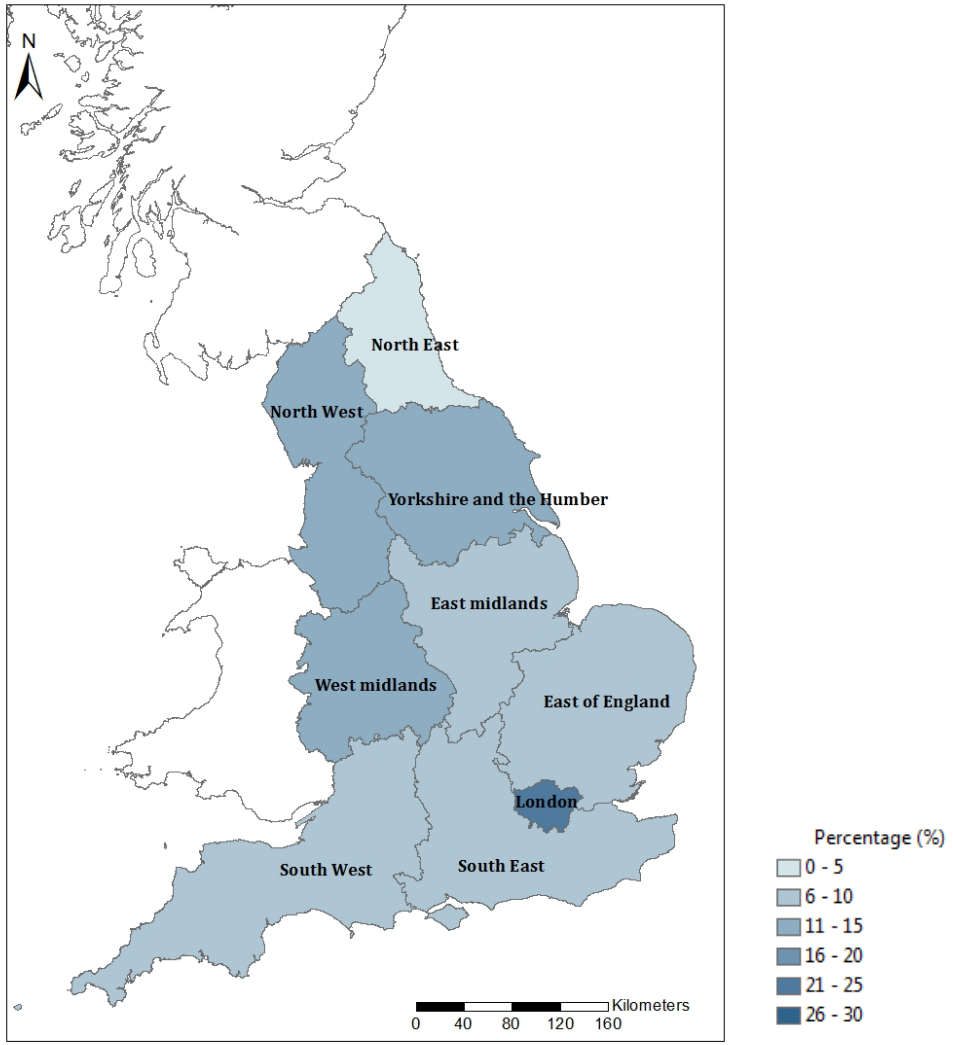


Figure 4.11bi. Preterm rate per 10,000 live, singleton births with gestation weeks at birth recorded in England by dataset by year from 2002-2010

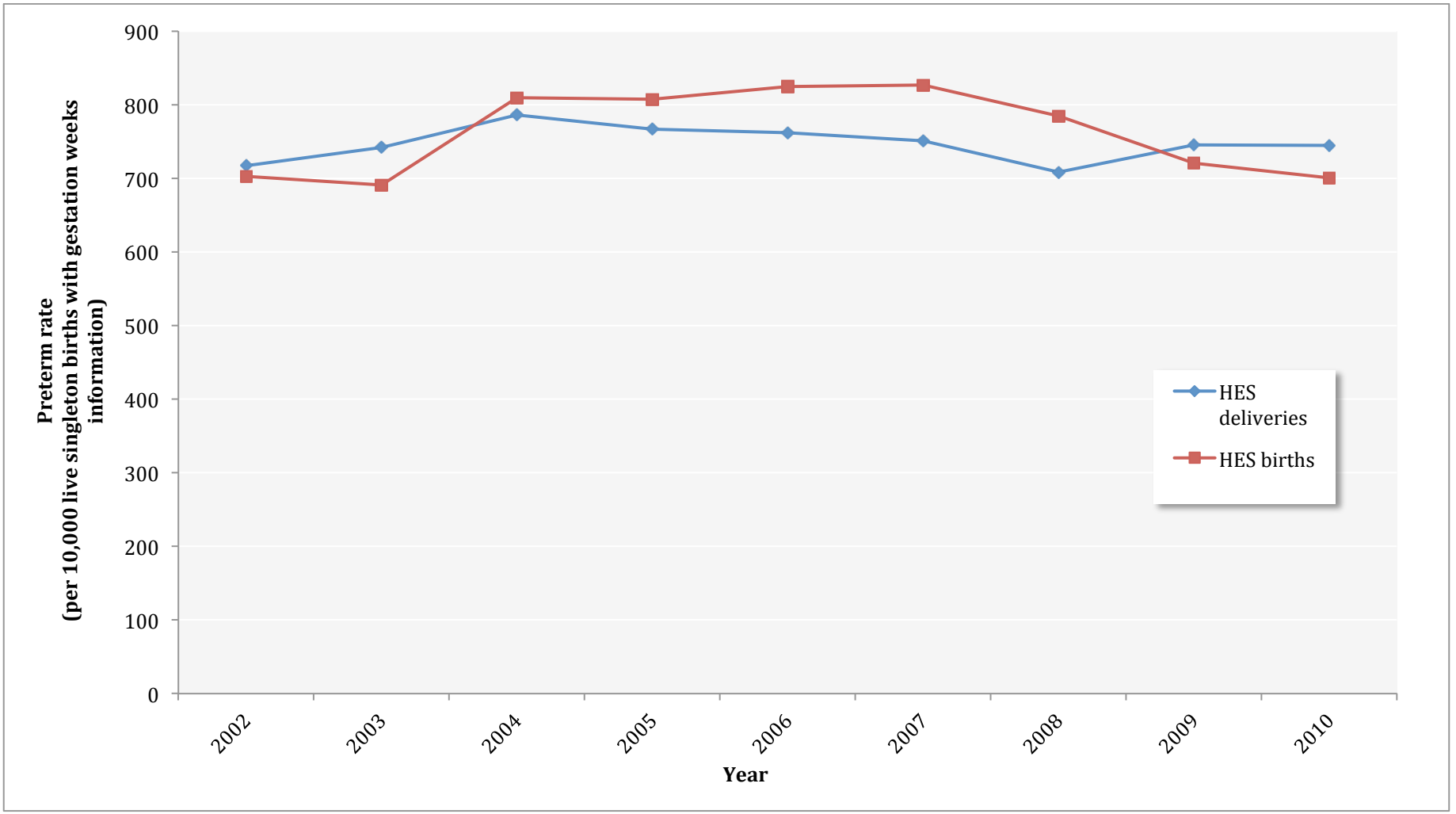


Figure 4.11bii. Proportion of preterm live singleton births by government office region (GOR) within HES deliveries from 2002-2010

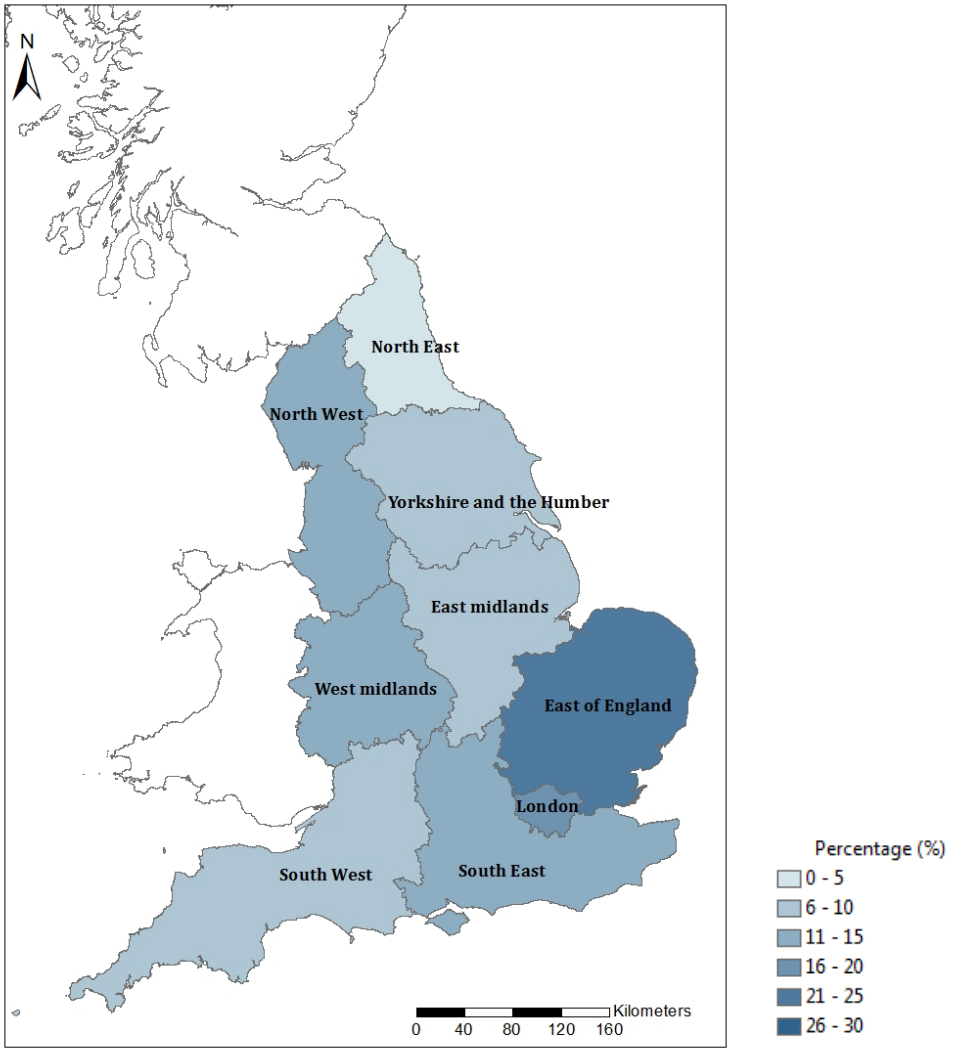


Figure 4.11c. Very preterm rate per 10,000 live, singleton births with gestation weeks at birth recorded in England by dataset by year from 2002-2010

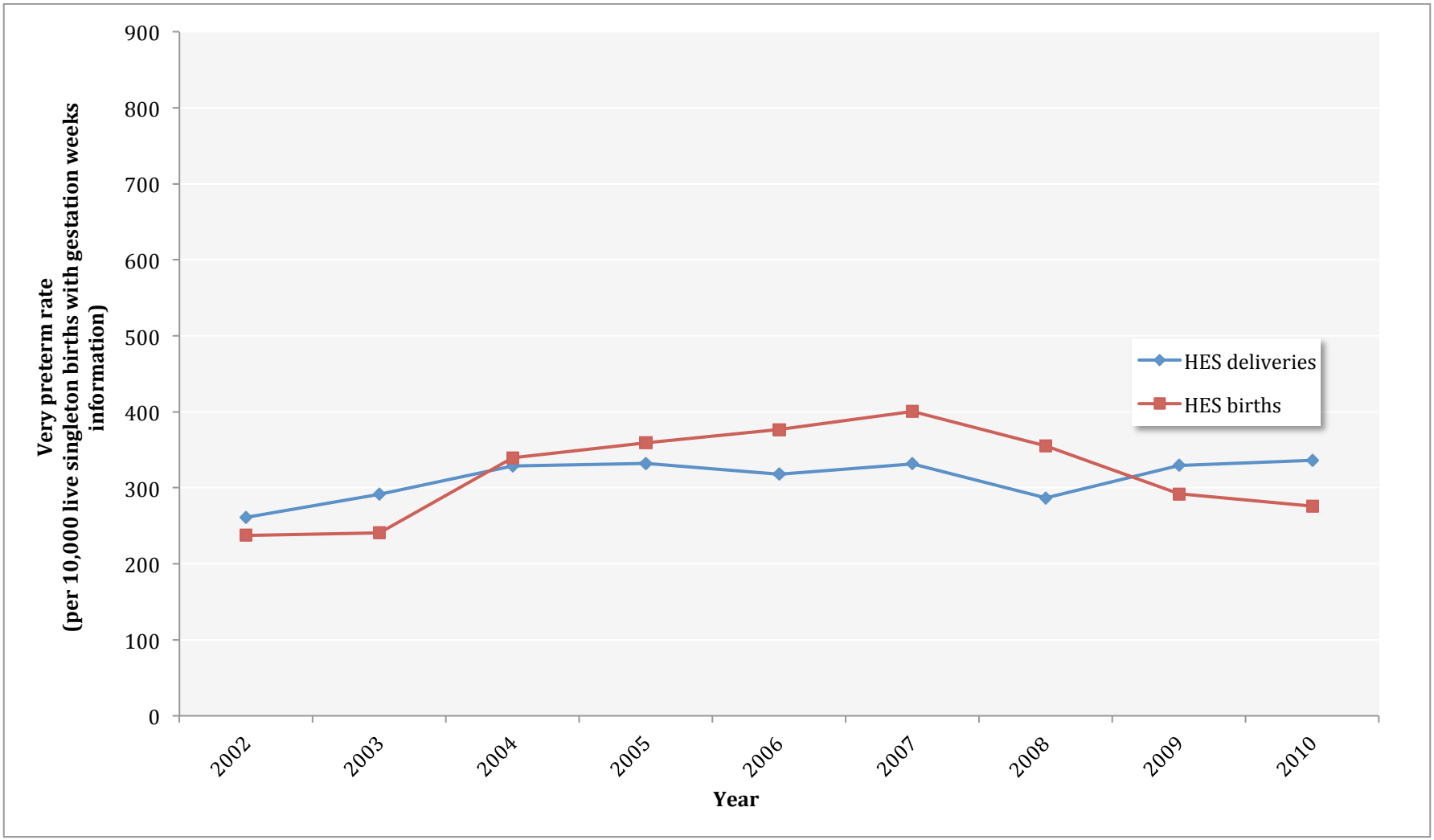


Table 4.29 Super Output Area (SOA) level comparison of the number of live births, stillbirths and average birth weight information by GOR

	Live births		Stillbirths		Continuous birth weight	
	HES deliveries	**ONS births**	**HES deliveries**	**ONS births**	**HES deliveries**	**ONS births**
National (SOA's=32,442)						
Mean	112.05	157.74	0.76	0.84	3369.97	3376.07
Standard deviation	68.72	74.13	2.34	1.09	122.79	94.9
Median	99	144	0	1	3379.47	3383.09
IQR	64-145	107-193	0-1	0-1	3307.56-3445.28	3316.47-3443.45
5-95th percentiles	29-238	70-291	0-3	0-3	3185.35-3533.02	3209.03-3518.70
Min-Max	0-1484	3-1900	0-63	0-11	606-4600	2955.77-3728.5
North East (SOA's = 1656)						
Mean	124.73	140.4	0.53	0.75	3386.66	3387.06
Standard deviation	54.47	61.67	0.83	0.98	87.56	86.72
Median	116	130	0	0	3388.08	3389.9
IQR	88-152	99-170	0-1	0-1	3327.02-3447.30	3329.04-3447.83
5-95th percentiles	56-221	63-254	0-2	0-3	3240.49-3530.71	3240.27-3534.29
Min-Max	21-756	21-905	0-5	0-7	3043.39-3665	3044.8-3683.36
South East (SOA's=5320)						
Mean	94.81	148.92	1.43	0.71	3406.81	3406.86
Standard deviation	57.76	68.38	5.25	0.95	89.5	77.36
Median	84	138	0	0	3408.78	3410.22
IQR	54-121	104-179	0-1	0-1	3349.95-3466.35	3357.84-3459.63
5-95th percentiles	28-199	68-269	0-5	0-3	3254.34-3547.43	3273.33-3526.70
Min-Max	6-681	27-1001	0-63	0-7	2988.68-3851.88	3051.33-3636.61

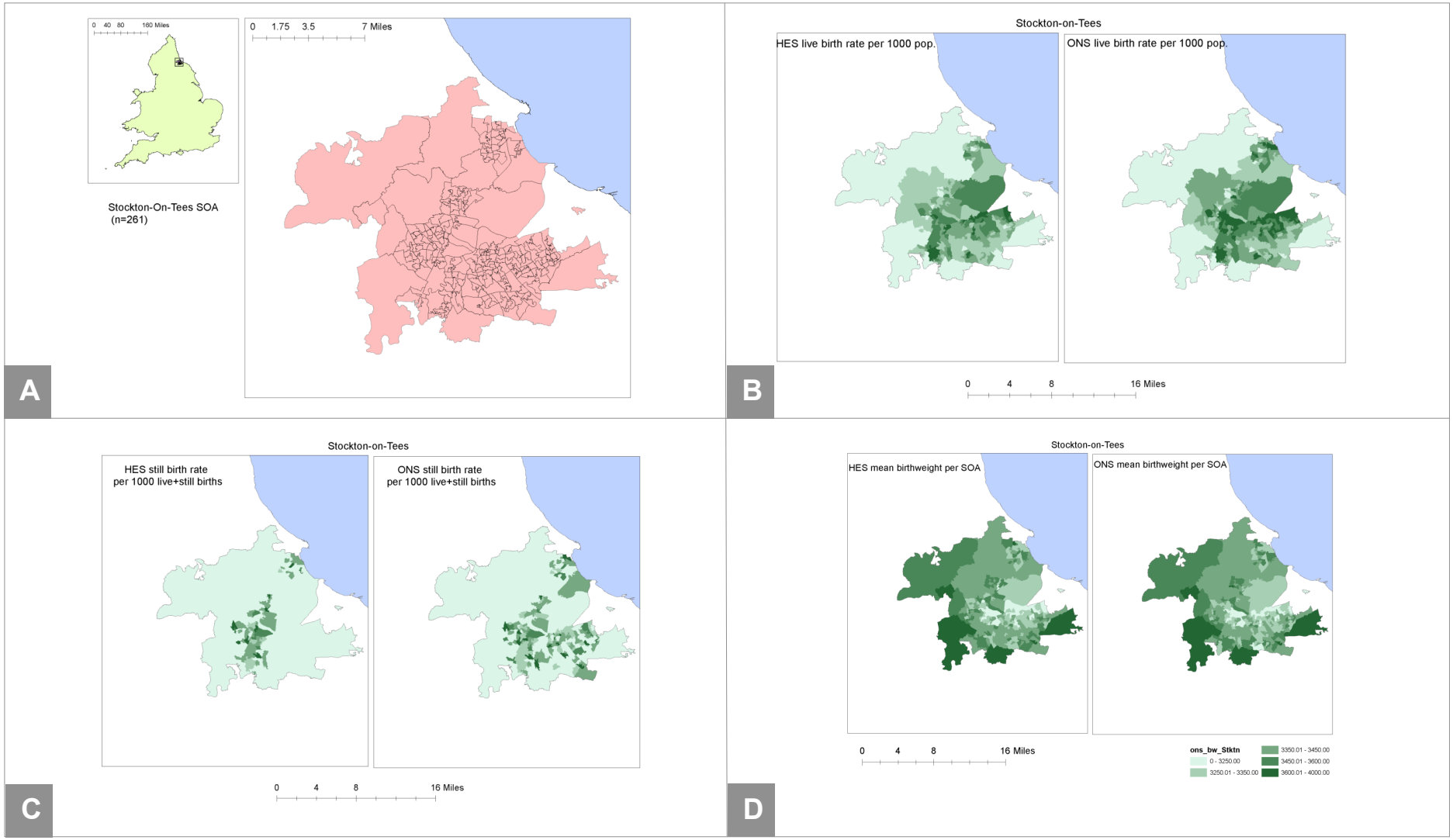
Table 4.30 Super Output Area (SOA) level comparison of the number of live births, stillbirths and average birth weight information within 10km from Marchwood MSWI and Stockton-on-Tees MSWI

	Live births		Stillbirths		Continuous birth weight	
	HES deliveries	**ONS births**	**HES deliveries**	**ONS births**	**HES deliveries**	**ONS births**
Stockton-on-Tees (SOA's = 259)						
Mean	128.19	155.88	0.33	0.85	3375.24	3375.74
Standard deviation	71.19	85.91	0.72	1.15	113.26	109.44
Median	119	144	0	1	3372.13	3367.78
IQR	84-163	102-198	0-0	0-1	3309.05-3439.04	3304.75-3443.84
5-95th percentiles	30-237	40-290	0-2	0-3	3197.14-3530.71	3204.01-3534.96
Min-Max	2-725	2-872	0-5	0-7	3001.67-3965	3096.75-3965
Marchwood (SOA's=261)						
Mean	61.84	144.32	0.05	0.69	3405.88	3402.45
Standard deviation	29.11	66.45	0.24	0.99	107.58	89.39
Median	59	142	0	0	3400.23	3407.23
IQR	42-80	102-182.5	0-0	0-1	3351.47-3473.52	3348.69-3456.10
5-95th percentiles	16-118	39-268	0-1	0-2.5	3225.30-3571.00	3272.06-3528.23
Min-Max	1-154	1-370	0-2	0-6	2988.68-4072.5	3058.65-3793

Figure 4.12 Super Output Area (SOA) level comparison of HES and ONS data surrounding the Marchwood MSWI. (A) Map showing the location of the Marchwood MSWI and its surrounding SOAs (B) Live birth rates by dataset (C) Stillbirth rates by dataset (D) Mean birth weight by dataset



Figure 4.13 Super Output Area (SOA) level comparison of HES and ONS data surrounding the Stockton-on-Tees MSWI. (A) Map showing the location of the Stockton-on-Tees MSWI and its surrounding SOAs (B) Live birth rates by dataset (C) Stillbirth rates by dataset (D) Mean birth weight by dataset



CHAPTER 5: DISCUSSION

Here the findings presented in chapter 4 are brought together and put into context in light of previous research, in addition to a discussion of the implication for future research in this field. The thesis addresses different issues concerned with the study of MSWI emissions and their potential effect on reproductive health. The work presented in this thesis provides proof of concept in support of SAHSU's national study investigating the association between MSWI emissions and adverse birth and neonatal health outcomes in GB. First, a detailed modelling exercise was undertaken to estimate potential population exposure to particulate matter pollution as a proxy for MSWI pollutants. Data for four MSWIs were modelled and will be used in the SAHSU study together with similar estimates for the remaining sites in the UK which have been obtained using the models developed in this thesis. Second, a biomonitoring study of dioxin exposures was undertaken, results of which will help the interpretation of the SAHSU study. Third, a comparison was undertaken of available datasets on births and birth outcomes from HES and ONS, again to inform selection of data sources and endpoints to be used in the SAHSU analyses.

5.1 SMALL AREA LEVEL EXPOSURE ASSESSMENT OF MUNICIPAL SOLID WASTE INCINERATOR EMISSIONS

The use of atmospheric dispersion models are well established within air quality management and risk assessment and are increasingly being used to assess environmental exposure in epidemiological studies. As part of this thesis a dispersion model was used to predict ambient levels of particulates around MSWI point sources at postcode level. This model, and the modelling outputs for the four MSWIs described, will be used in SAHSU's incinerators study to assess exposure to MSWI related pollutants for 22 MSWIs in GB operating to modern day standards between 2003 and 2010. The estimates of population exposure to MSWI emissions (modelled through particulate matter pollutants) produced will be used to investigate the association between MSWIs and adverse birth outcomes.

Extremely low concentrations of particulates (annual mean concentration ranging from 0.97-59.28 x 10^{-4} $\mu g/m^3$) were modelled for all four MSWIs, with peak concentrations never exceeding expected background levels. Modelled concentrations decreased with distance from the MSWI site with areas of higher estimated PM_{10} exposure found to the North East in all four sites, consistent with the prevailing South Westerly winds in the UK. Concentrations levelled out

beyond approximately 5 km from the MSWI site, with variability in modelled emissions well captured within the 10 km study area. Models were sensitive to model input parameters - including the dispersion site parameters, surface roughness length and MO length and meteorological data. This reinforces the importance of selecting representative model input parameters as any limitations in these parameters are likely to influence the validity of model output.

A comparison of distance to source and dispersion model outputs indicated that there is moderate agreement between these two methods of exposure assessment, with improvements in agreement when the number of exposure categories was reduced. This is due to the dispersion models capturing small area level variation in population exposure (with more variation captured as exposure categories increase), which cannot be accounted for using a distance model. Within tertile exposure categories there was good agreement between the two methods for both the lowest and highest exposure tertile. However there was poor agreement for the middle tertile where exposures did not conform to a circular pattern around the MSWI site and small area level variation was observed. One source characteristics considered within the dispersion model was the height of the MSWI stacks. This is the reason residents living close to the stack (within the first 500 m) have very low estimated exposures (the plume does not fall immediately to the ground). Since these residents would be the most highly exposed residents if distance alone were used, failure to take this factor into account in distance approaches could lead to important exposure misclassification. Allowing for a "shadow" area or "exclusion" zone immediately proximal to the site would go some way to dealing with this problem in future distance-based approaches. However there is then a need to consider the size of the zone, which will in part depend on the stack height (accounted for in dispersion models).

Exposure assessment methods used within previous epidemiological studies exploring the relationship between incineration and adverse health outcomes - in particular those focussed on birth outcomes - have predominantly used a simple distance metric as proxy for exposure (discussed in chapter 1). Of the six studies using dispersion models [125, 126, 131, 132, 136, 138], five explored dioxins [125, 126, 131, 132, 138]. The emissions input data for each varied from semi-quantitative estimates from experts (based on incinerator characteristics: capacity, type of functioning, dust control, fume treatment and year began operating) [125], to maximum allowable concentrations [131, 132] and one used annual dioxin measurements [138]. In the study by Cordier *et al* (2010) this information was not provided [126]. Similarly to what has been done in this thesis, Candela *et al* (2013) used PM as a tracer for all MSWI emissions due to the lack of temporal measurements of other pollutants, for the same time period (2003-2010)

[136]. Candela *et al* (2013) reports modelled concentration of 0.96 ng/m^3 in 2003 decreasing to 0.26 ng/m^3 in 2010. As shown in chapter 4, the results of this thesis are within the same order of magnitude, 0.18-5.93 ng/m^3 in 2003 and 0.16-5.09 ng/m^3 in 2010, with model outputs consistently higher for Edmonton, Marchwood (after 2005) and Stockton (before 2006).

Implications and recommendations

Each MSWI is unique

This thesis has shown that most of the variability in MSWIs in England is related to, the number and characteristics of individual flues, the daily MSWI particulate emissions data and their local topographic and meteorological conditions. This, alongside variability in model output and its sensitivity to input parameters, would imply that previous epidemiological studies based on dispersion modelling, which use default model parameters and mean annual emission levels, are liable to misspecification and potential exposure misclassification. This is particularly important for birth outcomes where the relevant window of exposure is either trimester specific or the term of pregnancy and therefore will be sensitive to season and other variables affecting emission concentrations in different parts of the year.

Distance vs dispersion model

Although a comparison of model output and distance to the source showed they were moderately correlated, distance does not account for the influence of the stack height which can result in peak concentrations being between ~600-1200 m from the MSWI stack. This agreement improves when the numbers of exposure categories is reduced, due to a reduction in the capture of small area level variation accounted for within dispersion models but not distance models. Kappa coefficients suggested fair agreement for deciles of exposure improving to moderate agreement for quintile and tertiles of exposure.

Bias and limitations

The modelled ecologic exposure estimates have a number of limitations. Many of these relate to assumptions about how representative the input data are (as discussed in chapter 3, section 3.1.1.2), in addition to limitations of the model itself, whereby these models are found to underestimate ambient concentrations by ~15-30% [29, 30, 32, 33]. As a whole dispersion models are disadvantaged by their vast demand for data and the expertise required to successfully run and interpret them [242]. Finally, the models built estimated PM_{10} exposure as a tracer for all emitted MSWI emissions, including those of particular interest such as dioxins

and heavy metals. The assumption that PM_{10} acts as an adequate tracer for all MSWI emissions was called into question during a correlation analyses, detailed in chapter 3, section 3.3.1, whereby PM exposures were shown to be weakly correlated with dioxin exposures. Although this weak correlation is likely a reflection of the scarcity of dioxin data it could indicate a source of bias in the form of exposure misclassification. However, as this misclassification of exposure would not be related to the birth outcome, and therefore non-differential, it would likely bias effect estimates towards the null. It is additionally noted that PM_{10} has considerable variability in its chemical properties, which are not accounted for in the models, in addition to variation by geographic location and by MSWI (waste load).However, the models employed have been justified by: firstly, the availability of temporally sensitive particulate concentration data, which allowed the generation of time sensitive models for trimester weighting exposure estimates, and secondly, the literature which detailed that dioxins adhere to particulate matter [7].

Dispersion models provide ambient concentrations of PM_{10} at population level, it is assumed that this reflects actual exposure to incineration by-products, of individuals. The exposure assessment is yet more complex as the internal dose received by individuals depend on a host of factors including daily activities, diet, mobility, time spent indoors and in the home. The Incinerators Biomonitoring Study will aid interpretation in this aspect as it will provide data on absorbed dose of dioxins amongst the target group (pregnant women). One important assumption is that exposure concentrations at place of residence are a useful proxy for an individual's total exposure to incineration by-products. The postcode level models developed within this thesis do not take into consideration factors such as an individual's occupation (short term maternal migration) and residential history (long term maternal migration) which are likely to play an important role in influencing individual exposure. Exposure levels assigned to residential postcodes are likely to be different to those in the workplace or at previous addresses, neither of which are likely to be within the same postcode, though evidence from this thesis suggests that most migration is to nearby areas. This misclassification of exposure is unlikely to be related to the health outcome and is therefore termed non-differential which would be expected to bias observed effect estimates towards the null [243].

Strengths

To the author's knowledge this thesis has for the first time estimated exposure to emissions from modern operating UK MSWIs using a dispersion modelling approach. As already noted its methodology will be used in the GB-wide study of MSWIs by SAHSU, in order to shed some light on the study questions: *Do the emissions from WID operating incinerators pose a risk to*

reproductive and infant health?" and "*Does living near a municipal solid waste incinerator pose a risk to reproductive and infant health?*".

The availability of emissions data with appropriate temporal resolution has enabled daily models of exposure to be developed. This resolution is required when exposure is estimated for windows of exposure which are less than a year, as required in a study of birth outcomes. The window of exposure most relevant is dependent on the outcome ranging from first trimester, most relevant for birth defects, to the third trimester, most relevant for stillbirths and fetal growth outcomes [244].

Dispersion models as a whole are advantaged by their inclusion of a wide range of information influencing both the pattern of exposure and the pollutants concentrations, in addition to the wide scope of validation undertaken on these models. ADMS-Urban has been validated for assigning exposure both at an individual and small area level and is universally used for regulatory purposes, policy support and providing information to the public [24, 242].

Dispersion modelling recommendations

Based on the exposure modelling work undertaken within this thesis, the following recommendations have been composed as guidance to researchers undertaking modelling of this nature. It is my recommendation that:

- The grid reference location of individual point sources including stack locations are verified
- When point source emission concentrations are sourced from external data providers, measurement methodologies alongside all data coding are disclosed and discussed in full before modelling is undertaken. This includes a review of commissioning dates including testing periods
- Default site characteristics, the MO length and surface roughness lengths, are scrutinised through sensitivity analysis. Appropriate lengths should be selected based on an exploration of land cover within the fetch of the point source (1km radius around source). Where land cover is variable, lengths should be assigned weighted by the proportion of the various land covers and their representative lengths
- Meteorological stations with less than 90% annual coverage of key climatic variables are disregarded and distance from the station to the MSWI is of greatest importance during the selection process

- Terrain files are included within models when greater than 5% of the study area has a gradient over 10%
- Excel VBA macros, or equivalent software, are used to automise the generation of input files if either temporally sensitive or spatially sensitive models are required

Ongoing exposure modelling work

The author is aware that since undertaking this work, several data issues and discussions with experts with potential implications for the exposure models presented within this thesis have come to light. Sensitivity analysis is currently being undertaken beyond those undertaken here. The main issues uncovered relate to the interpretation of the emission data provided. Firstly, it is not always clear whether emission records reported as zero correspond to days when the MSWI was not in operation or concentrations below the limit of detection. This will be investigated with reference to an analysis of daily records for other pollutants (SO_2, NOx) where available. Any changes to the interpretation of emission records reported as zero will additionally influence the imputation of the missing data. Finally the EA has made us aware that emissions records provided (obtained from reports operators provide to the EA to demonstrate WID compliance) for particulates have a 30% confidence interval subtracted to allow for allowable uncertainty. Discussions on implications of this systematic underestimate of emissions are currently ongoing.

As noted previously, the findings of the dispersion modelling carried out as part of this thesis were published in the Journal of Environmental and Public Health in 2013**(Appendix C)** [145].

Together with the Environmental Research Group (ERG) at Kings College London a validation study is being undertaken to fingerprint and detect in ambient air data, heavy metal stack emissions from MSWIs. This will further help delineate the importance of the modelled PM_{10} data in identifying heavy metal emissions from MSWIs with potential to identify regional and MSWI specific differences in PM composition of emissions. This work has been published in Atmospheric Environment **(Appendix F).**

Epidemiological analysis

At present the larger SAHSU study **(Appendix B), f**or which the work presented in this thesis is contributing, is in the preliminary stages. Delays in obtaining emissions data from the Environment Agency for all MSWIs has led to significant delays in the progress of the SAHSU incinerators study, however these delays had no affect on the specific goals of this thesis.

SAHSU's incinerators study is an individual-level population based cohort which aims to investigate the association between modelled ground level particulate concentrations as a proxy for all MSWI emissions and the following health endpoints; birth weight (continuous and term low birth weight), small for gestational age, stillbirths, PTD, infant mortality, sex ratio, twinning and congenital anomalies between 2003 and 2010. All births with and without the health endpoints in question will be selected the ONS births dataset, HES maternity dataset, ONS deaths dataset or BINOCAR congenital anomalies dataset depending on the outcome (details of these datasets are provided in chapter 3, Section 3.3.1 and in Section 5.3 of this chapter) within the study area (10km radius around the MSWI, as discussed in chapter 3, Section 3.1.1).

The method of analysis will be a generalised liner regression model with incinerator specific random effects. The epidemiological evidence indicates that there are a number of risk factors for adverse birth outcomes. Those risk factors that are also independently associated with incineration are potential confounders. Confounders need to be accounted for in the statistical analysis in order to help distinguish whether any associations, if found, are true associations or a reflection of these confounding variables. It is additionally noted that because the study population will be selected from within the study area these confounders are in part accounted for. Within the regression model only confounding variables with statistically significant changes in risk of the outcome (defined as >5% change in relative risk) will be included in the final models. The inclusion of these potential confounders in the statistical analysis will aid the interpretation of any associations under investigation and help distinguish whether associations with birth outcomes, if found, are reflective of a relationship between incinerators emissions and birth outcomes or rather alternative explanatory factors.

Potential confounders

Maternal age, Gender, Parity and Pregnancy and/or birth complications

There is strong evidence to support maternal age and fetal sex as risk factors for a number of adverse birth outcomes. Older mothers are at increased risk of having a stillbirth [245, 246] (supported by a systematic review by Huang *et al* 2008 [245]), to deliver preterm and have babies with birth weights below the 5th centile [246]. Male sex of a fetus has shown to hold a greater risk of preterm births, delivery by caesarean section and complications such as macrosomia [247-249], neonatal death and congenital anomalies [248]. The results presented in the thesis, shown in section 4.3, support this, showing preterm births to be proportionally higher in male births. All birth datasets record information on maternal age and sex fields at the

time of birth. It is noted however that within the ONS births dataset maternal age is provided in encrypted categories of two years (see table 4.22).

With regards to parity as a risk factor for adverse birth outcomes, a review by Shah *et al* 2010 reported an increase in risk of LBW and SGA for nulliparous women compared with multiparous women [250]. Parity is a data field collected within the ONS births dataset only. This is supported within the descriptive analysis undertaken within the thesis, Section 4.3 of the Results chapter shows LBW babies occurring more frequently in nulliparious women. Additionally it is known that complications occurring within pregnancy increase the risk of adverse birth outcomes. For example women diagnosed with gestational diabetes are at increased risk of preterm delivery [251]. Information on pregnancy complications are detailed only within the HES datasets.

Descriptive analysis of these risk factors by exposure category will help to determine if these are potential confounders however, as stated above, only variables which change the relative risk of the outcome explored will remain in the final model.

Deprivation

A systematic review and meta-analysis by Vos *et al* 2014 report that living in a deprived neighbourhood increases the risk of babies born preterm, SGA and stillborn by 20-30% [252]. As supported within the descriptive analysis in Section 4.3 of the Results chapter LBW babies, stillbirths, term LBW and preterm births occur more frequently in more deprived areas (Carstairs score). As detailed in Appendix B, SAHSU's scoping study reported that the population living near MSWIs tend to be more deprived than the general population. Information on deprivation will be derived from the 2011 Census data, with Carstairs scores provided at middle layer super output area. Deprivation is a known confounding variable in this analysis and therefore its inclusion is essential within the statistical analysis in order to ensure that any associations, if found, are not due to the effects of deprivation.

Maternal ethnicity

Racial disparities in birth outcomes are widely reported in the literature [253, 254], with higher rates of adverse outcomes reported within ethnic minority populations. This is further supported within the thesis, presented in Section 4.3 of the Result chapter. Information on maternal ethnicity is provided only within both HES datasets. For births not extracted from the

HES dataset, information on ethnicity will be sourced from the 2011 Census, with an extraction of ethnic category for all women of reproductive age at middle layer super output area.

Smoking

Smoking during pregnancy has been shown to increase the risk of adverse fetal outcomes such as fetal death, LBW and PTD [255-258], therefore inclusion of this information is vital. Information on smoking status will be extracted from weekly tobacco expenditure data per person in 2014 from CACI at the census output area level.

Maternal migration

Accounting for maternal migration during the pregnancy, and therefore any change in exposure status, helps to reduce the likelihood of introducing exposure measurement errors (as discussed in the Introduction, Section 1.6.2, and Discussion, Section 5.1, chapters). Information collected within the 2011 Census regarding individual's residency in the participants "last year", in addition to flow numbers, will be extracted for women at reproductive age at census output area level.

Other sources of MSWI emissions

Rural/Urban residency

In order to in part take into account the presence of other sources of MSWI emitting sources, rural/urban residency will be included as a confounding variable. Additionally is has been shown that the rate of adverse birth outcomes is greater in both remote rural areas and population dense areas [259]. Land cover classifications will be extracted from ONS land cover data at census output area level.

Other industrial sources

Due to the location of many of the MSWIs, often at industrial sites (as shown in the Results chapter (Section 4.1.1)) the presence of other industrial sources of MSWI emissions is highly likely. It is therefore essential that associations, if found, can be differentiated between MSWI and nearby industrial sources. Although disentangling this is likely to be difficult, adjustments

will be made for presence of other local industrial sources. It is however noted that it is assumed that the pattern of exposure for other industrial sources is not likely to mirror that of the MSWIs. A causal relationship between adverse birth outcomes and ambient pollution has been established for birth weight and to a lesser extent preterm births [260]. Within all statistical analyses, a binary confounder variable detailing the presence of other sources will be included. Information on the location of any additional industrial sources of MSWI emissions will be sought from the EA (the EA regulate all sites containing part A processes) within England and Wales, and from the Scottish Pollutant Release Inventory in Scotland. Additionally the emission concentrations of these pollutants can be provided by the sources described for more in-depth analysis. Additionally, to aid the interpretation of the epidemiological findings with regards to exposure from other sources, sensitivity analysis will be conducted excluding MSWIs from nearby sources. Finally it is noted that the dioxin congener profiling to take place from the Incinerators Biomonitoring Study (see Section 5.2 for details), which aims to detect a MSWI specific dioxin congener profile for MSWIs, will additionally aid interpretation and source appointment.

Road traffic

Epidemiological studies investigating the association between air pollutants and adverse birth outcomes require information on potential exposure from road traffic. Studies investigating the relationship between road traffic and adverse birth outcomes are sparse and show inconsistencies in exposure assessment which thereby limits their ability to infer a causal relationship [261]. The existing evidence, reinforced by a study by Brauer *et al* (2008) and the TRAFFIC study across Greater London, suggests a small but consistent increased risk of small for gestational age births with exposure to road traffic [261, 262]. Including information on road traffic within the vicinity of the MSWIs as a confounding factor is of particular importance because of the high influx of vehicle traffic as waste transportation to the plants. Road network data will be extracted from the Meridian 2 dataset, assembled from ordinance survey data, which will provide information on road networks and density as an indictor of traffic emissions.

5.2 BIOLOGICAL MONITORING OF DIOXINS- INCINERATORS BIOMONITORING STUDY

The aim of the Incinerators Biomonitoring Study undertaken as part of this thesis was to design, develop and undertake the data collection, including sample collection, for a study that aims to acquire a personal exposure profile to dioxins for a small group of pregnant women resident

within the vicinity of two MSWIs in England.

The pilot Incinerators Biomonitoring Study has developed and executed a study protocol, (with the exception of milk sample analysis), to establish an archive of breast milk samples for women resident near MSWIs. This study achieved a recruitment rate of 12.9% through postal invites and a 63.9% completion rate, to accomplish a study database of 97 participants with breast milk samples and completed study questionnaires. Participants from the Marchwood MSWI were found to be older, further along in their pregnancy and resident closer to the MSWI compared with the Stockon-on-Tees MSWI. A comparison of all recruited participates with those completing the study revealed that the latter group were also older, further along in their pregnancy, resident closer to the MSWI. These factors influencing study completion have been passed on to researchers undertaking the study expansion (details provided in future work section ahead) with the potential for use future targeted recruitment.

A comparison of recruitment methods within the Incinerators Biomonitoring Studies with existing literature was made difficult by the lack of information provided both on methods and recruitment rates [85, 87, 91-94]. In the biological studies detailing the method of recruitment, one study recruited through an appeal within a regional newspaper [86], another recruited from participants recruited to a population based cohort within the area [66] and within the SUREmilk study midwives undertook recruitment within postnatal wards and during home visits and therefore this study was able to gain a 80.9% recruitment rate [40].

For all participants who completed the Incinerators Biomonitoring Study and from whom a breast milk sample was received, a descriptive analysis of the demographic characteristics was compared with population level data extracted from the 2011 Census for women only within the same age categories of the Incinerators Biomonitoring Study. This showed that participants in the study were more likely to be married, less likely to be an ethnic minority and much more likely to have higher educational qualifications.

A comparison of characteristics relevant to dioxin exposure were analysed for participants resident near (within 3 km) and far (further than 3 km) from the MSWIs. Residents near the MSWIs were more likely to be older, have BMI scores within the normal BMI category, have moved residence within the last 5 years, and to a lesser extent worked in industrial production and ever smoked. These characteristics provide a complex picture for dioxin exposure because they influence dioxin levels in different directions. For example, there are studies supporting both a positive [263] and negative association [37] between dioxin levels and age. Additionally

due to the long half-lives of dioxins, a change in residence within 5 years suggests that dioxin levels may not represent exposure at current residence, i.e. near the MSWIs. For smoking and BMI their relationship with dioxin level is better established with smoking negatively associated [37, 263] and BMI positively associated [37, 264-267]. A higher BMI and therefore percentage body fat, enables more dioxin storage instead of elimination.

An analysis of daily dietary intake of dioxins for all participants completing the study ranged from 1.1-61.7 pg WHO-TEQ/day (0.02-1.10 pg WHO-TEQ/kg body weight/day) with an average of 27.5 pg WHO-TEQ/day (0.42 pg WHO-TEQ/kg body weight/day). Participants resident near the MSWIs showed slightly higher than average daily dietary intake of dioxins (28.5 pg WHO-TEQ/day or 0.45 pg WHO-TEQ/kg body weight/day) compared with participants resident far from the MSWIs (27.2 pg WHO-TEQ/day or 0.41 pg WHO-TEQ/kg body weight/day). For the 22 participants resident near the MSWIs, five (20%) had daily dietary intake of dioxins levels greater than 10 pg WHO-TEQ/day above the average for all participants. Dioxin intakes were similar to population levels reported by the FSA in 2001, calculated at 0.4 pg WHO-TEQ/kg body weight/day [230]. The maximum estimated dioxin intake level of 1.10 pg WHO-TEQ/ kg body weight/ day still falls below the EU exposure maximum of 2 pg WHO-TEQ/kg bodyweight/day.

Although daily dioxin dietary intake estimates for participants were equivalent to population levels reported by the FSA, the estimates were much lower than population levels reported in other European countries [268] (based on the body of literature detailing findings between 1999 and 2004). Estimated average population intakes within the European countries ranged from 0.9 pg WHO-TEQ/kg bodyweight/day in the Netherlands to 3.22 pg WHO-TEQ/kg bodyweight/day in Spain, with a mean estimate across all studies of 1.6 pg WHO-TEQ/kg bodyweight/day, over four times the levels reported in this study [268]. This discrepancy is likely explained by the study period, 1999 and 2004, in which the population estimates within these European countries took place. These higher population levels reflect the period before a number of major pollution controls regimes had been enforced, including WID (enforced in December 2002/2005) and EU limits on dioxins in food and animal feed (introduced in 2002). This temporal decline in dioxin levels is further supported in Figure 3.5, where the decreasing temporal trend in dioxin levels within UK food samples from the Total Diet Study are displayed.

Implications

The Incinerators Biomonitoring Study has demonstrated the feasibility of establishing an archive of breast milk samples for residents within the vicinity of MSWIs. This study addressed

and successfully overcame issues of study approval, recruitment of hospitals, recruitment of participants, coordination, collection, management and storage of breast milk samples.

Despite initial concerns about its nature, the study was positively received by midwives and participants. The author has no reason to believe that this study and its methodology could not be expanded to a greater number of MSWIs in the UK of a similar nature (see future work section below). This work has therefore made it possible to draw up the study recommendations below which relate to issues specific to biomonitoring studies of environmental pollutants in breast milk (general study design and set up recommendations have not been included).

- Considerations for study area selection:
  - Breastfeeding initiation rates
  - Concentrations of pollutant(s) of interest emitted from source(s) of interest
  - Surrounding sources of pollutant of interest
  - Size of recruiting hospital e.g. births per year
  - Geographical and social diversity
- Study materials should:
  - Be sensitive to the concerns of expecting mothers, particularly in relation to their views on breastfeeding
  - Consider individual feedback of results (an area of key consideration for ethics)
  - Consider a protocol in the event of a participant experiencing an adverse birth outcome. Including withdrawal, further contact from the study team and provision of contact information for organisations/charities with expertise in dealing with mothers experiencing adverse birth outcomes
  - Consider providing participants sample collection equipment e.g. manual/automatic breast pumps or breast shells
  - Consider more than one form of contact for ease following recruitment (new mothers are difficult to contact)
  - Consider storage procedures for breast milk samples to reduce the likelihood of spoiling samples
  - Consider requesting for a greater volume of breast milk than needed for chemical analyses
- Recruitment should:
  - Occur within a short period from when samples are to be requested
- Breast milk sample provision, storage and collection:

- Allow adequate time for sample collection, especially for first time mothers
- Ensure all study team members are informed on, and sympathetic to, issues and difficulties experienced during breastfeeding/expressing
- Recommend collecting breast milk samples from participant's houses to avoid issues of temperature controlled postage and to provide a personal and efficient collection service (enables the study team to ensure all study materials have been completed)

Bias and limitations

The Incinerators Biomonitoring Study is likely to have been subject to three forms of bias. The first relates to the selection process of the included MSWIs, as detailed in chapter 3. Each MSWI is unique in its location, design and operation, with great variation between MSWIs across the UK. MSWIs selected for inclusion in this study therefore may not accurately represent typical UK MSWIs. When selecting MSWIs the key areas of considerations were those relevant to dioxin exposure and recruitment, therein making the MSWIs unique. To increase the likelihood of MSWI dioxin detection, MSWIs within areas of high mean ambient dioxin levels and few additional dioxin emitting sources were selected. Therefore levels of dioxins in breast milk have the potential to be greater and MSWI derived at the selected MSWIs than around other MSWIs. However because MSWIs are most commonly located in industrial areas, alongside five of the 22 MSWIs in the UK with 10 km study areas overlapping with one another, the "cleaner" conditions selected for this study may lead to an underestimate of typical dioxin levels. It would have additionally been beneficial to include a low dioxin emitting MSWI within an area with few additional dioxin emitting sources. There by allowing a comparison to be made between MSWIs and therefore a better understanding of the contribution of MSWIs to total dioxin body burden. Finally, consideration of the number of years the MSWI had been operational was accounted for due to the long half-lives of dioxins, however as technology advances and abatement techniques improve, it is likely that newer MSWIs emit less dioxins and therefore levels measured during this study may be overestimated.

The second source of bias relates to the study inclusion criteria. This may mean the study participants are not representative of the population they come from. Firstly by measuring dioxins in breast milk, pregnant women unable or unwilling to breastfeed are automatically excluded. With the known social bias in breastfeeding uptake [40, 269, 270], more common amongst the least deprived population, this has the potential to influence dioxin exposure levels through occupational, residential and dietary means. Although the presence of this type of bias was suggested in practise, whereby the proportion of participants educated to a degree level or

above and those working in professional occupations were extremely high. Further exploration of this source of bias would require participants within the study to be assigned address level socio-economic levels and comparisons made with all pregnant women within the study areas.

Thirdly, because participation within the Incinerators Biomonitoring Study was voluntary, unavoidably self-selection bias will be present. This means that participants taking part may not accurately represent the population they come from. However because participants were blind to their dioxin exposure, this self-selection bias was hypothesised to be non-differential.

Finally, although biomonitoring studies are considered the "gold standard" in exposure assessment [20], they are greatly disadvantaged by the large resources they demand. These include time, staff and financial costs, alongside all the inherent difficulties in acquiring human tissue and the burden and potential risks to participants involved.

Strengths

To the authors knowledge this study will be the first to use breast milk to assess total body burden of dioxins in women resident within the vicinity of modern operating UK MSWIs. Within the body of studies investigating dioxin levels in breast milk from incinerators, the Incinerator Biomonitoring Study has a much larger sample size, than six of the eight identified studies [66, 86, 89, 92-94], the sample size is only exceeded by two studies [85, 87]. The first in Tokyo, Japan, recruited 240 women and the second 181 in Portugal (it is noted that the full biomonitoring study, following study expansion, has now exceeded both of these studies in size). The individual-level exposure uptake profiles developed from the Incinerators Biomonitoring Study (study outcomes discussed below) will help to interpret the finding of the national epidemiological study on MSWIs and birth outcomes being conducted by SAHSU. Enabling a comparison of both total concentrations and congener patters by, geographic location of participants, both from the MSWI and in relation model outputs (areas of modelled high and low dioxin levels) and between MSWI sites. In addition to shedding some light as to the different contributions of all exposure-relevant behaviours, for example lifestyle choices, dietary habits and distance to the MSWI source.

Future work

As outlined within the chapters 1 and 2, the design and development of the Incinerators Biomonitoring Study alongside data acquisition were included in the aims for this thesis

however; the full completion and data analysis of milk samples were not. This section details the future work to be undertaken for study completion.

Dioxin analysis

Frozen breast milk samples will be analysed by the Scientific Analysis Laboratories Ltd (SAL). SAL have expertise in this analysis for nearly 25 years and have BS EN ISO/IEC 17025/2005 accreditation. Samples will be analysed for 17 PCDDs/PCDFs by high-resolution gas chromatography/mass spectrometry.

Study outcomes

The Incinerators Biomonitoring Study will enable the development of an individual-level exposure uptake profile of dioxins for residents within the vicinity of modern MSWIs, accounting for all exposure-relevant behaviours, through lifestyle choices and dietary habits. Following laboratory analysis of dioxins (as discussed above) the study will explore the relationship between the breast milk dioxin levels and distance to the MSWIs, in addition to analyses with emphasis on factors of key consideration for dioxin exposure recorded within the study questionnaire, inclusive of: age, BMI, tobacco use, occupation and diet (both dietary habits and consumption of local produce). Participants diet is of particular interest for dioxin exposure because ingestion is the primary pathway of exposure [35]. This is further supported Frery *et al*, who conducted the largest biomonitoring study to date, who reported an increase in serum dioxin levels, within 1,030 resident around 3 MSWIs in France, with consumption of local produce of animal origin [59]. Additionally Chen *et al* 2003 reported that within 341 residents around 3 MSWIs in Taiwan, frequency of fish consumption was the most significant contributor to serum dioxin levels [80]. Comparisons will be made between dioxin congener profiles found in breast milk samples and fingerprint dioxin emissions from MSWIs, with additional comparisons between MSWIs and within different areas of exposure. The detection of a fingerprint or tracer of MSWIs in the breast milk of study participants would help to establish the relative contribution of MSWIs to body burden of dioxins for women living within the vicinity.

Study expansion

The success of the Incinerators Biomonitoring Study, both in recruitment (within North Tees the Incinerators Biomonitoring Study was the first reproductive health study in the top 5 recruiting studies within the trust, ranked at number three) and reaching its aim of collecting ~100 samples, has led to additional funding being granted by the MRC to expand the study.

These funds will be used to extend the study sample size from the original target of 100 to a new target of 170, thereby increasing the effect size the study is powered to detect to a 0.21 correlation coefficient.. This has enabled an additional MSWI site (SELCHP MSWI in Lewisham) to be included alongside an increase in biomarkers to be measured. A sub-set of samples will additionally be analysed for 7 heavy metals emitted by the MSWIs, namely copper, cobalt, nickel, arsenic, cadmium, mercury and lead. This expansion will further increase the power of the study, contribute to the limited body of evidence on this subject and help interpret the results from the initial study in the event of conflicting results from the two original locations.

Finally, collaboration with the University of Birmingham has been established to enable an analysis of novel brominated flame retardants within a subset of breast milk samples collected. Although the principal driver for this work will be to examine exposure levels, there has been concern expressed with regards to reproductive effects [271]. This work is being led by Professor Stuart Harrad who has considerable experience and expertise in this field of research [272-274].

5.3 USING NATIONAL BIRTH DATA WITHIN EPIDEMIOLOGICAL STUDIES OF BIRTH OUTCOMES

Two English national birth datasets were investigated with the aim of making recommendations to both the wider research community and for SAHSU's epidemiological analyses, on the most appropriate births dataset to use in epidemiological studies on birth outcomes. The birth outcomes investigated (LBW, vLBW, stillbirths, term LBW, preterm delivery and v preterm delivery) mirror a subset of birth outcomes within the SASHU study, including only the birth outcomes where there was a choice of dataset source. These outcomes were selected by SAHSU because of links between adverse birth outcomes and the chemicals of concern in the emissions from MSWIs. Extraction, data availability, quality and completeness of the HES maternity datasets (which were not created for use in research but for administrative purposes), were investigated and compared with the ONS births dataset and the epidemiology of the births outcomes in England updated for 2001 to 2010.

The first challenge encountered was during data extraction for the HES datasets. The lack of a generic framework made it difficult to extract, clean and de-duplicate HES maternity data, with considerable variability, over two fold, in birth counts depending on the extraction method.

Hospital data have the advantage of a wide-ranging collection of clinical data fields, which are not routinely collected at birth registration (ONS births). Those of particular importance for birth outcomes are number of previous children, ethnicity of mother and baby and gestational age. Of these, only information about previous numbers of children is included when a birth is registered. The "number of previous children" variable is essential in understanding trends and patterns of fertility, which help to inform policy and predict future fertility trends. Although documented when a birth is registered, this is only when that birth occurs within marriage. As births are increasingly occurring outside of marriage - in 1986 79% of births occurred in marriage decreasing to 53% in 2012 [275] - the capture is poor in the ONS data. It has been noted, however, that recent changes in legislation mean that from 2013 the information will be collected for all births within the ONS dataset [276]. Ethnic origin of mother and baby are both important covariates in many studies and essential to identify disparities in health and provision of health service. Gestational age at birth is a particularly useful indicator of fetal growth. Such data when used in conjunction with birth weight (routinely measured as a universal indicator of in utero fetal growth and development), can help distinguish between preterm babies and those with impaired growth [146, 244, 277]. Although information on gestational age for live births is not currently included in the ONS births dataset, ONS have linked their births data to the NN4B dataset held at the Health and Social Care Information Centre. This collects information on gestational age and has enabled the production of gestation-specific infant mortality statistics for 2006 onwards. In 2011, ONS linked 719,624 live births providing gestational age for 99.4% of these records [278]. Unfortunately these data are only available in ONS publications which limits their use to researchers.

Across the three datasets, ONS births provided the most complete record of the majority of variables, followed by HES deliveries. HES births was the least complete. Missing data is a major issue for the interpretation of results, as researchers are unable to determine whether births with missing or invalid data are different to those within the dataset. Both HES datasets underreported the number of births in England, particularly in the first year of study (2001) and hence 2001 was excluded from further analyses. This underestimate within HES data is likely due to the exclusion of births occurring at home and those in private hospitals [210, 236]. From 2002 onwards, HES captured over 95% of ONS births. In 2010 ONS [279] published a report that showed approximately 3.1% of all births in England occurred at home or in private hospitals (2.5% at home and 0.4% in non-NHS and other hospitals [279]). Overall at the national level, the HES information, when present, was in reasonable agreement with ONS, although the likelihood of reporting errors was much greater. It should be noted, however, that the large sample size of this analysis means that even small differences in percentages between datasets,

corresponds to a large differences in the number of births, which is of particular importance for rare birth outcomes.

Common national trends in the epidemiology of births that are LBW, vLBW, stillbirths, term LBW, preterm and very preterm in England were observed across the three datasets. Overall these outcomes were found to be disproportionately common in the Asian population (reported in HES only) and among the most deprived. These results are supported by other studies using routine data [280-283]. Although the total number of births increased over the study period across the datasets, the rate of LBW births declined and stillbirth rates remained stable. HES reported a distinct peak in stillbirths in 2007, however this was related to coding issues in which one NHS trust reported 99% of their deliveries as stillbirths (5,459 deliveries [284]). This highlights one of the many difficulties encountered when using HES data.

A spatial analysis of counts and rates of live births, stillbirths and birth weights between HES deliveries and ONS births at SOA level demonstrated great variability between datasets and by GOR and MSWI. Greatest disparity between datasets was revealed in the South East around the Marchwood MSWI. This variation is hypothesised to have occurred due to differences in hospital providers and therefore data reporting. This variation limits HES's use to the national scale, as using HES at a small area level when exposures vary geographically would inevitably lead to arte factual differences.

Research papers in which HES maternity data has been used can be categorised into three themes; those exploring trends and updating the descriptive epidemiology of maternal outcomes [285-291]; linkage studies [292-295] and those exploring data quality [238, 291, 296].

Papers reporting trends and updates on the descriptive epidemiology of maternal outcomes [285-290] used HES maternity data for either, delivery method (births delivered by caesarean section) or gestation age at birth. Studies exploring births delivered by caesarean section (CS) [285, 287, 290, 291] (CS defined using the HES procedure codes (OPCS4: R17-25) in preference to the "delivery method" field in the "baby tail") assessed variation in CS rates by maternal characteristics, clinical risk factors [285], across NHS trusts [287], by previous delivery methods [288] and by post-delivery complications [290]. Information on gestational age at birth enabled Castanon *et al* (2012) to explore the association between women treated at colposcopy (by biopsy or excisional treatment) and preterm delivery [286] and O'Sullivan *et al* (2007) to

investigate the association between congenital adrenal hyperplasia, due to 21-hydroxylase deficiency and length of gestation [289].

Although linkage of HES and ONS datasets is by no means a straightforward process (requiring governance and ethical permissions), it has been successful in previous studies. Linkage studies aim to create a single enhanced births datasets by combining maternity information from two or more birth datasets. Abrahams and Davy [292] conducted linkage between HES and ONS records in February 1997, this was later improved on by Hockley *et al* (2008) [295] who additionally linked interview data of parents from the Millennium Cohort study with ONS and HES records to investigate the validity of mothers recall from the interview. Both Abrahams and Davy and Hockley *et al* (2008) successfully performed linkage. Dattani *et al* [297] first conducted a linkage of ONS births data and NHS Number for Babies (NN4B) dataset and then more recently for HES, ONS and NN4B between 2005-2007 [293, 294]. These papers included a comprehensive examination of the completeness of HES maternity and concluded that linkage rates were good despite high rates of missing data in HES maternity records.

Finally papers have explored HES data quality, with comparative assessments made between maternity data fields and data fields derived from a general record [291, 296] and more recent studies have begun exploration of the using HES data to construct birth cohorts to allow follow up within research [238].

Compared with the considerable body of epidemiological studies exploring birth outcomes and studies using the main HES dataset, those using the HES maternity dataset are sparse and are mostly used to acquire information on delivery methods most frequently extracted from procedure codes i.e. not the maternity fields. No studies have used the HES maternity dataset in epidemiological analysis as per ONS births and the use of linked datasets within epidemiological analyses is complicated by issues of record matching, validation of matching and also the time needed to obtain ethical and governance permissions.

Within the UK, large birth cohorts also provide a wealth of information that can be used to examine birth outcomes at a smaller scale. These birth cohorts include: the National Study of Health and Development [298], the National Child Development study [299], the 1970 British birth cohort [300] and the Millennium Cohort [301], all of which collected detailed information at an individual level. These cohorts have the advantage over nationally collected data in that they collect much more detailed information, often including biological samples, and offer the ability to follow up individuals over time. The data collected are also related to the research aim

in question and therefore tailored to the research needs. Despite the clear advantages of birth cohorts they do not provide the national coverage that national datasets capture.

Implications & recommendations

Based on this work, I have recommended to SAHSU that for the following outcomes the datasets below are used;

- Stillbirths - ONS data
- At a national scale: LBW, vLBW, term LBW, preterm delivery and v preterm delivery (all of which require gestational age) - HES deliveries

  With the recommendation to:
  - Use data from 2002 onwards only
  - Undertake descriptive analysis by hospital to ensure differences or mistakes in reporting are identified
- At a small area scale: For epidemiological studies exploring exposures at a geographical level I would not recommend using HES maternity data at a small scale due to the large variability in NHS trust reporting.

Bias

Minimal selection bias will be present in the ONS birth data. Although these data may encompass non-differential coding errors, they are collated by a single organisation using a standard procedure for recording data which incorporate validation checks for all records and cover the UK population. Therefore the influence of these errors within this thesis are likely to be negligible.

Although HES captures all NHS or NHS funding hospital inpatients, there is inevitability variation by hospital in the information recorded, as well as recording systems used, staff and finances. These hospital provider effects include data completeness, hospital beds, admissions policies and hospital access [302]. The occurrence of misclassification of birth outcome when using the HES maternity dataset due to these differences is therefore likely. As observed within the stillbirths data in 2007, this relates to the miscoding of almost all delivery episodes by a single trust [303]. Although this misclassification is unlikely to match the spatial pattern of an environmental exposure, this may occur.

Strengths

To the author's knowledge this thesis is the first to undertake an in depth comparison of the only two national birth datasets in England. It is therefore able to provide information to and recommendations on the most appropriate dataset for researchers undertaking epidemiological studies on birth outcomes. This analysis was possible due to the availability of the datasets from SAHSU.

Future work

The finding of great variability in hospital data quality at small area level indicates the importance of hospital provider in all analysis using HES data. It would therefore be of great interest to explore the extent to which the hospital accounts for variability in births across the country.

As noted previously, a manuscript, based on the work presented in this thesis, has been accepted for publication at the Archives of Disease in Childhood **(Appendix E).** The author is additionally involved in work by Dr Kevin Garwood within SAHSU which aims to develop a generic, automatic method to identify, clean and de-duplicate HES delivery records. The development, publication and accessibility of a standardised protocol (and SQL scripts) for processing HES delivery records would provide a consistent, transparent framework for data extract for all future epidemiological papers using this dataset.

SAHSU's epidemiological analyses – health data sources

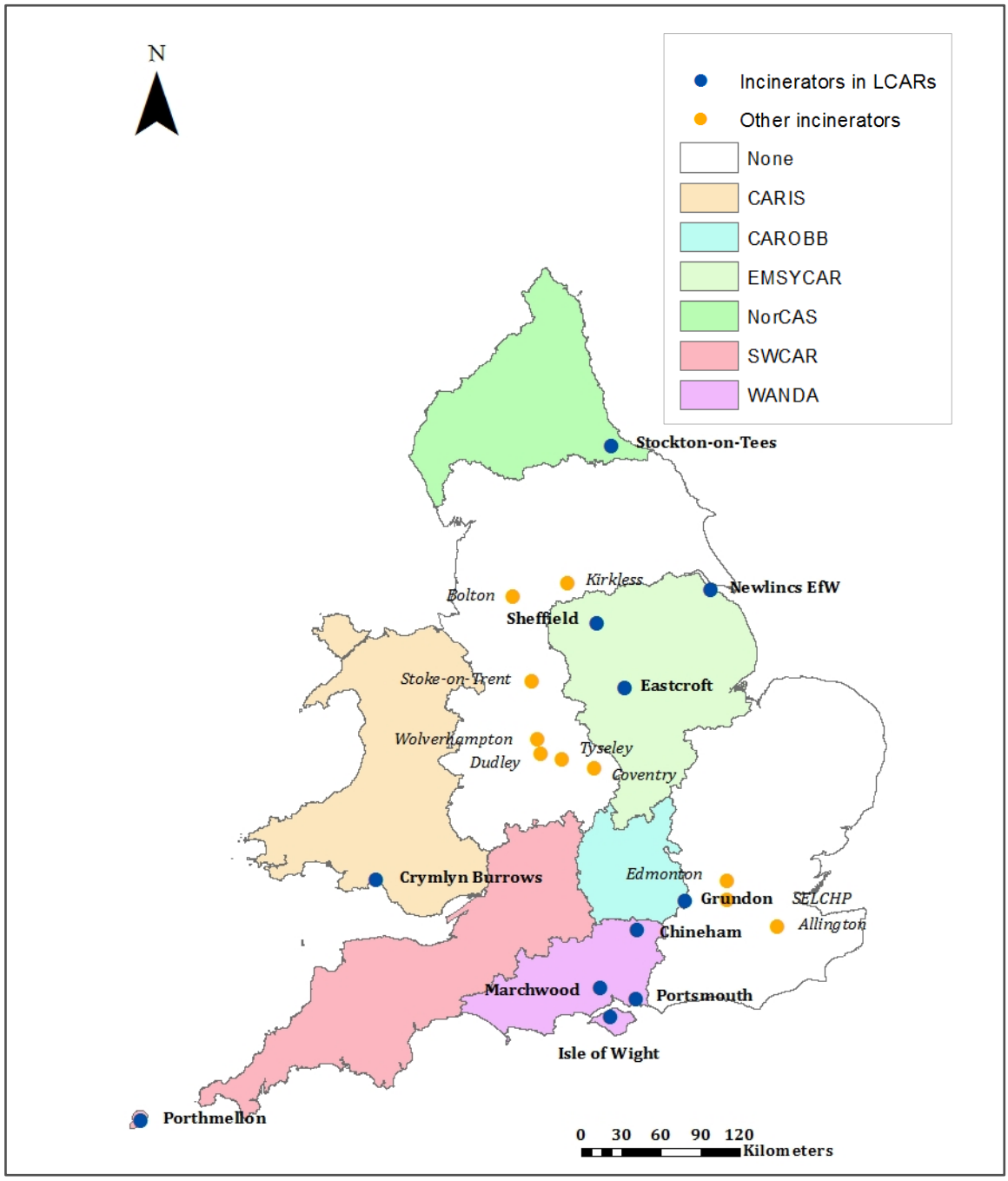
SAHSU will investigate the association between modelled ground level particulate concentrations and; LBW, stillbirths, PTD, infant mortality, sex ratio, twinning and congenital anomalies. As outlined above all recommendations relating to data use for LBW, stillbirths and PTD outcomes have been presented in "Implications & recommendations" above. For sex ratio and twinning outcomes SAHSU will use the ONS births dataset (a description of the ONS births dataset has been provided in the Methods chapter, section 3.3.1).

All recommendations relating to data use for LBW, stillbirths and PTD outcomes have been presented in "Implications & recommendations" above. For sex ratio and twinning outcomes SAHSU will use the ONS births dataset (a description of the ONS births dataset has been provided in the Methods chapter, section 3.3.1).

Infant deaths will be extracted from routine sources of mortality data, the ONS mortality dataset. As prescribed in the Births and Deaths Registration Act (1836) [304], since 1837 it has been a legal requirement that all deaths in England and Wales are registered at a local Registrar of births and deaths within 5 days of the death [305]. This includes deaths occurring in adulthood, childhood, infancy and neonatal deaths. On a weekly basis ONS are provided data collected when deaths are certified and registered. The information reported to the Registrar is supplied by the informant (usually a family relation) however the death is required to be certified by an attending medical practitioner or coroner [305]. Information collected within the death certificate includes personal details of the deceased (name, address, age, occupation), personal details of the informant (name, address and relation to deceased) and details of the death, including: date, place, immediate cause of death and all underlying or contributing factors. Although annual mortality statistics published by the ONS group childhood (under 16 years), infant and prenatal mortality together (Series DH3), stillbirths are not collected within this dataset (detailed on stillbirths data is provided in the Methods chapter, section 3.3.1). As per the ONS births data, ONS mortality data is highly completed, however is disadvantaged by lack of information on important factors such as ethnicity in addition to data quality issues experienced for cause of death which showing great variability due to influencing factors such as the experience of the attending medical staff.

Congenital anomaly data will be extracted from British Isles Network of Congenital Anomaly Registers (BINOCAR). Within the British Isles, population-based congenital anomaly data is collected within regional registers, local congenital anomaly registers (LCARs), which collectively are held by BINOCAR. BINOCAR was established in 1998 as a system that combines data from regional and disease specific registries and since 2010 is the only source of this data for England and Wales [306]. The National Congenital Anomaly System (NCAS) predates BINOCAR as a voluntary notification system run by ONS between 1964 until 2009. NCAS relied on reports from acute hospital trusts, child health systems, public health departments and midwifery units [307], which were often incomplete sources of data. To address data quality issues and with the aim to provide a more comprehensive ascertainment of anomalies, LCARs were established and in 1998 LCAR data was fed into NCAS. LCARs continue to collect data, which is fed to BINOCAR [306, 307]. Within the SAHSU epidemiological analysis of congenital anomalies, only MSWIs located within the 6 LCARs will be included due to the poor completeness of the NCAS data. Figure 5.1 shows the location of the LCARs in relation to the inclusive MSWIs.

Figure 5.1 Location of all local congenital anomaly registers (LCARs) in England and Wales and all 21 MSWIs



CONCLUSIONS

This thesis provides proof of concept for a number of methodological issues concerning the study of MSWI emissions and risk of adverse birth and neonatal outcomes. The results and conclusions drawn from this thesis will contribute to SASHU's study of the association between MSWI emissions and adverse birth outcomes. The thesis addresses a number of the gaps identified in the literature, first; an estimation of population exposure to MSWI emissions using a dispersion model; second, a biological monitoring study to estimate individual level dioxin uptake in women resident around two MSWIs and finally a comparison of the quality and availability of English birth datasets for use in epidemiological studies of birth outcomes.

Key study findings

The four key findings of the small area level exposure assessment were (a) modelled ground level concentrations of particulates from currently operating MSWIs never exceed expected background levels (b) spatial variability in modelled particulate concentrations show higher exposure in North East quadrants consistent with the South Westerly prevailing winds in the UK (c) the model was sensitive to model input parameters (d) proximity and modelled exposure were well correlated, however greatest disparity between these methods occurs near the MSWI site (due to the effect of the stack) and within 5 km from the MSWI. These findings show that compared with dispersion modelling using distance as a proxy measure for exposure may increase the risk of exposure misclassification.

The three key findings from the incinerators biomonitoring study were (a) proof of concept for a study of this nature with scope for expansion (b) age, gestational age and residence relative to the MSWI influenced study completion (c) estimated daily dietary intake of dioxins were equivalent to those reported for the FSA with maximum exposures falling below EU exposure maximums.

The five key findings from the analysis of national birth data were (a) the difficulties and therefore need for a standardised protocol in extracting, cleaning and de-duplicating HES maternity data (b) HES deliveries dataset is recommended for use in preference to HES births (c) both HES datasets did not provide the capture in births or the completeness in matching fields that ONS provided, but both have shown considerable improvements in data quality between 2002-2010 (d) spatial and temporal trends in birth outcomes were in good agreement between HES and ONS datasets (e) at the small area level live and still birth counts showed

considerable variation between HES deliveries and ONS births, due to differences in hospital operators and therefore reporting. Therefore HES deliveries is not appropriate for epidemiological analysis of birth outcomes at a small area level.

Contribution of this thesis

This thesis addressed the knowledge gaps relating to the poor exposure assessment methods used in previous epidemiological studies of modern MSWI emissions, the lack of individual level uptake assessment of dioxins from MSWIs in the UK, in addition to the small number of birth outcomes and lack of information on availability of national birth datasets explored within the epidemiological evidence thereby limiting the power of these studies to detect an effect of incinerators if present. As noted, to the author's knowledge, this is the first study to date to estimate exposure to modern operating UK MSWIs and to provide recommendations to researchers on their use of national birth datasets.

This thesis forms a vital part of SAHSU's national study investigating the associations between MSWI emissions and adverse birth and neonatal health outcomes in GB, by providing proof of concept and piloting a number of methodologies all of which, including the results of this thesis, will be used in the SASHU study. This thesis did not aim to undertake the entire SAHSU study which is a highly complex study involving over 20 researchers, still ongoing after 7 years of investigation. Research to date exploring the relationship between MSWI exposure and birth outcomes has been limited and with inconsistent findings, with the available studies being carried out on older generation MSWIs, pre WID, where operating standards and emissions limits were much less stringent. These studies have additionally lacked the power to detect the effect of incinerators if present. SAHSU's incinerators study is the first to characterise the national UK experience and address such a crucial public concern and the finding of this thesis have been vital for the SAHSU study.

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APPENDICES

APPENDIX A

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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.

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☆ 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.,

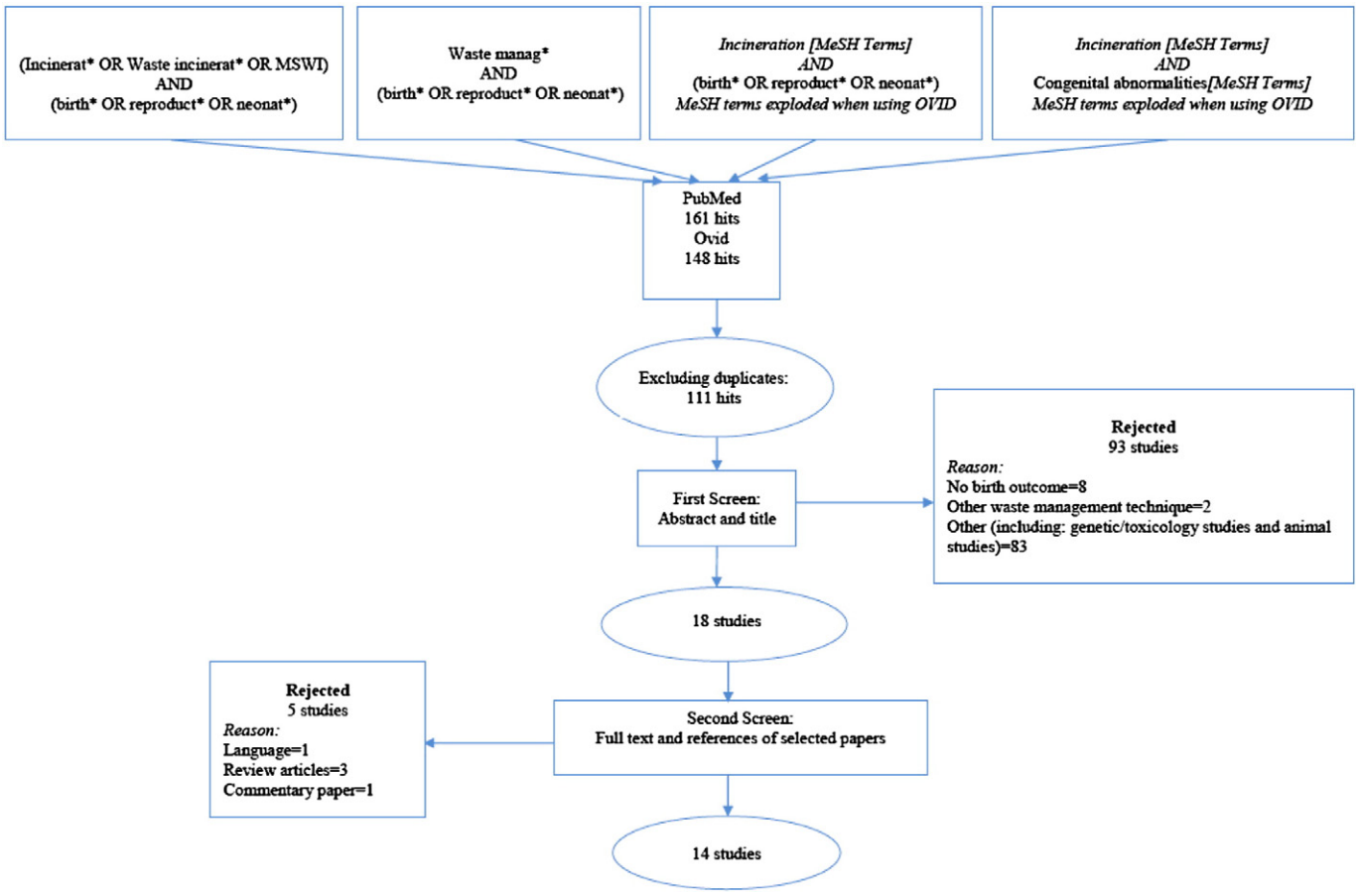


Fig. 1. Selection and review method for all identified studies.

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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APPENDIX B

SAHSU will undertake epidemiological analyses to examine the association between MSWI emissions and birth outcomes. Specifically, SAHSU will undertake an individual-level population based birth cohort study using the following exposures measures: (a) dispersion modelled particulate emissions between 2003-2010 (b) distance from the MSWI stack (c) time before and after the implementation of the WID; from all 22 operational MSWIs in England, Wales and Scotland between 2003 and 2010. The health endpoints to be considered are twinning, stillbirths, infant mortality, birth weight (continuous and term low birth weight), small for gestational age, preterm delivery and congenital anomalies (all and selected groups). Using exposure measure (a) and (b) all cases (infants with the endpoints of interest within 10km from an MSWI) and controls (all other births between 2003-2010 within 10km from an MSWIs, or births selected at random from control areas not within 10km from an MSWIs) will be assigned trimester specific estimated exposure to incinerator emissions at the location of the residence. Generalised linear regression will be used with incinerator specific random effects adjusted for potential confounders. For exposure measure (c) this analysis will be a Bayesian space-time model accounting for the MSWI commissioning dates and the implementation of the WID comparing rates of the health end points before and after the change but accounting for secular trends unrelated to incinerators.

APPENDIX C

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Research Article

Comparative Assessment of Particulate Air Pollution Exposure from Municipal Solid Waste Incinerator Emissions

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Background. Research to date on health effects associated with incineration has found limited evidence of health risks, but many previous studies have been constrained by poor exposure assessment. This paper provides a comparative assessment of atmospheric dispersion modelling and distance from source (a commonly used proxy for exposure) as exposure assessment methods for pollutants released from incinerators. *Methods.* Distance from source and the atmospheric dispersion model ADMS-Urban were used to characterise ambient exposures to particulates from two municipal solid waste incinerators (MSWIs) in the UK. Additionally an exploration of the sensitivity of the dispersion model simulations to input parameters was performed. *Results.* The model output indicated extremely low ground level concentrations of PM_{10}, with maximum concentrations of $<0.01\,\mu g/m^3$. Proximity and modelled PM_{10} concentrations for both MSWIs at postcode level were highly correlated when using continuous measures (Spearman correlation coefficients ~ 0.7) but showed poor agreement for categorical measures (deciles or quintiles, Cohen's kappa coefficients ≤ 0.5). *Conclusion.* To provide the most appropriate estimate of ambient exposure from MSWIs, it is essential that incinerator characteristics, magnitude of emissions, and surrounding meteorological and topographical conditions are considered. Reducing exposure misclassification is particularly important in environmental epidemiology to aid detection of low-level risks.

1. Introduction

Incineration is being increasingly used as a waste management option in the United Kingdom (UK). This is in response to EU legislation restricting the amount of waste disposed of in landfills [1]. Up until the 1990s incineration in the UK was largely uncontrolled. Legislation pertaining to all incinerators in the UK, the EU Waste Incineration Directive (WID) (2000/76/EC), came into operation for new incinerators in 2002 and older ones in 2005. This has set strict limits on emissions into the air [2]; nonetheless, there remains public concern and scientific uncertainties about possible health risks from pollutants emitted from incinerators.

European waste legislation uses the Waste Hierarchy Framework to guide the use of different waste management options, prioritising the more environmental desirable and sustainable options. Incineration falls above disposal of waste in landfills within this framework but is not as desirable as recycling and composting, reuse, and prevention [3]. Municipal solid waste incinerators (MSWIs) burn waste assembled by collection authorities [4], at high temperatures, reducing the volume of waste, eliminating pathogens and are capable of recovering energy from the waste [5].

To date a number of epidemiological studies have investigated the relationship between incineration and health [4–12], with most focused on its association with risk of cancer

and more recently, the risk of adverse birth outcomes [8, 12–24]. The UK Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment released a statement about MSWIs and cancer in 2000 (updated in 2009), stating that, "*...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*" [6, 7]. This was supported by the UK Health Protection Agency's' statement in 2009 "*...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*" [25]. However, the evidence base investigating this issue remains limited and most existing studies suffer from incomplete information on potential confounders, lack of statistical power, and poor exposure assessment.

Exposure assessment is often referred to as the "Achilles heel" of environmental epidemiology [26, 27]. Inaccurate and imprecise exposure estimates, leading to exposure misclassification, can create biases in health risk estimates. In many environmental epidemiology studies, exposure misclassification is unrelated to the health outcome, termed nondifferential exposure misclassification, which would be expected to bias observed effect estimates towards the null [28]. Accurate exposure assessment is particularly important for studies trying to detect/exclude small excesses in risk in relation to environmental exposures [29], such as due to incineration, in order to enable true risks, if present, to be detected.

The methods used to assess exposure to an environmental source, such as an incinerator, range in design and complexity, from simple proxy methods to detailed individual level measures of exposure. Simple proxy methods, such as distance to the incinerator, assume a linear decrease in exposure with distance from source but benefit from the ease of implementation and the limited data and resources required to undertake a study using this exposure assessment method. However, this approach is crude and does not account for the magnitude of emissions, incinerator characteristics, or the propagation of the emissions due to local meteorological and topographic conditions. Individual level direct measures of exposure, such as biomarkers in human tissue, provide an objective assessment of exposure to chemicals and are considered "gold standards" in exposure assessment [30]. Biomarkers are often not feasible in large studies due to the high cost of laboratory analysis, the difficulties in acquiring human tissue, and the burden and potential risks to participants involved [30]. Exposure modelling has largely bridged the gap between the need for more accurate exposure assessment and the practical and financial constraints of large epidemiological studies. Atmospheric dispersion models use monitored emission data along with information on local topographic and meteorological conditions, within a Gaussian framework, to estimate the concentration and dispersion pattern of pollutants around an identified source [31, 32]. New generation dispersion models have an updated understanding of atmospheric turbulence and boundary layer structure [33] and have been extensively evaluated [34–37].

Many studies investigating the relationship between incineration and adverse health outcomes have used distance as a proxy for exposure. Some studies have included additional information alongside proximity to strengthen this method, including wind patterns, soil concentrations [18], local topography, and complaints of nuisance caused by the plumes [24]. Only a limited number of more recent studies have used dispersion models [8, 12, 13, 17, 23] to assess exposures. As far as the authors are aware, no existing studies on incinerators have compared these two exposure assessment methods and quantified the extent of exposure misclassification between the two. Modelled exposure patterns are expected to be different when using the two comparative methods. The distance method will predict greatest exposure adjacent to the stack and will decrease linearly with distance from the stack. These exposures will also be fixed in time and will be homogenous in space at a given distance from the stack. In contrast, because stack height above ground is considered, the dispersion model will predict low concentrations of incinerator emissions near to the stack. Greatest concentrations will be at a distance from the stack (determined by the release conditions and meteorology) after which concentrations will decrease nonlinearly with distance. Temporal changes in release conditions and meteorology are taken into account to produce a concentration field that varies in time. Here, we provide a detailed comparison of atmospheric dispersion modelling and a distance based method to assess exposure to particulates from two MSWIs and explore issues of exposure misclassification.

2. Methods

2.1. Study Area and Study Population. Two UK MSWIs were included in this study, Crymlyn Burrows, located approximately 5 km east of Swansea, Wales and Marchwood, approximately 3 km west of Southampton, England. These two MSWIs are representative of operational MSWIs in Wales and England in terms of the operational standards they were built to (both have only ever operated to the most recent European Waste Incineration Directive [2]); their size (Crymlyn Burrows and Marchwood licensed throughput of 52,500 tonnes and 210,000 tonnes of MSW a year, respectively, where the typical median throughput of all operational UK MSWIs is 165,000 tonnes, ranging from 3,500 to 750,000 tonnes); and their rural locations (within 10 km surrounding Crymlyn Burrows 70% of the land is rural land and 69% for Marchwood, median for all operational MSWIs of 69%). The two selected incinerators additionally provided a number of contrasting features. Crymlyn Burrows has a single flue, is surrounded by hills, and lies 850 m from the coast, whereas Marchwood has two flues, is surrounded by flat land, and lies more inland. Incinerator characteristics and daily emissions data from their commissioning date (January 2003 for Crymlyn Burrows, January 2006 for Marchwood) until December 2010 were provided by the UK Environment Agency (EA).

The study area was defined as a 10 km radius around each MSWI. The 10 km distance was chosen for consistency with screening criteria used for implementing the Habitats

Table 1: Source characteristics of the two inclusive municipal solid waste incinerators.

Incinerator	County	Permitted throughput (tonnes/year)	Flue	Stack height (m)	Stack diameter (m)	Flue exit flow rate (m^3/s)	Flue exit velocity (m/s)	Temperature (°C)
Crymlyn Burrows	Neath Port Talbot (South Wales)	52,500	1	40	0.95	12.3	17.6	136
Marchwood	Hampshire (England)	210,000	1	65	1.25	30.3	24.7	150
			2	65	1.25	30.9	25.2	148

Flue exit flow rate, velocity, and temperature for Crymlyn Burrows provided are a mean of biannual measurements for most years of operation, whereas for Marchwood these measures are single measures derived from the permit application.

Regulations: incineration plants that are within 10 km of a European Site require an assessment of their impact for short range air emissions.

The study population was defined as all residents within the study area, calculated by extracting postcode headcount data from the 2001 census [38], where one UK postcode represents on average 12–15 properties and 40–45 people.

2.2. Emissions Dispersion Modelling. The Atmospheric Dispersion Modelling System Urban (ADMS-Urban) v2.3 modelling package was used [39] to model the dispersion pattern and ground level concentration of particles with a diameter <10 μm (PM_{10}) from both incinerators. ADMS-Urban is a new generation Gaussian plume air dispersion model that uses an updated understanding of turbulence and atmospheric boundary layer structure [33] and is capable of simulating the atmospheric dispersion patterns of pollutants from multiple sources and within complex terrain [40].

ADMS-Urban calculates atmospheric boundary layer parameters such as boundary layer height and Monin-Obukhov length from a variety of input parameters [40]: air temperature (°C), wind speed (m/s), wind direction (°), and cloud cover (oktas). The Monin-Obukhov length is an indicator of the atmospheric stability and is a key parameter in the dispersion of pollutant. It is defined by a quotient of heat flux at ground level by frictional velocity. It provides a height at which turbulent flows are created by buoyancy and not wind shear. In ADMS-Urban a minimum value for the Monin-Obkhov length is set, with the default value set to 30 m in order to account for the heat island effect of major cities and to prevent the model from stabilising [40, 41].

Another key model parameter that has impact on the dispersion of pollutants is the surface roughness length. Surface roughness length characterises the roughness of the terrain, providing an indicator of how much drag the wind experiences from the ground. Surface roughness is required to calculate convective turbulence.

2.2.1. Model Input Data. For each MSWI, information on the location of the stack, year commissioned, total annual waste licensed to incinerate and stack characteristics was extracted from their environmental permit application to the EA. The precise location of the stacks was verified by checking the incinerator address and postcode against six-figure grid references (georeferenced location of the stack in British National Grid projection), in addition to visually searching for stacks on satellite maps in Google maps. Stack data included number of lines, stack height (m), stack diameter (m), exit velocity (m/s), exit flow (m^3/s), and exit temperature (°C) (Table 1). For Marchwood only one measure of flue gas flow, velocity, and temperature was available from 2006 till 2010. For Crymlyn Burrows quarterly measures of these flue gas metrics were available for most years of operation. Annual averages of these quarterly measures were calculated and used. When quarterly measures were unavailable, the overall representative flue gas measures for Crymlyn Burrows were used. The concentration of total particulates at the flue exit for each MSWI was measured as daily means.

Sensitivity analysis of the dispersion conditions was conducted to select the most appropriate and representative surface roughness and Monin-Obukhov lengths. The fetch for roughness is defined by the US Environmental Protection Agency (US EPA) as 1 km surrounding the source [42]. Land cover data, extracted from the CORINE Land Cover Map 2000 [43] (Figure 1), was used to characterise the 1 km area around each MSWI. CORINE is an EU-wide dataset, generated by semiautomatic classification of satellite imagery [43] and comprises 44 land cover classes, of which 11 relate to urban land. Based on the land cover data around each MSWI, an array of relevant lengths was selected. As both MSWIs were partly surrounded by urban land cover (Marchwood 20% and Crymlyn Burrows 26%, resp., see Figure 1), a number of different surface roughness lengths and minimum Monin-Obukhov lengths were explored. Output concentrations were then compared when using the different values for both lengths.

The surface elevation in the area surrounding the MSWIs was extracted from Ordnance Survey PANORAMA digital terrain model (DTM), which has a horizontal resolution of 50 m [44]. As shown in Figure 1 the terrain surrounding Marchwood is low lying with a mean elevation of 23 m above sea level. However for Crymlyn Burrows there is a significant variation in elevation, with a range of 370 m. In order to account for this variation in terrain and therefore changes in the dispersion pattern of particulates, the hill option in ADMS-Urban was selected and a preprepared terrain file was extracted from the DTM and input into the model.

Meteorological conditions greatly influence the observed spatial pattern of emitted pollutants from a point source. Selecting an appropriate meteorological station, that best represents the area surrounding the MSWI, is therefore crucial. Hourly land surface meteorological observations from all Met Office stations in England and Wales between 2003 and 2010 were obtained from the British Atmospheric Data Centre

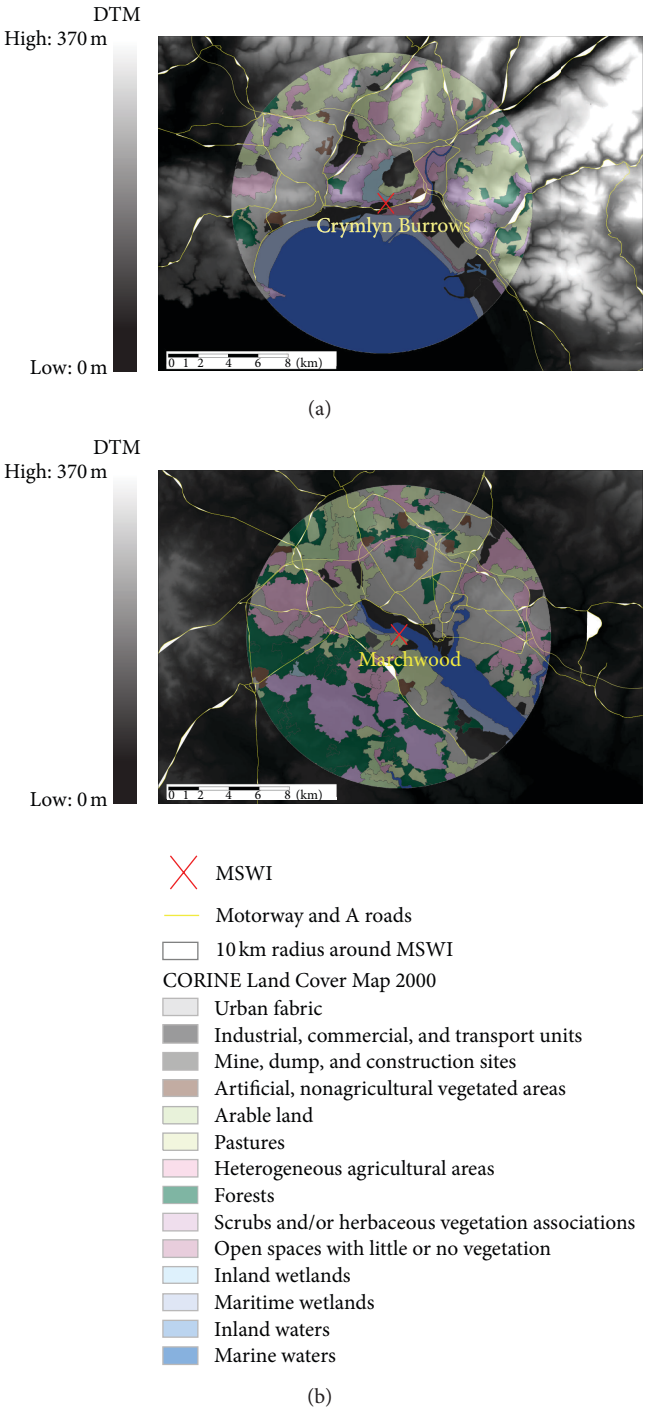


Figure 1: Land cover data from CORINE-Land 2001 and topography data from PANORMA 10 km around Crymlyn Burrows (a) and Marchwood (b) incinerators.

(BADC). Candidate meteorological stations located within approximately 30 km from the selected MSWIs were identified. Meteorological stations considered were those with 90% completeness for all weather variables (excluding cloud cover), for each year. The Air Quality Modelling Assessment Unit (AQMAU) at the EA advised that incorporating cloud cover from alternative nearby stations makes a very small contribution to overall modelling uncertainties. Therefore, cloud cover was obtained from the nearest station with 90% completeness where necessary [45]. Following the selection of candidate meteorological stations, wind roses were plotted for each station. These wind roses were used to spot anomalies in the data (e.g., apparent gaps in wind from a given sector) and comparisons were made between the sites. Following this, CORINE land cover and DTM data were extracted and compared for a 1 km radius around each meteorological station in order to select a meteorological station with similar surrounding topography and land use to the MSWI. The dispersion model was then run using these different meteorological stations and their outputs compared.

2.2.2. Model Output. Bag-filtered stack emissions from the MSWIs were not considered to contain a significant amount of particulates greater than 10 μm diameter. Emitted particulates were therefore modelled as PM_{10} and considered to disperse in the same manner as a gas.

Modelled ground level concentrations of PM_{10} for the sensitivity analysis were estimated for receptors in a 200 m × 200 m grid within the study areas. For Marchwood sensitivity analysis was performed for 2006 and Crymlyn Burrows for 2003.

For the exposure analysis, all residential postcode centroids within the study area were used as receptors and ground level concentrations of PM_{10} were modelled. For Marchwood models were run for 2006–2010 and Crymlyn Burrows 2003, 2005–2010.

For the exposure analysis, each modelled day required input of single daily mean particulate concentrations at the flue exit together with hourly meteorological data to produce a daily ground level PM_{10} concentration field. These daily modelled concentrations were aggregated to calculate annual means. Model outputs were mapped in ESRI ArcMap 10.0 [46].

2.3. Distance to Source. All residential postcode centroids within the study area were assigned a distance to their respective MSWI using the NEAR function in ArcGIS. The distance metric was chosen as distance from the edge of the study area rather than distance from the incinerator. This was termed proximity and had its greatest value at the incinerator and least value at the edge of the study area. The ordering of the magnitude of the proximity metric allowed a clearer comparison of the distance and dispersion approaches with the greatest proximity value and highest concentration found closest to the incinerator.

2.4. Comparison of Exposure Assessment Methods. All residential postcodes within the study areas were assigned both an average modelled PM_{10} concentration over the period in which the MSWI was in operation and a distance to the MSWI. Postcodes were classified into deciles, quintiles, and tertiles from high to low exposures (modelled PM_{10} concentrations sorted from high to low, distance to MSWI from low to high). A population was additionally assigned to each postcode using headcount data extracted from the 2001 census [38].

The comparison of exposure assessment by the dispersion model and by the distance method was undertaken in three ways.

(1) Calculation of Cohen's kappa coefficients of agreement between exposure deciles, quintiles, and tertiles as calculated by the distance method versus the dispersion model. Cohen's kappa coefficient provides a statistical measure of interobserver agreement taking into account chance, that is, a quantification of precision [47, 48]. Kappa coefficients range from 0 to 1, with 0 indicating no agreement and 1 perfect agreement between methods. As our exposure tertiles, quintiles, and deciles are ordinal categories, equal weighted kappa coefficients were calculated in addition to unweighted Cohen's kappa coefficients [49]. Weighted Cohen's kappa coefficients account for ordinal differences in categories; that is, a difference of two categories between the indices of exposure is a more severe misclassification error than a difference of one category.

(2) Calculation of weighted and unweighted Cohen's kappa coefficients of agreement between the distance method and the modelled particulate concentrations by population weighted exposure deciles, quintiles, and tertiles.

(3) Plotting of modelled long-term average PM_{10} concentrations against distance from the MSWI at each postcode centroid, with calculation of Spearman's correlation coefficients.

3. Results

3.1. Particulate Emissions from MSWI. Figures 2(a) and 2(b) display the daily concentrations of total particulates measured at the flue exit for Crymlyn Burrows and Marchwood, respectively. Figure 2(a) demonstrates the variability in concentrations for Crymlyn Burrows over the study period, 2003–2010, with the maximum concentration of 9.87 mg/m^3. The gap in the data shown for 2004 was due to a fire during the last quarter of 2003 causing Crymlyn Burrows to stop operation during 2004. Figure 2(b) shows the daily particulate concentrations for both flues for the Marchwood incinerator. Again, there was considerable variability in concentrations over time and also between the two flues. Both Flue 1 and 2 had a maximum concentration of 10 mg/m^3, the Waste Incineration Directive limit. Both MSWIs show a decreasing trend in particulate emissions from 2008 (Crymlyn Burrows) and 2009 (Marchwood) until 2010, from daily emissions of ~10 mg/m^3 to 1-2 mg/m^3. The maximum particulate emissions took place in 2008 for both MSWIs.

3.2. Dispersion Modelling. For Marchwood, three candidate meteorological stations were located within 30 km. The nearest meteorological station was Southhampton Oceanography Centre located 3.3 km east of Marchwood, followed by Solent (19.1 km south-east) and Middle Wallop (29.2 km north) (see Figure 3). For Crymlyn Burrows only one meteorological station was available located 9.4 km south-west from the incinerator.

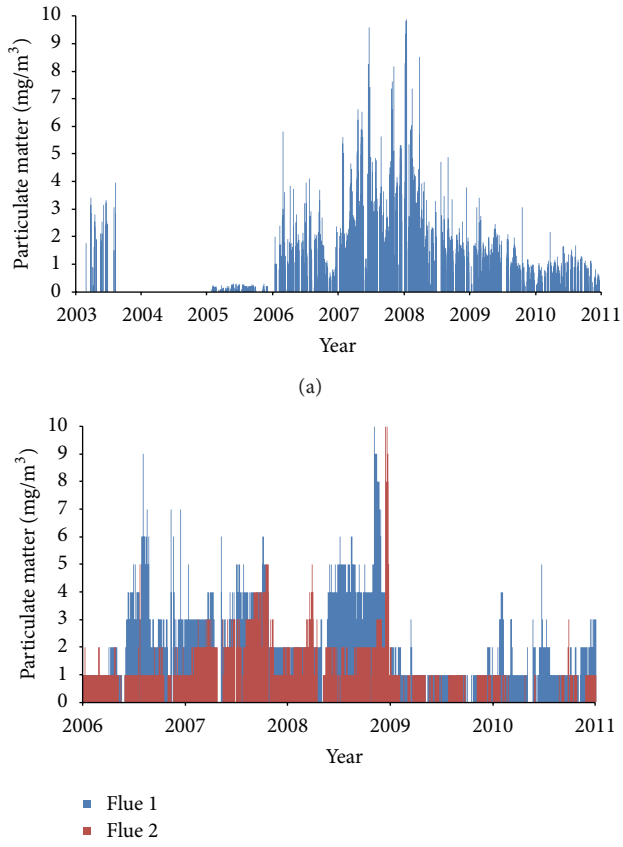
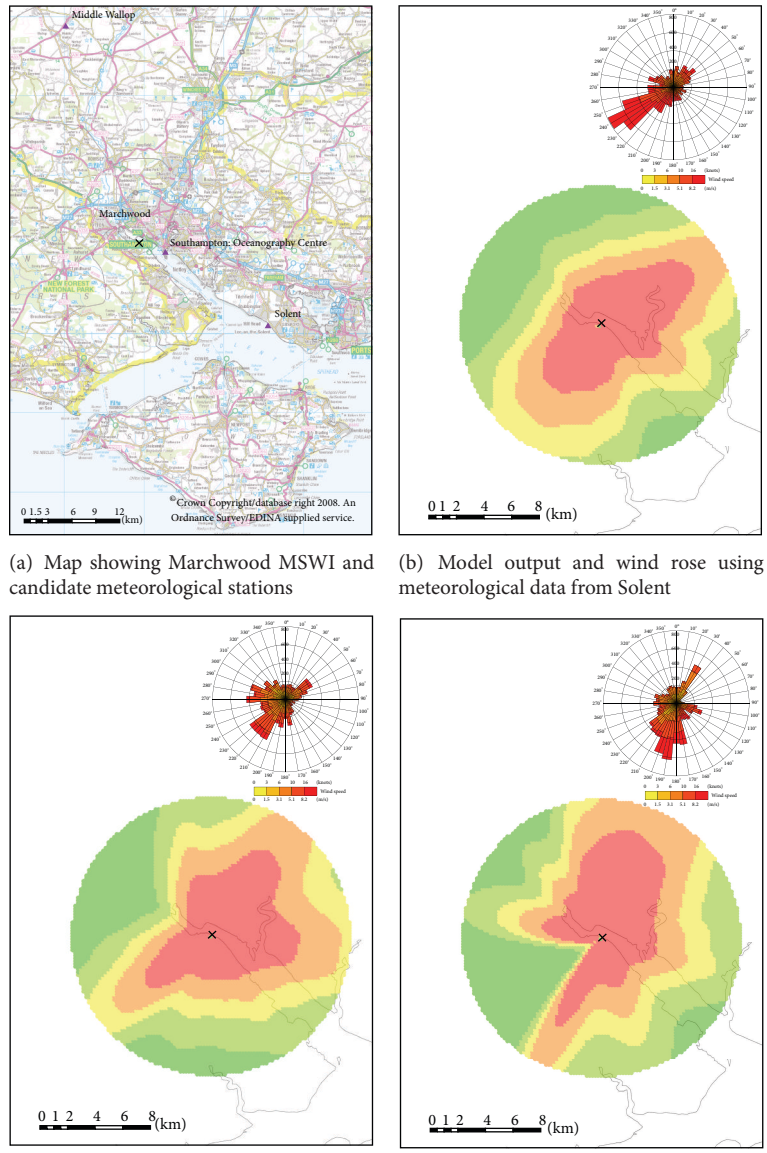


Figure 2: (a) Daily particulate concentrations measured at flue exit for Crymlyn Burrows from 2003 to 2010. (b) Daily particulate concentrations measured at flue exit for Marchwood from 2006 to 2010.

Comparisons were made between the three meteorological stations available for Marchwood. First, the wind roses for the three meteorological stations were compared. The wind rose for the Southhampton Oceanography Centre displayed very low frequency of wind from the north-east, between 50 and 80 degrees, for all years of operation (2006–2010) (Figure 3(d)). The other two meteorological stations, however, did not show this pattern (Figures 3(b) and 3(c)). The effect of this apparent gap in wind direction becomes particularly evident when using the data from these meteorological stations in our dispersion model simulations. Figure 3 shows the modelled annual mean particulate concentrations in 2006 using the three meteorological stations around Marchwood MSWI. The PM_{10} annual mean concentration using the Southampton Oceanographic Centre clearly shows a gap in the predicted concentrations south-west of the incinerator (Figure 3(d)), not seen when using the other two meteorological stations (Figures 3(b) and 3(c)). Based on this comparison the data from Southampton Oceanographic Centre meteorological station was deemed erroneous for unknown reasons and was therefore not used in subsequent



(a) Map showing Marchwood MSWI and candidate meteorological stations

(b) Model output and wind rose using meteorological data from Solent

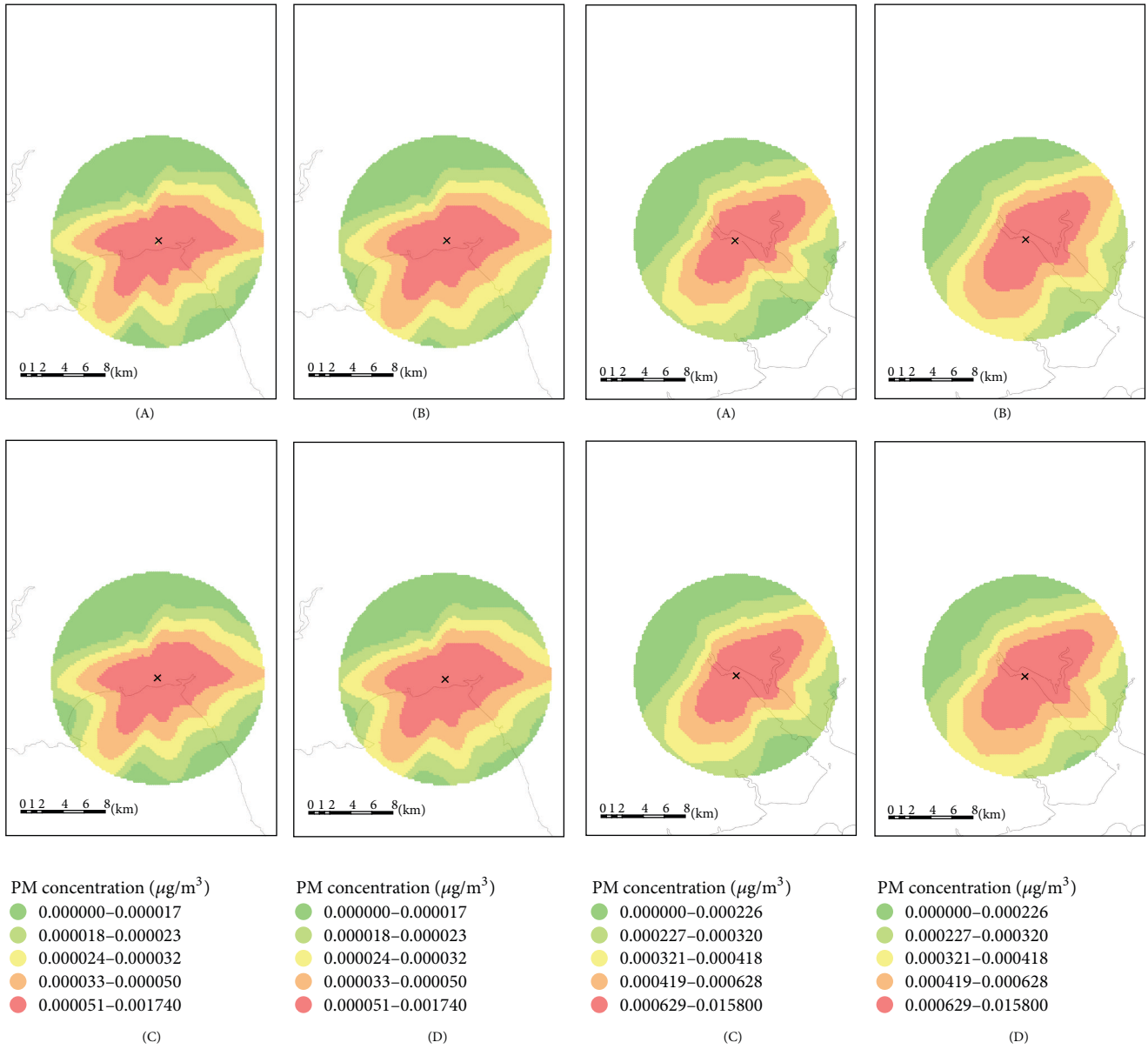
(c) Model output and wind rose using meteorological data from Middle Wallop

(d) Model output and wind rose using meteorological data from Southampton Oceanography Centre

FIGURE 3: Sensitivity of the model to the selected meteorological stations for Marchwood in 2006. Maps (b)–(d) use the same site surface roughness length and minimum Monin-Obukhov length.

analysis. The wind and dispersion patterns were similar for Solent and Middle Wallop, with higher PM_{10} concentrations in the SW-NE diagonal. Therefore the closest station, Solent, was selected for the exposure analysis. However when Solent cloud cover fell short of 90% capture annually, cloud cover data from Middle Wallop was used.

An exploration of surface roughness for both MSWIs showed little variation in the model output for surface roughness lengths varying from 0.2 m to 1 m (see Figures 4(a) and 4(b)). Only 7.7% of the model receptors had a difference in modelled particulate concentrations greater than 25% in Marchwood and 3.1% for Crymlyn Burrows



(a) (A) Model output using surface roughness length 0.2 m. (B) Model output using surface roughness length 1 m. (C) Model output using no set minimum Monin-Obukhov length. (D) Model output using 30 m set minimum Monin-Obukhov length

(b) (A) Model output using surface roughness length 0.2 m. (B) Model output using surface roughness length 1 m. (C) Model output using no set minimum Monin-Obukhov length. (D) Model output using 30 m set minimum Monin-Obukhov length

Figure 4: (a) Sensitivity of the model to site surface roughness length and minimum Monin-Obukhov length for Crymlyn Burrows. Maps (A)–(D) use the same meteorological station data for 2003. (b) Sensitivity of the model to site surface roughness length and minimum Monin-Obukhov length for Marchwood. Maps (A)–(D) use the same meteorological station data for 2006.

(Table 2). The difference in modelled particulate patterns and concentrations between no set minimum Monin-Obukhov length and 30m showed little variation, with a maximum percentage difference of 31% for Marchwood and 18% for Crymlyn Burrows (Table 2).

Table 3 demonstrates the extremely low concentrations of modelled annual PM_{10} concentrations within 10 km from the MSWI both for all days of the year (Table 3(a)) and also for only the days of operation (Table 3(b)). The modelled ground level concentrations of PM_{10} were extremely low for both MSWIs, with a mean concentration of 0.000117 μg/m^3 for Crymlyn Burrows for all days and 0.000334 μg/m^3 for operational days only; and 0.00129 μg/m^3 for Marchwood for all days and 0.00205 μg/m^3 for operational days only. Modelled long-term average PM_{10} concentrations were very small (maximum of 0.0022 μg/m^3 for Crymlyn Burrows and 0.0089 μg/m^3 for Marchwood). Figure 5 shows the modelled long-term average PM_{10} concentrations for both MSWIs

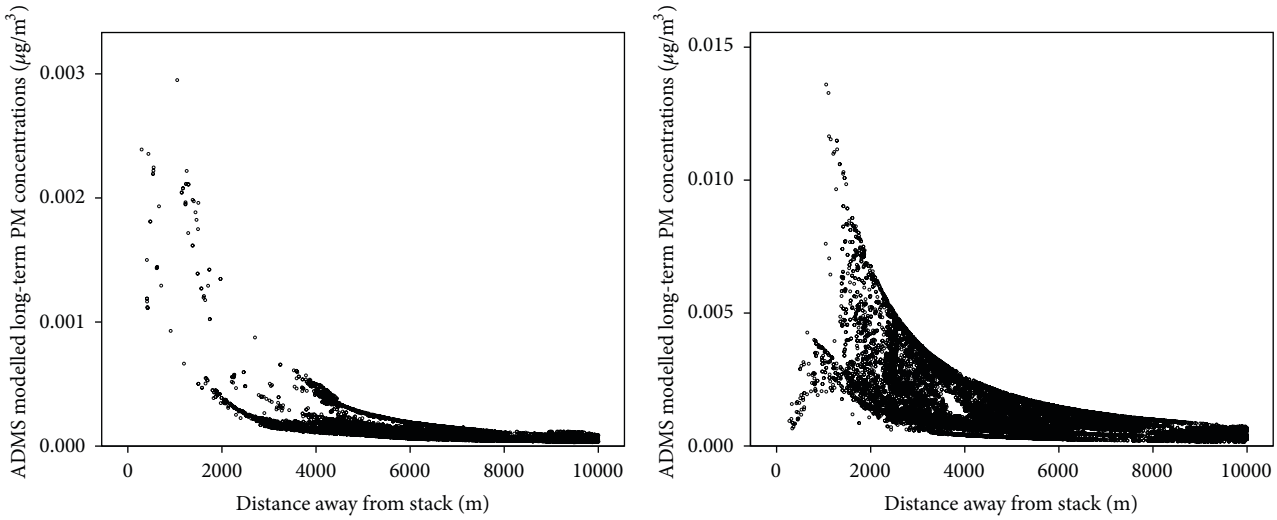


Figure 5: (a) Modelled long-term PM concentrations ($\mu g/m^3$) plotted against distance away from the MSWI (m) at postcode centroid for Crymlyn Burrows. (b) Modelled long-term PM concentrations ($\mu g/m^3$) plotted against distance away from the MSWI (m) at postcode centroid for Marchwood.

Table 2: Surface roughness sensitivity analysis. Percentage difference between extreme surface roughness values at all model receptors.

Percentage difference	Crymlyn Burrows	Marchwood
Surface roughness		
Mean (%)	8.7	12.3
Median (%)	6.9	11.2
Minimum (%)	0	0
Maximum (%)	116.6	117.5
Receptors > 25% difference (%)	3.1	7.7
Monin-Obukhov length		
Mean (%)	6.4	11.5
Median (%)	5.5	10.2
Minimum (%)	0	0
Maximum (%)	17.6	30.6
Receptors > 25% difference (%)	0	6.6

against distance from the MSWI at each postcode centroid. It is clear from Figure 5 that the concentrations at the 10 km edge of the modelled domain were <7% of the maximum concentration.

The pattern of the final dispersion model for Crymlyn Burrows showed irregular shapes, with symmetrical bands of increasing exposure from the source. This irregular dispersion pattern might be due to the hilly topography in the Swansea area that modifies the wind patterns and, therefore, the dispersion of emissions from the MSWI. Due to its coastal location a large proportion of the modelled area has no population. For Marchwood the final dispersion pattern was much more elliptical with the greatest PM_{10} concentration extending to the north-east of the MSWI following the main wind direction.

3.3. Distance to Source. Table 4 shows the number of postcodes and the population count in relation to distance from the two MSWIs. The area around the Marchwood MSWI is more densely populated (361,005 people within 10 km) than Crymlyn Burrows (248,937 people within 10 km). The population around Marchwood MSWI also resides closer to the MSWI than that at Crymlyn Burrows with the greatest population density between 3 km and 7 km.

3.4. Comparison of Exposure Assessment Methods. The agreement between exposure categories, as calculated by the dispersion modelling and distance methods, is shown in Table 5. Better agreement was achieved when using tertiles (Cohen's kappa coefficient of 0.424 unweighted and 0.553 weighted and 0.308 unweighted and 0.448 weighted from Crymlyn Burrows and Marchwood, resp.) compared with deciles and quintiles (Cohen's kappa coefficient ranging from 0.068 to 0.201 unweighted and 0.198 to 0.519 weighted).

Table 6 shows the population weighted agreement of the two exposure methods. Again, agreement improved with a reduction in the numbers of exposure categories. Best agreement between methods was displayed for Crymlyn Burrows exposure tertiles (but here the unweighted Cohen's kappa coefficient only reached 0.425, equally weighted Cohen's kappa coefficient only reached 0.548) and the poorest agreement for Marchwood exposure deciles (unweighted Cohen's kappa coefficient 0.0644, equally weighted Cohen's kappa coefficient 0.150).

Figure 5 shows the long-term mean PM_{10} concentration at each postcode centroid against distance from MSWI for Crymlyn Burrows (Figure 5(a)) and Marchwood (Figure 5(b)). Spearman correlations (R) for modelled long-term PM_{10} concentrations versus proximity from the edge of the modelling domain at postcode level were 0.765 and 0.688

Table 3: (a) Annual mean, median, and interquartile range of modelled PM_{10} concentration in the postcodes 10 km around Crymlyn Burrows (2003–2010) and Marchwood (2006–2010) weighted by postcode. (b) Annual mean, median, and interquartile range of modelled PM_{10} concentration in the postcodes 10 km around Crymlyn Burrows (2003–2010) and Marchwood (2006–2010) weighted by postcode for operational days only.

(a)

	Mean ($\times 10^{-5}$ $\mu g/m^3$)	Median ($\times 10^{-5}$ $\mu g/m^3$)	Interquartile range ($\times 10^{-5}$ $\mu g/m^3$)
Crymlyn Burrows			
2003	3.7	3.0	2.5
2005	0.8	0.6	0.5
2006	10.8	8.2	6.8
2007	29.4	24.2	17.1
2008	22.0	16.5	15.2
2009	10.3	7.7	7.1
2010	4.9	3.9	3.0
Marchwood			
2006	121.5	80.0	101.6
2007	186.3	127.7	149.9
2008	229.5	139.5	200.8
2009	59.6	44.5	50.3
2010	48.9	36.4	32.2

(b)

	Mean ($\times 10^{-5}$ $\mu g/m^3$)	Median ($\times 10^{-5}$ $\mu g/m^3$)	Interquartile range ($\times 10^{-5}$ $\mu g/m^3$)	Days of operation		
Crymlyn Burrows						
2003	51.5	4.25	31.7	33		
2005	2.61	2.10	1.59	150		
2006	29.1	23.6	17.1	204		
2007	61.2	51.1	33.6	264		
2008	52.7	42.6	32.6	227		
2009	23.1	18.8	13.8	225		
2010	13.3	10.6	7.77	188		
				Flue 1	Flue 2	Either one or both flues in operation
Marchwood						
2006	207.3	140.9	154.3	308	240	334
2007	290.6	204.1	221.5	325	327	344
2008	338.1	212.7	262.7	340	325	358
2009	96.9	72.5	72.0	296	192	357
2010	91.7	69.8	59.1	323	104	356

for Crymlyn Burrows and Marchwood, respectively (both significant at the 0.01 level).

4. Discussion

The majority of the studies exploring the relationship between incineration and health have used a simple distance metric as a proxy for exposure. Here we have provided a comparison of distance from source and emissions modelling to assess exposure to particulates emitted by two MSWIs in the UK. Our results suggest that epidemiological studies requiring an assessment of exposure to airborne pollutants from MSWIs, at a small scale level, would benefit from a dispersion modelling approach compared to a simple distance based approach. Although the use of distance as a proxy for exposure has limited data requirements, it does not account for source characteristics, the concentrations of pollutants emitted, local meteorological conditions, and topography [31, 50] all of which are incorporated in Gaussian dispersion models, such as ADMS-Urban. Dispersion models provide a different exposure assessment to distance from source. This approach is expected to be more realistic than a simple distance proxy as it tries to capture the physical processes that determine the dispersion of emissions from a point source

Table 4: Distance of the study population (all residents within 10 km) to the incinerators, Crymlyn Burrows and Marchwood.

Distance to source (km)	Crymlyn Burrow				Marchwood			
	Number of PCs	Percentage of total PCs (%)	Population count	Percentage of total population (%)	Number of PCs	Percentage of total PCs (%)	Population count	Percentage of total population (%)
0–<1	22	0.2	165	0.1	87	0.5	1677	0.5
1–<2	69	0.5	834	0.3	813	4.2	12829	3.6
2–<3	229	1.8	5067	2.0	2363	12.3	31729	8.8
3–<4	777	5.9	14590	5.9	2720	14.2	46690	12.9
4–<5	2623	20.1	38736	15.6	2969	15.5	59070	16.4
5–<6	2496	19.1	49338	19.8	2999	15.6	69784	19.3
6–<7	2365	18.1	51665	20.8	2171	11.3	48832	13.5
7–<8	1982	15.2	39467	15.9	1378	7.2	25298	7.0
8–<9	1256	9.6	25853	10.4	1611	8.4	32654	9.0
9–10	1251	9.6	23222	9.3	2055	10.7	32442	9.0
Total	13070	100	248937	100	19166	100	361005	100

PC: postcodes.

Table 5: Measure of agreement Kappa coefficient (where 0 = no agreement; 1 = perfect agreement) between modelled long-term PM_{10} concentrations and distance away from stack categorised in deciles, quintiles, and tertiles at postcode level.

	N	Type of Kappa	Deciles	Quintiles	Tertiles
Crymlyn Burrows	13069	Unweighted	0.0684	0.210	0.424
		Weighted-Equal	0.307	0.519	0.553
Marchwood	19166	Unweighted	0.0734	0.177	0.308
		Weighted-Equal	0.198	0.446	0.448

Table 6: Measure of agreement Kappa coefficient (where 0 = no agreement; 1 = perfect agreement) between population weighted modelled long-term PM_{10} concentrations and distance from the stack categorised in deciles, quintiles, and tertiles at postcode level.

	N	Type of Kappa	Deciles	Quintiles	Tertiles
Crymlyn Burrows	5269	Unweighted	0.0932	0.251	0.425
		Weighted-Equal	0.334	0.535	0.548
Marchwood	8102	Unweighted	0.0644	0.169	0.219
		Weighted-Equal	0.150	0.380	0.345

including topographic and meteorological information that influence where and how emissions are dispersed. ADMS-Urban has been successfully used and validated when assigning exposure at an individual or small area level [34–37] and is frequently used for regulatory purposes, policy support, and providing information to the public [32]. Dispersion modelling can additionally help determine the distance to which a particular source influences exposures, as shown in Figure 5, where modelled PM_{10} falls to <7% of peak concentrations at 1000 m to 2000 m away from the MSWI. The comparison between dispersion modelling and distance for the two MSWIs studied here (see Table 5 and Figure 5) reveals poor to moderate agreement only when using distance compared with dispersion modelling. Both methods assigned a decreasing exposure with an increasing distance from source (as shown by the strong spearman's correlations with continuous measures). However, when using categorical metrics (as are often employed in epidemiological studies) distance was a fairly good proxy in distinguishing highest and lowest exposure tertiles, but the dispersion model was able to capture the pattern of small area level variation in population exposure (Figures 3 and 5), which did not conform to circular dispersion around the source as would be predicted using a distance model.

The influence of stack height on the dispersion pattern was especially apparent for the Marchwood MSWI, which shows very small PM_{10} concentrations up to approximately 500 m (Figure 5(b)), after which they peak between 1000 and 2000 m, depending on the direction. This pattern was less apparent at the Crymlyn Burrows MSWI, mainly due to the lack of postcodes within 2000 m of the MSWI.

Both Figures 5(a) and 5(b) show a flattening in modelled PM_{10} concentrations beyond approximately 5 km, suggesting that, at least for the Crymlyn Burrows and Marchwood

MSWI, most variability in exposure occurs within 5 km of a MSWI and this was therefore captured well within the 10 km distance chosen in this assessment.

Model input parameters influenced both the pattern and concentration of the modelled PM_{10}, in turn affecting the modelled exposed population. It is therefore essential that the quality of the model input parameters is assessed. It was found that the model was sensitive to surface roughness length, Monin-Obukhov length, and meteorological conditions. The model output showed little relative variation in output concentrations with different input parameters with the exception of changes in meteorological station. We demonstrate here that the choice of meteorological input data is crucial. As shown in Figure 3, possible misclassification of exposure is evident from the use of different meteorological stations, particularly in the case of the south-west part of the Marchwood MSWI.

The dispersion model simulations in this study were subject to a number of limitations that would contribute to the uncertainty in the ground level exposure estimates produced. Firstly, Marchwood only had a single measure of flue gas flow, velocity, and temperature for the duration of its operation (2006 till 2010), whereas Crymlyn Burrows had quarterly measures of these flue gas metrics for most years of operation which showed substantial variation. The assumption that these flue exit parameters are constant over such long periods of time is therefore not representative of true conditions. Additionally, due to data availability, poor data quality, and completeness, the choice of meteorological sites was limited and it was challenging to find meteorological sites representative of the surrounding area. This was especially evident for Marchwood where the selected meteorological site (Solent) was located 19 km away from the MSWI. Additionally, although ADMS-Urban has been validated as a point source modelling tool in other scenarios, the long-term mean concentrations of modelled PM_{10} in this study were exceptionally low, and therefore model validation would not be possible, as they fall below the limit of detection for regulatory ambient measurements.

There are a number of disadvantages to using dispersion models, including their large input data demands, which are often unavailable, and the expertise required to successfully run and interpret the models [31]. To meet the EU Directive requirements the MSWIs in this study, along with those elsewhere in Europe, are now required to have daily measurements of particulate emissions. This allows time varying emissions to be included in modelled assessments for the first time. This is beneficial for calculating exposures linked to health endpoints with critical exposure periods, for example, trimester specific exposures for birth outcomes.

Although long-term ground level PM_{10} levels from these MSWIs were found to be approximately thousandths of regional background levels, it is hypothesised that particulates from MSWIs may possibly have different impacts on health than those from other ambient sources of particulate matter due to their metal or dioxin content, for instance. The modelled concentrations of PM_{10} may act as a proxy for the concentration fields for these and other primary emissions from MSWIs. While long-term PM_{10} concentrations from dispersion modelling may provide a good indication of ambient concentrations, this will still be an imperfect marker of personal exposure. An alternative individual level exposure could be measured by personal monitoring or collection and analysis of biomarkers. However, such personal exposure approaches, aside from being very expensive and time-consuming and (for biomarkers) potentially invasive, may not adequately capture exposures specific to MSWIs.

5. Conclusions

Using distance as a proxy measure of exposure to emissions from incinerators is a simple, quick, and cheap approach; however, when compared with dispersion modelling, there is indication of exposure misclassification. Dispersion models incorporate information on individual incinerator characteristics, emission concentrations, local meteorological conditions, and topography, all of which contribute to the observed concentrations and spatial patterns of incinerator emissions. The additional detail included in these models enables a more appropriate and informative exposure assessment from incinerators, which is important in an epidemiological context in order to reduce risk of bias in risk estimates due to exposure misclassification.

Disclaimer

This report is a work commissioned by the National Institute of Health Research. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health.

Conflict of Interests

All authors declare no conflict of interests with any trademarks mentioned in this paper.

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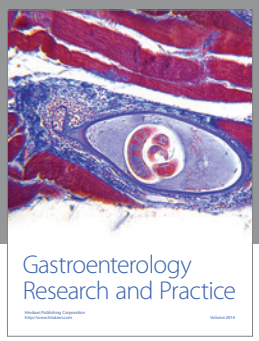
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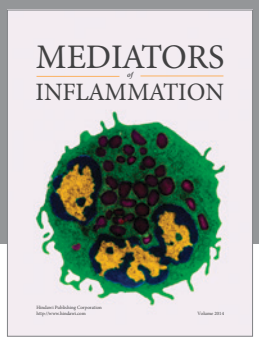
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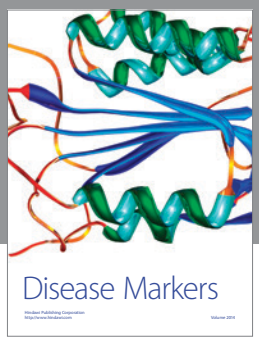
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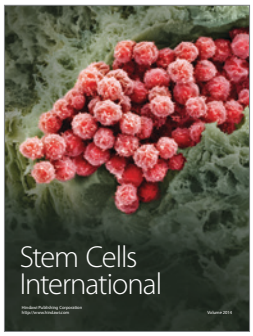


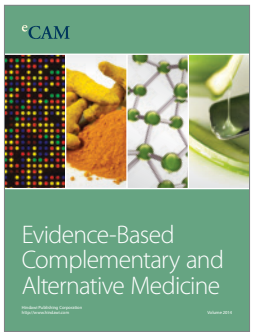




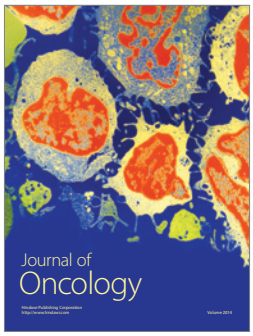


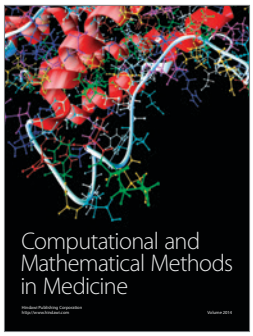


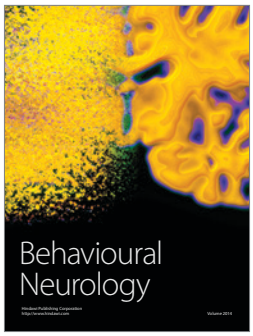




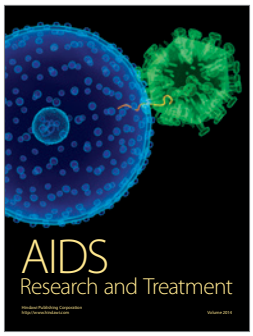


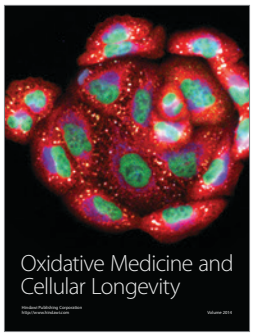












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APPENDIX D

Does the rubbish you create affect your health?

Incinerators Biomonitoring Study

Version 2
12th April 2013

Main sponsor: Imperial College London and Imperial College Healthcare NHS trust
Funder: MRC Centenary Award awarded by the MRC-HPA Centre for Environment and Health
Research site: Department of Epidemiology and Biostatistics, Faculty of Medicine, Imperial College London

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- University Hospital Southampton NHS foundation trust
- South Tees Hospitals NHS foundation trust
- North Tees & Hartlepool NHS foundation trust

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Funder

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Glossary of abbreviations

PCDD	Dibenzo-*p*-dioxin
PCDF	Diobenzofurans
SAHSU	Small Area Health Statistics Unit
MSWI	Municipal Solid Waste Incinerator
HPA	Health Protection Agency
EA	Environment Agency
BINOCAR	British Isles Network of Congenital Anomaly Registers

ADMS	Atmospheric Dispersion Modelling System
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
PIC	Participant Identification Centre
NIHR	National Institute for Health Research
CRN	Clinical Research Network
CLRNs	Comprehensive Local Research Network
PIS	Participant information sheet
CDC	Centers for Disease Control and Prevention
cPCBs	Polychlorinated biphenyl
SCF	Scientific Committee for Food
WHO	World Health Organisation

Abstract

This is a protocol for a biomonitoring study, the Incinerators Biomonitoring Study, which is an academic study to be conducted as part of Danielle Ashworths' PhD at Imperial College London. The Incinerators Biomonitoring Study is a standalone study linked to the Small Area Health Statistics Unit (SAHSU) study on municipal solid waste incinerators (MSWI) and adverse birth and neonatal outcomes. The SAHSU study was initiated in response to ongoing public concern about health risks associated with pollutants emitted from incinerators. Incinerators release a number of pollutants including a group of chemicals that are persistent in the environment, known as dioxins. The Incinerators Biomonitoring Study will investigate the relationship between modelled ambient dioxin exposure and individual level breast milk dioxin exposure, in approximately 100 pregnant women. Dispersion models will be used to identify areas of modelled high and low dioxin exposure from two selected MSWIs, Marchwood and Stockton-on-Tees. Eligible study participants will be identified through their maternity hospitals, located near the selected MSWIs. Eligible participants are women in their second and third trimester of their first pregnancy, living in modelled high and low dioxin exposure zones, over 18 years of age. These women will be invited to take part in this study via post. Following consent, women will be asked to complete a questionnaire (during pregnancy) and provide a breast milk sample (between 1-6 weeks after birth). Breast milk samples will be sent to the Organic Analytical Toxicological Branch laboratories at the Centers for Disease Control and Prevention, Atlanta, USA for dioxin analysis. This study will acquire a personal biomarker of dioxin exposure for a small group of pregnant women, using this we will be able to investigate the relationship between; modelled ambient dioxin exposure and individual level dioxin exposure and individual dioxin exposure and distance to a MSWI. Additionally the Incinerators Biomonitoring Study will aid the interpretation of the SAHSU study results and enhance this important, high profile, national study.

Study summary

Title	Incinerators Biomonitoring Study
Methodology/Design	-Questionnaire study -Biomonitoring study of breast milk samples (tissue collection)
Aims	To investigate the relationship between modelled area level ambient dioxin

	exposure and individual level breast milk dioxin exposure in residents living near two municipal solid waste incinerators in England
Outcome measures	*Primary outcome measure:* The correlation coefficient between individual milk dioxin levels and modelled ambient dioxin concentrations. *Secondary outcome measures*: To acquire a personal biomarker of dioxin exposure for a small group of pregnant women and allow the exploration of individual dioxin exposure and its relationship with; distance to a dioxin emitting source, an incinerator, and dietary habits. The study results will additionally help interpret the results of the national epidemiological study on municipal solid waste incinerators and birth outcomes being conducted by the Small Area Health Statistics Unit at Imperial College London.
Study population	100 pregnant women
Eligibility	Primiparous pregnant women in their second and third trimester of pregnancy, resident in modelled high and low dioxin exposure areas, over 18 years of age
Study duration	Approximately 10 months

This protocol describes the Incinerators Biomonitoring Study and provides information about the procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

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1. Introduction

1.1 Background

EU legislation has placed restrictions on the amount of municipal waste disposed of in landfills[1]. This has increased the use of incineration as a waste management method in the UK. To date there is considerable public concern over potential health risks associated with incineration and in particular with incinerator emissions. Incinerators emit a number of pollutants, including; particulates, heavy metals and polychlorinated dibenzo-*p*-dioxins (PCDDs) and diobenzofurans (PCDFs), known from now on as "dioxins". To address public concerns, researchers from the Small Area Health Statistics Unit (SAHSU) at Imperial College London, have initiated an epidemiological study to investigate the association between municipal solid waste incinerator (MSWI) emissions and adverse birth and neonatal outcomes (Appendix 1). This SAHSU study is funded by the Health Protection Agency (HPA) and the Environment Agency (EA) and is in collaboration with British Isles Network of Congenital Anomaly Registers (BINOCAR). Specifically, the SAHSU study is investigating the relationship between dispersion modelled ground level concentrations of particulates, heavy metals and dioxins, from MSWIs in England and Wales, operating under current legislation (EU directive 2000/76/EC[2]), and low birth weight, stillbirths, small for gestational age, preterm delivery, sex ratio, infant deaths and congenital anomalies. Ground level concentrations of particulates, heavy metals and dioxins from MSWIs are currently being modelled using the second generation dispersion model Atmospheric Dispersion Modelling System (ADMS), developed by Cambridge Environmental Research Consultants. These models require information on incinerator stack characteristics, surrounding topographic and metrological conditions and the concentration of emitted pollutants. The concentration of heavy metals, dioxins and particulates emitted at each incinerator, measured at the flue exit, between 2003-2010 are being provided to SASHU by the EA. The dispersion models built will be used to estimate trimester-specific exposures from MSWIs for individuals at their birth postcode.

This protocol is for the Incinerators Biomonitoring Study that is a standalone study linked to SAHSU's study investigating the association between exposure to MSWIs emissions and birth and neonatal outcomes (covered by the SAHSU ethics: Appendix A: 12 LO 0566 Favorable opinion letter) and Appendix B: 12 LO 0567 Decision Letter).

1.2 Rational for study

The aim of the Incinerators Biomonitoring Study is to assess the relationship between modelled area level ambient dioxin exposure and individual level breast milk dioxin exposure in residents

living near two MSWIs, Marchwood in Hampshire and Stockton-on-Tees in Cleveland, in England.

Epidemiological studies on environmental exposures often involve trying to detect small excess risks[3]. Unfortunately these studies are also often limited to surrogate, indirect measures of exposure at the ecological level. While the SAHSU MSWI study is using dispersion modelling as the primary means of exposure assessment, an improvement on the use of simple distance based measures used in most previous studies[4-10], it is still possible that there will be misclassification of exposure and that the semi-ecological design will not accurately reflect exposure at an individual level. The Incinerators Biomonitoring Study proposes to use personal biomarkers of dioxin exposure for a small group of pregnant women to investigate the relationship between modelled ambient dioxin concentrations and breast milk dioxin levels. This study will help to understand whether the built exposure models reflect exposure to dioxins at an individual level. Additionally this study will aid the interpretation of the findings of the important, high profile, national epidemiological study around MSWI conducted by SAHSU. Ideally it would be best to obtain biomarkers of dioxin exposure for all study participants, however the resources required to undertake this type of study are unavailable. Therefore the study participants will be pregnant women within the study area, 10km around the selected MSWIs.

We propose this study to include two key components:

- Study questionnaire- to acquire information on individual study participants' socio-demographic characteristics, lifestyle factors and dietary habits.
- Self-collected 20mL breast milk sample- for dioxin analysis.

2. Study aim and objectives

Aim: To investigate the relationship between modelled area level ambient dioxin exposure and individual level breast milk dioxin exposure in residents living near two MSWIs in England.

Objectives: To gather a detailed personal exposure profile to dioxins for approximately 100 pregnant women residing near two MSWIs in England, Marchwood and Stockton-on-Tees.

3. Study design

3.1 Individual level dioxin exposure

Dioxins are both persistent and lipophilic. These properties mean that dioxins are stored in adipose tissue for long periods of time. There are approximately 75 congeners of PCDD's and 135 PCDF's[11], each with different half-life's in the human body. A review by Milbrath *et al*[12] on dioxin half lives, showed that in most studies exposure to dioxins was occupational or from contamination incidents, e.g. the contamination of rice oil in Japan, Yusho, and Taiwan, Yu-Cheng. The most commonly studied dioxin congener was 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), which, based on 14 studies, has a half life ranging from 1.5 to 11.3 years in adults[12]. Half

lives show considerable variation by congener and within individuals, influenced by age, body fat, smoking and breast feeding[12].

To quantify an individuals' exposure to dioxins, biomarkers of dioxins can be measured in blood serum and breast milk. Dioxin congeners partition from adipose tissue into milk in a different way to serum[13]. Studies investigating the relationship between dioxin concentrations in both matrices show very similar trends in the distribution of dioxin congeners. Wittsiepe *et al*[14] collected blood during pregnancy and breast milk after delivery for 160 study participants and reported a very good correlation of dioxins levels in blood and milk, with a Pearsons correlation coefficient of 0.83. The authors reported WHO-TEQ in blood ranged from 2.73 to 55.07pg/$g_{\text{lipid base}}$ (mean:16.79, median:15.32) and 1.80 to 34.70pg/$g_{\text{lipid base}}$ (mean:13.84 and median:13.30) in breast milk. This study is unique in that both matrices were derived from each participant, whereas most studies exploring dioxin levels in blood and breast milk collect samples from different participants. A literature view by Mannetje *et al*[13] showed mean serum/milk ratios to increase with dioxin molar volume, hydrophobicity and halogen substitutes.

This study requires a measure of individual uptake of dioxins which could be measured in either blood serum or breast milk. Dioxin analysis in blood serum is advantaged in that it provides the best estimation of body burden, additionally blood can be drawn from a wider population than breast milk, including men and women who do not breastfeed. The disadvantages of dioxin analysis in blood serum include; the amount of blood required for analysis (50mL), the preparatory laboratory analysis required before the dioxin analysis (serum extraction) and the practical difficulties of collecting blood samples. The key advantages of using breast milk over serum are both the practical advantages, collecting breast milk is both non invasive and simple, in addition to the lower detection limit for dioxins in breast milk compared with serum as a result of the higher fat content in milk. Weighing up the advantages and disadvantages of dioxin analysis in both matrices it was decided that for this study dioxins will be measured in breast milk.

There are a number of issues which need to be taken into consideration when dioxins are measured in breast milk. The composition of breast milk changes with both time from birth and in the duration of a feed. For approximately one week after birth breast milk is known as colostrum, milk that is high in protein (10%) and low in fat (1%). Following this, more mature milk is produced which is lower in protein (1%) and higher in fat (4%)[15]. Additionally the amount of fat in breast milk increases over each feed, starting with the most watery thirst quenching milk then moving towards the fattier milk towards the later part of the feed[15]. The Incinerators Biomonitoring Study will therefore ask participants to provide a small (20mL) breast milk sample at the end of a feed between 1-6 after birth. This time frame will ensure mature milk is collected and also that the greatest number of women are incorporated in the study, as the number of infants breastfeeding dramatically decreases after 6 weeks following birth.

3.2 Inclusive municipal solid waste incinerators

The potentially inclusive MSWI's for the Incinerators Biomonitoring Study were identified as all 20 operational MSWI's in England in 2010. Following this, both island MSWI's, one on the Isles of Scilly and one on the Isle of Wight, were excluded. Of the remaining 18 MSWI's, Marchwood

and Stockton-on-Tees were selected for inclusion. Marchwood and Stockton-on-Tees were chosen because they are both located in areas with; 1) relatively high ambient dioxin levels area[16] (helping to ensure dioxins can be detected) 2) a limited number of additional dioxin emitting sources. Table 1 below provides the characteristics of the five MSWI's in England with the highest mean dioxin concentrations within a 10km radius around the incinerator. Figure 1 displays the location of the 21 operational MSWI in England and Wales in 2010, with the selected MSWI's for this study shown in red.

Table 1: Characteristics of five English MSWIs with the highest mean dioxin concentrations within a 10km radius.

MSWI	Mean dioxin concentration	Dioxin range (Maximum-Minimum)	Number of surrounding dioxin sources (ranging from 1-11)	Tonnage (tonnes per year)	Date commissioned
Dudley	0.0467	12.8	11	105,000	1998
Sheffield	0.0240	5.93	10	225,000	2006
Stockton-on-Tees	**0.00994**	**2.42**	**5**	**263,000**	**1998**
SELCHP	0.00649	0.0822	9	420,000	1994
Marchwood	**0.00607**	**0.705**	**6**	**165,000**	**2006**

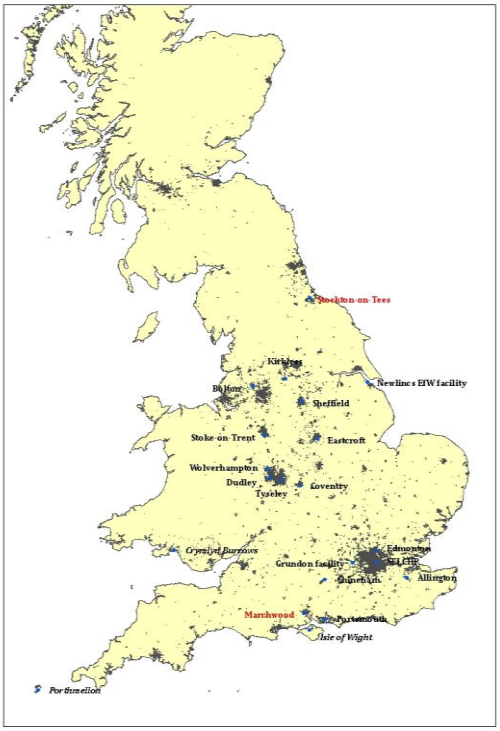


Figure 1: Location of 21 operational MSWI's in England and Wales in 2010.

3.3 Study location and setting

The research for the Incinerators Biomonitoring Study will be conducted at Imperial College London. However, the identification of participants and study invitation letters will be sent from maternity hospitals, participant identification centres (PICs), situation within 10km from the two MSWIs, Marchwood, located near Southampton in Hampshire, and Stockton-on-Tees, located near Middlesbrough in Cleveland (Appendix 2). Local collaborators at two NHS foundation trusts have been identified. One at the University Hospital Southampton NHS foundation trust and one at the South Tees NHS foundation trust.

In order to gain support for this study, in particular for the recruitment of study participants, an application was been made for this study to be adopted into the National Institute for Health Research (NIHR) portfolio. This study was assessed as eligible for consideration for Clinical Research Network (CRN) support and has been included in the NIHR portfolio. As the Marchwood MSWI falls within the Hamphire and Isle of Wight Comprehensive Local Research Networks (CLRN), it has been confirmed that the Hampshire and Isle of Wight will act as the lead CLRN on this project and therefore the University Hospital Southampton NHS Foundation Trust will be the lead NHS organisation.

3.4 Study design

Study type: Questionnaire and biomonitoring (tissue collection study)

Duration of study: We anticipate that the Incinerators Biomonitoring Study will take approximately 10 months to conduct. Study participants could potentially be involved in the study for a maximum of 7 and a half months. This maximum time would be for women who were both; recruited, provided consent, on the first day of their second trimester of pregnancy and provided a breast milk sample at the latest available day, 6 weeks after birth.

- End of data collection: the last breast milk sample collected.
- End of dioxin analysis: results of dioxin analysis received by study team at Imperial College London from the analyzing laboratory.
- Preliminary study end: data analysis has been conducted and study aims addressed, all study results written up in chief investigators PhD thesis.
- Final end of study: study results submitted to peer reviewed journals.

Number and type of subjects: Recruitment to the Incinerators Biomonitoring Study will be for women in their second and third trimester of their first pregnancy (primiparous pregnant women), over 18 years of age, living in areas defined by ADMS dispersion models as high or low dioxin areas surrounding each of the two selected MSWIs. We aim to recruit approximately 100 participants to this study. All eligible participants will be identified by the PICs (maternity hospitals) through database searches and these women will be invited to take part in this study via a letter. All study invitation packs will be provided by the study team to the maternity hospitals and postages costs covered. The study invitation packs will include:

- A study invitation letter (Appendix 3).
- A participants information sheet (PIS), (Appendix 4), providing the potential study participant with information about the study and what it will involve if they decide to take part.

- A consent/recruitment form (Appendix 5).
- A prepaid addressed envelope to Imperial College London. This will allow participants to post their completed consent forms back to the study team at Imperial College London.

As the study invitation packs will be sent from the maternity hospitals, no investigators from the study team will have any information on, or contact with, potential study participants until consent forms have been received. The consent form (Appendix 5) requires the participant to provide a written signature. Additionally this form collects information on the study participants' residential address, expected due date and whether they intend on breast feeding. Only once the consent forms have been received by the study team at Imperial College London, will a participant be enrolled in the study and assigned a unique study ID.

A list of the participants who consented to take part in the study will be sent to the local collaborators at the PICs. Following this, the two local collaborators will check the maternity records of the study participants regularly (weekly or every fortnight) and provide the study team with information on whether any of the participants have given birth or experienced any adverse birth outcomes, for example in the case of a miscarriage or stillbirth. Women who have had a miscarriage or stillbirth will be automatically withdrawn from the study and will not be contacted by the study team.

All participants progressing normally in pregnancy will be sent a study pack to their home address at approximately 6 weeks before their due date. The study pack will include:

- A study questionnaire (with only the participants study ID's documented on the questionnaire) (Appendix 6).
- A manual breast pump.
- A glass screw-capped bottle for milk storage and shipping (pre-labelled with study ID only).
- Instructions on how and when to take the breast milk sample (Appendix 7).
- A form for the participants to fill in about when the breast milk sample was taken (Appendix 8).

After a participant has expressed their milk sample, using the breast pump provided, they will be asked to store it in the glass bottle provided in their domestic freezer. Once the breast milk samples have been collected the study participants will be asked to contact the chief investigator to arrange a suitable time for their; frozen breast milk sample, breast milk sample form and completed study questionnaire to be picked up from their home. If a participant has not contacted the study team by 4 weeks after their due date, the study team will contact the participant using the contact details they provided on their consent form. Please note, as discussed above, because maternity records will be checked on a regular basis by the local collaborators, no women who have experiences adverse birth outcomes will be approached.

Frozen breast milk samples will then be shipped to the Organic Analytical Toxicological Branch laboratories at the Centers for Disease Control and Prevention (CDC) in Atlanta, USA on dry ice for chemical analysis. The CDC has long-standing analytical expertise in the measurement of dioxins. Samples will be analysed for 21 PCDDs/PCDFs and dioxin like Polychlorinated biphenyl (cPCBs) by high-resolution gas chromatography- isotope dilution mass spectroscopic analysis. Contact has been established with the CDC and in principal they have agreed to perform the

dioxin analysis.

3.5 Study outcomes

The primary outcome measure for the Incinerators Biomonitoring Study is the correlation coefficient between individual milk dioxin levels and modelled ambient dioxin concentrations. This will answer the study aim and determine if modelled area level ambient dioxin exposure is reflected in individual level breast milk dioxin exposure in residents living near two MSWIs in England.

As a secondary outcome measure this study will acquire a personal biomarker of dioxin exposure for a small group of pregnant women and allow the exploration of individual dioxin exposure and its relationship with; distance to a dioxin emitting source, a MSWI and dietary habits. Finally, the results of the Incinerators Biomonitoring Study will help interpret the results of the national epidemiological study on MSWIs and birth outcomes being conducted by SAHSU.

4. Participant entry

The identification of study participants and invitation to the Incinerators Biomonitoring Study will occur through participant identification centres (PICs), maternity hospitals, surrounding Marchwood and Stockton-on-Tees MSWI, with the aim to recruit 100 participants. Study participants will be recruited antenatally because postnatal recruitment was thought to be approaching women in a particularly vulnerable time, in addition to not allowing the women sufficient time to consider whether they want to take part in the study.

Women eligible to take part in the Incinerators Biomonitoring Study are; primiparous pregnant women in their second and third trimester of pregnancy who are resident in areas modelled as high and low dioxin exposure over 18 years of age. These eligible participants will be identified by the PIC through a database search. Women with previous children were excluded from this study because there is a substantial volume of literature linking parity and the concentration of fat-soluble contaminates, such as dioxins, in breast milk[17]. It is suggested that this maybe a result of lactation reducing the amount of stored dioxins in breast milk. Dioxins are therefore expected to be highest, maximising detection, for primparious pregnant women. Furthermore, pregnant women under 18 years of age were excluded from this study. This ensures consent to take part in this study is only required from the participant themselves and not additional parties i.e parents or guardians.

Funding limits the ability for this study to account for potential participants who do not adequately understand the study information provided in English. Therefore participants without a good understanding of English will be excluded from the study. Due to: a) dropout/non-compliance b) women unable or choosing not to breast feed c) women losing their baby, we will aim to over recruit initially.

As stated in the study invitation letter (Appendix 3), the PIS (Appendix 4) and the consent form (Appendix 5) participation in this study is entirely voluntary and any woman is free to withdraw from the study at any time without their medical care being affected in any way. No

children or adults unable to provide consent for themselves will be approached to take part in the study.

5. Study stages

The stages of the Incinerators Biomonitoring Study are outlined below:

1) PICs to conduct a database search to identify eligible study participants.
2) Study invitation packs sent out to approximately 500 potential study participants, 250 in Southampton and 250 in Middlesbrough, from the two maternity hospital via post (all packs previously provided and postages covered by the study team at Imperial College). The study invitation pack will contain; i) an invitation letter (Appendix 3), ii) a PIS (Appendix 4) iii) a consent/recruitment form (Appendix 5) iii) a prepaid envelope addressed to Imperial College London. The study invitation packs will be sent out in batches, 100 at a time, in order to monitor response rates and most efficiently use resources.
3) Study participants to complete consent/recruitment forms (Appendix 5) and send this back to Imperial College London in prepaid envelope provided in their invitation packs.
4) A list of study participants providing consent sent to the local collaborators at the PICs. Routine checks by the local collaborators to identify participants who have given birth and those with adverse birth outcomes.
5) At approximately 6 weeks before a participants due date, participants who have not experienced an adverse birth outcome will be sent a study pack by the study team at Imperial College. The study pack will include; i) a study questionnaire (Appendix 6) ii) a manual breast pump iii) a glass screw-capped bottle for milk storage and shipping (prelabelled with study ID only) iii) instructions on how and when to take the breast milk sample (Appendix 7) iv) a short form to be filled in by the participant on the time/date of when breast milk sample taken (Appendix 8). Within this week study participants will be contacted by the study team to ask how they are progressing and remind participants to fill out their study questionnaire as soon as possible (during pregnancy) and to take a breast milk sample 1-6 weeks after birth if possible. Additionally this will provide participants with the opportunity to ask any questions about the study.
6) Study participants to complete the study questionnaire during pregnancy and provide a breast milk sample between 1-6 weeks after giving birth using the breast pump provided. Breast milk samples to be stored in the glass bottles provided in their domestic freezer.
7) Study participants to contact the study team once they have collected their breast milk sample and arrange a day to collect the frozen breast milk samples, breast milk sample forms and the completed study questionnaires. If the participant has not contacted the study team by 4 weeks after their due date, the study team will contact the participants using contact details provided in the consent form.
8) Two members of the study team to collect questionnaires, breast milk sample forms and all frozen breast milk samples from the participants' homes.
9) All frozen breast milk samples to be boxed and sent to the CDC for dioxin analysis.

6. Participants requirements and burdens to participants

There are a number of potential burdens for participants if they decide to take part in this study. The section below explored these burdens and discusses how they have been minimised and addressed.

- Participants to complete consent forms and mail them to Imperial College London.

To encourage participants to mail back their consent forms and to ensure that taking part in this study does not cause any financial burden to participants, each study participant will receive a pre-paid addressed envelope in their study invitation pack. This envelope will be used to mail back their consent forms to the study team at Imperial College.

- Participants to complete study questionnaire.

In order not to burden participants or reduce compliance, the number of questions asked in the questionnaire (Appendix 6) was limited. The questionnaire is expected to take approximately 20 minutes. The questionnaires will collect information on:

Personal details and risk factors/potential confounders:

- Gestation weeks
- Due date
- Intention on breast feeding
- Maternal age
- Marital status
- Ethnicity
- Educational attainment

Dioxin exposure

- Residential history
- Parity
- Maternal obesity measures
- Employment before/during pregnancy including occupational information- this information will be used to ascertain whether the women are working or have previously worked in specific jobs that are the main contributors to dioxin exposure
- Work place address
- Tobacco use
- Dietary habits
- Locally sourced food consumption

- Participants to provide breast milk sample

We are aware that new mothers are vulnerable and expressing breast milk can be very difficult particularly in the early days after birth. To order to help mothers provide their breast milk sample and encourage participation in this study we will provide each participant with a manual breast pump. Additionally it clearly states, on all the study documentation, that we are only asking women to provide a breast milk sample if they can and feel happy to do so and that participation in this study is entirely voluntary and any participant is free to withdraw at any time throughout the study without their medical care being affected. Furthermore, studies using breast milk in the USA, tend to collect a complete milk expressions from women. However, for

the Incinerators Biomonitoring Study we will not ask for a complete milk expression as this means infants are required to miss a feed. In order not to burden the participants we will ask the women to provide a small 20mL breast milk sample at the end of a feed between 1-6 after birth.

7. Statistics, data analysis and dissemination of study results

7.1 Sample size

Due to funding limitations, we will aim to recruit a sample size of approximately 100 women. Accounting for a number of exclusions, with a sample size of 90, n=90, and 90% power and 5% statistical significance, we will be able to detect a correlation coefficient of at least 0.34[18] between breast milk dioxin concentrations and modelled ambient dioxin concentrations. With 80% power a correlation coefficient of at least 0.26 will be detected. The limited body of literature in this area of research makes it difficult to ascertain whether this minimum detectable correlation coefficient is sufficient because most studies have focused on exploring how well ambient concentrations of pollutants act as proxies for personal exposure[19]. One study evaluated the association between serum dioxin concentrations and atmospheric dispersion modelled ambient dioxin concentrations within 5km from one MSWI in Northern Taiwan and found no significant correlation[20] .

7.2 Data analysis and dissemination of study results

The statistical analysis for this study will be made up of the following steps:

a) Descriptive analysis of the characteristics of the study participants
b) Descriptive analysis of study participants by modelled zone and milk dioxin concentration
c) Mean, range and standard deviation of milk dioxin levels by modelled zone
d) Correlation between milk dioxin levels and modelled ambient dioxin concentrations
e) Milk concentrations by dioxin congener
f) Milk concentrations by dioxin congener by modelled zone
g) Investigations of the relationship between milk dioxin concentrations and distance from the incinerator
h) Investigations of the relationship between milk dioxin concentrations and dietary habits

No individually identifiable data from this study will be published, only the results of the study published in peer reviewed journals and Danielle Ashworths' (Chief Investigator) PhD thesis.

8. Ethical considerations

The section below summarises the main ethical issues arising from this study and how these issue have been addressed.

8.1 Informed consent

All participants invited to take part in this study will receive a PIS (Appendix 4) with their invitation letter (Appendix 3). The PIS will provide eligible women with information on the purpose of the Incinerators Biomonitoring Study and also what will happen if they decide to take part. A participant may only take part in this study if they provide consent. Consent will be in the form of a written consent form (Appendix 5), requiring the participant to provide a written signature. Only once signed consent forms have been received by the study team at Imperial College (posted in a prepaid envelope provided to the participant), will a participant be enrolled in the study. The invitation letter, the PIS and the consent form all clearly state that; participation in this study is entirely voluntary, any woman is free to withdraw from the study at any time and whatever their decision their medical care will not be affected in any way. No children or adults unable to provide consent for themselves will be approached to take part in the study. Additionally funding limits our ability to account for women unable to adequately understand the study information provided in English. Therefore women without a good understanding of English will be excluded from the study.

8.2 Data storage and confidentiality

All individually identifiable data will be dealt with in the strictest confidence and access to personal identifying information will be limited to the study team. Paper records of the consent forms (Appendix 5) and study questionnaires (Appendix 6) will be kept in locked cabinets at the department of epidemiology and biostatistics, Imperial College London. These locked cabinets are kept in a locked room on a floor that can only be accessed via security card. The front entrance of the department has a manned security desk. The study questionnaires will not document the name of the study participant only a unique patient identifier, the study ID. The consent forms will be linked to the questionnaires by this study ID. Consent forms will be kept in a separate cabinet and room to the study questionnaire. Anonymised study data from the questionnaires will be transferred into an electronic database, using only the study ID. All electronic data will be stored securely on a password protected private computer network (an airgapped network that is not connected to any other network) at Imperial College London. Within the study pack only the study ID will be used on the; questionnaire, the form recording the time/date of when breast milk sample taken (Appendix 8) and the breast milk collection tube. The analyzing laboratory will not have access to any individually identifiable data, samples will only be labelled with the study ID.

8.3 Feedback to participants on milk dioxin levels

It has been decided that no feedback will be provided to the study participants on their milk dioxin levels. It has been made clear, see PIS (Appendix 4), that study participants will be providing their breast milk sample as a "gift" to the study and are able to withdraw at any point in the study without this affecting their medical care, see PIS and consent form (Appendix 5). No feedback will be provided to the participants because currently there is very limited evidence on any adverse health effects to the mother or baby from dioxins in breast milk. The few studies exploring this relationship show very inconsistent findings. Additionally the level at which dioxins may cause harm or any potential affects remains unknown. The evidence suggests that higher dioxin concentrations in breast milk does not necessarily mean a feeding infant or

mother is at risk of adverse health outcomes. Additionally the advice from expert groups, the Scientific Committee for Food (SCF) and World Health Organisation (WHO), both encourage and support breastfeeding, stating that it is thought that the benefits of breastfeeding outweigh any potential negative effects from dioxins. For these reasons no feedback will be provided to the study participants in order to prevent them from unnecessary concerns.

8.4 Adverse birth outcomes

The issue of potential distress to participants if their pregnancy has resulted in an adverse outcome was raised by the ethics committee. In order to ensure that study participants are not approached following an adverse birth outcome, i.e. a miscarriage or a stillbirth, the study team will feedback to the local collaborators at the PICs a list of women who have consented to be in the study. This will allow the local collaborators to regularly check the maternity records of the study participants and inform the study team if a woman has had an adverse birth outcome. If a study participant experiences an adverse birth outcome they will automatically be withdrawn from the study and will be not be contacted.

8.5 Indemnity

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

8.6 Sponsor

Imperial College London and Imperial College Healthcare NHS Trust will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the local collaborators at the participant identification centres, NHS trusts, taking part in this study.

8.7 Funding and conflicts of interest

The Incinerators Biomonitoring Study is funded by the MRC Centenary Award awarded by the MRC-HPA Centre for Environment and Health (Appendix C: Confirmation of funding). No conflicts of interest are declared. Danielle Ashworth (Chief Investigator) is a PhD candidate funded by the MRC-HPA Centre for Environment and Health. The main academic supervisor, Dr Mireille B Toledano, is a member of the MRC-HPA Centre for Environment and Health, however she is a senior lecturer at Imperial College London and therefore her salary is funded by Imperial. The funders have had no role in the design of this study.

8.8 Audits

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

9. Study team and scientific oversight

Danielle Ashworth is a PhD candidate at Imperial College London. The Incinerators Biomonitoring Study will form part of her PhD and she will act as Chief Investigator. This research will be overseen by two academic supervisors: Dr Mireille B Toledano, senior lecturer in epidemiology in the department of epidemiology and biostatistics at Imperial College London and Professor Paul Elliott, chair in epidemiology and public health at the department of epidemiology and biostatistics at Imperial College London. Both Dr Mireille B Toledano and Professor Paul Elliott are investigators on the larger SAHSU study on MSWI emissions and adverse birth and neonatal outcomes and have substantial expertise in environmental reproductive epidemiology. Dr Rebecca Ghosh is a researcher at Imperial College London, who will additionally form part of the study team.

10. Timeline

Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Preparation of materials										
Ethical approval										
Recruitment of study participants										
Box and send samples to CDC										
Dioxin analysis of samples										
Data analysis and write up										

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12. Appendices

Appendix 1: Health Protection Agency incinerators press realease
Appendix 2: Study invitation letter
Appendix 3: PICs invitation letter
Appendix 4: Participant information sheet
Appendix 5: Consent/recruitment form
Appendix 6: Study questionnaire
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Appendix A: SAHSUs incinerator study: Favorable opinion letter (12 LO 0566)
Appendix B: SAHSUs incinerator study: Decision Letter (12 LO 0567)
Appendix C: Letter of confirmation of funding

MRC-HPA Centre for Environment & Health
Imperial College London

Imperial College London

Does the rubbish you create affect your health?

Incinerators Biomonitoring Study

Chief investigator: **Danielle Ashworth**

Version 2
12th April 2013

Ms Jane Doe
Department of Epidemiology and Biostatistics
St Mary's Campus, Norfolk Place
London W2 1PG

April 2013

Dear Ms Doe,

I would like to **invite you to take part in a research study** being conducted by Imperial College. This study is investigating whether incinerator pollutants can be detected in breast milk.

I am sending you this mailing on behalf of Imperial College in order to protect your confidentiality. The accompanying information leaflet explains more about why this study is being carried out and what is involved if you decide to take part.

Your participation in this study is entirely **voluntary**. If you decide to take part in this study and later change your mind, you are free to withdraw at any time. Whatever you decide, your medical care will not be affected in any way.

If you would like to take part in this study, please complete the enclosed consent and recruitment form and return it to Imperial College London in the pre-paid envelope provided.

If you decide to take part in this study, you will then be sent:

- A study **questionnaire** that should take no longer than 20 minutes to complete (includes a 24 hour food diary)
- A **breast pump** and will be asked to provide a **small breast milk sample** (20mL, 4 teaspoonfuls), if possible, within the first few weeks following birth

Thank you for taking the time to read this letter.

Yours sincerely
Maternity Centre

MRC-HPA Centre for Environment & Health

Imperial College London

PARTICIPANT INFORMATION SHEET

Does the rubbish you create affect your health?

Incinerators Biomonitoring Study

Chief Investigator: **Danielle Ashworth**

You are being invited to take part in a research study. This study has been set up by Imperial College to investigate whether incinerator pollutants can be detected in breast milk. Before you decide if you would like to take part in this study, it is important for you to understand why this research is being done and what it will involve. Please take the time to read the following information carefully.

Version 2
12th April 2013

➢ What is the purpose of this study?

There is an ever increasing amount of rubbish in the world today. In the past, most UK household waste was dumped in landfill sites. We now get rid of rubbish in more environmentally friendly ways like burning it in incinerators. With more and more waste being incinerated, there are an increasing number of incinerators in the UK.

Incinerator pollutants are released into the environment and can make their way into the human body. Some of these pollutants can be stored in fat tissue for long periods of time. It may be possible to measure these pollutants in breast milk.

Researchers at Imperial College London are conducting a study to see if they can detect these incinerator pollutants in breast milk.

➢ Why have I been invited to take part in this study?

All pregnant women in their second (weeks 14-26) and third trimester (weeks 27-birth), attending this maternity unit and living in selected areas around incinerators have been invited to take part in this study.

➢ Do I have to take part in this study? What if I want to withdraw?

Taking part in this study is voluntary and it is up to you to decide whether or not to take part. If you decide you want to take part in this study and later change your mind, you are free to withdraw at any time without giving a reason. Whatever you decide, your medical care will not be affected in any way.

Your maternity centre will contact us, the study team, if during the course of your pregnancy there is any reason why you can no longer participate

in this study, for example in the case of a miscarriage or stillbirth. If this is the case you will be automatically withdrawn from the study and we will not contact you again. Please note we do not have access to your medical records, these are held in confidence by the maternity centre.

Please see page 7 for additional information on who to contact for support in the case of a stillbirth or miscarriage.

➢ What will I have to do if I decide to take part?

If you decide to take part in this study, you will be asked to:

1. Complete a **study consent and recruitment form** and post it to Imperial College London in a prepaid envelope. Both the consent, recruitment form and prepaid envelope can be found enclosed.

Once you have provided consent to take part in this study and are approximately 6 weeks from your expected due date, you will be sent;

2. A **short study questionnaire** to your home address. This questionnaire should take no longer than 20 minutes to complete and we ask that you complete it during your pregnancy. The questionnaire includes questions about yourself and a 24 hour food diary which will be used to help us interpret the results of this study.
3. A **breast pump**. We ask you to provide a 20mL (4 teaspoonfuls) **breast milk sample** between 1-6 weeks after birth, if possible, using the provided breast pump.

If you would like more in depth information about either the study questionnaire or the breast milk sample, please feel free to contact the chief investigator by email: danielle.ashworth09@imperial.ac.uk or call on 02075941892.

➢ Will my taking part in this study and my results be kept confidential?

All the information collected about you during the course of this study will be kept strictly confidential. No individually identifiable data from this study will be published and therefore you will not be identified in any report or publication.

➢ What are the possible benefits of taking part in this study?

This is your chance to be part of groundbreaking research in environment and health. The advantages of taking part in this study are that:

1. You will receive a **free breast pump** for you to keep.
2. You will be helping us in our efforts to determine if incinerator pollutants can be detected in breast milk.

➢ Should I be worried about living near an incinerator?

No, you should not be worried about living near an incinerator. Modern incinerators are tightly regulated and very safe.

➢ Should I worry about incinerator pollutants in my breast milk?

The European Scientific Committee for Food and the World Health Organisation both encourage and support breastfeeding, stating that the benefits of breastfeeding outweigh any potential negative effects that small levels of incinerator pollutants may have on both a feeding baby or a mother.

➢ What if I can't breast feed?

We are aware that expressing breast milk can be very difficult particularly in the early days after birth. We are inviting women to take part in this study who currently intend to breast feed and feel that they would be happy to provide a small sample after they have given birth. If you change your mind at any point in the study and no longer want to provide a breast milk sample or are unable to, you can withdraw from the study at any time, without providing any explanation or your medical care being affected.

➢ Will I receive feedback on the level of incinerator pollutants in my breast milk?

We would like you to think of the breast milk sample you are providing us with as a "gift" to this study. There is little evidence on the levels of incinerator pollutants which may adversely affect you or your child's health. To ensure we do not cause any unnecessary concern or anxiety we will not be providing you with any feedback on the levels of incinerator pollutants in your breast milk sample. However, overall study findings will be written up and published in a scientific journal. You will be able to read this publication by obtaining a copy from the research team.

➢ I want to take part in the study, what do I do?

What do I do now: Please complete the enclosed consent form as soon as possible and send this to Imperial College London using the pre-paid envelope enclosed.

What happens next: Once your completed consent form has been received by the study team at Imperial College London, a study pack will be dispatched to your home address.
The study pack will include;

- A study questionnaire,

- A manual breast pump,
- A glass screw-capped bottle to store your breast milk sample in,
- Instructions on how to provide the breast milk sample,
- A form to document when you took the breast milk sample.

Once you have received the study pack, we would like you to complete the questionnaire immediately (before you give birth) and store it somewhere safe. Then, between 1 to 6 weeks after giving birth we would like you to provide a 20mL breast milk sample. We ask that you store your sample in the glass screw-capped bottle provided in your domestic freezer, until a member of the study team comes to pick it up from your home at a convenient time.

➢ Who is organising/funding this study?

This study is part of a PhD research project at Imperial College London. The study team are all researchers from Imperial College London. This study is funded by the MRC Centenary Award awarded by the MRC-HPA Centre for Environment and Health (http://www.environment-health.ac.uk/).

➢ Contact us

If you would like any more information about this study or if you have any concerns, please feel free to contact:

Danielle Ashworth
Department of Epidemiology and Biostatistics,
Room 171, Imperial College London, St Mary's Campus,
Norfolk Place, Paddington, London, W2 1PG, UK
E-mail: danielle.ashworth09@imperial.ac.uk
Telephone number: 02075941892

If you have any **complaints** about this study please contact the study team in first instance. If you would like to contact someone independent from the study team, please feel free to contact any member of the

The Joint Research Compliance Office (JRCO)
Website:http://www3.imperial.ac.uk/clinicalresearchgovernanceoffice

➢ Additional contacts

For advice and support if you have been affected by a miscarriage or the death of a baby:

Miscarriage association:
Contact number: 019 2420 0795
Helpline: 019 2420 0799 (Monday - Friday 9am - 4pm)
Website: http://www.miscarriageassociation.org.uk/

Sands (Stillbirth & neonatal death charity):
Contact number: 020 7436 7940 (Monday - Friday 10am - 5pm)
Helpline: 020 7436 5881 (Monday – Friday 9.30am – 5.30pm and Tuesday & Thursday 6pm-10pm)
Website: http://www.uk-sands.org/home.html

Thank you for your time.

We couldn't do this research without your help!

MRC-HPA Centre for Environment & Health
Imperial College London

Imperial College London

Does the rubbish you create affect your health?

Incinerators Biomonitoring Study

Chief investigator: **Danielle Ashworth**

Version 2
12th April 2013

CONSENT FORM

1. I confirm that I have read and understand the information sheet dated 12/04/2013 (version 2) for the above study.

2. I understand that my participation in this study is voluntary and I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

3. I agree to complete a study questionnaire, which will include a 24 hour food diary, for use in the above study.

4. I agree to provide a breast milk sample, if possible, as a "gift" to the above study. I understand that I will not receive any individual feedback on the levels of incinerator pollutants in my breast milk.

5. I understand that my medical notes and data collected from the study may be looked at by regulatory authorities or by persons from the Trust where it is relevant to my taking part in this research. I give permissions for these individuals to have access to this information.

6. I confirm agreement to take part in the above study.

_____	_____	_____
Name of Patient/Participant	Signature	Date

RECRUITMENT FORM

Forenames	
Surname	
Date of birth	*Day* ☐☐ *Month* ☐☐ *Year* ☐☐☐☐
Address **Postcode**	
Main contact number	
Number of previous live births *(do not include miscarriages, terminated pregnancies or stillbirths)*	None ☐ 1 ☐ >1 ☐
How many weeks pregnant are you today?	Weeks ☐
Expected due date	*Day* ☐☐ *Month* ☐☐ *Year* ☐☐☐☐
Do you intend on breast feeding your child for the first 6 weeks (or longer) after birth?	Yes ☐ No ☐
Do you have access to a freezer to store your breast milk sample in, for use in the above study? *(excludes freezer boxes within fridges)*	Yes ☐ No ☐
Would you like us to send you a breast pump, free of charge, to your home address?	Yes ☐ No ☐

MRC-HPA Centre for Environment & Health
Imperial College London

Imperial College London

QUESTIONNAIRE:

Does the rubbish you create affect your health?

Incinerators Biomonitoring Study

STUDY ID: **November 2013**

TO BE COMPLETED DURING PREGANCY

TO BE COLLECTED ALONGSIDE BREAST MILK SAMPLES

Completing this questionnaire should take approximately 20 minutes of your time

How to complete this questionnaire:

The information you supply in the following questionnaire is helping groundbreaking research in environment and health. All the information you provide will remain confidential. Please answer the questions below to the best of your ability and check boxes with a tick (✓) when required.

Q1. How many weeks pregnant are you today? ☐ *weeks*

Q2. What is your expected due date

Day ☐☐ Month ☐☐ Year ☐☐☐☐

Q3. Do you intend on breast feeding your baby for the first 6 weeks (or longer) after birth?

☐ Yes ☐ No

Q4. Have you lived at your current address for the duration of your pregnancy?

☐ Yes ☐ No

Q5. Have you lived at your current address for the last 5 years (since the beginning of 2008)?

☐ Yes ☐ No

If you answered **no** to Q5 please could you provide all of your previous addresses for the last 5 years:

1. Years _____

Address: _____

City: _____ Postcode: _____

2. Years _____

Address: _____

City: _____ Postcode: _____

3. Years _____

Address: _____

City: _____ Postcode: _____

Q6. Age ☐ *years*

Q7. Height ☐ *cm or inches*

Q8. Weight at beginning of pregnancy ☐ *Kgs or stone*

Q9. Marital status

☐ Single ☐ Married ☐ Other

Q10. Number of previous live births *(do not include miscarriages, terminated pregnancies or stillbirths)*

☐ None ☐ 1 ☐ >1

Q11. Please tick the group which best describes your ethnicity

☐ British/Irish (White)
☐ Other White background
☐ Black-Caribbean
☐ Black-African
☐ Black-Other
☐ Indian
☐ Pakistani
☐ Bangladeshi
☐ Chinese
☐ Other Asian background

☐ White and Black-Caribbean/African/Other (mixed)

☐ White and Asian (mixed)

☐ Black-Caribbean/African/Other and Asian (mixed)

☐ Other mixed background

☐ Other ethnic group

Q12. Age at which you left school ☐ *years*

Q13. What is the highest educational or school qualification you have completed?

☐ University higher degree (e.g. MSc/MA, PhD)

☐ First degree level (e.g. BSc/BA)

☐ A level or equivalent

☐ GCSE/O level or equivalent

☐ Other school

☐ None of the above

Q14. Were you employed (full or part time) during any part of your pregnancy?

☐ Yes ☐ No

If you answered **yes** to Q14, did you work in one of the following industries:

1. Industrial production (e.g. incinerators, petroleum refinery, cement and glass production, metal production or paper industry)

☐ Yes ☐ No

2. Chemical or textile industry

☐ Yes ☐ No

Q15. Have you ever been employed in one of the following industries:

1. Industrial production (e.g. incinerators, petroleum refinery, cement and glass production, metal production or paper industry)

☐ Yes ☐ No

2. Chemical or textile industry

☐ Yes ☐ No

If you answered **yes** to either Q14 or Q15, approximately how long did you work in these industries for in total;

☐ <1 month ☐ 1-6 months ☐ 6-12 months

☐ 1-5 years ☐ 5-10 years ☐ ≥10 years

Q16. Are you currently a smoker?

☐ Yes ☐ No

If you answered **yes** to Q16 approximately how many cigarettes do you smoke per day

☐ <5 ☐ 5-10 ☐ 10-20 ☐ >20

Q17. Did you smoke before you became pregnant (within the last 10 years)?

☐ Yes ☐ No

If you answered **yes** to Q17 approximately how many cigarettes did you smoke per day

☐ <5 ☐ 5-10 ☐ 10-20 ☐ >20

Q18. Have you smoked at any point during your pregnancy?

☐ Yes ☐ No

If you answered **yes** to Q18 approximately how many cigarettes did you smoke per day

☐ <5 ☐ 5-10 ☐ 10-20 ☐ >20

Q19. Do you have any dietary restrictions?

☐ Yes ☐ No

If yes please indicate the type of dietary restrictions you adhere to

☐ Vegetarian ☐ Vegan ☐ Other If other please state_____

Q20. Do you avoid any of the following food types; meat and/or seafood?

☐ Yes ☐ No

Please indicate which food type you avoid

☐ Avoid meat ☐ Avoid seafood ☐ Avoid both

Q21. Do you consume milk?

☐ Yes ☐ No

If you answered **yes** to Q21 please indicate what type of milk you consume

☐ Soya milk ☐ Goat's milk ☐ Cow's milk ☐ Other

If you answered **cow's milk in** Q21 please indicate what type cow's milk you consume

☐ Whole milk ☐ Semi-skimmed milk ☐ Skimmed milk

☐ Long life (UHT) ☐ Dried milk ☐ Other

Q22. Do you eat any of the following food items from local sources (i.e. your own garden or from a farm within 10km from your house)

Food item	Do you eat the food item from local sources? *Please circle your answer*		Approximately how many times would you consume this item in a typical week?
Meat	Yes	No	
Poultry	Yes	No	
Fish	Yes	No	
Eggs	Yes	No	
Dairy products	Yes	No	

Q23. Please complete the table below which is asking about the food and drinks you have consumed in the last 24 hours:

Today's date

Day ☐☐ Month ☐☐ Year ☐☐☐☐

Which day of the week does this record?

☐ Monday ☐ Tuesday ☐ Wednesday ☐ Thursday

☐ Friday ☐ Saturday ☐ Sunday

Does this day represent your typical eating habits?

☐ Yes ☐ No

Have your eating habits changed during pregnancy?

☐ Yes ☐ No

24 HOUR RECORD

Time	Occasion *Please circle appropriate*	Food/Drink Please include the amount/serving size (how much eaten or drank?)	Where food was from? *Please circle most appropriate*
Example: *8:30 am*	***Breakfast*** ***Brunch*** ***Lunch*** ***Dinner*** ***Snack*** ***Other***	*2 Weetabix* *Approximately ¼ pint of semi-skimmed milk* *Approximately 2 tablespoons of sugar* *1 tea with semi-skimmed milk* *1 glass of orange juice*	***Homemade/locally grown*** ***Readymade supermarket/deli*** ***Restaurant/take out***
	Breakfast **Brunch** **Lunch** **Dinner** **Snack** **Other**		**Homemade/locally grown** **Readymade supermarket/deli** **Restaurant/take out**
	Breakfast **Brunch** **Lunch** **Dinner** **Snack** **Other**		**Homemade/locally grown** **Readymade supermarket/deli** **Restaurant/take out**
	Breakfast **Brunch**		**Homemade/locally grown** **Readymade supermarket/deli**

Lunch **Dinner** **Snack** **Other**		**Restaurant/take out**
Breakfast **Brunch** **Lunch** **Dinner** **Snack** **Other**		**Homemade/locally grown** **Readymade supermarket/deli** **Restaurant/take out**
Breakfast **Brunch** **Lunch** **Dinner** **Snack** **Other**		**Homemade/locally grown** **Readymade supermarket/deli** **Restaurant/take out**

Thank you for your time. We couldn't do this research without your help!

For additional information, concerns or queries about this study please contact:
Miss Danielle Ashworth
Department of Epidemiology and Biostatistics,
Imperial College London,
St Mary's Campus,
Norfolk Place, Paddington,
London, W2 1PG, UK
Telephone number: 02075941892
E-mail: danielle.ashworth09@imperial.ac.uk

Breast milk sample:

Does the rubbish you create affect your health?

Incinerators Biomonitoring Study

August 2013

STUDY ID:

If you are able to provide a breast milk sample please could you complete the form below. Please keep the completed form somewhere safe, it will be collected by an Imperial College London researcher along with the breast milk sample at a date convenient for you.

Date breast milk sample expressed:

Day Month Year

☐☐ ☐☐ ☐☐☐☐

Time milk expressed: ☐ am or pm

Were you able to express 20mL (4 teaspoonfuls or ~1 fl oz) of breast milk?

☐ Yes ☐ No

Were you able to freeze your sample within 30 minutes after expressing?

☐ Yes ☐ No

Once you have collected your sample please contact a member of the study team via email danielle.ashworth09@imperial.ac.uk or call on 02075941892 to arrange a suitable time for your frozen breast milk sample, this form and your questionnaire to be picked up from your home.

If we have not heard from you 4 weeks after your due date, the study team will contact you using the contact details you provided.

Does the rubbish you create affect your health?

Incinerators Biomonitoring Study

November 2013

QUESTIONS ON EMPLOYMENT

1. **Job title at current/last employer – please specify** *e.g. Manager of restaurant- managing approximately 10 employees*

2. **Work address at current/last employer**

   Address (line one): _____

   Address (line two): _____

   _____

   City: _____ Postcode: _____

3. **Current/former employment status**

   ☐ Full time

   ☐ Part-time (< 35 hrs a week)

   ☐ Temporary (1 month)

4. **How long have you/had you worked at the last place of employment**

   ☐ <1 month ☐ 1-6 months ☐ 6-12 months
   ☐ 1-5 years ☐ 5-10 years ☐ ≥10 years

Health Research Authority
National Research Ethics Service

NRES Committee North West - Preston
HRA NRES Centre - Manchester
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7818
Facsimile: 0161 625 7299

25 April 2013

Miss Danielle C Ashworth
Imperial College London
Room 171, Department of Epidemiology and Biostatistics
St Mary's Campus, Imperial College London
Norfolk Place, Paddington, London
W2 1PG

Dear Miss Ashworth

Study title:	**Does the rubbish you create affect your health?(Incinerators Biomonitoring Study)**
REC reference:	**13/NW/0202**
IRAS project ID:	**123638**

Thank you for your letter of 19 April 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Mrs Carol Ebenezer, nrescommittee.northwest-preston@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see

"Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Evidence of insurance or indemnity		30 July 2012
GP/Consultant Information Sheets	1	27 February 2013
Investigator CV	Danielle Ashworth	
Investigator CV	Mireille Toledano	
Investigator CV	Prof Paul Elliott	
Letter from Sponsor		06 March 2013
Letter of invitation to participant	2	12 April 2013
Other: Letter from Funder		06 February 2013
Other: Health protection Agency Incinerator Study	1	24 January 2013
Other: 12/LO/0566 - Favourable Letter		18 May 2012
Other: 12/LO/0567 - Favourable Letter		18 May 2012
Other: Recruitment Form		
Other: 24 Hour Record		
Other: FAQs	2	12 April 2013
Other: Sample Form	2	12 April 2013

Participant Consent Form	2	12 April 2013
Participant Information Sheet	2	12 April 2013
Protocol	2	12 April 2013
Questionnaire	2	12 April 2013
REC application	3.4	07 March 2013
Response to Request for Further Information		19 April 2013
Summary/Synopsis		27 February 2013

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/NW/0202	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely



Dr Patricia Wilkinson
Chair

Email:nrescommittee.northwest-preston@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Dr Mireille B Toledano*
Ms Lucy Parker

University Hospital Southampton NHS Foundation Trust

Please reply to: Research and Development
SGH - Level E, Laboratory & Pathology Block, SCBR - MP 138
Southampton University Hospitals NHS

Telephone: 023 8079 5078
Fax: 023 8079 8678
E-mail: sharon.atwill@uhs.nhs.uk

Mrs Jane Forbes
Princess Anne Hospital
Room F84, MP 815, F Level
Research Office
Coxford Road
Southampton
SO16 5YA

12 June 2013

Dear Mrs Forbes

ID: RHM O&G0206 Does the rubbish you create affect your health? (Incinerators Biomonitoring Study)

Thank you for submitting all the required documentation for Trust review of your request to act as a Participant Identification Centre for the above named study. I write to inform you that your request has full UHS R&D approval.
As a Participant Identification Centre (PIC) you are ONLY authorised to refer potential participants to the research team based in another organisation, for assessment and possible recruitment to this study. A PIC can also undertake support functions, such as project management, site monitoring, data analysis or report writing. As a PIC you are not considered to be a research site, and as such, cannot conduct participant-related research procedures specified in the protocol, including recruitment and informed consent.

You are required to keep copies of all your essential documents relating to this study.

Please note: A condition of approval is that any changes need to be timeously notified to the R&D office. This includes providing copies of:
. All NRES substantial amendments and favourable opinions that have implications for the SUHT site;
. NRES Annual Progress Reports;
. NRES End of Study Declaration;
. Notifications of significant breaches of GCP or protocol

Please quote the above RHM No. on any correspondence with our office.

Should you, or any of your team, require training in any of the policies and procedures required to ensure compliance with the conditions of approval, please refer to the R&D Training website http://tinyurl.com/prkd65 for an up-to-date calendar of training events.

Yours sincerely

Sharon Atwill

Research Governance Officer

Appendix for R&D approval letter dated: 12 June 2013

RHM O&G0206
Study Title: Does the rubbish you create affect your health? (Incinerators Biomonitoring Study)

The following documents have been reviewed as part of the R&D approval.

Document	Version	Date
Protocol	1	25 February 2013
CV – Mrs J Forbes	n.a.	12 March 2012
REC approval letter	n.a.	25 April 2013
Letter of Invitation	2	12 April 2013
Information Sheet	2	12 April 2013
Consent Form/Recruitment Form	2	12 April 2013
Breast Milk FAQs	1	27 February 2013
Breast Milk Sample	1	27 February 2013
Questionnaire	1	27 February 2013
Sampling & Mailing Strategy Marchwood study area	1	June 2013

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14 May 2013

Miss Danielle Ashworth
Department of Epidemiology and Biostatistics
Imperial College London
Room 171, St Mary's College
Norfolk Place
Paddington
London
W2 1PG

Dear Miss Ashworth

Study Title: Does the rubbish you create affect your health? Incinerators Biomonitoring Study: INCINERATOR
Local Collaborator: Mrs Janet Mackie
CSP ID: 123638
REC Ref: 13/NW/0202
R&D Ref: OBS-060

I am pleased to confirm NHS approval for North Tees and Hartlepool NHS Foundation Trust to act as a Participant Information Centre (PIC) for the above study. The documents listed below have been reviewed in order to confirm this decision.

• Protocol	Version 2	12.04.13
• Participant letter of invitation	Version 2	12.04.13
• Participant information sheet	Version 2	12.04.13
• Consent form	Version 2	12.04.13
• Patient Questionnaire	Version 2	12.04.13
• Breast milk sample FAQs	Version 2	12.04.13
• Breast milk sample date & amp	Version 2	12.04.13
• NHS Ethics approval letter	Dated	25.04.13
• Caldicott approval	Dated	08.04.13

It is the sponsor's responsibility to notify participating sites of any information relating to a change to the status of the project. If amendments do not impact this Trust an R&D amendment approval letter will not be issued.

It is important that you / delegated nominee inform us of any of the following:

- **Change in Chief Investigator (CI)**
- **Changes in protocol or study documentation.**
- **Changes to the time frame of the study.**

We require you to provide regular updates on request and a final report on completion of this project.

We wish you every success with your research project.

Professor Volker Straub
Research & Develop ment Director
Harold Macmillan Chair for Medicine, FRCPCH
Direct Line: 01642 624090

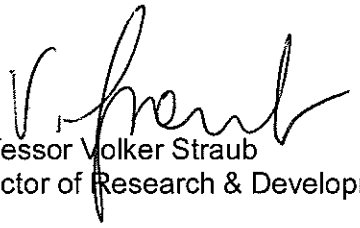
Professor Samir Gupta
Deputy Research & Developm ent Director
Consultant Neonatologist
Direct Line: 01642 624090

Paul Garvin
Chairman

Alan Foster
Chief Executive

NTH115

Best Wishes



Professor Volker Straub
Director of Research & Development

Cc

Dr Mireille B Toledano
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Mrs Janet Mackie
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31st May 2013

Mr Aethele Khunda
Consultant Obstetrician & Gynaecologist
The James Cook University Hospital
Marton Road
Middlesbrough
TS4 3BW

Dear Mr Khunda

Re: UKCRN ID: 123638
2013019 - Does the rubbish you create affect your health? (Incinerators Bio monitoring Study)

I am writing to confirm that South Tees Hospitals NHS Foundation Trust agree to act as a Participation Identification Centre (PIC) for the above study.

If the R&D Department can be of any further assistance, please do not hesitate to contact us.

Kind regards.



Mr A Owens
Research & Development Director
GMC 3485934

APPENDIX E

Downloaded from http://fn.bmj.com/ on September 4, 2016 - Published by group.bmj.com
ADC-FNN Online First, published on February 2, 2016 as 10.1136/archdischild-2015-309540

Routinely collected English birth data sets: comparisons and recommendations for reproductive epidemiology

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▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/archdischild-2015-309540).

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Received 11 August 2015
Revised 23 December 2015
Accepted 31 December 2015

ABSTRACT

Background In England there are four national routinely collected data sets on births: Office for National Statistics (ONS) births based on birth registrations; Hospital Episode Statistics (HES) deliveries (mothers' information); HES births (babies' information); and NHS Numbers for Babies (NN4B) based on ONS births plus gestational age and ethnicity information. This study describes and compares these data, with the aim of recommending the most appropriate data set(s) for use in epidemiological research and surveillance.

Methods We assessed the completeness and quality of the data sets in relation to use in epidemiological research and surveillance and produced detailed descriptive statistics on common reproductive outcomes for each data set including temporal and spatial trends.

Results ONS births is a high quality complete data set but lacks interpretive and clinical information. HES deliveries showed good agreement with ONS births but HES births showed larger amounts of missing or unavailable data. Both HES data sets had improved quality from 2003 onwards, but showed some local spatial variability. NN4B showed excellent agreement with ONS and HES deliveries for the years available (2006–2010). Annual number of births increased by 17.6% comparing 2002 with 2010 (ONS births). Approximately 6% of births were of low birth weight (2.6% term low birth weight) and 0.5% were stillbirths.

Conclusions Routinely collected data on births provide a valuable resource for researchers. ONS and NN4B offer the most complete and accurate record of births. Where more detailed clinical information is required, HES deliveries offers a high quality data set that captures the majority of English births.

What is already known on this topic

- Routinely collected birth data sets provide an important resource for epidemiological studies and for surveillance of reproductive health.
- Of the four national sources of birth data ONS births and NN4B offer the most complete and accurate record of all births in England.
- But ONS births and NN4B do not provide the detailed clinical information held in HES.

What this study adds

- HES deliveries are recommended for use over HES births.
- Researchers should undertake a descriptive analysis of the data to identify any temporal or spatial trends.
- Policies are required to reduce the high burden of permissions and information governance required to obtain and link birth data sets.

INTRODUCTION

Routinely collected data on births are a valuable resource for use in epidemiological studies of reproductive outcomes and surveillance.[1 2] In England there are four national births data sets: Office for National Statistics (ONS) births based on birth registrations; Hospital Episode Statistics (HES) deliveries; HES births; and National Health Service (NHS) Numbers for Babies (NN4B) which is based on ONS births plus gestational age and ethnicity information.

ONS births consists of information on births in England and Wales (live or still) registered within 42 days of birth, a statutory requirement. ONS births is a complete, high quality data set that holds some sociodemographic information, but lacks key information such as gestational age. ONS provides detailed metadata as well as produces annual publications on a range of summary birth statistics and trends.[3] This data set has also been used in studies of reproductive health and environmental exposures,[1 2 4–6] sociodemographic effects,[7–9] temporal trends in birth weight[10 11] and survival.[12]

HES from the Health and Social Care Information Centre (HSCIC), documents all admissions into English NHS hospitals and facilities funded by NHS and routinely publishes descriptive statistics and data quality summaries of their maternity data.[13] The HES maternity records are a subset of HES and include two data sets: HES births (babies record), and HES deliveries relating to the birth process (mothers record with information on each baby). HES deliveries contains detailed clinical information and has been used to investigate obstetric surgery outcomes and practice.[14–17] HES births has been mainly used for methodological papers creating linked birth cohorts[18] and linkage with other routine data sets.[19 20]

NN4B was created to allocate NHS numbers to babies who are notified (within a few days of birth)

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to a Central Issuing System and for 2006 onwards NN4B is available from ONS. NN4B is a high quality record of births with additional key variables including gestational age[21] and has been linked to birth and death registrations by ONS to produce gestation-specific infant mortality statistics.[22] From 2015 NN4B functions have been replaced by the Personal Demographics Service on the NHS Spine but the information currently being collected will remain comparable to NN4B.

The specific aims of this study were to: (1) assess, for the first time, the quality of all four national data sources on birth outcomes; (2) to produce comparative statistics for each data set for several common outcomes in reproductive epidemiology; and (3) make recommendations to researchers on the most appropriate data set(s) for use in epidemiological studies.

METHODS

Data were extracted from ONS births registrations and HES maternity records for all English births for calendar years 2002–2010; (NN4B from 2006 the earliest available year from ONS). For ONS births and NN4B, each record relates to one birth. In HES maternity, records relate to an episode of care during pregnancy rather than a birth and contain variables that are also held in standard HES records. HES deliveries and HES births hold space for up to nine additional fields known as a 'baby tail; in which variables relate to the delivery and babies.

Online supplementary table S1 and figure S1 document an exploration of the different criteria, filtering conditions and deduplication that can be used to define a birth within HES. This was conducted in accordance with previously published papers,[18 19] reports[23] and personal communication with the HES team.

Data analysis

Variables available, total numbers of births and missing data in each data set were compared for the whole period (2002–2010) and by year. Descriptive statistics were produced for the following four common adverse birth outcomes:[24 25]

1. Low birth weight (LBW): Live singleton births with a birth weight between 200 g and 2500 g
2. Stillbirths: Births coded as stillbirths occurring ≥24 weeks of pregnancy
3. Term LBW: Live singleton births with a birth weight between 200 g and 2500 g born ≥37 weeks of pregnancy
4. Preterm delivery (PTD): Live singleton birth occurring <37 weeks of pregnancy but >10 weeks of gestation.

Variability in rates and counts was investigated by maternal age, plurality, region, deprivation (quintiles of the Carstairs index[26] of Census Output Areas (COAs) 2001 defined by residential postcode), birth weight, sex, parity (number of previous children), ethnicity, previous pregnancies, delivery method, delivery place and gestational age.

Geography: COA are the smallest geographical areas for which census data are published. They are created from census data using clusters of adjacent postcodes and are designed to have similar characteristics and population sizes (on average around 100 people). Lower Layer Super Output Areas (LSOAs) are geographical areas built up from groups of adjacent COAs with similar characteristics and for the 2001 census LSOAs had a mean population of 1514.[27]

For the two most complete data sets (ONS and HES deliveries) the numbers of live births and stillbirths and the average birth weight were calculated at a small area level (LSOA 2001—LSOA) across: (A) England and (B) two regions, the North-East and Greater London. The rates of live births per 10 000 population (using ONS midyear population estimates) of the two regions were then mapped at LSOA level.

All data handling and analysis was performed in R V.2.14.2 and STATA V.13 (Stata Corp, College Station, Texas, USA); maps were produced using Arc GIS 10.1 (Environmental Systems Research Institute, California, USA).

Table 1 Availability of data by birth data set

Fields of information	HES deliveries	HES births	ONS births	NN4B
Birth status	✓	✓	✓	✓
Birth weight	✓	✓	✓	✓
Sex of baby	✓	✓	✓	✓
Mother's date of birth	✓	✓	*	*
Residential postcode	✓	✓	✓	✓
Residential address			✓	✓
Gestational age (still)	✓	✓	✓	✓
Gestational age (live)	✓	✓		✓
Ethnicity of mother	✓			
Ethnicity of baby		✓		✓
Previous pregnancies	✓	✓		
Previous children			✓	✓
Delivery method	✓	✓		
Delivery place	✓	✓		

*Although mother's date of birth is recorded in the ONS births data set to comply with legislation on disclosure Small Area Health Statistics Unit (SAHSU) researchers are only provided with 2-year maternal age bands.
HES, Hospital Episode Statistics; ONS, Office for National Statistics; NN4B, NHS Numbers for Babies.

RESULTS

All data sets contain information on birth status and weight, sex, mothers' date of birth and residential postcode (table 1). ONS and NN4B have residential address while the HES maternity data sets only have information at postcode level. The HES data sets and NN4B include information on gestational age and ethnicity, with HES providing the mothers' ethnic group and NN4B providing the ethnic category of the baby as defined by the mother. HES maternity also provides additional clinical information.

Total births and time trends

There were clear differences in capture across the study period (see online supplementary Figure S2) and in 2001 HES deliveries captured only 73.0% of ONS. Capture was much higher thereafter, so 2001 was excluded from subsequent comparisons. From 2002 to 2010, ONS recorded 5 727 407 births, HES deliveries 5 545 905 and HES births 5 534 194, while NN4B recorded 3 333 154 in 2006–2010 (table 2). From 2002 to 2010, HES deliveries captured 96.8% of all ONS births, HES births captured 96.6% and for 2006–2010 NN4B captured 99.8%.

ONS had few missing or unavailable data except for parity which was only recorded for married mothers (51.6% of births) and gestational age (stillbirths only); NN4B also had few missing data (table 2). The HES data sets had more variables with larger proportions of missing data than ONS, with HES births being worse than HES deliveries. ONS and NN4B had

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Table 2 Missing data in selected birth outcome variables (2002–2010)

Variable	HES deliveries		HES births		ONS births		NN4B births*	
	n missing	Missing, %	n missing	Missing, %	n missing	Missing, %	n missing	Missing, %
Total births or deliveries (2002–2010)	5 545 905		5 534 194		5 727 407		3 333 154	
Maternal age	14 605	0.3	2 128 620	38.5	0	0	2	0
Plurality	905 313	16.3	1 563 918	28.3	N/A†		N/A†	
Residential postcode	36 185	0.7	4 088 071	73.9	318	0	885	0.0
Government Office Region (GOR)	32 245	0.6	4 086 574	73.8	0	0	6300	0.2
Carstairs score‡	49 526	1	3 473 637	71.4	8625	0.2	6300	0.2
Birth status (live/still)	1 540 412	27.8	2 072 393	37.4	N/A§		N/A§	
Birth weight¶	1 300 202	23.4	2 085 549	37.7	36 224	0.6	20 327	0.6
Sex of baby	1 326 373	23.9	5 409 048	97.7	0	0	2	0
Parity (previous children)**	NI		NI		2 480 180	48.4	NI	
Mothers' ethnicity	943 329	17.0	NI		NI		NI	
Babies' ethnicity	NI		1 441 154	26.0	NI		260 112	7.8
Previous pregnancies	2 061 539	37.2	5 390 377	97.4	NI		NI	
Delivery method	1 294 750	23.3	1 742 960	31.5	NI		NI	
Delivery place	1 881 901	33.9	2 213 562	40.0	NI		NI	
Gestational age	2 201 195	39.7	2 227 618	40.3	N/A		32 039	1

*2006 to 2010 only.
†ONS and NN4B codes multiple births as 1, all other births are considered singleton. Coverage is therefore 100%.
‡No data for 2010, results displayed for years 2002–2009, NN4B 2006–2010.
§ONS tables are split into stillbirths and live births. Coverage is therefore 100%.
¶Valid birth weights for HES include 1–7000 g, for ONS 1–9997 g and for NN4B 200–5000 g.
**Applies to live births and stillbirths within marriage only.
HES, Hospital Episode Statistics; ONS, Office for National Statistics; NA, not applicable; NI, not included; NN4B, NHS Numbers for Babies.

little variation in missing data by year, both HES data sets showed a decrease in missing data over time but with a spike in missing data in 2007 (see online supplementary table S2). For HES births the sex of the baby was not collected from 2003 and for key variables there was an increase in missing data over time.

A comparison of selected variables for each data set is presented in online supplementary table S3. For total births the

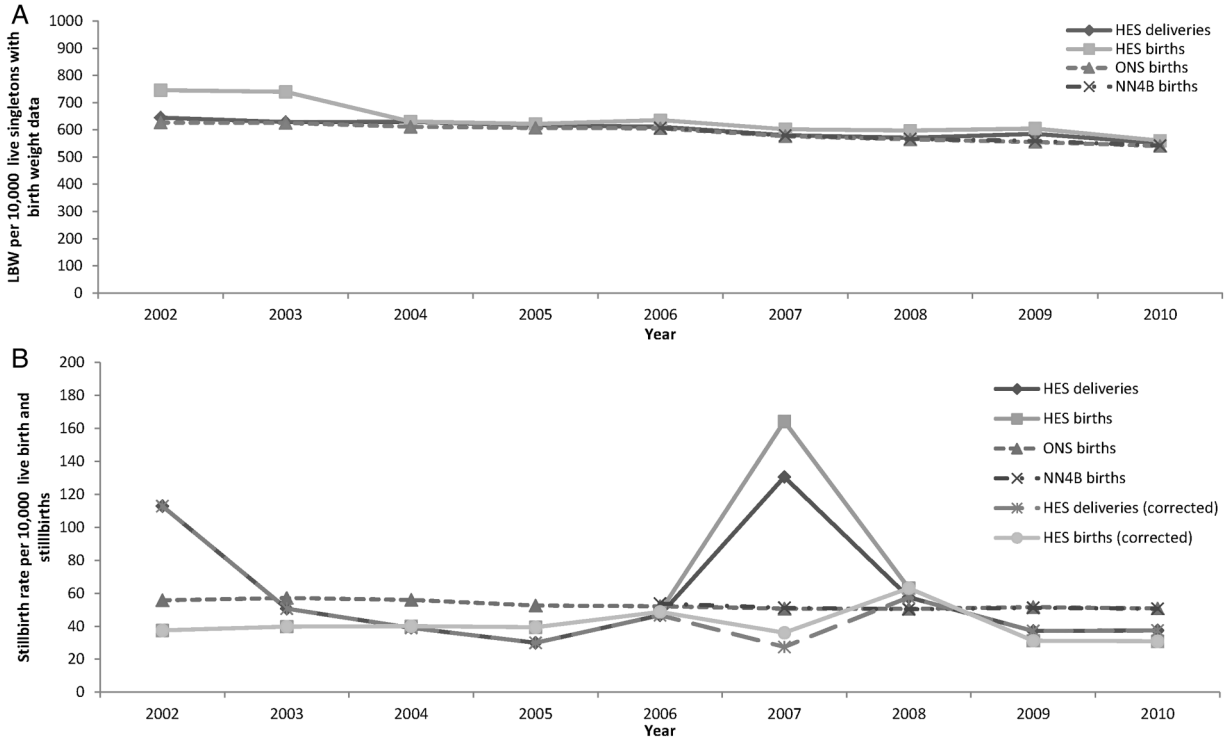


Figure 1 Annual rates of (A) low birthweight births per 10 000 live singleton births and (B) stillbirths per 10 000 total births (live and still) in each birth datasets from 2002 to 2010. *HES deliveries and HES births presented with and without inclusion of one NHS trust with known stillbirth reporting issues.[27] HES, Hospital Episode Statistics; LBW, low birth weight; ONS, Office for National Statistics; NN4B, NHS Numbers for Babies.

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HES data sets were broadly consistent with ONS and NN4B data, with fewer multiple births (HES deliveries 2%; ONS 3.1%) and more female births (HES deliveries 49.6%; ONS 48.7%).

LBW births and stillbirths

Similar proportions of births were recorded as LBW in all data sets (ONS=5.9%; HES deliveries=6%; HES births 6.3%; NN4B=5.5%) (see online supplementary table S4) and all showed a decreasing trend in LBW rates (figure 1A). When comparing specific variables in each data set for LBW births only, HES deliveries was similar to ONS but HES births was not, especially when comparing sex and region. When comparing the characteristics of LBW births with those of all births (see online supplementary table S3), LBW births were more likely to be Asian (NN4B Asian LBW births=16.9%; NN4B Asian births =10.4%), delivered more frequently by Caesarean section and in the most deprived Carstairs quintile.

Similar proportions of all births were stillborn in all data sets (ONS 0.5%; HES deliveries 0.6%; HES births 0.5%; NN4B 0.5%) (see online supplementary table S4). Between 2002 and 2010 there was a slight decrease in the annual rate of stillbirths with a large peak in 2007 in HES (figure 1B). This was due to reporting issues with one NHS trust (which has previously been reported in HES data quality notes) and after excluding this trust, the rates of stillbirths in HES were lower than in ONS. When comparing specific variables in each data set for stillbirths only, HES deliveries was generally similar to ONS, but HES births showed larger discrepancies. Compared with all births (see online supplementary table S3) stillbirths were more often multiple births (ONS multiple births=3.1%, ONS multiple stillbirths=7.7%), in deprived areas, of LBW and from non-white ethnic groups.

Term LBW deliveries and PTDs

Analysis of term LBW deliveries and PTDs requires information on gestational age which is held in HES data sets and NN4B only (see online supplementary table S5). Using data for 2006–2010, the proportion of live singleton births that were term LBW varied from 2.5% in NN4B to 2.7% in HES births. Compared with all births (see online supplementary table S3) term LBW babies were more likely to be female, Asian (HES deliveries Asian births=11.5%, HES deliveries Asian term LBW births=23.1%) and from deprived areas.

The two HES data sets recorded a similar, higher proportion of PTDs than NN4B (HES deliveries=7.4%; NN4B=5.9%) (see online supplementary table S5) and the HES deliveries data set was more similar to NN4B than HES births. Compared with all births, PTDs were more likely to be LBW (HES deliveries LBW births=5.8%; HES deliveries preterm LBW births=45.9%) and from the most deprived areas.

Regional spatial analysis

The national HES deliveries data set had fewer live births per LSOA than ONS (HES mean 122.8 live births per LSOA; ONS=175.1) with this difference being most marked in London (table 3). Stillbirth counts at LSOA level were similar in both data sets at a national level (mean 0.9 stillbirths per LSOA), but lower in HES deliveries in the North-East and London. The birthweight data at LSOA level showed good agreement between HES deliveries and ONS but differences were observed in the variability. A similar pattern was seen for the North-East and London regions.

The spatial distribution of the rates of live births in London and the North-East at LSOA level (2002–2010) is shown in figure 2. In London there were clear spatial differences in the live birth rates, with the South-East and North-West of London showing particularly low rates of HES deliveries compared with ONS births (figure 2A). In the North-East the distribution of births by LSOA was broadly similar in both data sets (figure 2B).

DISCUSSION

This is the first study to provide a detailed assessment of the quality of reproductive health data from all four national routine births data sets in England. Overall the ONS births data set is the most complete and accurate record of all births in England (2002–2010) and NN4B is a valuable enhancement to this data set. HES deliveries is more complete than HES births and captures the majority of English births (96.8%) with good comparability to ONS but still has inaccuracies relating to missing data resulting in temporal and spatial anomalies. However HES deliveries offers detailed clinical information that cannot be obtained from the ONS data sets.

Descriptive statistics and trends for the birth outcomes were broadly similar for ONS, NN4B and HES deliveries, but less so for HES births due to missing data. The prevalence of LBW babies in ONS (5.9%) was similar to a WHO estimate for similar European countries (6.6%),[28] as was the prevalence of stillbirths in ONS (0.5%) which also was consistent with other European countries (<1%).[29] The prevalence of PTDs in the NN4B data (5.9%) was similar to recent 2010 estimates for other northern European countries (5%).[30] Known risk factors for LBW, PTD and stillbirth include deprivation and non-white ethnicity;[31] this was consistent with our results which found term LBW, LBW birth, PTD and stillbirth were more likely in non-white ethnic groups and in the most deprived Carstairs quintiles.

Our recommendations for those considering using the four national routine births data sets in England for epidemiological studies of birth outcomes are:

- For studies where clinical and lifestyle data are not required, for example, birth rates/prevalence studies, time trend studies, etc, ONS birth registrations is preferred.
- For studies that require information on gestational age and potential confounders such as ethnicity, NN4B is preferred but is currently only available from ONS from 2006 onwards.
- If clinical or pre-2006 information is needed HES deliveries is preferred over HES births unless, for example, information on the child's ethnicity is required over mother's ethnicity.
- Temporal and spatial trends in HES data should be thoroughly explored before use especially if HES data prior to 2002 are to be used.
- Any spatial and temporal trends identified should be interpreted in the light of changes in reporting.
- Despite information governance and technical challenges, linkage between data sets has the greatest potential to provide the richest and best quality data sets for use in research.

Previous studies of birth outcomes in England have primarily used ONS,[1 2 7–12] and HES data have seldom been used for peer reviewed research papers.[14–17 32] It is unclear why HES data sets have been underused but could be due to concerns over data quality or being a more complicated data set to work with. Differences in how the data are collected may also influence the choice of data set.

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Table 3 LSOA level comparison of live births, stillbirths and average birth weight by selected government office regions 2002–2010

	Live births		Stillbirths		Continuous birth weight*	
	HES deliveries	ONS births	HES deliveries	ONS births	HES deliveries	ONS births
National (LSOAs=32 470)						
Mean	122.8	175.1	0.9	0.9	3368.6	3375.0
SD	75.6	80.8	2.6	1.2	121.9	94.0
Median	109	160	0	1	3378.4	3383.9
IQR	70–159	119–214	0–1	0–1	3306.8–3443.5	3316.4–3441.8
5–95th centiles	30–262	79–321	0–3	0–3	3185.0–3529.6	3208.4–3514.8
Min–max	0–1491	3–1940	0–63	0–12	606–4600	2961.6–3734.1
North-East (LSOAs=1656)						
Mean	137.8	156.2	0.6	0.8	3380.1	3384.9
SD	59.4	67.2	0.9	1.0	86.8	84.7
Median	128	145	0	1	3382.1	3386.4
IQR	97–168	111–188	0–1	0–1	3321.6–3442.2	3329.0–3443.8
5–95th centiles	64–240	72–279	0–2	0–3	3231.6–3521.5	3241.6–3521.8
Min–max	21–792	26–952	0–5	0–7	3020.0–3651.4	3072.8–3663.4
London (LSOAs=4765)						
Mean	156.2	226.7	0.9	1.4	3324.0	3321.6
SD	80.8	77.7	1.2	1.4	92.5	85.3
Median	149	220	1	1	3322.7	3321.4
IQR	94–207	174–269	0–1	0–2	3265.0–3385.3	3264.9–3380.9
5–95th centiles	41–298	114–359	0–3	0–4	3170.0–3472.1	3178.4–3461.9
Min–max	2–674	3–1082	0–9	0–10	2971.3–3708.0	3013.1–3580.7

*Live singletons.
HES, Hospital Episode Statistics; LSOA, Lower Layer Super Output Area; ONS, Office for National Statistics.

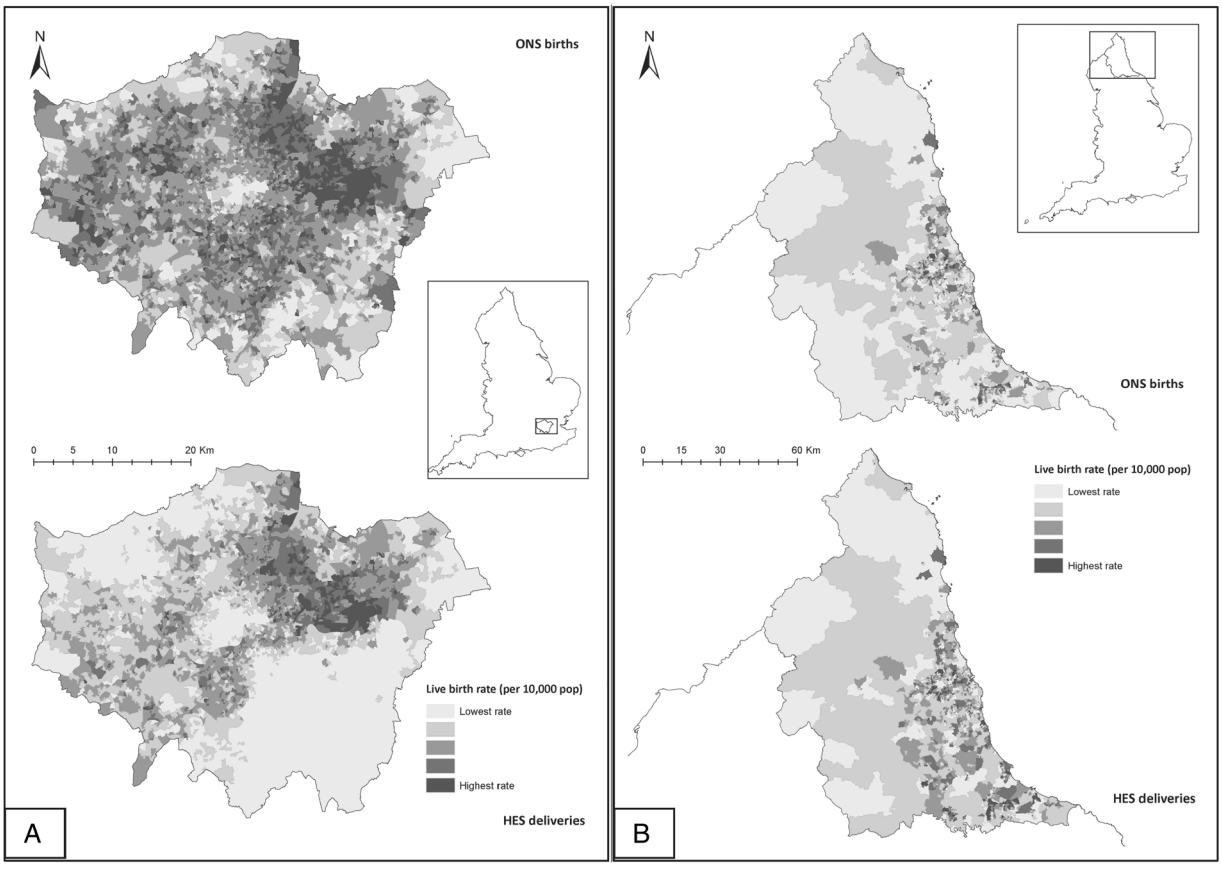


Figure 2 Super Output Area level live birth rates in ONS births and HES deliveries in (A) London (B) the North-East (2002–2010). *Actual live birth rates are not provided to prevent any potential identifiability of the data. HES, Hospital Episode Statistics; ONS, Office for National Statistics.

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While ONS birth registrations have remained consistently high quality, the HES data set had poorer capture and more missing data in earlier years, particularly pre-2002. Completeness has improved considerably and HES currently captures almost all English births in hospitals, although it does not record births outside NHS hospitals (eg, 2.8% of births occurring at home[33] or in private hospitals). Moreover, geographical identifiers in all the data sets are based on residential postcode of the mother. ONS and NN4B capture English resident mothers who give birth in Welsh, Scottish or northern Irish hospitals. HES will not capture English mothers who give birth outside England, although numbers of these are likely to be small.

HES data sets remain susceptible to data artefacts due to the nature of their collection and recording processes across many different hospitals. HES data quality is investigated and reported in HES data quality notes. There are various methods for selecting and deduplicating HES maternity records and the choice of method may influence the final data set. The Dr Foster method used in this paper[34] is not the only available method.[35] The apparent large peak in stillbirths in 2007 was the result of one NHS trust recording 99% of all its delivery episodes as stillborn and was reported in the annual HES data quality note.[36] The increase in missing HES data for 2007 is related to cessation of intensive manual data cleaning for 2007–2008.[36]

While HES deliveries data on a national scale were similar to ONS, we found spatial variations at the small area level. Low rates were observed in the South-East of London caused by under-reporting or lack of reporting of births by several hospitals. One method to deal with any variations in quality in HES data is to focus research or surveillance only on hospitals with high completeness of recording;[18] another is to link birth data sets. Linking ONS to HES deliveries would combine the completeness of ONS with additional information from HES. Pilot studies testing linkage between HES and ONS records have found that a high rate of linkage can be achieved.[37] However the linkage rate will depend on the years of data investigated, with the most recent pilot studies (2005–2007) able to link between 91–93% of HES deliveries to ONS births.[19 20] ONS routinely links infant mortality records with births to produce statistics on infant and perinatal mortality[38] as well as linking NN4B with births to produce gestation-specific infant mortality statistics.[22]

While administrative data sets are a rich data source for epidemiological studies, gaining access can be a slow process taking many months. Access to routinely available births data sets that are not publicly available (ie, with sensitive and/or personal information) is only possible with appropriate ethical approval, Health Research Authority Confidentiality Advisory Group governance approval, and data provider approval in place. Researchers will also need to use approved suitably secure facilities, either at their own institution or those provided by ONS or the Administrative Data Service. Changes to legislation and/or data provider changes may introduce further delays to obtaining data; HSCIC updating of data access processes as part of the Health and Social Care act 2012 and issues relating to the introduction of the care. data project have recently resulted in substantial delays. Linkage between HES and ONS data sets is not available routinely and there are additional technical challenges related to record matching and validation. Due to these constraints it is currently more common for researchers to use only one birth data set, therefore reducing the possible data coverage or depth of clinical information.

CONCLUSION

Routine birth data sets in England provide a valuable resource for epidemiological research on birth outcomes, surveillance of reproductive trends and provision of maternity services. The NN4B data set appears to be a promising addition for years from 2006, as it has the quality and coverage of ONS births but includes gestational age and ethnicity. The HES deliveries data set, currently underused, contains rich clinical information unavailable elsewhere but an appreciation of potential data anomalies is important for researchers. Streamlining data access procedures and routine linkage between these data sets would provide the best use of resources possible and improve use of these data by the research community.

Acknowledgements Hospital Episode Statistics data 2014 are reused with the permission of the Health and Social Care Information Centre. The ONS births data used were supplied by the Office for National Statistics (ONS), derived from the national birth registrations.

Contributors MBT conceived the study. KG was responsible for data extraction and KG and DCA were responsible for data cleaning and preparation. DCA and REG carried out the statistical analyses and drafted the initial report. REG carried out the mapping. The analyses were interpreted by REG, DCA, ALH, PE and MBT. All coauthors revised the report and approved the final version. MBT is the guarantor of this paper.

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Competing interests PE and ALH report grants from the Medical Research Council & Public Health England, during the conduct of the study.

Ethics approval Governance statement SAHSU holds approvals from the National Research Ethics Service—reference 12/LO/0566 and 12/LO/0567—and from the Health Research Authority Confidentiality Advisory Group (HRA-CAG) for Section 251 support (HRA—14/CAG/1039).

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Routinely collected English birth data sets: comparisons and recommendations for reproductive epidemiology

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APPENDIX F

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Using metal ratios to detect emissions from municipal waste incinerators in ambient air pollution data

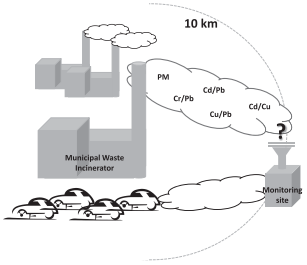
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HIGHLIGHTS

- Metal ratios used to fingerprint emissions from UK municipal waste incinerators.
- Weekly ambient metals data and high-resolved met data were used.
- No evidence of incinerator emissions within 10 km around four installations.
- Ambient metal ratios agreeing with emissions in sites within 10 km of two plants.
- Plume grounding detected for less than 0.2% of the time, contributing little to PM.

GRAPHICAL ABSTRACT



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ABSTRACT

This study aimed to fingerprint emissions from six municipal waste incinerators (MWIs) and then test if these fingerprint ratios could be found in ambient air samples. Stack emissions tests from MWIs comprised As, Cd, Cr, Cu, Pb, Mn, Ni, V and Hg. Those pairs of metals showing good correlation ($R > 0.75$) were taken as tracers of MWI emissions and ratios calculated: Cu/Pb; Cd/Pb; Cd/Cu and Cr/Pb. Emissions ratios from MWIs differed significantly from those in ambient rural locations and those close to traffic. In order to identify MWI emissions in ambient air two analysis tests were carried out. The first, aimed to explore if MWI emissions dominate the ambient concentrations. The mean ambient ratio of each of the four metal ratios were calculated for six ambient sampling sites within 10 km from a MWI under stable meteorological conditions when the wind blew from the direction of the incinerator. Under these meteorological conditions ambient Cd/Pb was within the range of MWI emissions at one location, two monitoring sites measured mean Cr/Pb ratios representative of the MWI emissions and the four sites measured values of Cu/Pb within the range of MWI emissions. No ambient measurements had mean Cd/Cu ratios within the MWI values. Even though MWI was not the main source determining the ambient metal ratios, possible occasional plume grounding might have occurred. The second test then examined possible plume grounding by identifying the periods when all metal ratios differed from rural and traffic

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values at the same time and were consistent with MWI emissions. Metal ratios consistent with MWI emissions were found in ambient air within 10 km of one MWI for about 0.2% of study period. Emissions consistent with a second MWI were similarly detected at two ambient measurement sites about 0.1% and 0.02% of the time. Where plume grounding was detected, the maximum annual mean particulate matter (PM) from the MWI was estimated to be 0.03 μg m^{-3} to 0.12 μg m^{-3}; 2–3 orders of magnitude smaller than background ambient PM_{10} concentrations. Ambient concentrations of Cr increased by 1.6–3.0 times when MWI emissions were detected. From our analysis we found no evidence of incinerator emissions in ambient metal concentrations around four UK MWIs. The six UK MWIs studied contributed little to ambient PM_{10} concentrations.

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1. Introduction

Municipal waste consists of a mix of combustible and non-combustible materials such as paper, plastic, food waste, glass, defunct household appliances and other non-hazardous materials (EMEP- EEA, 2013) that might vary by time and by city, town or village. The use of Municipal Solid Waste Incinerators (MWIs) has been increasing in the United Kingdom (UK) as a means to treat municipal waste due to European Union (EU) restrictions on the use of landfills. Modern European MWIs have operated under the EU Waste Incineration Directive (EU-WID) 2000/76/EC which set limits on emissions for heavy metals, dioxins and furans, carbon monoxide, dust, total organic carbon, hydrogen chloride, hydrogen fluoride, sulphur dioxide and nitrogen oxides. The EU-WID came into operation in 2002 for new MWIs and applied to all existent ones from 2005. The later Directive on Industrial Emissions (IED) (2010/75/EU) merged seven directives, including the EU-WID, into one piece of legislation, in order to harmonise the various strands of industrial regulation. The implementation of the IED in the UK was set to 2013 for new installations and 2014 for the existing ones.

Despite the strict limits on emissions, there is still considerable public concern about possible health effects associated with incineration. Some epidemiological studies have reported significant positive relationships with broad groups of congenital anomalies in populations living near MWIs. However, the results from these studies remain inconclusive due to limitations on exposure assessment, possible confounding risk factors and lack of statistical power (Ashworth et al., 2014).

Previous studies found no evidence that incinerators had a major or modest impact on particulate concentrations either in the United States (Shy et al., 1995) or in the UK (Ashworth et al., 2013). Despite this, older MWI have been found to be a source of heavy metals to the atmosphere (Sakata et al., 2000; Hu et al., 2003; Moffet et al., 2008) and high concentrations could be found in soil and vegetation samples in the vicinities of MWIs (Morselli et al., 2002).

In this study we aimed to fingerprint emissions from UK MWIs by identifying characteristic metal emission ratios and then test if these fingerprint ratios can be found in ambient air samples around MWI. Our analysis was part of a UK Public Health England (PHE) project investigating birth outcomes in the population living around (10 km distance) MWIs in England, Wales and Scotland.

2. Methods

2.1. Metals emissions from MWI and ambient concentrations

Quarterly stack emissions tests from MWIs were made available by the UK Environment Agency (EA). Particulate matter was sampled isokinetically from each MWI stack onto quartz filters. Following acid digestion with a mixture of nitric and hydrofluoric acid, stack samples were analysed by Inductively Coupled Plasma - Mass Spectrometry (ICP-MS) according to EN 14385:2004. This method is validated against matrix reference material BCR-037. Samples were analysed for Arsenic (As), Cadmium (Cd), Chromium (Cr), Copper (Cu), Lead (Pb), Manganese (Mn), Nickel (Ni), Vanadium (V) and Mercury (Hg). Emissions data were available from 2003 until 2010. For most of the samples the metals concentrations were aggregated for reporting purposes (EU-WID compliance) and the concentration for each metal was not available. Only 52 tests among all the UK MWI had detailed concentration values for each metal and these were used for fingerprinting. This detailed metals emissions data came from 10 (of a total of 22) UK MWIs: Crymlyn Burrows, Chineham, Coventry, SELCHP, Dudley, Bolton, Stockton-on-Tees, Stroke-on-Trent, Tyseley and Wolverhampton.

Ambient concentrations of As, Cd, Cr, Cu, Iron (Fe), Hg, Mn, Ni, Pb, Platinum (Pt), V and Zinc (Zn) in PM_{10} (particulate matter with aerodynamic diameter <10 μm) were measured by sampling onto a filter (cellulose ester) for weekly periods using a Partisol 2000 sampler according to EN12341:2014. The ambient air filters were digested in a mixture of nitric acid and hydrogen peroxide in a microwave oven, according to EN 14902:2005, and followed by analysis by ICP-MS. This procedure was validated by the digestion and measurement of suitable matrix reference materials, such as NIST SRM 1648a – urban particulate matter. The recoveries of all relevant metals were consistent with the certified values within the uncertainty of the measurements. The analysis was undertaken by the National Physical Laboratory (NPL) for sites belonging to the urban and industrial metals network; and by the Centre for Ecology and Hydrology (CEH) for the rural metals network. These data are available as monthly means at http://uk-air.defra.gov.uk/.

Due to high sampling temperatures the stack filters are quartz and a hydrofluoric (HF) acid matrix is required to digest them to ensure that any deeply trapped PM is recovered, and to perform an appropriate blank correction. By contrast only nitric acid digestion is needed to fully digest cellulose ester filters used for ambient measurements and HF digestion is not required. Kulkarni et al. (2007) underlined the importance of HF digest for ambient PM samples with high silica mineral content. This was unlikely to be an issue in our study since large mineral particle emissions from the MWI would have been preferentially trapped in the bag filtration system that have higher efficiency for larger particles (Buonanno et al., 2009; Ashworth et al., 2013) and mineral dust episodes such as those from the Sahara are rare in the UK (Ryall et al., 2002).

In order to fingerprint emissions from MWIs, the correlation coefficient between metals was calculated from the stack measurements. Those pairs of metals showing good correlation ($R > 0.75$) across all MWI sites were taken as potential tracers for MWI emissions. Ratios were then calculated by means of Reduced Major Axis (RMA) regression (Ayres, 2001; Warton et al., 2006). Due to insufficient samples it was not possible to create fingerprint

profiles for individual MWI.

Ratios for the same metals were calculated from ambient samples from the rural network (n = 579 samples from 11 sites in 2010) and from Cromwell Road site in London as representative of metal ratios from traffic sources (data from 2004 to 2011, n = 311).

2.2. Detecting MWI emissions in ambient air

Six metals sampling sites were located within 10 km of a MWI in the UK (Fig. 1; Table 1) with weekly samples of ambient metals concentrations. Most of the ambient metals sampling sites were located close to heavily industrialized areas. The sampling sites Walsall Bilston Lane (Background metals site) and Walsall Centre (Industrial metals site), near the Wolverhampton and Dudley MWIs respectively, had multiple industries related to metals refining and finishing located nearby. Although the Redcar Normanby site was an urban background site, the same wind direction towards the Stockton-on-Tees MWI included industrial premises such as chemical, plastics and acrylics manufacturers and an oil refinery. London Westminster and Sheffield Centre were urban background sites located near traffic. London Westminster site had no industrial sources nearby. NE of the Sheffield Centre metals site (in the same direction as the MWI) there were several industries producing industrial alloys, cast products and steel. The Swansea Morriston sampling site was located just off a main road running SW – NE. The Crymlyn Burrows MWI was located SE of the metals site with the UK's largest steel production plant (Port Talbot) located ~3 km to the east of the MWI.

The analysis period for each MWI was determined by the operational times for each MWI and the coincidental availability of ambient metal measurements (Table 1).

To assess if emissions from MWIs were detected at the metals sites, two sets of analysis were undertaken: the first aimed to explore if MWI emissions dominate the ambient concentrations; the second tested if all four ratios differed from rural or traffic values at the same time and were consistent with MWI emissions. For the first analysis, bivariate polar plots (BPP) of those metal ratios that were identified as good tracers of MWI emissions were calculated using the Openair R-package (Carslaw and Ropkins, 2012). BPP determine the mean value of an ambient metals ratio against wind direction and wind speed. BPP have been used previously in receptor analysis to identify the location of potential sources of air pollution (Carslaw, 2005). For the second analysis, the Polar Annulus (PA) function of the Openair R-package was calculated. PA plots show the time series of the measured ambient ratio by wind direction.

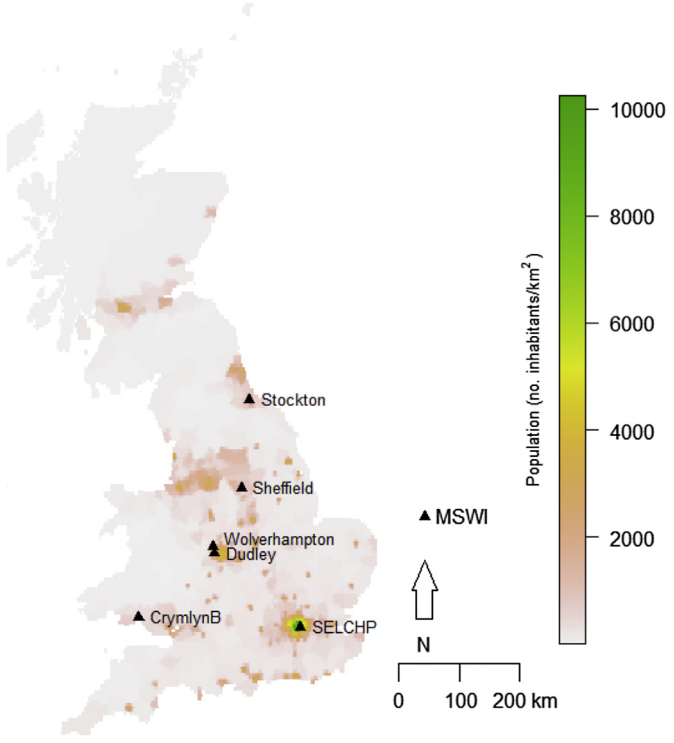


Fig. 1. Map of the UK MWI included in this study. Base map: population density in 2000 (CIESIN, 2011).

Previous studies have successfully determined the sources and their contribution to pollutant concentrations measured at low-frequency (e.g. daily, weekly). Different techniques have been proposed in the literature based on the frequency of the wind for a given wind sector (e.g. Cosemans et al., 2008; Godri et al., 2010). Here, high resolution (hourly) meteorological measurements were used to compute BPP and PA. The same weekly metals concentration was assigned to each hourly measurement of wind speed and direction.

Meteorological data were obtained from weather stations within 30 km of a MWI and processed using the Atmospheric Dispersion Modelling System Urban (ADMS-Urban). ADMS-Urban uses meteorological variables including wind speed, wind direction, temperature and cloud cover to calculate parameters that are used in the dispersion algorithms such as boundary layer height, Monin-Obukhov length, etc. The meteorological input data was extracted from the closest weather station following the MetOffice quality standards. Missing cloud cover records were completed using data from the nearest met station with 90% completeness where necessary.

During unstable meteorological conditions buoyant motions are enhanced causing rapid dispersion of emissions. Under poor mixing (stable) conditions MWI plume will mix less with the surrounding air keeping its chemical composition. Highest concentrations attributable to the MWI at the ambient metal sites are therefore expected under stable atmospheric conditions. For this reason, analysis of ambient data was focused on the times when stable atmospheric conditions were met.

Atmospheric stability conditions were defined as:

$$z^{*}\mathrm{L} = z^{*}1/\mathrm{L_{MO}}$$

where z is the boundary layer height and $\mathrm{L_{MO}}$ is the Monin-Obukhov length. Stability conditions were classified as unstable for $-1000 < z^{*}\mathrm{L_{MO}} \leq -0.2$; neutral for $-0.2 < z^{*}\mathrm{L_{MO}} \leq -0.2$; and stable for $0.2 < z^{*}\mathrm{L_{MO}} \leq 50$.

During stable conditions an elevated point source (such as the MWI chimney) may be above the boundary layer height (z). At these times emissions can be released above the temperature inversion and hence not influence ground-level concentrations. With the exception of SELCHP MWI, z was lower than the MWI chimneys at all times. At SELCHP, the stack was above the boundary layer for 22% of the hours when stable conditions were met.

$\mathrm{NO_X}$, $\mathrm{SO_2}$ and PM emissions reported by the MWI operators were used to assess the days when the plants were operating for inclusion in the BPP and PA calculations. The total analysis period covered 11,437 days.

In order to test our assumptions about higher attributable MWI emissions under stable conditions and whether emissions from stacks could be identified using weekly samples instead of highly-resolved data (i.e. hourly concentrations), two sensitivity tests were undertaken. These used air quality data from the Harwell monitoring site (1.3265°W, 51.5711°N). Harwell is a rural monitoring site

Table 1
List of MWI and ambient metals sites (AMS) within 10 km.

MWI	Stack height (m)	Start year	Median PM emissions (kg day^{-1})	Ambient metals site (AMS)	Type of AMS	Distance MWI to AMS (km)	Analysis period (no. days)
Crymlyn Burrows	40	2003	0.7	Swansea Morriston	Traffic	5.2	847
Dudley	47	1998	1.8	Walsall Bilston Lane	Background	9.7	1578
Dudley	47	1998	1.8	Walsall Centre	Industrial	10.3	1515
Stockton-on-Tees	70	1998	4.5	Redcar Normanby	Background	9.1	745
Sheffield	76	1990	0.7	Sheffield Centre	Background	1.9	910
SELCHP	100	1994	14.8	London Westminster	Background	6.0	1889
Wolverhampton	76	1998	3.0	Walsall Bilston Lane	Background	5.8	1996
Wolverhampton	76	1998	3.0	Walsall Centre	Industrial	8.1	1957

belonging to the UK Automatic Urban and Rural Network (AURN) located 7.3 km from the coal-fired Didcot Power Station, a well known source of atmospheric SO_2 (McGonigle et al., 2004; Charron et al., 2005). The first test was based on BPP for SO_2 concentrations under unstable, neutral and stable conditions. BPP for SO_2 concentrations under stable conditions showed higher concentrations in the direction of the Power Station compared to those measured under unstable conditions (Supplementary Figure A1). Moreover, under unstable conditions, the source of SO_2 in the direction of the Power Station was spread over a wider range of wind sectors and wind speeds due to enhanced atmospheric mixing conditions. In the second test, BPP and PA for weekly SO_2 concentrations were compared to those using hourly data. Under stable conditions, using weekly mean SO_2 with hourly resolved meteorological data, BBP analysis located the same source of SO_2 as using hourly data (Supplementary Figure A2). The PA time series of the trends of the SO_2 source computed from the hourly and weekly datasets were also similar (Supplementary Figure A3). The use of weekly means combined with high-resolved meteorological data can therefore be confidently used to detect point sources of atmospheric pollution and to assess the temporal changes in their intensity.

2.3. Quantification of ambient MWI PM using a single metals tracer

Analysis of ambient metal ratios can be used to detect MWI emissions but not quantify their impacts on ambient PM concentrations. To quantify Particulate Matter (PM) at receptor locations the ratio of PM/metal emitted by the MWIs was calculated from stack emissions tests by RMA regression.

ADMS-Urban was also used to model daily mean PM concentrations at post-code resolution for each MWI following the methods detailed in Ashworth et al. (2013). Metals concentrations were then estimated at the receptor (ambient metal site) based on modelled PM and calculated stack emission ratios.

3. Results

3.1. Metals emissions from MWI

The MWI listed in Table 1 were installations that were adapted to the EU-WID except Crymlyn Burrows which was commissioned following EU-WID. Results from MWI stack tests are summarized in Table 2. The ambient concentrations measured at rural metals sites are also given for comparison. Sorted from largest to smallest emissions concentrations (median values), MWI were emitters of Pb > Cr > Ni > Mn > Cu > Cd > As > V. When compared to the median rural background concentrations, MWI emissions contained greater quantities of Cr (41×10^3 times larger than rural concentrations), Cd (22×10^3 times larger), Ni (13×10^3), Pb (5×10^3) and Cu (3×10^3).

Emissions of Cu–Pb showed a good correlation ($R = 0.91$, $N = 18$, $p < 0.001$) followed by Cd/Pb ($R = 0.86$, $N = 19$, $p < 0.001$), Cd/Cu ($R = 0.77$, $N = 50$, $p < 0.001$) and Cr/Pb ($R = 0.68$, $N = 19$, $p < 0.05$) (Table 3). We therefore selected the emissions ratios of these four pairs of metals as potential tracers for MWI emissions. Additionally their values also differed from those found in rural and traffic locations (Table 4). However, these four ratios represented only three pieces of independent information since (Cd/Pb)/(Cd/Cu) = (Cu/Pb).

Since Cr and Cd were the two metals with the greatest enrichment factors (Table 2), ratios of PM/Cd and PM/Cr were calculated from emissions samples. Emissions rates of PM/Cd showed a good correlation coefficient ($R = 0.94$, $p < 0.01$, $n = 34$) while PM/Cr was weaker ($R = 0.41$, $p < 0.05$, $n = 33$). Cd therefore was therefore additionally selected as tracer for PM emitted by MWI using a ratio of 6724 [5999–7647, 2σ] mgPM (mgCd)$^{-1}$ (Table 5).

3.2. Detecting MWI emissions in ambient air

Fig. 2a shows an example of BPP for the Cr/Pb ratio calculated using weekly samples from the Redcar Normanby site, 9.1 km from the Stockton-on-Tees incinerator. Values of Cr/Pb fell within the range of MWI emissions for wind speeds higher than 10 m s^{-1} when the wind blew from the direction of the incinerator (Fig. 2b). For wind speeds lower than 10 m s^{-1}, values of Cr/Pb ranged between that found in rural areas and the ratio expected from traffic sources.

Ambient ratios measured at the metal sites from the wind direction of each MWI were compared with the values from MWI stacks (Table 6). With the sole exception of the Walsall Centre sampling site in the direction of Wolverhampton incinerator, mean Cd/Pb, mean Cd/Cu and mean Cd/Pb were not within the range of MWI emissions for any of the ambient measurements near a MWI. However, near the Dudley, Stockton-on-Tees and Wolverhampton MWI ambient ratios were above the rural background values for Cd/Cu; and above the traffic values for Cd/Pb near Stockton-on-Tees and Wolverhampton. The metals sites near Stockton-on-Tees and Sheffield measured Cr/Pb ratios representative of the MWI emissions. The values of the Cu/Pb ratio near Dudley, Stockton-on-Tees, Sheffield and Wolverhampton fell within the range of values representative of the MWI emissions.

From analysis of the mean ambient metal ratios when the wind blew from the direction of an incinerator it was clear that the MWIs were not the main source of the tracer metals. Only Redcar Normanby measured mean ratios within the MWI emissions range (Cr/Pb and Cu/Pb) and different from the rural (Cd/Cu) and traffic values (Cd/Pb). However, emissions from MWI might influence the burden of metals in the area and grounding of MWI plume might have occasionally occurred. This would lead to a mixture of sources on a weekly filter producing a ratio that was between rural conditions and the incinerator emissions. Fig. 3 shows the time series of the Cr/

Table 2
Minimum, mean and maximum metal concentrations from MWI stack tests from 2003 to 2010. Ambient concentrations measured at rural metals sites in 2010 are also shown.

	MWI stack emissions (2003–2010)				Ambient rural concentration (2010)			
Metal	Min (μg m^{-3})	Median (μg m^{-3})	Max (μg m^{-3})	*N*	Min (ng m^{-3})	Median (ng m^{-3})	Max (ng m^{-3})	*N*
As	0.00	0.85	97.00	50	0.05	0.40	13.6	579
Cd	0.00	1.30	26.50	52	0.01	0.06	2.05	579
Cr	0.00	10.60	94.00	51	0.24	0.26	7.06	579
Cu	1.00	6.10	160.00	50	0.12	1.98	60.3	579
Pb	0.00	16.00	200.00	19	0.36	3.38	184	579
Mn	0.40	6.30	92.30	52	0.04	1.55	52.1	579
Ni	0.00	6.80	177.50	49	0.06	0.52	9.74	579
V	0.00	0.75	12.20	49	0.12	0.74	11.2	579

Table 3
Correlation coefficients between the metals emitted by the MWI in the UK from 2003 to 2010.

	As	Cd	Cr	Cu	Pb	Mn	Ni	V
As	1							
Cd	−0.05	1						
Cr	0.08	0.36	1					
Cu	0.00	**0.77**	0.57	1				
Pb	0.03	**0.86**	**0.68**	**0.91**	1			
Mn	0.02	0.42	0.13	0.39	0.42	1		
Ni	−0.06	0.06	0.03	0.06	−0.04	0.24	1	
V	0.11	0.40	0.02	0.20	−0.05	0.42	0.05	1

Pb ratios measured at the Swansea Morriston metals site when the wind blew from Crymlyn Burrows MWI. Despite the Cr/Pb mean ratio being between the rural and traffic values (Table 6), some of the measured ratios measured fell within the MWI emissions range (Fig. 3).

Most of the MWI are located in areas of diverse industrial sources which could confound the analysis. Even though an ambient metal ratio was within the range of MWI emissions (Fig. 3), we could not with certainty attribute ambient metals concentrations to direct emissions from MWIs. It was clearly not possible to fingerprint all of the potential emissions sources. We therefore considered the time series of the four ratios measured at each site to determine whether all the metal ratios were consistent with MWI emissions or were different from rural or traffic values at the same time. Fig. 4 shows the time series of the four metal ratios measured at Redcar Normanby from the direction of the Stockton-on-Tees incinerator. Measurements of Cr/Pb were within the range of MWI emissions on three occasions and these were coincidental

Table 4
Mean and 95% confidence interval of the metals ratio values representative of MWI emissions, ambient rural and ambient traffic locations.

Metals ratio	MWI (mean ± 2σ)	Rural (mean ± 2σ)	Traffic (mean ± 2σ)
Cd/Cu	0.14 [0.12–0.17]	(0.26 [0.24–0.28])·10^{-1}	(0.07 [0.06–0.08])·10^{-1}
Cd/Pb	0.08 [0.06–0.10]	(1.31 [1.27–1.35])·10^{-2}	(0.17 [0.16–0.18])·10^{-1}
Cr/Pb	0.56 [0.38–0.75]	0.13 [0.12–0.14]	0.28 [0.25–0.31]
Cu/Pb	0.83 [0.67–0.99]	0.51 [0.47–0.54]	2.38 [2.14–2.63]

Table 5
Mean and 95% confidence interval of the PM_{10}/Cd and PM_{10}/Cr ratios representative of MWI emissions.

	Cd	Cr
PM_{10}/metal (mean ± 2σ)	6724 [5999–7647]	1708 [1166–2249]
R	0.94	0.41
N	34	33

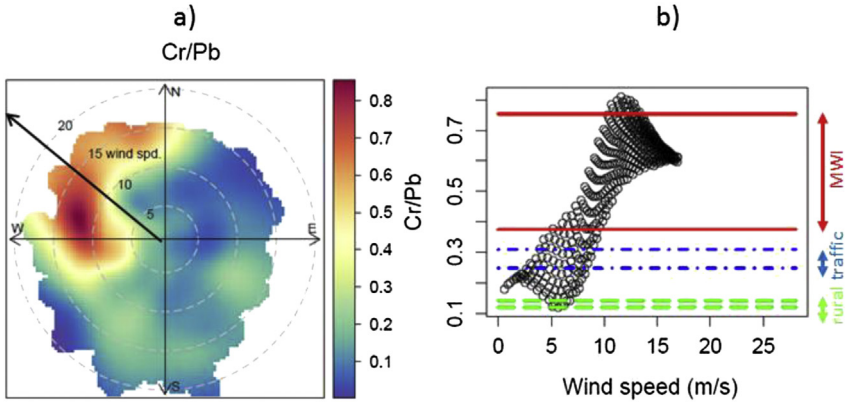


Fig. 2. (a) BPP for the Cr/Pb ratio measured at Redcar Normanby metals site under stable atmospheric conditions. Radially wind direction is plotted from north (N). The concentric lines indicate increasing intensity of the wind speed and the shading shows the mean ratio value. The arrow indicates the direction where the Stockton-on-Tees MWI is located. (b) Distribution of the ratio values against wind speed for the direction where the Stockton-on-Tees MWI is located. Solid red horizontal lines indicate the range of MWI emissions for the Cr/Pb ratio; green and blue dashed lines indicate the range for the rural and traffic, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 6
Minimum and maximum ambient values for the four metal ratios measured in the ambient metals sites near a MWI when the wind blew from the incinerator (30° sectors). Numbers in italics indicate ratios that are different from rural or traffic ratios. * indicates ratios were within the MWI emissions representative values.

Metals site	MWI	Cd/Cu	Cd/Pb	Cr/Pb	Cu/Pb
Swansea Morriston	Crymlyn Burrows	0.01–0.02	0.01–0.02	0.03–0.27	1.21–1.79
Walsall Bilston Lane	Dudley	*0.04–0.06*	*0.03–0.06*	0.03–0.10	0.73–1.47*
Walsall Centre	Dudley	*0.02–0.05*	*0.02–0.04*	0.08–0.17	0.70–0.93*
Redcar Normanby	Stockton-on-Tees	*0.03–0.05*	*0.02–0.02*	*0.12–0.81**	0.49–0.82*
Sheffield Centre	Sheffield	0.01–0.02	0.01–0.02	*0.02–0.51**	0.89–1.93*
London Westminster	SELCHP	0.01–0.02	0.01–0.03	0.14–0.34	1.32–1.80
Walsall Bilston Lane	Wolverhampton	*0.03–0.06*	*0.04–0.06*	0.06–0.19	0.78–1.91*
Walsall Centre	Wolverhampton	*0.02–0.10*	*0.02–0.08**	0.08–0.20	0.65–0.99*

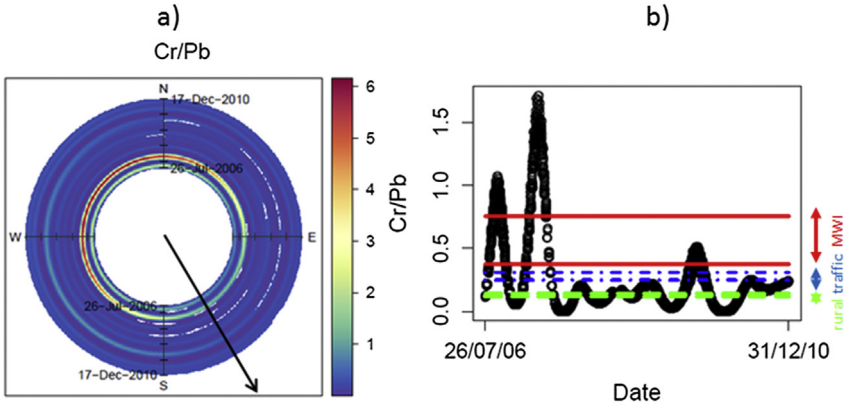


Fig. 3. (a) PA for the Cr/Pb ratio measured at Swansea Morriston metals site under stable atmospheric conditions. The arrow indicates the direction where the Crymlyn Burrows MWI is located. (b) Time series of the Cr/Pb ratio at the direction where the Crymlyn Burrows MWI is located. Solid horizontal red lines indicate the range of MWI emissions for the Cr/Pb ratio; green and blue dashed lines indicate the range for the rural and traffic representative values, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

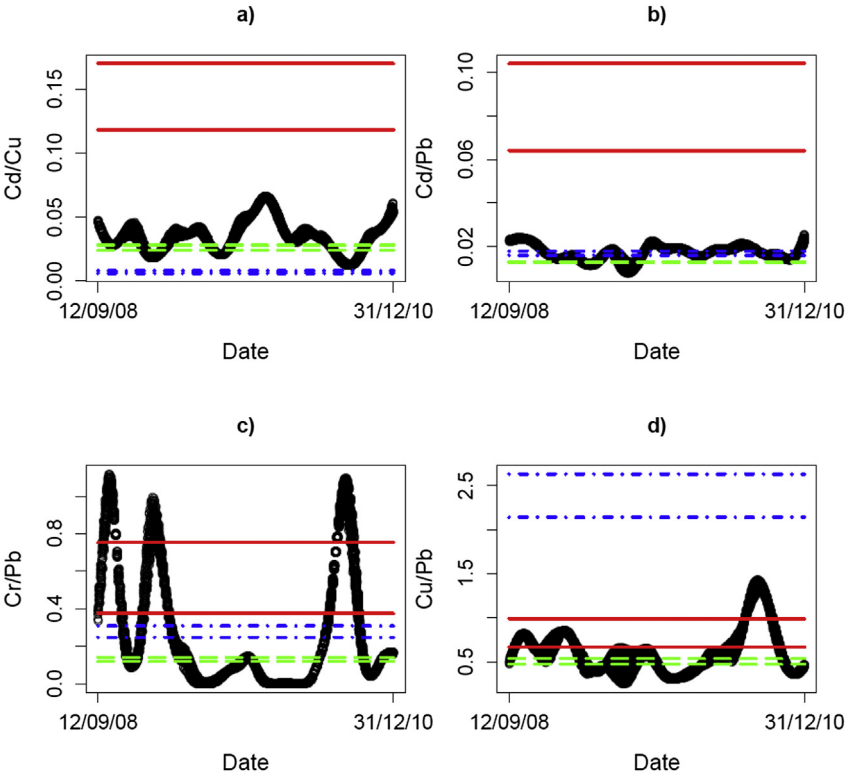


Fig. 4. Time series of Cd/Cu (a), Cd/Pb (b), Cr/Pb (c) and Cu/Pb (d) measured at Redcar Normanby when the wind blew from the direction where the Stockton-on-Tees MWI is located. Solid horizontal red lines indicate the range of MWI emissions; green and blue dashed lines indicate the range for the rural and traffic representative values, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

with Cu/Pb values expected from MWI emissions. Measured Cd/Cu ratios were similar to the rural concentrations but some peaks were different from rural values indicating the presence of a source changing the metals ratio that might have been the incinerator. Similarly, Cd/Pb ratios ranged between the rural and traffic values with some peaks moving towards the MWI values.

A further example of this approach is shown in Fig. 5 which depicts the time series of the metal ratios measured at London Westminster for the wind sector where SELCHP MWI is located. Some peaks of the Cr/Pb ratio fell within the MWI ratio (Fig. 5c) but those peaks were identified as traffic sources by the other tracers, which was consistent with this being a highly trafficked location in central London, leading to the conclusion that these peaks were not due to the MWI plume grounding.

For the majority of the metals sampling sites located near an incinerator it was rare to measure simultaneously the four ratios within MWI values or different from the rural and traffic values (Table 7). Only the Redcar Normanby, Walsall Centre and Walsall Bilston Lane metals sites measured all four ratios coincidently; for 5.4%, 2.6% and 0.5% of the time, respectively, that the wind blew from the incinerator Stockton-on-Tees (Redcar Normanby) and Wolverhampton (Walsall Centre and Walsall Bilston Lane) in stable conditions.

For the metals sampling sites near Stockton and Wolverhampton MWIs, PM emitted by the MWI was estimated using the Cd concentration measured when grounding of the MWI plume was detected by all four tracer ratios; and assuming zero PM concentration from MWI when plume grounding was not detected. It is therefore an estimated maximum PM from MWI at the ambient metals site. The maximum PM concentration in ambient air from MWI emissions ranged from 0.029 μg m^{-3} (Stockton-on-Tees MWI) to 0.123 μg m^{-3} (Wolverhampton MWI). This differed from the mean PM concentrations predicted from the ADMS-Urban model that were 1–2 orders of magnitude smaller (Table 8).

The ambient concentration of heavy metals during plume grounding was compared with the mean concentration measured from other wind sectors (Table 9). The concentrations of Cr was higher at all measurement sites when MWI emissions were detected: 3.0 (at Redcar Normanby), 1.6 (Walsall Bilston Lane) and 2.4 (Walsall Centre) times larger compared with the mean concentration measured from the other wind sectors. Ni concentrations were higher at Walsall Bilston Lane when MWI emissions from Wolverhampton were detected (14.3 ± 2.3 ng m^{-3}) compared to the mean concentration measured from the other wind sectors (4.6 ± 5.8 ng m^{-3}). The other metals sites (Redcar Normanby and Walsall Centre) also measured higher mean concentrations but differences were not statistically significant.

The emission ratio in Table 5 can be combined with the ADMS-Urban PM estimates to calculate a metal concentration at each ambient metals site, as shown in Supplementary Material (Part B). This shows that the contribution of MWI emissions to the ambient levels of Cd and Cr were very small (ranging from 0.001% to 0.08%).

4. Discussion and conclusions

In our study we aimed to pin-point emissions from MWI using measurements of ambient heavy metal particle concentrations. Several studies have used receptor models to apportion particulate matter sources or to apportion bulk deposition near a MWI (Venturini et al., 2013). Receptor models are useful when the aim of the study is to identify the sources of pollution affecting an ambient measurement site. However, in our study we aimed to pin-point only one source of pollution (incinerator) instead of explaining all sources influencing the measured metals concentrations.

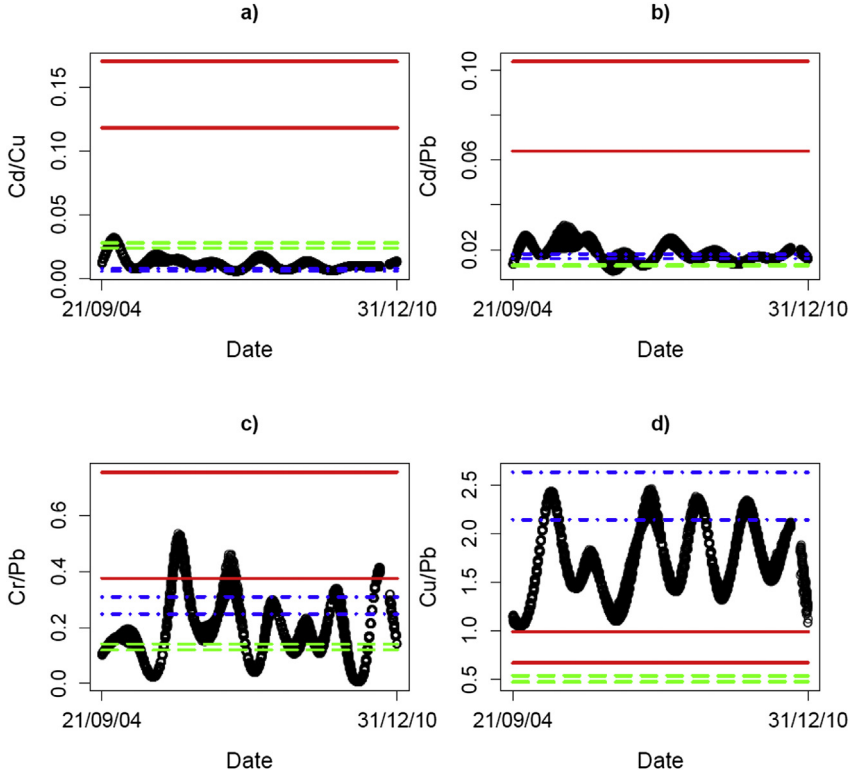


Fig. 5. Time series Cd/Cu (a), Cd/Pb (b), Cr/Pb (c) and Cu/Pb (d) ratios measured at London Westminster at the direction where the SELCHP MWI is located. Solid horizontal red lines indicate the range of MWI emissions; green and blue dashed lines indicate the range for the rural and traffic representative values, respectively. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 7
Percentage of time that the four tracers were simultaneously within the range of MWI emissions or different from rural and traffic ambient sources.

MWI	Ambient metals site	% time with wind from MWI under stable conditions	% of the study period
Crymlyn Burrows	Swansea Morriston	0.0	0.0
Dudley	Walsall Bilston Lane	0.0	0.0
Dudley	Walsall Centre	0.0	0.0
Stockton-on-Tees	Redcar Normanby	5.4	0.2
Sheffield	Sheffield Centre	0.0	0.0
SELCHP	London Westminster	0.0	0.0
Wolverhampton	Walsall Bilston Lane	0.5	0.0
Wolverhampton	Walsall Centre	2.6	0.1

Table 8
Estimated PM from MWIs at ambient metals sites.

MWI	Ambient metals site	Maximum PM from MWI ambient data (mean ± σ) (μg m^{-3})	PM from MWI ADMS-Urban (mean ± σ) (μg m^{-3})
Stockton-on-Tees	Redcar Normanby	0.029 ± 0.002	$0.008 \cdot 10^{-1}$ ± 0.002
Wolverhampton	Walsall Bilston Lane	0.038 ± 0.002	0.002 ± 0.003
Wolverhampton	Walsall Centre	0.123 ± 0.007	0.001 ± 0.002

First, we successfully fingerprinted emissions from modern MWI in the UK using stack emissions samples of heavy metals. The ratios used to fingerprint MWI emissions in UK were consistent with emissions from burning electronic waste (that emits Cu and Pb) (Gullett et al., 2007), mixed paper and plastics (which emit Pb and Cd), and batteries (which emit Cd; Hasselriis and Licata, 1996; WHO, 2010), materials all expected to be found in municipal waste. Cr is emitted when burning coloured newsprint and mixed paper, plastic film, lawn waste, wood, textiles, footware and fines (Hasselriis and Licata, 1996). It has not been previously used as a tracer of MWI emissions despite being emitted in high abundance relative to rural concentrations (Table 2).

Unfortunately the number of stack samples available to calculate emission ratios was not enough to calculate individual source profiles for each MWI or to assess their changes over time. However, emission ratios of heavy metals were expected to be consistent between MWI for two reasons. First, the metals with best correlation coefficients share common origins within waste material. In a previous study from a MWI in British Columbia found that many waste types contributing to Pb emissions also exhibited high levels of Cr. Garden waste and certain type of paper fractions (commonly found in municipal waste) contain the highest concentrations of Pb, Cr and Cd. Emissions of Cr and Cd versus Pb also showed a linear relationship (Hasselriis and Licata, 1996). This is in agreement with our results. Second, all MWI in England and Wales used the same abatement techniques for heavy metals. These include injection of activated carbon (to capture mercury) and bag filters (to remove particulates). Furthermore the Cd/Pb ratio in our study was almost identical to that reported for modern European MWI in Nielsen et al. (2010) (Table 10). Other ratios were more similar to Nielsen et al. (2010) values than the older studies of Morselli et al. (2002) and Hu et al. (2003). Although it did not affect our study, the revised Restriction of the use of certain Hazardous Substances (RoHS) directive (2011/65/EU), that became effective on January 2013, limits the use of hazardous substances (such as Pb, Hg, Cd, and Cr (VI), among other substances) in electrical and electronic equipment. Emissions of heavy metals from incinerators are therefore expected to decrease and this will impact on future emission ratios.

In order to properly detect sources of atmospheric pollution in ambient data three requirements are needed: i) the dataset collected must include daily, seasonal and yearly variations of the source (Cohen et al., 2014); ii) the emissions tracers are not transformed in the atmosphere between emission and detection; and iii) the ambient measurements should include the chemical species emitted by the source (Cohen et al., 2014) at a measurable concentration.

The stack emissions used to fingerprint MWI emissions

Table 9
Mean ± standard deviation of heavy metals concentration (ng m^{-3}) measured at the ambient metals site when MWI emissions were detected and for the other wind directions. Bold numbers indicate those heavy metals that concentrations (within 95% confidence) were higher when MWI plume was detected.

	Redcar Normanby (Stockton-on-Tees)	Walsall Bilston Lane (Wolverhampton)	Walsall Centre (Wolverhampton)
As MWI plume	0.20 ± 0.03	0.88 ± 0.06	1.17 ± 0.08
As other sectors	0.40 ± 0.21	1.17 ± 0.38	1.05 ± 0.34
Cd MWI plume	0.08 ± 0.01	1.17 ± 0.06	0.71 ± 0.03
Cd other sectors	0.09 ± 0.04	2.58 ± 1.30	0.61 ± 0.40
Cr MWI plume	**2.32 ± 0.80**	**5.84 ± 0.21**	**6.08 ± 0.78**
Cr other sectors	**0.78 ± 0.90**	**3.66 ± 1.78**	**2.50 ± 1.77**
Cu MWI plume	2.58 ± 0.20	27.22 ± 1.06	17.94 ± 1.23
Cu other sectors	2.71 ± 1.06	50.3 6 ± 17.57	16.74 ± 6.63
Pb MWI plume	3.50 ± 0.39	48.09 ± 1.57	22.57 ± 1.25
Pb other sectors	5.70 ± 2.85	70.1 4 ± 31.76	19.90 ± 6.46
Mn MWI plume	4.20 ± 1.19	9.72 ± 0.26	8.56 ± 0.72
Mn other sectors	5.19 ± 3.89	11.25 ± 2.75	9.67 ± 1.97
Ni MWI plume	0.60 ± 0.42	**14.26 ± 2.33**	8.34 ± 2.81
Ni other sectors	0.45 ± 0.42	**4.59 ± 5.83**	3.84 ± 6.33
V MWI plume	0.86 ± 1.13	2.44 ± 0.10	5.27 ± 1.13
V other sectors	0.91 ± 1.25	1.87 ± 1.22	2.45 ± 3.15

Table 10
Value for the ratios representative of MWI emissions reported in this study and in the literature.

	This study	Nielsen et al. (2010)	EMEP-CORINAIR (2006) Morselli et al. (2002)	Hu et al. (2003)	Mamuro et al. (1980)
Cu/Pb	0.83 [0.67–0.99]	0.24 [0.17–0.32]	(0.89 [0.39–0.84])·10^{-3}	–	–
Cd/Pb	0.08 [0.06–0.10]	0.08 [0.07–0.09]	0.03[0.03–0.03]	0.05	0.03
Cd/Cu	0.14 [0.12–0.170]	0.34 [0.28–0.41]	36.56 [83.61–17.66]	0.21	–
Cr/Pb	0.564 [0.38–0.75]	0.28 [0.25–0.32]	(0.02 [0.01–0.04])·10^{-1}	–	–

comprised only a short snapshot of the MWI output throughout the study period (daily emissions on quarterly basis). Metals emissions from the MWI might change weekly, seasonally and/or on yearly basis. However the standard deviation in the four metal ratios was small meaning that these could be used with confidence as MWI tracers.

The ambient dataset available for this study ranged from 2 to 5.5 years depending on the MWI (Table 1). It comprised weekly samples of heavy metals and hourly meteorological information. Wind direction dependent emission ratios have been used successfully elsewhere in receptor analysis; for instance Johnson et al. (2014) recently used V, Ni, sulphur and black carbon ratios to examine the influence of shipping emissions on ambient air pollution in Brisbane, Australia. Although daily variations of the source cannot be observed in the weekly samples, analysis on a test dataset from the Harwell – Didcot Power Station showed that weekly mean concentrations combined with hourly meteorological data can accurately detect a point source and track temporal changes under stable meteorological conditions. Following results from the Harwell – Didcot Power Station test, the analysis of UK MWIs focused on stable meteorological conditions. These were met between 51–68% of the time when the wind blew from the direction of the MWIs.

The fingerprint metal ratios from MWI stack emissions were found to be very different to those in ambient rural environments and those close to traffic. Particulate metals are a primary emission from MWI (Table 2) and bag-filtered stack emissions from MWIs do not contain a significant amount of particulates greater than 10 μm diameter (Buonanno et al., 2009; Ashworth et al., 2013). Over the maximum 10 km distance considered in the study the different particulate metals should therefore be subject to the same rates of dispersion and deposition. Although concentrations of particulate metals would be expected to decrease with distance from the stack, the emissions ratios will be conserved in the MWI plume.

Detecting stack emissions using ratios in ambient data is most likely to be successful if the stack is the only source of the tracer species. The presence of other sources emitting the same species at different rates might change the ratios in ambient data making difficult to isolate sources. Some studies have used the ratio of heavy metals (e.g. Cd) related to Pb to detect the influence of MWI emissions in urban ambient air (e.g. Sakata et al., 2000). However, Pb emissions in Europe mainly come from area sources such as traffic (Pacyna et al., 2007, 2009; Noble et al., 2008) while Cd is emitted primarily from point sources (e.g. waste incinerators). The dissimilar distribution of emissions of Cd and Pb would represent a challenge for the detection of MWI emissions in ambient air as the emissions from other sources would modify the ratio measured at the measurement site. Ambient ratios different from the rural and traffic values might indicate the presence of other sources emitting metals to the atmosphere (e.g. MWIs). Most of the MWI in the UK are located in heavily industrialized areas and these might also modify the ambient metal ratios. In order to overcome this type of confounding behaviour, we used four tracer ratios to identify emissions from MWIs. Our technique identified that traffic was the main source of metals in central London demonstrating its specificity. Despite three of the four ratios used to fingerprint MWI emissions being related (Cd/Pb, Cd/Cu and Cu/Pb) the combination provided specific source information. For example, at the end of the time series shown in Fig. 4 ambient values of Cu/Pb were within the MWI emissions value although Cd/Cu and Cd/Pb values clearly indicated the dominance of traffic emissions.

In summary we did not detect incinerator source profiles in ambient particulate matter metal concentrations around four UK MWIs. However, MWI emissions might still influence ground-level concentrations but the location of the sampling sites did not detect them. Despite the ambient sampling locations were not ideally placed to detect the influence of the MWIs (e.g. not downwind in the prevalent wind direction, near other metals emitting industrial sources, etc.) and the time resolution of measurements were only weekly samples, we successfully identified emissions from MWI for two installations in UK. Metal ratios consistent with MWI emissions were found in ambient measurements within 10 km of the Stockton MWI for about 5.4% of the time when the wind blew from the incinerator under stable conditions. The Wolverhampton MWI was similarly detected at two ambient metals sites, about 2.6% and 0.5% of the time when the wind blew from the incinerator under stable conditions. This was 0.2% of the total study period at Stockton and a maximum of 0.1% of the study period at Wolverhampton. Stockton-on-Tees and Wolverhampton are the second and third largest UK MWI in terms of daily PM emissions (Table 1), which might explain their detection in the study. Using metal tracers we estimated a maximum ambient PM from these two MWIs between 0.03 and 0.12 μg m^{-3} at our receptor sites. These concentration estimates were one to two orders of magnitude larger than the dispersion-modelled mean PM concentrations which were between 10^{-4} and $2 \cdot 10^{-3}$ μg m^{-3} at the metals sites. It must be remembered that our tracer method assumed that all Cd during plume grounding arose from the MWI which would lead to an overestimate of the ambient contribution. Importantly, however, both the emission ratio and dispersion modelled estimates were very low compared to background levels. Annual PM_{10} ambient levels ranged from 20 to 31 μg m^{-3} at urban background and roadside sites between 2003 and 2010 (DEFRA, 2014); 2–3 (compared to emission ratio estimates) and 3–4 (ADMS) orders of magnitude larger. It is not feasible to measure increments of this order of magnitude above background PM values using state-of-the-art instruments. For all the metals sites where MWI emissions were detected, higher of Cr concentrations were detected during the grounding periods compared with other wind sectors; Ni concentrations were also higher at 95% confidence interval for one metals site. This is consistent with the relative abundance of these metals in MWI emissions.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.atmosenv.2015.05.002.

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