Articles

Risk of congenital anomalies near hazardous-waste landfill sites in Europe: the EUROHAZCON study

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Summary

Background Waste-disposal sites are a potential hazard to health. This study is a multicentre case-control study of the risk of congenital anomalies associated with residence near hazardous-waste landfill sites in Europe.

Methods We used data from seven regional registers of congenital anomalies in five countries. We studied 1089 livebirths, stillbirths, and terminations of pregnancy with non-chromosomal congenital anomalies and 2366 control births without malformation, whose mothers resided within 7 km of a landfill site; 21 sites were included. A zone within 3 km radius of each site was defined as the "proximate zone" of most likely exposure to teratogens.

Findings Residence within 3 km of a landfill site was associated with a significantly raised risk of congenital anomaly (295 cases/511 controls living 0–3 km from sites, 794/1855 living 3–7 km from sites; combined odds ratio 1·33 [95% CI 1·11–1·59], adjusted for maternal age and socioeconomic status). There was a fairly consistent decrease in risk with distance away from the sites. A significantly raised odds ratio for residence within 3 km of a landfill site was found for neural-tube defects (odds ratio 1·86 [1·24–2·79]), malformations of the cardiac septa (1·49 [1·09–2·04]), and anomalies of great arteries and veins (1·81 [1·02–3·20]). Odds ratios of borderline significance were found for tracheo-oesophageal anomalies (2·25 [0·96–5·26]), hypospadias (1·96 [0·98–3·92]), and gastroschisis (3·19 [0·95–10·77]). There was little evidence of differences in risk between landfill sites but power to detect such differences was low.

Interpretation This study shows a raised risk of congenital anomaly in babies whose mothers live close to landfill sites that handle hazardous chemical wastes, although there is a need for further investigation of whether the association of raised risk of congenital anomaly and residence near landfill sites is a causal one. Apparent differences between malformation subgroups should be interpreted cautiously.

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See Commentary page XXXX

Introduction

Waste disposal by landfill is a cause for environmental concern. People who live near landfill sites may be exposed to chemicals released into the air, water, or soil.[1] Air contamination includes off-site migration of gases, dust, and chemicals bound to dust, especially during operation of the site. Local surface water and groundwater can become contaminated, and these may in turn contaminate potable water supplies or water for recreational use. Chemical contamination of air, water, or soil may also affect locally grown and consumed food produce. Thus, a landfill site may be a health risk for local residents and their children. Information on the potential risks to health should aid the future design, location, and operation of landfill sites.

To date, however, there is little epidemiological evidence on which to base health-risk assessments of landfill sites. Studies of pregnancy outcomes among women who live near landfill sites have been done in the USA, including the well-known contamination incident at Love Canal[2,3] and multiple-site assessments.[4–8] Some of these studies show raised risks of congenital anomalies in babies whose mothers live near landfill sites, but no clear pattern of risk has yet emerged. The potential teratogenicity of many of the chemicals dumped in landfill sites, such as heavy metals, pesticides, and solvents, is known, but chemical dose may have to reach a threshold level before significant teratogenic effects appear.

Communities close to waste-disposal sites are concerned about the potential health risk of the sites, and may link local "clusters" of adverse health outcomes to exposure to chemicals from nearby sites. However, even with a random spatial pattern of adverse health outcomes, localised clusters will occur, and distinction of these random clusters from those in which there is a common underlying local cause is difficult. It is desirable to move beyond post-hoc study of clusters, to study of waste-disposal sites specified a priori. We studied whether pregnant women living near landfill sites would be exposed to sufficient chemical doses for there to be any risk of congenital anomalies in their children. We present the first results of a collaborative European study of the risk of congenital anomaly among people living near hazardous-waste landfill sites. These first results concern non-chromosomal congenital anomalies.

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Register centre and study area	Number of landfill sites	Study period	Cases (n=1089)	Controls (n=2366)
Funen County (Denmark)				
1	1	1987–93	19	44
2	1	1986–93	28	68
Western North Thames (UK)				
3	1	1990–93	50	124
4	1	1990–93	10	30
Lyon (France)				
5	1	1990–94	35	78
Antwerp (Belgium)				
6	1	1990–93	73	160
7	3	1990–93	35	82
8	1	1992–93	6	16
Tuscany (Italy)				
9	1	1982–93	60	67
10	1	1982–93	121	138
11	1	1987–93	45	53
Northern Region (UK)				
12	1	1989–93	120	300
13	4	1986–93	296	740
14	1	1990–93	23	58
Glasgow (UK)				
15	2	1990–91	168	408

Table 1: **Background information on cases of congenital anomaly and controls**

Methods

Data collection

We used data from seven research centres in five European countries—Belgium, Denmark, France, Italy, and the UK. The centres maintain regional population-based registers of congenital anomalies that include data on livebirths, stillbirths, and terminations of pregnancy after prenatal diagnosis. Five of these centres are in the EUROCAT network of regional registers of congenital anomalies in Europe—register methods have been described elsewhere.[9–12] Three other centres participated in the study, but two of these only register Down's syndrome (Slovenia, UK), and one had too few people resident within the study area around the landfill site for meaningful data analysis (north-east Italy).

The landfill sites studied were located in areas covered by the registers of congenital anomalies. The sites contained hazardous waste of non-domestic origin, as defined in the EC Directive on Hazardous Waste.[13] We studied 21 suitable landfill sites, of which nine closed before the start of the study period and ten were in operation for more than 20 years before the end of the study period.

An area of 7 km radius around each landfill site defined each study area. Each study area contained a "proximate" zone of 3 km radius from the site within which most exposure to chemical contaminants would occur, according to expert advice. If two or more landfill sites were within 7 km of each other, and the proximate zones nearly overlapped, these study areas were combined as one large study area. If the landfill sites were 7–14 km from each other, any study-area overlap was split along a median line, the study population was allocated to the nearest site, and then each study area was analysed separately. The study period for each study area started when the registration of anomalies started, and after at least 5 years' operation of the nearest landfill site to allow for the time it takes for off-site contamination to occur. The study period ended on Dec 31, 1994, at Lyon, and on Dec 31, 1993, at the other sites.

We searched the registers for routinely registered cases of liveborn children with malformations, malformed fetal deaths of 20 weeks' gestation or later, and terminations of pregnancy after prenatal diagnosis of anomaly. Cases had to be born within the study period, and the mother had to be resident in a study area. Congenital anomalies were those on the EUROHAZCON list, which includes most major birth defects but excludes familial syndromes, neoplasms, metabolic diseases, and minor malformations. Chromosomal anomalies were excluded from the current analysis. Cases of congenital anomaly were further classified into non-exclusive subgroups (a baby could have more than one anomaly) based on EUROCAT subgroups.[9] Cardiac anomalies were classed as follows (with International Classification of Diseases, tenth revision, code): malformations of cardiac chambers and connections (Q20); malformations of cardiac septa (Q21); malformations of cardiac valves and other heart malformations (Q22–Q24); anomalies of great arteries and veins (Q25–Q26, except patent ductus arteriosus). Anomalies were multiple if a baby had two or more apparently unrelated anomalies, including recognised associations. All cases of possible syndromes and sequences were reviewed by the medical geneticists and by paediatric members of the collaborative group, who were not told the place of residence in each case. A baby with multiple anomalies was included both in the component anomaly subgroups and as a single case of multiple anomaly. A baby with a non-familial syndrome was included only in the syndrome subgroup. Recognised sequences were classed only in terms of the primary anomaly.[14] Numbers in any subgroup refer to cases, not to the numbers of anomalies.

For every case, two controls were randomly selected from all children without malformations born (liveborn or stillborn) on the nearest following day in the same study area. Two centres (Northern Region, Glasgow, UK) selected controls as a random sample of all livebirths in the same year of birth as the case. In Tuscany there was only one control per case. Twin-pairs were treated as one outcome, and classed as a case if one or both were malformed. Siblings were classed as separate outcomes.

Study area	0–3 km from site		3–7 km from site		Odds ratio (95% CI)	Adjusted odds ratio* (95% CI)
	Cases	Controls	Cases	Controls		
All study areas	295	511	794	1855	1·37 (1·14–1·63)	1·33 (1·11–1·59)
Single study areas						
1	7	23	12	21	0·49 (0·15–1·63)	0·43 (0·11–1·65)
2	11	25	17	43	1·26 (0·47–3·40)	1·23 (0·41–3·67)
3	25	59	25	65	1·16 (0·60–2·26)	0·76 (0·34–1·69)
4	6	18	4	12	1·12 (0·19–6·42)	0·83 (0·11–6·07)
5	4	14	31	64	0·58 (0·17–1·91)	0·45 (0·13–1·60)
6	18	21	55	139	2·19 (1·08–4·45)	2·08 (0·98–4·41)
7	11	11	24	71	2·92 (1·11–7·70)	3·93 (1·20–12·80)
8	0	1	6	15	0	. .
9	21	15	39	52	2·09 (0·92–4·75)	1·29 (0·48–3·49)
10	17	15	104	123	1·38 (0·65–2·94)	1·40 (0·62–3·15)
11	28	38	17	15	0·65 (0·28–1·52)	0·72 (0·17–2·97)
12	23	50	97	250	1·16 (0·67–2·02)	1·26 (0·71–2·22)
13	64	113	232	627	1·52 (1·08–2·15)	1·50 (1·05–2·13)
14	1	4	22	54	0·63 (0·07–6·16)	0·94 (0·09–9·74)
15	59	104	109	304	1·58 (1·07–2·33)	1·63 (1·09–2·44)

*Adjusted for socioeconomic status and maternal age.

Table 2: **Odds ratios for non-chromosomal congenital anomalies for each study area**

Cases and controls were geographically located with the address or postcode of the mother's place of residence, with an accuracy of 100 m or less. The distance of the mother's place of residence from the nearest landfill site was used as a surrogate measurement of exposure to chemical contaminants from the landfill site.

Socioeconomic status and maternal age were recorded for cases and controls. Socioeconomic status was measured in different ways in each country: as a quintile of a deprivation score based on enumeration-district data in the UK;[15] as one of five social classes of parental occupation in Funen County; as one of five classes of maternal education in Tuscany; as one of five occupation groups in Lyon; and in quintiles of average income in the area of residence in Antwerp. Socioeconomic status was recorded for more than 97% of cases and controls overall, and for more than 86% of the cases and controls in individual regions.

Statistical methods

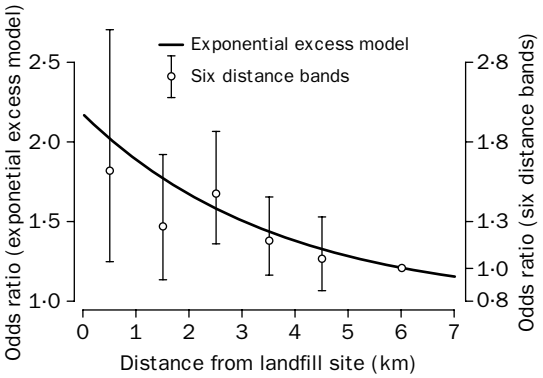
We used logistic and related binomial regression models to investigate the association between residence near hazardous-waste landfill sites and risk of congenital anomaly.[16] All controls, including those selected for cases with chromosomal anomalies, were included in the data analysis, including the subgroup analysis. Case-control matching was not retained in the data analysis, but data were stratified by study area and year of birth. Socioeconomic status was modelled separately for each country because of the different measures used.

Data from all study areas combined were grouped into six distance bands and distance was used as a continuous measure in explicit models. We fitted several models, including one in which the risk of congenital anomaly (odds ratio) declined exponentially with distance from a landfill site.[17] We also fitted various models that allowed for random variation in odds ratios between study areas.[18] We report results from a Bayes random-effects model with a normal distribution of underlying log odds ratios, and "non-informative" gamma (0·001, 0·001) prior for the inverse variance of this normal distribution. Other approaches gave similar results.

Results

We studied 1089 cases of non-chromosomal congenital anomaly and 2366 controls (table 1). We assessed the potential for confounding by maternal age and socioeconomic status. Maternal age had a positive but non-significant relation with risk of congenital anomaly. There was no clear relation between risk of congenital anomaly and socioeconomic status in any of the centres except in the UK, where there was a significant (p=0·04), trend of greater risk of anomaly with increasing deprivation, adjusted for distance from landfill sites (odds ratio for the most deprived quintile relative to the most affluent 1·37 [95% CI 0·98–1·93]). The maternal age and socioeconomic profiles of residents within 3 km of landfill sites and those who lived further away differed within some study areas, but there was no consistent pattern whereby older or more socially deprived people lived closer to landfill sites. Nonetheless, both these variables were included in our statistical models.

The overall odds ratio for congenital anomalies associated with residence within 3 km of a hazardous-waste landfill site, for all study areas combined, adjusted for maternal age and socioeconomic status, was 1·33 (95% CI 1·11–1·59; table 2). Adjustment for confounders did not substantially change the odds-ratio estimates for the combined or for most of the individual study areas. There were four sets of siblings in our sample in which both were malformed, but all lived more than 3 km from landfill sites.



Odds ratios for congenital anomalies with distance from landfill sites

Different scales are needed for the two models because the baseline differs: circle at 6 km represents 5–7 km baseline (odds ratio=1·0, righthand scale) for logistic regression of six distance bands; solid curve at this point represents estimated risk 6 km from site relative to risk infinitely far from site (odds ratio=1·22, lefthand scale).

There was little evidence of heterogeneity in the odds ratios between study areas (p=0·31). Adjusted odds ratios for three of the study areas (7, 13, and 15) were significant (p=0·02, 0·03, 0·02, respectively). The odds ratio for study area 6 was of borderline significance (p=0·05). The lack of evidence of heterogeneity of the odds ratios across study areas was reflected in the Bayes random-effects analysis, the results of which differed little from those of the simple combined analysis (median odds ratio 1·35 [1·07–1·68]).

There was a fairly consistent decrease in risk of congenital anomalies with increasing distance from a landfill site, although CIs in the six distance bands were wide (figure). All models that used distance as a continuous variable fitted our data well, although the exponential-excess model in the figure fitted somewhat better than the logistic models with distance or its reciprocal. All models showed a significant decrease in risk of congenital anomaly with increasing distance from a landfill site (p values ranged from 0·001 to 0·012).

Congenital anomaly	Number of cases	Odds ratio (95% CI)
Neural-tube defects	130	1·86 (1·24–2·79)
Hydrocephaly	32	1·06 (0·44–2·59)
Other central-nervous-system defects	23	1·03 (0·36–2·94)
Malformations of cardiac chambers and connections	45	0·91 (0·42–1·97)
Malformations of cardiac septa	248	1·49 (1·09–2·04)
Malformations of valves and other heart malformations	109	1·17 (0·73–1·88)
Anomalies of great arteries and veins	63	1·81 (1·02–3·20)
Cleft palate	38	1·63 (0·77–3·41)
Cleft lip with or without cleft palate	72	1·18 (0·66–2·12)
Tracheo-oesophageal fistula, oesophageal atresia and stenosis	25	2·25 (0·96–5·26)
Digestive system and upper alimentary tract	59	0·98 (0·49–1·93)
Atresia and stenosis of rectum and anal canal	20	1·02 (0·33–3·15)
Hypospadias	45	1·96 (0·98–3·92)
External genitalia (female + indeterminate)	10	0·89 (0·18–4·53)
Renal abnormalities	75	1·30 (0·73–2·31)
Urinary-tract abnormalities	69	1·14 (0·62–2·11)
Limb reduction defects	41	1·27 (0·61–2·62)
Exomphalos	12	0·26 (0·03–2·19)
Gastroschisis	13	3·19 (0·95–10·77)
Skin and other integument abnormalities	30	1·92 (0·78–4·73)
Syndromes, presumed de-novo mutations	29	1·48 (0·63–3·49)
Multiple anomalies	84	1·21 (0·71–2·06)

Table 3: **Odds ratios for congenital anomalies among residents within 3 km of a hazardous-waste landfill site**

The combined odds ratios for selected subgroups of congenital anomalies among residents within 3 km of a landfill site (table 3) were not changed substantially after adjustment for socioeconomic status and maternal age. Significant unadjusted odds ratios were found only for neural-tube defects (p=0·003), malformations of the cardiac septa (p=0·014), and abnormalities of the great arteries and veins (p=0·041). Odds ratios for tracheo-oesophageal anomalies, hypospadias, and gastroschisis were of borderline signifance (p=0·06). However, there were few cases in most of the subgroups analysed, and thus CIs were wide.

Discussion

We have shown a small, but statistically significant, excess risk of non-chromosomal congenital anomalies among people who live within 3 km of hazardous-waste landfill sites. There is no evidence that the risk of anomalies differs between sites, although our study has limited statistical power to address this issue. The fundamental question is whether the relation observed is causal. In our opinion, the results of previous epidemiological multisite studies[4–6] do not greatly strengthen any conclusion of causality in our study.

Socioeconomic status is the most obvious potential confounder in any spatial analysis of health outcomes. There has been little research on the strength of the relation between socioeconomic status and risk of congenital anomaly.[19–23] Our work suggests a positive relation between non-chromosomal malformations and social deprivation in the UK, but little evidence for the same relation elsewhere in Europe. There was no overall evidence that socioeconomically more deprived communities live near to landfill sites. Moreover, adjustment for socioeconomic status in our statistical analyses, although hampered by the lack of standard socioeconomic classification in Europe, did not greatly change the odds ratios. We therefore think that socioeconomic confounding is unlikely to explain the excess risk of congenital anomaly found near landfill sites.

A second possible confounder is the presence of other industrial sites or toxic environmental exposures near landfill sites. However, there has been little study of the risk of congenital anomaly near any type of industrial site; our results would be of equal interest if the observed association was with other industrial sites, instead of or as well as landfill sites. A further possibility is that mothers resident near landfill sites have jobs with high risks to health, at the landfill site or at other industrial sites. However, it would be unusual for enough of the women in any area to be employed in high-risk industrial occupations for the mean risk of adverse birth outcomes for resident women to be significantly raised.

Congenital anomalies may have been more fully reported close to landfill sites (ascertainment bias). However, the registers used many information sources and active case-finding, they collected data routinely, with no knowledge of the study hypothesis, and an examination of our data by hospital of birth shows that hospital-based ascertainment differences, at least, do not explain the excess risk found near landfill sites.

Women may move house between exposure to potential teratogens and pregnancy outcome, and this can lead to migration bias whereby true excess risk is underestimated. Unlike most chronic effects of exposure to harmful chemicals, teratogenic effects may be detected as early as a few months after exposure to the teratogen. Thus, the potential for migration bias is limited. However, for chemicals that accumulate in the body over time, the length of residence of the mother near the landfill site may be important. There are few estimates of the proportion of mothers who move house during pregnancy, but figures from the UK suggest that about 25% of women move house during pregnancy; of these, about 50% move less than 1 km.[24] We estimate that this migration would lead to roughly a 10% underestimation of any true excess risk of congenital anomaly related to exposures during early pregnancy.[25] There is public concern about the effects on health of several of the landfill sites included in our study. This concern has not, to our knowledge, been specifically related to birth defects, but there may have been more migration in areas close to the landfill sites than is usual because of these health concerns.

Congenital anomalies are heterogeneous in pathogenesis and aetiology, and it would be of interest to investigate whether any particular anomalies are linked to either landfill sites in general or to particular chemicals dumped in them. However, there are no robust a-priori hypotheses about which anomalies occur most commonly around landfill sites, or which anomalies occur after exposure to specific chemicals or chemical mixtures. Furthermore, landfill sites cannot be easily classified according to the chemicals they contain, because each site contains a range of chemicals, and because information on the chemicals dumped is usually incomplete; record keeping has not always been a legal requirement. We have found increased risks of many types of congenital anomaly near the landfill sites, although not all of these findings were significant. There was a significantly overall increased risk of neural-tube defects, malformations of the cardiac septa, and malformations of the great arteries and veins in residents near the landfill sites in our study, and borderline significantly increased risk of tracheo-oesophageal anomalies, hypospadias, and gastroschisis. These findings should be used as hypotheses to inform further study, because no clear interpretation of differences in risk between congenital anomalies can be made. However, increased risk of hypospadias is of particular interest in relation to concern about male reproductive abnormalities related to endocrine-disrupting chemicals.[26]

The environmental hazardousness of a landfill site may be more a result of geology, engineering, and management practices than of the type or amounts of chemicals dumped there.[27] We now aim to rank landfill sites according to "hazard potential" by expert consensus, with concealment of risk status. A "dose-response" effect, in which the sites of highest hazard potential are associated with the highest risk of congenital anomaly, would strengthen the case for a causal association between risk of congenital anomaly and residence near sites. Direct measurement of exposure to chemicals for residents near landfill sites would also help to assess whether the association is causal, but this research has not yet been done.

Our study was limited to landfill sites that handle hazardous industrial wastes. However, municipal landfill sites that take domestic wastes can be as environmentally hazardous as those categorised as hazardous-waste sites,[28] and indeed, in the UK, codisposal (mixture of domestic

and industrial wastes) is recommended. We believe that systematic "environmental health surveillance" is needed for municipal landfill sites and other pollution sources that cause public or scientific concern. Surveillance should make use of the registers of congenital anomaly, should include assessment of people's exposure to chemicals, and should encourage regular communication between departments with health and environment responsibilities. It is unfortunate, for example, that one of the original participants in our study withdrew because the local environment department was unwilling to provide information about the landfill sites in the area covered by the register of congenital anomalies.

Environmental problems cross political boundaries, and a coordinated policy response is necessary, informed by coordinated research. Our results show the need for further investigation of the potential environmental and health risks of landfill sites, and for a more systematic environmental-health surveillance system in Europe.

Contributors

Helen Dolk, Martine Vrijheid, and Ben Armstrong wrote the first draft of the paper. Helen Dolk led the project, designed the study protocol, and supervised quality-control and data analysis. Martine Vrijheid coordinated data collection, did the statistical analysis, and took part in study protocol design. Ben Armstrong supervised the statistical analysis. Leonore Abramsky, Fabrizio Bianchi, Ester Garne, Vera Nelen, Elisabeth Robert, John Scott, David Stone, and Romano Tenconi took part in study protocol design, advised on classification of cases, and supplied data from participating centres. All investigators contributed to writing of the paper.

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