multiple partners, participation in sex work, and increase in risk of rape in adulthood.1 Intergenerational sex also fuels the HIV-1 epidemic by providing foci of infection within every emerging age group, leading to transmission of the virus to peers once children reach the stage of consensual sexual activity. Many girls are forced to leave school because of pregnancies fathered by teachers and because of harassment by teachers.4 A girl’s ability to reach her economic and social potential is thus reduced, and likelihood of subsequent dependency on sex for payment rises. They and their children are also placed at much greater risk of many other health problems.

Our findings confirm that rape of girls, especially in school, is a substantial public-health problem in South Africa. Research is needed to understand its broader social context, nature, and magnitude, and to develop interventions for primary prevention and prevention of its long-term health consequences. Effective action to address rape and sexual harassment of girls in schools is needed. South Africa has only recently made sexual relations, consensual or otherwise, between staff and students a serious offence that results in dismissal of staff. Many countries do not have such legislation. Enforcement still presents a substantial challenge.

Contributors
R Jewkes designed the questions on child sexual abuse, ensured adherence to ethics, and wrote the report. J Levin was the study statistician, and analysed the data. D Bradshaw was the main investigator, and N Mbananga was the project manager. All researchers contributed to all decisions on planning, design, and project implementation, and writing of the report.

Conflict of interest statement
None declared.

Acknowledgments
The 1998 South Africa Demographic and Health Survey was initiated and mostly funded by the National Department of Health. The survey was coordinated by the Medical Research Council, with technical assistance from MACRO International. Fieldwork was done by the Centre for Health Systems Research and Development of the Free State University, and USAID provided additional funding. The Department of Health of each province provided provincial co-ordinators who assisted in facilitating the survey. Statistics South Africa provided the sampling frame and sample details, and the Human Sciences Research Council monitored the quality of fieldwork. The study sponsors had no role in study design, data collection, data analysis, or data interpretation or in the writing of the report.

We thank the many field workers, supervisors, editors, and provincial managers for their contribution, and the people who shared intimate details of their lives in the interviews.


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Chromosomal congenital anomalies and residence near hazardous waste landfill sites


Previous findings of the EUROHAZCON study showed a 33% increase in risk of non-chromosomal anomalies near hazardous waste landfill sites. Here, we studied 245 cases of chromosomal anomalies and 2412 controls who lived near 23 such sites in Europe. After adjustment for confounding by maternal age and socioeconomic status, we noted a higher risk of chromosomal anomalies in people who lived close to sites (0–3 km) than in those who lived further away (3–7 km; odds ratio 1·41, 95% CI 1·00–1·99). Our results suggest an increase in risk of chromosomal anomalies similar to that found for non-chromosomal anomalies.


EUROHAZCON study findings1 have shown a 33% increase in the risk of non-chromosomal anomalies for residents living within 3 km of 21 European hazardous waste landfill sites. We report findings from the EUROHAZCON study on chromosomal anomalies. EUROHAZCON study methods have been described in detail.1 We obtained data from regional population-based registers of congenital malformations in five European countries. In addition to the regions included previously (table 1), we included data from the England and Wales Down’s Syndrome register, selecting only two regions (Essex 1989–92, and Mersey 1989–93) because resources were insufficient to provide case data with full postcodes for all regions. These two regions were selected because of good collaboration with local environment agencies and presence of hazardous waste landfill sites which conformed to our criteria for inclusion.1 In total, we included 23 landfill sites in 17 study areas (table 1). Details of site characteristics have been published.1 One landfill site included in the non-chromosomal part of the study was excluded because geographical site co-ordinates proved incorrect. Exclusion of this site (study area 14) did not change findings published for non-chromosomal anomalies: the odds ratio for living within 3 km of a landfill site including site 14 was 1·33 (95% CI 1·11–1·59) for non-chromosomal anomalies.1 After exclusion of site 14 this estimate was 1·34 (1·12–1·60).

On a-priori advice of landfill specialists, we defined a 0–3 km proximate zone around each site to represent the zone of most likely exposure.1 This zone was compared with a 3–7 km distant zone. We defined cases as livebirths, stillbirths, and terminations of pregnancy with chromosomal anomalies (International Classification of Disease [ICD] 9 codes 7580–89) registered on malformation registers. Controls were normal live births, around two per case, selected from the same year of birth and 7 km study area as the case.1 In the Essex Region (study areas 16 and 17), controls were selected by random selection of two neonates from all normal births on the day after the birth of the case, within the same 7 km study area. In the Mersey region (study area 18), controls were a random sample of all live births in the same year of birth and study area as the case. These different methods were used in order to obtain complete maternal age information for controls. In analyses we used the total pool of controls selected for non-chromosomal and chromosomal cases in each 7 km study area, giving about 10 controls per
chromosomal case. We included a total of 245 cases and 2412 controls. The geographical locations of cases and controls were determined with an accuracy of 100 m or less by use of the mother’s address or postcode of residence at time of birth. The association between distance of residence from the nearest waste site and risk of chromosomal anomalies was analysed with logistic and related binomial regression models. Terms for study area and year of birth, were included in all models, and analyses were adjusted for maternal age and socioeconomic status.1 Distance of residence was fitted as a dichotomous measure (0–3 km and 3–7 km zones) and as a continuous measure only in analyses pooling data over all study areas. We fitted the same continuous distance models as in the non-chromosomal part of the study, including one model in which risk declines exponentially with distance.1,3

The adjusted odds ratio for living near a site, for all chromosomal anomalies combined, was 1·41 (95% CI 1·00–1·99, table 2). Adjustment for confounding factors increased the crude odds ratio slightly (from an unadjusted odds ratio of 1·32, 0·96–1·81), almost entirely because of adjustment for maternal age. Odds ratios did not vary significantly between study areas (p=0·79). A similar odds ratio was found for the fifteen study areas on which previous non-chromosomal analyses had been based (table 2). Point estimates of odds ratios for Down’s syndrome and non-Down’s syndrome separately were greater than 1, but were not significant (table 2). Risk did not decline consistently with increasing distance from sites: various models fitting distance as a continuous measure and six distance zones showed no significant trends (p > 0·10).

Odds ratios were highest in the 0–1 km (1·68, 0·72–3·89) and 2–3 km (1·74, 1·12–2·70) distance zones, and lowest in the 1–2 km (1·08, 0·61–1·93) and 3–4 km (1·05, 0·69–1·60) zones compared with a 5–7 km baseline. In most individual study areas, odds ratios were not significant before or after adjustment for maternal age (table 1). However, numbers of cases were small and 95% CI wide.

Risk estimates for chromosomal anomalies were similar to those noted for non-chromosomal anomalies, in pooled analyses and in individual study areas. This similarity can be interpreted in two main ways. Either landfill exposures are causally related to risk of congenital anomaly and have

Table 1: Odds ratios for chromosomal anomaly in residents within 3 km of a hazardous waste landfill site

<table>
<thead>
<tr>
<th>Study area</th>
<th>Number of sites</th>
<th>Distance from site (km)</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95% CI)</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Funen County (Denmark)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>&lt;3</td>
<td>2</td>
<td>23</td>
<td>1·83 (0·15–21·64)</td>
<td>2·53 (0·16–40·09)</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>3–7</td>
<td>1</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td>25</td>
<td>1·72 (0·32–9·18)</td>
<td>1·32 (0·20–8·80)</td>
</tr>
<tr>
<td><strong>North Thames (West) (UK)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>0–3</td>
<td>4</td>
<td>59</td>
<td>0·55 (0·16–1·92)</td>
<td>0·76 (0·17–3·28)</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>3–7</td>
<td>8</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td></td>
<td>3</td>
<td>18</td>
<td>1·00 (0·15–6·91)</td>
<td>1·00 (0·11–8·79)</td>
</tr>
<tr>
<td><strong>Lyon (France)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0–3</td>
<td>1</td>
<td>14</td>
<td>0·00</td>
<td>--</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>3–7</td>
<td>4</td>
<td>64</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antwerp (Belgium)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>0–3</td>
<td>2</td>
<td>21</td>
<td>2·65 (0·48–14·53)</td>
<td>2·73 (0·49–15·19)</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>3–7</td>
<td>5</td>
<td>139</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>0–3</td>
<td>4</td>
<td>11</td>
<td>1·29 (0·14–12·11)</td>
<td>2·33 (0·21–26·15)</td>
</tr>
<tr>
<td><strong>Tuscany (Italy)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>0–3</td>
<td>2</td>
<td>15</td>
<td>1·39 (0·24–7·88)</td>
<td>1·07 (0·17–6·81)</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>3–7</td>
<td>5</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td>0–3</td>
<td>4</td>
<td>15</td>
<td>0·40 (0·09–1·79)</td>
<td>0·35 (0·06–1·98)</td>
</tr>
<tr>
<td><strong>Northern region (UK)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>0–3</td>
<td>6</td>
<td>50</td>
<td>1·36 (0·53–3·53)</td>
<td>1·30 (0·48–3·54)</td>
</tr>
<tr>
<td>13</td>
<td>4</td>
<td>0–3</td>
<td>14</td>
<td>113</td>
<td>1·59 (0·85–2·97)</td>
<td>1·50 (0·78–2·90)</td>
</tr>
<tr>
<td><strong>Glasgow (UK)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>2</td>
<td>0–3</td>
<td>11</td>
<td>104</td>
<td>1·69 (0·78–3·67)</td>
<td>1·77 (0·80–3·88)</td>
</tr>
<tr>
<td>16‡</td>
<td>1</td>
<td>3–7</td>
<td>1</td>
<td>1</td>
<td>2·13 (0·12–38·48)</td>
<td>1·98 (0·06–62·49)</td>
</tr>
<tr>
<td>17‡</td>
<td>1</td>
<td>3–7</td>
<td>8</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18‡</td>
<td>1</td>
<td>3–7</td>
<td>4</td>
<td>14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR=odds ratio. *Adjusted for maternal age (<20, 20–24, 25–29, 30–34, >35 years). Adjustment for socioeconomic status and maternal age led to unstable odds ratio estimates and is therefore not presented. Adjustment for socioeconomic status did not result in a shift in the OR point estimate. †In areas 16 and 17, controls were included by random selection of two neonates from all non-malformed births on the day after the birth of the case, within the same 7 km study area. In area 18, controls were a random sample of all live births in the same year of birth and study area as the case. ‡Down’s syndrome only. §There are 3 cases with the same postcode within this distance band. Comparison of the exact address, date of birth, and age of mother gave no evidence that these cases were duplicates or siblings.
both teratogenic and mutagenic effects, or the relation is not causal and findings indicate a common bias, or a chance effect in the selection of a common pool of control births. Potential sources of bias, including misclassification of exposure, ascertainment bias, migration bias, and occupational and industrial exposure have been discussed in detail and apply to the present findings. The similar increase in risk of chromosomal and non-chromosomal anomalies renders residual socioeconomic confounding unlikely as an explanation for findings as socioeconomic status affects risks of chromosomal and non-chromosomal anomalies differently. We noted higher risks of non-chromosomal anomalies and lower risks of chromosomal anomalies in groups with lower compared with higher socioeconomic status, mainly because of differences in maternal age distribution. Maternal age is a confounding factor in analysis of chromosomal anomalies, but adjustment for maternal age shifted odds ratios away from unity. A previous study reported on chromosomal anomalies near hazardous waste landfill sites. The similar increase in risk of chromosomal and non-chromosomal anomalies near waste sites and showed an increased risk of chromosomal anomalies near hazardous waste landfill sites in Europe. In: Lawson AB, Biggar A, Bobone D, Lesaffre E, Vield JP, Bertollini R, et al, eds. Disease Mapping and Risk Assessment for Public Health. Chichester: Wiley, 1999.

More study into the chemical causes of chromosomal anomalies and exposure of residents to landfill sites is needed to interpret our findings.

Contributors
M Vrijheid and H Dolk wrote the paper and coordinated the study. M Vrijheid did analyses of chromosomal congenital anomaly risk near landfill sites and reviewed the literature. B Armstrong supervised statistical analyses. The other authors took part in protocol design of the study (including advice on data collection, classification of cases, &c), and supplied data from participating registries. All authors contributed to revision of the paper.

Conflict of interest statement
None declared.

Acknowledgments
We thank colleagues from the participating registries and laboratories contributing data to the Down Syndrome Register. The main study was funded by the EC DG XII BIOMED programme, this work was carried out specifically under a Research Fellowship for M Vrijheid from the Wolfson Institute of Medicine and Dentistry, London, UK.

Table 2: Odds ratios for chromosomal anomaly in residents within 3 km of a hazardous waste landfill site

<table>
<thead>
<tr>
<th>Distance from site (km)</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All study areas pooled</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All chromosomal anomalies</td>
<td>&lt;3</td>
<td>70</td>
<td>536</td>
<td>1.32 (0.96–1.81)</td>
</tr>
<tr>
<td></td>
<td>3–7</td>
<td>175</td>
<td>1876</td>
<td></td>
</tr>
<tr>
<td>Study areas 1–15 pooled†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All chromosomal anomalies</td>
<td>&lt;3</td>
<td>56</td>
<td>507</td>
<td>1.36 (0.96–1.92)</td>
</tr>
<tr>
<td></td>
<td>3–7</td>
<td>142</td>
<td>1801</td>
<td></td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td>&lt;3</td>
<td>38</td>
<td>507</td>
<td>1.33 (0.87–2.04)</td>
</tr>
<tr>
<td></td>
<td>3–7</td>
<td>89</td>
<td>1801</td>
<td></td>
</tr>
<tr>
<td>Non-Down’s syndrome</td>
<td>&lt;3</td>
<td>18</td>
<td>507</td>
<td>1.43 (0.81–2.52)</td>
</tr>
<tr>
<td></td>
<td>3–7</td>
<td>53</td>
<td>1801</td>
<td></td>
</tr>
</tbody>
</table>

OR=odds ratio compared with 3–7 km zone. *Adjusted for maternal age (<20, 20–24, 25–29, 30–34, 35–37, 38–40, 41–43, and >44 years) and socioeconomic status measures of area deprivation in UK and Belgium study areas, parental occupation in Denmark and France, maternal education in Italy.†Study areas as included in previous non-chromosomal analyses.‡Adjusted for maternal age only (adjustment for both maternal age and socioeconomic status led to unstable estimates, adjustment for socioeconomic status only did not result in a shift in the OR point estimate).

Asthma and infectious respiratory disease in children – correlation to residence near hazardous waste sites

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Summary Rates of hospitalization for asthma and respiratory infectious disease in children were modeled as a function of residence: (1) in a zip code containing a hazardous waste site with persistent organic pollutants (POPs); (2) in a zip code with a waste site that did not contain POPs (‘other’); or (3) in a zip code without any identified waste site (‘clean’), as well as other demographic covariates. After adjustment, living in a zip code containing a POPs waste site significantly increased the frequency of hospitalization for asthma and infectious respiratory disease. Living in a zip code with an ‘other’ waste site also increased hospitalization frequencies for both diseases. The association was strongest for zip codes whose residents were in the lowest quartile of medium family income. This evidence supports the hypothesis that living near a hazardous waste site increases risk of respiratory disease in children.

KEYWORDS
polychlorinated biphenyls; dioxins; chlorinated pesticides; hospitalization

Persistent organic pollutants (POPs) include dioxins, furans, polychlorinated biphenyls (PCBs) and chlorinated pesticides, such as dichlorodiphenyltrichloroethane (DDT). These substances are very persistent in both the environment and in the human body. They also have adverse health effects on several different organ systems, including immune system function. Dioxins, furans and PCBs are known to suppress immune function in animals1–3 and humans.5 Chlorinated pesticides also perturb immune function in humans,5 causing induction of Th2-type cytokines. While human exposure to these POPs commonly occurs via consumption of contaminated animal fats and fish in particular,6 recent evidence has shown that inhalation of these semi-volatile compounds is also a significant route of exposure.7,8

A depressed immune system would be expected to increase the incidence of infectious diseases, since an immunosuppressed individual would be less able to defend against infection. There are a number of reports of increased rates of infectious diseases in children exposed to POPs.9,10 Some studies have also demonstrated elevations in respiratory infections in exposed children.11,12 Living near a hazardous waste site increases the likelihood that one will be exposed to contaminants through
ASTHMA AND INFECTIOUS RESPIRATORY DISEASE IN CHILDREN 293

migration of the contaminant into soils, water and air. Many identified hazardous waste sites contain POPs, although these compounds are also present in low levels in the general food supply.14 There are also many other hazardous compounds frequently found in waste sites, including metals, volatile organics, polyaromatic hydrocarbons and radioactive substances, all of which have a variety of adverse human health effects.15 Exposure to all of these substances can occur via ingestion, dermal absorption or inhalation.

We have tested the hypothesis that living in a zip code containing a hazardous waste site increases the risk of childhood asthma and respiratory infectious disease. The general hypothesis was that residence near a hazardous waste site promotes exposure to the chemicals contained therein, which in turn, promotes the development of disease and increases the rate of hospitalization. We have used two New York State data sets. All state-regulated hospitals (i.e. all hospitals except federal hospitals such as those of the Veterans Administration) must report all diseases (up to 15) identified in each inpatient to the New York State Department of Health (NYSDOH). This information is available with age, race, sex and zip code of the patient. In addition, New York has an excellent state registry of hazardous waste sites. This registry includes identification of the major contaminants and the location of the waste site. We have classified all the zip codes in New York (except for New York City) as (1) containing or abutting a hazardous waste site with POPs, (2) containing or abutting a hazardous waste site but not one with POPs, or (3) not containing or abutting any hazardous waste site. Then we determined the rates of hospitalization for asthma and infectious respiratory disease in children aged from birth to 9 years in these three categories from 1993 to 2004.

MATERIALS AND METHODS

Study population

We examined hospital discharge diagnoses for children aged up to 9 years in New York State, excluding New York City. New York City was excluded from this analysis because it maintains a hospitalization listing, which is separate from that maintained by the NYSDOH. In addition, New York City differs significantly from the rest of the state in population density and composition, and in social and economic status. We used zip codes as the unit of analysis since this is the smallest unit for which hospitalization data was available. The study population consisted of residents from 1402 zip codes. Zip codes whose boundaries had changed during the period 1993–2004 or who were listed as having zero population were excluded.

Hospital discharge data were obtained from the New York Statewide Planning and Research Cooperative System (SPARCS) for the years 1993–2004. SPARCS requires all state-regulated hospitals to report the principle diagnosis and up to 14 other diagnoses of each inpatient upon discharge to the NYSDOH, according to the International Classification of Disease, Ninth Revision (ICD-9). The SPARCS data provides the age, race, gender and zip code of residence for each patient. In this study, we selected hospital discharge data that had a diagnosis of (1) asthma (ICD-9: 493) and/or infectious respiratory disease, which included acute respiratory infections (ICD-9: 460–466), (2) bronchitis (ICD-9: 490–491) and (3) pneumonia and influenza (ICD-9: 480–487).

The SPARCS data available to us does not contain personal identifiers. Therefore, this study has the limitation that the outcome variable is the number of discharges and not the number of individual patients. We are not able to distinguish multiple hospital discharges by a single individual from hospital discharges by more than one individual with the same disease. However, the rate of hospital discharges in a zip code is still an adequate and interpretable measure of the presence of disease. New York State residents who seek out-of-state healthcare are not included in this dataset, nor are patients in federally regulated hospitals. Since the outcome counts only discharge of hospitalized patients this, in general, is a population with relatively severe illness, not individuals seeking outpatient or emergency room care. However, the dataset is comprehensive and contains about 2.5 million discharges per year for 12 years.

Zip code-level population data derived from the US Census were obtained from Claritas Inc., stratified by age, race and gender.16 Age was divided into the following groups: <1 year, 1–2 years, 3–4 years, 5 years, 6 years and 7–9 years. We considered only two racial groups – Caucasian and African American – since these accounted for more than 95% of the population. We used Claritas Inc. zip code level medium-household income to control for social economic status.

Exposure assessment

The New York State Department of Environment Conservation (NYSDEC) has identified 818 sites in New York State that pose potential threats to human health. These include National Priority List sites as well as state superfund sites. For each site, the major contaminants are identified.16 To identify a ‘POPs’ site, we scanned the listing of major contaminants for the words: PCB, Pyranol, Aroclor, pesticide, chlordane, dieldrin, endosulfan, heptachlor, herbicide, 1,1-dichloro-2,2,2-trifluoroethane (DDT), dichlorodiphenyltrichloroethane (DDE), dioxin, furan, aldrin, endrin, hexachlorobenzene, mirex and toxaphene. A total of 118 zip codes were found that contained or abutted a POPs waste site. In addition, we included as POPs sites all zip codes directly abutting bodies of water known to be contaminated, including the Hudson River from Hudson Falls to New York City and the six ‘Areas of Concern’ in New York as identified by the International Joint Commission.17 This gave a total of 195 POPs zip codes.
The primary objective of this study was to assess the association of residential proximity to hazardous waste sites and hospital discharges for asthma or infectious respiratory diseases in children. Since we record hospitalizations, which indicate a serious condition, there is the possibility that concurrent asthma plus infection may be common. Since asthma and infectious respiratory disease have distinct etiologies, it is important to distinguish the effects of exposure for each of the outcomes. In addition, if we select one of the outcomes then not controlling for the other may result in a confounded measure of exposure. To mitigate the confounding that results from using only one disease outcome, asthma or infectious respiratory disease, when both could be present, we conducted a separate analysis for each of following distinct combinations of disease: (1) discharge with asthma independent of whether or not there is concurrent infection, (2) discharge with asthma but no coexisting respiratory infection, (3) discharge with infectious respiratory disease whether or not there is concurrent asthma, (4) discharge with infectious respiratory disease without concurrent asthma, and (5) discharge with diagnosis of both asthma and infectious respiratory disease.

The unit of analysis was zip codes and covariate patterns were formed that controlled for age, gender, race, urban/rural, medium household income (MHI) and exposure. Urban was defined as zip codes with more than 1000 person per square mile (386 person per square kilometer). MHI was divided into four levels by quartile: >$34,410, $34,411–44,906, $44,906–63,455 and >$63,455. The outcome for each covariate pattern was the number of hospital discharges across all the zip codes having that covariate pattern. Thus the outcome was a counting variable. Initially Poisson regression was considered the appropriate model. However, the deviance and residual plots for the Poisson regression model indicated over-dispersion. Therefore, a negative binomial regression model was examined and found to fit. The final model for the log of the expected rate of hospital discharges was:

\[
\log(\text{Expected rate of hospital discharge}) = \text{Intercept} + b_1 \times \text{POP} + b_2 \times \text{Other} + 
\]

\[
+b_3 \times \text{2ndQ MHI} + b_4 \times \text{3rdQ MHI} + b_5 \times \text{4thQ MHI} + 
\]

\[
+b_6 \times \text{Urban} + b_7 \times \text{Black} + b_8 \times \text{Female} + 
\]

\[
b_9 \times \text{Age1} - 2 + b_{10} \times \text{Age3} - 4 + b_{11} \times \text{Age5} + b_{12} \times \text{Age6} + b_{13} \times \text{Age7} - 9
\]

Although the full 200 miles of the Hudson River from Hudson Falls to Manhattan are classed as a National Priority Site, most of the zip codes along the river are not listed on the NYSDEC listing of state superfund sites. Furthermore, our analysis showed that those zip codes along the upper and middle Hudson (from Hudson Falls to Poughkeepsie) behaved differently from those below Poughkeepsie (unpublished observations), where contamination levels are less. For all of these reasons, in a follow-up analysis we excluded all zip codes along the Hudson River and the six ‘Areas of Concern’ except those 118 zip codes specifically listed by the NYSDEC from our ‘POPs’ list.

Interaction terms were added to the model in order to identify effect modifiers. We found statistically significant evidence that the exposure effects for both ‘POPs’ and ‘other’ sites were stronger for zip codes whose residents were in the lowest quartile of MHI. However, there was no significant improvement in the overall quality of fit (deviance/degree of freedom) upon addition of these interaction terms. In addition, the summary effects of exposure from the interaction model are consistent with the effects of exposure in the main effect model. Consequently, only results from the main effect model are presented.

All statistical analysis was performed with SAS software, Version 9.1 (SAS Institute Inc.).

RESULTS

Table 1 presents results of the regression analysis for rates of hospitalization for asthma and infectious respiratory disease when we consider all zip codes listed by NYSDEC.
as containing POPs, plus all zip codes along the Hudson River and the ‘Areas of Concern’ to be included as POPs sites. Residents in ‘POPs’ zip codes have a significantly elevated rate ratio for both asthma (RR = 1.12) and infectious respiratory disease (RR = 1.13). The rate ratio for children diagnosed with both asthma and infectious respiratory diseases was slightly higher (RR = 1.15). There was no significant difference when we examined relationships for children who had asthma but no coexisting respiratory infectious disease (‘asthma only’), or who had respiratory infectious disease but no asthma (‘infectious only’), suggesting that neither outcome is severely confounded by the presence of the other. There was also a statistically significant elevated rate of hospitalization for both asthma (RR = 1.10) and infectious respiratory disease (RR = 1.12) in children living in zip codes in the ‘other’ category.

The other factors that influence rates of hospitalization for the various models are shown in Table 1. As expected, lower MHI was a significant risk factor. The RR for both diseases declined significantly as MHI increased. This may reflect better nutrition, sanitation, health insurance coverage and access to preventive healthcare. It is likely that children in homes with higher socioeconomic status receive earlier treatment as outpatients and are less likely to require hospitalization. Residents in urban areas showed significantly higher rates of hospitalization for asthma (RR = 1.22) than those in rural areas, while there was no significant difference between urban and rural for infectious respiratory disease. African-American children were much more likely to be hospitalized than Caucasian children. This was especially true for asthma (RR = 2.45), but was also the case for infectious respiratory disease (RR = 1.71). Girls had lower rates than boys, and the difference was more pronounced for asthma than infectious respiratory disease. Hospitalization for both diseases was most frequent in children at young ages. For asthma the peak age was from 1 to 2 years, whereas for infectious respiratory disease the peak was in the first year of life and fell dramatically at older ages. Asthma hospitalization also declined with age, but more slowly.

Because our preliminary analysis indicated that we might be underestimating the magnitude of effect by including zip codes for those along contaminated bodies of water not listed by the NYSDEC as ‘POPs’ sites, we repeated the analysis using only the NYSDEC dataset. Fig. 2 shows the
exposure effect for these 118 ‘POPs’ zip codes and 227 ‘other’ zip codes. The number of ‘other’ sites is larger than that in the preliminary analysis because some Hudson River zip codes contain ‘other’ waste sites. The effect for ‘POPs’ is higher in this group of zip codes: 1.17 for asthma, 1.15 for infectious respiratory diseases, and 1.24 for coexisting asthma and infectious respiratory disease. The effects of ‘other’ sites are similar to that shown in Table 1.

For all regressions, the deviance values per degree of freedom are very close to one, indicating adequate fit. We also checked the residual plots and did not find outliers or any indication of extreme or influential values.

DISCUSSION

Dioxin causes thymic atrophy and immunosuppression in animals, which results in a decreased resistance to bacterial, viral and parasitic infections.\(^{18,19}\) Most of the immune system effects of dioxin and PCBs are believed to be mediated via the aryl hydrocarbon (Ah) receptor,\(^{20}\) which has been reported to suppress Th cell differentiation into Th2 cells.\(^{21}\) However, both Ah-receptor dependent and independent immunosuppression has been reported.\(^{22}\) Many pesticides are also immunosuppressive.\(^{23}\)

While clear effects of dioxin exposure on immune system function of adults are not very well documented,\(^{24}\) Lu and Wu\(^{25}\) reported decreased immunoglobulin M (IgM) and IgA and alterations of T cells in Yucheng patients who were exposed to a mixture of PCBs and furans. Natural killer lymphocytes have been found to be reduced in adults exposed to dioxins, furans, PCBs,\(^{26}\) and organochloride pesticides.\(^{27}\) There is stronger evidence for perturbation of immune system function in children exposed to POPs. Yucheng children were found to have more bronchitis, influenza and middle ear infections than controls.\(^{28}\) Elevated rates of infectious diseases have also been reported in other POPs-exposed children.\(^{5,10,12}\)

The collection of diseases commonly referred to as asthma is quite different to infections, and is characterized by airway hyper-responsiveness. Asthma appears to be secondary to a deviation of immune response toward a Th2 profile, with excess release of proinflammatory cytokines.\(^{29}\) There has been relatively little investigation into the role of chemicals as risk factors for asthma compared with air pollution or allergens. Rumchev et al.\(^{30}\) have reported elevated asthma on exposure to volatile organic compounds, and Karmaus et al.\(^{31}\) found that elevated levels of DDE resulted in a significant OR of 3.71 for asthma. There is some evidence that children who spend time near indoor chlorinated swimming pools have elevated rates of asthma.\(^{32}\) The relationship between frequency of respiratory infections and incidence of asthma is also uncertain, with some evidence that frequent infections protect against asthma (the ‘hygiene hypothesis’),\(^{33}\) while other investigators fail to find any such effect.\(^{34,35}\)

There have been few studies of respiratory diseases or immune function in relation to residence near hazardous waste sites. Vine et al.\(^{36}\) reported that residents living closer to a pesticide dump site in North Carolina had significantly lower mitogen-induced lymphoproliferative activity than those living further away. We have previously reported elevated rates of chronic bronchitis and chronic obstructive pulmonary disease in adults living near ‘POPs’ waste sites.\(^{37}\)

Our studies show statistically significant elevations in the rates of hospital discharge for both asthma and infectious respiratory disease in children who live near hazardous waste sites after adjustment for a variety of factors, including MHI, an indicator of socioeconomic status. This relationship is somewhat stronger for waste sites containing POPs, but is also significant for hazardous waste sites that do not contain POPs. Many of these have volatile organic compounds, which may be risk factors.\(^{30,32}\) Most of the POP sites in our study contain PCBs, while relatively few contain dioxins in any significant amount. It is interesting to note...
that Weisglas-Kuperus et al.\textsuperscript{10} found that Dutch children exposed to both dioxins and PCBs showed more infections but fewer symptoms of asthma, while Van Den Heuvel et al.\textsuperscript{13} found that, in Flemish children, dioxin was protective against asthma, whereas PCBs increased risk.

There are some serious limitations to our study in that our only measure of exposure is residence in proximity to a hazardous waste site. Our unit of analysis is the zip code, and we have no information on duration of residence or migration patterns. Our analysis is conducted on an aggregate level, and there are a number of individual level confounders (nutrition, smoking, air pollution, allergens, exercise) that we cannot control. However, this study also has many strengths, primarily in the large sample size and the multiple years of data. The analysis controlled for potential confounders, such as age, race, gender and urban/rural residence. Furthermore, we used zip code level MHI as a proxy for socioeconomic status, which in turn on a population level is a surrogate for many individual level behaviors.

The highly significant elevations in rates of hospital discharges that we found for both diseases suggests that an even stronger association may exist between exposure and disease if we could refine the measure of exposure or use individual level data. Further studies with individual data are needed to confirm our observations. However, our results are consistent with the hypothesis that living near a hazardous waste site increases the risk of exposure to toxic chemicals, and that this exposure in turn elevates the rate of being hospitalized for both asthma and infectious respiratory disease.

REFERENCES


