

## Hazardous waste disposal sites: summary of epidemiologic evidence

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### 1. Overall summary

This section summarizes epidemiologic evidence cited in the tables below and will be updated as new evidence becomes available. I would appreciate feedback on any errors or omissions. [don.wigle@sympatico.ca](mailto:don.wigle@sympatico.ca)

Health effect	Level of evidence <sup>a</sup>	Comments
Early fetal deaths (spontaneous abortion)	Inadequate	A case-control study in Massachusetts found a borderline association between early fetal deaths and drinking water mercury but not arsenic levels (both contaminants occurred at low concentrations) (Aschengrau et al. 1993). A retrospective cohort study of pregnant women in California showed a dose-response relationship between spontaneous abortion and tap water consumption (Dean et al. 1989, 1992, Wrensch et al. 1990). A recent review concluded that there is inadequate evidence for an association between fetal deaths and maternal residential proximity to hazardous waste landfill sites or incinerators (Rushton 2003).
Late fetal deaths (stillbirths)	Inadequate	A case-control study of stillbirths caused by anencephaly (a severe neural tube birth defect) in Canada found no association with community water supply concentrations of lead, mercury, cadmium or other elements (Elwood and Coldman 1981). A case-control study within the 1988 National Maternal and Infant Health Survey showed a borderline weak association between late fetal deaths and maternal residential proximity to EPA National Priority List hazardous waste disposal sites in the USA (Sosniak et al. 1994). Ecologic studies in the UK found no association between late fetal deaths and maternal residential proximity to hazardous waste landfill sites (Elliott et al. 2001, Morris et al. 2003) or incinerators (Dummer et al. 2003). The latter study found a weak but significant association between stillbirths and maternal residential proximity to crematoria (mercury is a major toxicant in such emissions). A recent review concluded that there is inadequate evidence for an association between fetal deaths and maternal residential proximity to hazardous waste landfill sites or incinerators (Rushton 2003).
Intrauterine growth retardation (IUGR), small for gestational age (SGA), birth weight adjusted for gestation length	(Inadequate)	A population-based case-control study in Montreal found no association between SGA and maternal residential proximity to a large municipal solid and industrial waste disposal site (Goldberg et al. 1995). A retrospective cohort study of Camp Lejeune in North Carolina showed no overall association between SGA and maternal prenatal/preconceptional exposure to drinking water contaminated with tetrachloroethylene from a dry-cleaning operation; among offspring of women age 35 years or older, such exposure was associated with SGA and inversely with birth weight

		adjusted for gestation length (Sonnenfeld et al. 2001). An ecologic study in Nova Scotia (Canada) found no association between low birth weight (any gestation length) and maternal residence in region with a large hazardous waste disposal site (Dodds and Seviour 2001). An ecologic study in New York State found a weak but statistically significant association between low birth weight but not very low birth weight rates (adjusted for gestation length) and maternal residential proximity to hazardous waste disposal sites containing PCBs; the mean birth weight was about 22 g less ( $p < 0.001$ ) among offspring of women living near such sites (Baibergenova et al. 2003).
Term birth weight	(Inadequate)	A case-control study within the 1988 National Maternal and Infant Health Survey found no association between term low birth weight and maternal residential proximity to hazardous waste disposal sites (Sosniak et al. 1994). A retrospective cohort study in New Jersey found an association between term low birth weight and maternal residential proximity to a large hazardous waste disposal site; the association was stronger for women who lived downwind of the site (Berry and Bove 1997). A retrospective cohort study in California found slightly reduced birth weight at term among infants of women living in high-odour regions near a large landfill site (Kharrazi et al. 1997).
Low birth weight (not adjusted for gestation length)	Proximity to hazardous waste sites Limited  Proximity to incinerators Inadequate	A literature review (Vrijheid 2000) concluded that there was limited evidence for an association between reduced birth weight and maternal residential proximity to hazardous waste disposal sites. A population-based case-control study in Montreal found no association between low birth weight or very low birth weight and maternal residential proximity to a large municipal solid and industrial waste disposal site (Goldberg et al. 1995). A retrospective cohort study in New Jersey found that average term birth weight in the region close to a large hazardous waste disposal site increased after the high-exposure period ended (Berry and Bove 1997). An ecologic study in the UK found a weak but significant association between low birth weight and maternal residential proximity to hazardous waste disposal sites (Elliott et al. 2001). An ecologic study in Nova Scotia (Canada) found no association between low birth weight (any gestation length) and maternal residence in region with a large hazardous waste disposal site (Dodds and Seviour 2001). An ecologic study in Scotland also found no association between low birth weight and maternal residential proximity to hazardous waste disposal sites (Morris et al. 2003). A recent review concluded that there is limited evidence for an association between low birth weight and maternal residential proximity to hazardous waste disposal sites but few epidemiologic studies and inadequate evidence for an association between low birth weight and maternal residential proximity to incinerators (Rushton 2003).
Preterm birth, gestation length	(Inadequate)	A population-based case-control study in Montreal found no association between preterm birth and maternal residential proximity to a large municipal solid and industrial waste disposal site (Goldberg et al. 1995). A retrospective cohort study in New Jersey found an association between preterm birth and maternal residential proximity downwind to a large hazardous waste disposal site (Berry and

		<p>Bove 1997). A retrospective cohort study in California found slightly reduced gestational age among normal birth weight infants of women living in high-odour regions near a large landfill site (Kharrazi et al. 1997). A retrospective cohort study of Camp Lejeune in North Carolina showed that preterm birth was not associated with maternal prenatal/preconceptual exposure to drinking water contaminated with tetrachloroethylene from a dry-cleaning operation (Sonnenfeld et al. 2001). An ecologic study in Nova Scotia (Canada) found no association between preterm birth and maternal residence in region with a large hazardous waste disposal site (Dodds and Seviour 2001).</p>
Total birth defects	Limited	<p>A small cohort study in Missouri found no association between total birth defects and maternal residence in areas with TCDD-contaminated soil and dust (Stockbauer et al. 1988). A population-based case-control study in New York State found a weak but statistically significant association between total birth defects and maternal residential proximity to hazardous waste disposal sites and an index of exposure likelihood (Geschwind et al. 1992). A case-control study found no association between total birth defects and maternal residential proximity to EPA National Priority List (NPL) hazardous sites (Sosniak et al. 1994). A literature review (Vrijheid 2000) concluded that there was inadequate evidence for an association between birth defects and maternal residential proximity to hazardous waste disposal sites. A population-based case-control study in five European countries found a weak association between total birth defects and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found a slightly increased risk of total birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between total birth defects and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An extension of the population-based case-control study in five European countries by Dolk et al. (1998), described above, found a borderline dose-response relationship between total birth defects and the estimated hazard from contaminants released into water but not those released into air from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002). A large case-control study found a weak association between total birth defects and maternal residential proximity to NPL hazardous waste sites in California (Orr et al. 2002). A review by Dolk and Vrijheid (2003) concluded that there is limited epidemiologic evidence for an association between birth defects and maternal residential proximity to hazardous waste disposal sites while a review by Rushton (2003) concluded that there was inadequate epidemiologic evidence; both reviews concluded that the few existing epidemiologic studies provided inadequate evidence for an association between birth defects and maternal residential proximity to incinerators. An ecologic study in Scotland found no association between total birth defects and maternal residential proximity to hazardous waste sites (Morris et al. 2003).</p>
Central nervous system (CNS) birth	(Limited)	<p>A case-control study of stillbirths caused by anencephaly (a severe neural tube birth defect) in</p>

defects		<p>Canada found no association with community water supply concentrations of lead, mercury, cadmium or other elements (Elwood and Coldman 1981). A population-based case-control study in New York State found an association between CNS birth defects and maternal residential proximity to hazardous waste disposal sites but not with an index of exposure likelihood (Geschwind et al. 1992). An enlarged population-based case-control study in New York State found no association between CNS birth defects and maternal residential proximity to hazardous waste disposal sites or with likelihood of exposure to solvents from such sites by routes other than drinking water; there were borderline associations with maternal residential proximity to industrial facilities emitting solvents or metals but irregular dose-response relationships (Marshall et al. 1997). A population-based case-control study in California found a non-significant association between NTDs and maternal residential proximity to NPL hazardous sites; there were borderline or significant associations between NTDs and proximity to sites with contaminated surface or ground water, sites containing cyanides, lead, pyrene, PCBs, benzene or pesticides (Croen et al. 1997). A population-based case-control study in five European countries found an association between NTDs and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found an increased risk of NTDs in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between NTDs and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An extension of the population-based case-control study in five European countries by Dolk et al. (1998), described above, found a borderline dose-response relationship between NTDs and the estimated hazard from contaminants released into air but not those released into water from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002b). A large case-control study found a borderline association between NTDs and maternal residential proximity to NPL hazardous waste sites in California (Orr et al. 2002). An ecologic study in Scotland found no association between NTDs and maternal residential proximity to hazardous waste sites (Morris et al. 2003). A retrospective cohort study in the UK found a weak association between NTDs and maternal residential proximity to hazardous waste sites but not to incinerators (Dummer et al. 2003). A large retrospective cohort study in France found no association between NTDs and maternal residence in a community with a solid waste incinerator or expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004).</p>
Cardiovascular birth defects	(Limited)	<p>A case-control study in Massachusetts found no association between total cardiac birth defects and detectable lead or arsenic in community drinking water; there were associations between patent ductus arteriosus and detectable mercury and between coarctation of the aorta and detectable arsenic (Zierler et al. 1988). A population-based case-control study in Tucson found an association between cardiovascular birth defects and parental residence in a region served by a drinking water well contaminated by trichloroethylene, dichloroethylene and chromium; this association was not</p>

		<p>observed after the well was closed (Goldberg et al. 1990). A population-based case-control study in California found non-significant associations between conotruncal heart birth defects and maternal residential proximity to NPL hazardous sites or to sites containing heavy metals, inorganics or semi-volatiles; there was no association with sites containing VOCs (Croen et al. 1997). A population-based case-control study in five European countries found associations between cardiac septa and great artery/vein birth defects and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found a borderline increased risk of cardiovascular birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between cardiovascular birth defects and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An extension of the population-based case-control study in five European countries by Dolk et al. (1998), described above, found a non-significant dose-response relationship between cardiac septal defects and the estimated hazard from contaminants released into water but not those released into air from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002b). An ecologic study in Scotland found no association between cardiovascular birth defects and maternal residential proximity to hazardous waste sites (Morris et al. 2003). A retrospective cohort study in the UK found a weak association between cardiac birth defects and maternal residential proximity to hazardous waste sites but not to incinerators (Dummer et al. 2003). A population-based case-control study in Maryland and northern Virginia found an association between l-transposition of great arteries and maternal residential proximity to four NPL hazardous waste disposal sites, including two sites that released large amounts of chlorinated solvents into air (Kuehl and Loffredo 2003). A large retrospective cohort study in France found no association between cardiac birth defects and maternal residence in a community with a solid waste incinerator or expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004).</p>
Orofacial birth defects	(Inadequate)	<p>A population-based case-control study in New York State found a borderline association between oral cleft birth defects and maternal residential proximity to hazardous waste disposal sites (Geschwind et al. 1992). A population-based case-control study in California found no associations between oral cleft birth defects and maternal residential proximity to NPL hazardous sites or to sites containing heavy metals, inorganics, semi-volatiles or VOCs (Croen et al. 1997). A large retrospective cohort study in France found a weak association between facial clefts and maternal residence in a community with a solid waste incinerator but no association with expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004).</p>
Musculoskeletal birth defects	(Inadequate)	<p>A population-based case-control study in New York State found a weak but statistically significant association between musculoskeletal birth defects and maternal residential proximity to hazardous waste disposal sites and an index of exposure likelihood (Geschwind et al. 1992). An enlarged</p>

		<p>population-based case-control study in New York State found no associations between musculoskeletal birth defects and maternal residential proximity to any hazardous waste disposal site or to industrial facilities releasing solvents or pesticides; there was also no association with the likelihood of exposure to solvents or pesticides from waste disposal sites (Marshall et al. 1997). A population-based case-control study in five European countries found an association between gastroschisis and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found no increased risk of musculoskeletal birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). A large retrospective cohort study in France found no association between limb reduction birth defects and maternal residence in a community with a solid waste incinerator (Cordier et al. 2004).</p>
Genitourinary birth defects	(Limited)	<p>A population-based case-control study in five European countries found a borderline association between hypospadias and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found no increased risk of genitourinary birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between hypospadias and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An ecologic study in Scotland found no association between hypospadias and maternal residential proximity to hazardous waste sites (Morris et al. 2003). A large retrospective cohort study in France found an association between renal dysplasia and maternal residence in a community with a solid waste incinerator but not with expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004). The latter study found a borderline association between obstructive urinary tract birth defects and maternal residence in a community with a solid waste incinerator and no association between hypospadias and such exposure.</p>
Gastrointestinal birth defects	(Inadequate)	<p>A population-based case-control study in five European countries found an association between tracheo-esophageal birth defects and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). A large retrospective cohort study in France found a borderline association between megacolon and maternal residence in a community with a solid waste incinerator (Cordier et al. 2004).</p>
Chromosomal abnormalities (structural)	(Inadequate)	<p>A population-based case-control study in New York State found a borderline association between chromosomal abnormalities and maternal residential proximity to hazardous waste disposal sites (Geschwind et al. 1992). An ecologic study in Sydney, Nova Scotia (Canada) found a slight and non-significantly increased risk of chromosomal abnormalities in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An extension of the population-</p>

		based case-control study in five European countries by Dolk et al. (1998), described above, found a borderline dose-response relationship between chromosomal abnormalities and the estimated hazard from contaminants released into water but not those released into air from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002b). The latter authors also found borderline associations between both Down's syndrome and non-Down's syndrome chromosomal abnormalities and maternal residential proximity to hazardous waste disposal sites (Vrijheid et al. 2002a). A large retrospective cohort study in France found no association between chromosomal abnormalities and maternal residence in a community with a solid waste incinerator (Cordier et al. 2004).
All childhood cancers	Inadequate	An ecologic study in the UK found a possible association between childhood cancer and early life residential proximity to municipal waste incinerators but not hazardous waste landfill sites (Knox 2000). A review by Rushton (2003) concluded that the few epidemiologic studies provide inadequate evidence for an association between childhood cancer and waste disposal by incineration or deposition in landfill sites.
Leukemia	(Inadequate)	A very small case-control study in Holland found an association between childhood leukemia/lymphoma and swimming in a pond contaminated by DDT, PAH and benzene and subject to runoff from intensive horticultural pesticide use (Mulder et al. 1994). An ecologic study of childhood leukemia in New Jersey found an association between leukemia in young girls but not boys and municipal drinking water trichloroethylene levels (Cohn et al. 1994). The childhood leukemia incidence rate in Woburn (Massachusetts) during 1966-1986 was elevated almost 5-fold (Durant et al. 1995). A subsequent case-control study in Woburn found a borderline association between childhood leukemia and likelihood of exposure to drinking water contaminated by trichloroethylene and other solvents; there was some evidence that the association was greater for prenatal compared to childhood exposure (Costas et al. 2002). An ecologic study in the UK found no association between leukemia and residential proximity to general or hazardous waste disposal sites (Jarup et al. 2002).
Lymphoma	(Inadequate)	A very small case-control study in Holland found an association between childhood leukemia/lymphoma and swimming in a pond contaminated by DDT, PAH and benzene and subject to runoff from intensive horticultural pesticide use (Mulder et al. 1994).
Reproductive system development: summary	(Inadequate)	A cross-sectional study of youth in Belgium found no association between testicular volume and serum dioxin-like compounds (Den Hond et al. 2002). This study found associations between delayed male genital development and reduced pubic hair growth and serum PCB but not dioxin-like compounds. Delayed breast development in girls was associated with serum dioxin-like compounds but not PCBs.

Thyroid function	(Inadequate)	A cross-sectional study of German children living near a toxic waste incinerator showed dose-response relationships between increased blood TSH and decreased blood FT3 levels and blood levels of cadmium and certain PCB congeners; there were no associations with blood lead or urinary mercury levels (Osius et al. 1999).
Kidney function	(Inadequate)	A cross-sectional study of youth in Belgium living near lead, waste incineration and other industries found dose-response relationships between serum cystatin-C and urinary $\beta$ 2-microglobulin levels (biomarkers of reduced renal filtration rates and renal tubular damage) and blood lead levels (Staessen et al. 2001).

## 2. Fetal death

Reference, location	Design	Exposure	Results	Association <sup>1</sup>	DR <sup>2</sup>	Covariates
(Elwood and Coldman 1981), Canada	Case-control study, 468 stillbirths caused by anencephaly, 4129 live birth controls, mothers resident in 142 communities population 10,000 or greater	Measured municipal drinking water calcium, magnesium, copper, zinc, nickel, lead, selenium, mercury, chromium, silver, cobalt, cadmium and molybdenum levels; mean drinking water lead levels in case and control communities were 10.3 and 11.5 µg/L	No association between anencephaly and municipal drinking water levels of lead, mercury, cadmium or any other element tested			Average family income, population, latitude, longitude, percent of married women employed
(Aschengrau et al. 1989), Massachusetts	Case-control study, 286 cases of spontaneous abortion, 1391 live birth controls	Measured trace element levels in drinking water supplies for communities where women lived while pregnant; mercury levels were all quite low (< 1.1 µg/L) as were arsenic levels (< 2 µg/L)	Borderline association between spontaneous abortion and detectable mercury levels in municipal water supply (odds ratio for 0.2-1.1 µg/L vs undetectable)	1.5 (CI 1.0-2.3)		Water source, maternal age, maternal education, previous spontaneous abortion
			Non-significant association between spontaneous abortion and detectable arsenic in municipal water supply (odds ratio for 1.4-1.9 µg/L vs undetectable)	1.5 (CI 0.4-4.7)		As above
(Deane et al. 1989; Wrensch et al. 1990; Deane et al.	Re-analysis, retrospective cohort study, 349 women in	Residence in two census tracts, one of which had a water supply contaminated with organic	Spontaneous abortion associated with tap water consumption in both census	exposed census tract 13, 31, 24		

<sup>1</sup> Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>2</sup> 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

(1992), Santa Clara County, California	two census tracts who became pregnant during 1980-1981; 39 spontaneous abortions	solvents including trichloroethane, a possible teratogen	tracts (rates per 100 pregnancies among women drinking 1,2-3 or 4+ glasses/day); spontaneous abortion rate did not increase over the 2 years during which contaminant levels increased	unexposed census tract 7, 9, 16	
			Spontaneous abortion associated with tap water consumption (odds ratio per category change in tap water consumption – 0 (referent), 1-3 and 4+ glasses/day)	2.2 (1.2-4.0)	+ 1 <sup>st</sup> trimester smoking and alcohol, maternal education and employment during pregnancy, age, ethnicity, prior fetal loss
(Sosniak et al. 1994), National Maternal and Infant Health Survey, USA	Case-control study, 1791 late fetal deaths, 5490 term live birth controls, USA, 1988	Linked subject records to 1990 EPA national priority list hazardous waste sites; 10% of subjects were exposed (defined as maternal residence $\leq$ 1.6 km from a hazardous waste site)	Weak association of borderline statistical significance between late fetal deaths and maternal proximity to a hazardous waste disposal site	1.14 (0.95-1.36)	Prenatal care, maternal age, smoking, alcohol, illicit drug use, employment, education, income, infant sex
(Elliott et al. 2001), UK	Ecologic study, pregnancy outcomes, UK 1982-1997; over 8 million live births, 43,471 late fetal deaths, 124,597 birth defects	Maternal residence within 2 km of any of 9,565 landfill sites operational during 1982-1997; included 774 hazardous waste sites	Stillbirths not associated with maternal residence near hazardous waste sites (odds ratio for residence <2 vs $\geq$ 2 km)	0.99 (CI 0.95-1.03)	Low income
(Rushton 2003), UK	Review of literature on health effects of waste disposal by incineration or deposition in landfill sites	Waste disposal in landfill sites	Inadequate evidence for an association between fetal death and maternal residential proximity to hazardous waste sites		

		Incineration – major toxicants include particulate matter, acidic gases and aerosols, heavy metals, dioxins/furans	The few epidemiologic studies of incinerators provide inadequate evidence for an association with fetal death		
(Morris et al. 2003), Scotland	Ecologic study, adverse pregnancy outcomes, 1982-1997; 1849 stillbirths, 11,138 birth defect cases, 324,167 live births	Maternal residence proximity to one of 61 special waste disposal sites	Stillbirths not associated with maternal residential proximity to hazardous waste disposal sites (relative risk <2 vs ≥2 km)	0.9 (0.8-1.1)	YOB, infant sex, SES
(Dummer et al. 2003), UK	Retrospective cohort study, 3234 stillbirths during period of crematoria operation, 1956-1993; 612 stillbirths during period of incinerator operation, 1977-1993; 244,758 total births	Maternal residential proximity to 4 incinerators and 3 crematoria in northwest England; birth certificate information on paternal occupation; mercury is major pollutant from crematoria; major incinerator emissions incl dioxins/furans, heavy metals, particulates, VOCs	Borderline and weak associations between stillbirths and maternal residential proximity to crematoria; odds ratio for distance D computed as $1/(D + 0.1)^2$	incinerators 1.04 (0.90-1.19) crematoria 1.04 (1.01-1.07)	YOB, SES, birth order, multiple birth

### Fetal death: summary

#### *Early fetal deaths (spontaneous abortion)*

A case-control study in Massachusetts found a borderline association between early fetal deaths and drinking water mercury but not arsenic levels (both contaminants occurred at low concentrations) (Aschengrau et al. 1993). A retrospective cohort study of pregnant women in California showed a dose-response relationship between spontaneous abortion and tap water consumption (Dean et al. 1989, 1992, Wrensch et al. 1990). A recent review concluded that there is inadequate evidence for an association between fetal deaths and maternal residential proximity to hazardous waste landfill sites or incinerators (Rushton 2003).

#### *Late fetal deaths (stillbirths)*

A case-control study of stillbirths caused by anencephaly (a severe neural tube birth defect) in Canada found no association with community water supply concentrations of lead, mercury, cadmium or other elements (Elwood and Coldman 1981). A case-control study within the 1988 National Maternal and Infant Health Survey showed a borderline weak association between late fetal deaths and maternal residential proximity to EPA National Priority List hazardous waste disposal sites in the USA (Sosniak et al. 1994). Ecologic studies in the UK found no association between late fetal deaths and maternal residential proximity to hazardous waste landfill sites (Elliott et al. 2001, Morris et al. 2003) or incinerators (Dummer et al. 2003). The latter study found a weak but significant

association between stillbirths and maternal residential proximity to crematoria (mercury is a major toxicant in such emissions). A recent review concluded that there is inadequate evidence for an association between fetal deaths and maternal residential proximity to hazardous waste landfill sites or incinerators (Rushton 2003).

### 3. Low birth weight, intrauterine growth retardation, preterm birth

Reference, location	Design	Exposure	Results	Association <sup>3</sup>	DR <sup>4</sup>	Covariates
(Sosniak et al. 1994), National Maternal and Infant Health Survey, USA	Case-control study, 4690 low birth weight, 813 term low birth weight and 4612 preterm low birth weight infants, 5490 term live birth controls (birth weight > 2500 g), USA, 1988	Linked subject records to 1990 EPA national priority list hazardous waste sites; 10% of subjects were exposed (defined as maternal residence ≤1.6 km from a hazardous waste site)	Term low birth weight not associated with maternal proximity to a hazardous waste disposal site	1.1 (0.9-1.4)		Prenatal care, maternal age, smoking, alcohol, illicit drug use, employment, education, income, infant sex
(Goldberg et al. 1995), Montreal	Population-based case-control study, 7403 preterm birth (<37 wk), 7977 low birth weight (<2500 g), 937 very low birth weight (<1500 g), 6705 SGA (≤3 <sup>rd</sup> percentile of Canadian sex-gestation-week-specific birth weights) and 7856 live birth controls among Montreal Island residents, 1979-1989	Large municipal solid waste site with about 36 million tons of domestic, commercial and industrial waste; biogas emission was the principal environmental and health concern; drinking water source not exposed to leachates from waste site; spot measurements of methane up to 25 ppm on streets near site; other air contaminants include combustion products from burning of biogas and heavy diesel truck traffic; exposure index based on residential proximity to waste site	Preterm birth not associated with maternal residential proximity to waste site (odds ratios for low, medium and high exposure vs referent population)	1.0 (0.9-1.1) 1.0 (0.9-1.1) 1.0 (0.9-1.1)		Mother's marital status, language, education, age, infant sex, season
			Low birth weight not associated with maternal residential proximity to waste site	0.9 (0.8-1.0) 1.1 (1.0-1.2) 1.1 (1.0-1.2)		Above plus preterm birth

<sup>3</sup> Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>4</sup> 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

			(odds ratios for low, medium and high exposure vs referent population)		
			Very low birth weight not associated with maternal residential proximity to waste site (odds ratios for low, medium and high exposure vs referent population)	1.3 (0.8-2.2) 1.1 (0.7-1.7) 1.1 (0.7-1.7)	Above plus preterm birth
			SGA not associated with maternal residential proximity to waste site (odds ratios for low, medium and high exposure vs referent population)	1.0 (0.9-1.1) 1.2 (1.1-1.3) 1.1 (1.0-1.2)	Mother's marital status, language, education, age, infant sex, season
(Kharrazi et al. 1997), California	Retrospective cohort study, 25,216 live births and fetal deaths, mothers living within 3 miles of landfill site, 1978-1986; analyses focused on term (gestation length $\geq 37$ wk), not low birth weight ( $\geq 2500$ g) infants	Maternal residential proximity to a hazardous waste landfill site, odour complaints per 100 households 1984-1985; peak exposure thought be during 1981-1984	Gestational age during 1981-1984 slightly reduced in high-odour region (difference in mean gestational age, high-odour vs referent no-odour region); no monotonic dose-response relationship	-1.8 d (p = 0.02)	Maternal age, parity, race/ethnicity, infant sex, delayed prenatal care, multiple births; education and % high school graduates and median family income at census tract level
			Birth weight during 1981-1984 slightly reduced in high-odour region (difference in mean birth weight,	-59 g (p = 0.05)	As above

			high-odour vs referent no-odour region; no monotonic dose-response relationship		
			Gestational age and birth weight not associated with maternal residential proximity to hazardous waste site (respective differences in means, distance <0.7 vs 0.7-3 miles)	gestational age 0 d (p=0.94) birth weight -20 g (p=0.25)	
(Berry and Bove 1997), New Jersey	Retrospective cohort study, 11,579 singleton live births in 4 municipalities close to hazardous waste disposal site, 1961-1985; birth certificate information on birth weight and gestation length	Main human exposure routes were inhalation of volatile chemicals; drinking water not contaminated by leachate from site; assessed region $\leq$ 1 km from site, subdivisions of this region based on prevailing wind direction and surrounding region >1 km from site; liquid hazardous wastes dumped in site during 1958-1969; period of peak exposure estimated to be late 1960's to mid 1970's with minimal exposure before 1966 or after 1980	Term low birth weight during the high-exposure period (1971-1975) associated with maternal residential proximity to hazardous waste disposal site (odds ratio, $\leq$ 1 vs >1 km)	1.9 (1.0-3.6)	Infant sex, maternal age, parity, prenatal care, previous stillbirths, education
			Term low birth weight during the high-exposure period (1971-1975) associated with maternal residential proximity to hazardous waste disposal site (odds	5.1 (2.1-12)	As above

			ratio, $\leq 1$ and <i>downwind</i> vs $>1$ km)		
			Avg term birth weight increased in region $\leq 1$ km from site but not in comparison region after the high-exposure period ended		
			Preterm birth during the high-exposure period (1971-1975) associated with maternal residential proximity to hazardous waste disposal site (odds ratio, $\leq 1$ and <i>downwind</i> vs $>1$ km)	2.1 (1.0-4.4)	As above
(Vrijheid 2000), UK	Review of literature on health effects of residential proximity to hazardous waste sites, 1980-1998	Existing epidemiologic studies in this field have methodologic problems, potential biases and confounding factors	There is limited evidence for an association between reduced birth weight and maternal residential proximity to hazardous waste sites		
(Dodds and Seviour 2001), Sydney, Nova Scotia, Canada	Ecologic study, birth weight, gestation length and birth defect incidence rates in a community with a large hazardous waste site; compared rates to remainder of county and	Hazardous waste from a coke oven that operated for over 80 yr; chemicals include PAHs, PCBs, benzene, arsenic, lead, other heavy metals; also a waste incinerator in community	Low birth weight (any gestation length), preterm birth and IUGR rates not increased in Sydney (respective relative risks, Sydney vs Nova	1.0 (0.8-1.1) 1.1 (1.0-1.3) 0.9 (0.8-1.0)	Maternal age, smoking, parity

	province, 1988-1998; 4128 births in Sydney, 11620 in remainder of Cape Breton and 109437 in Nova Scotia minus Cape Breton		Scotia minus Cape Breton)		
(Elliott et al. 2001), UK	Ecologic study, birth defects and low birth weight, UK 1982-1997; over 8 million live births, 43,471 late fetal deaths, 124,597 birth defects	Maternal residence within 2 km of any of 9,565 landfill sites operational during 1982-1997; included 774 hazardous waste sites	Low birth weight associated with maternal residence near hazardous waste sites (odds ratio for residence <2 vs ≥2 km)	1.05 (CI 1.04-1.06)	Low income
(Sonnenfeld et al. 2001), Camp Lejeune, North Carolina	Retrospective cohort study, 6117 births among exposed women and 5681 births among unexposed women, Camp Lejeune residents, 1968-1985; birth certificate information on birth weight and gestation length	2 of the 15 housing areas were supplied with water from contaminated wells; maternal prenatal exposure to drinking water contaminated by tetrachloroethylene based on birth certificate address and knowledge of water distribution systems on base; average drinking water tetrachloroethylene levels were 76-104 µg/L during 1982 and 215 µg/L during early 1985	SGA not associated with contaminated drinking water exposure (odds ratio, entire pregnancy and for ≥1 yr before conception vs never exposed)	1.1 (0.9-1.4)	
			Preterm birth not associated with contaminated drinking water exposure (odds ratio, entire pregnancy and for ≥1 yr before conception vs never exposed)	0.8 (0.6-1.1)	
			Birth weight inversely associated with exposure status among	age <35 yr -2 g (-17 to +13)	Gestation length, previous fetal loss, race, SES and infant

			women age $\geq 35$ yr (birth weight deficits and 90% CIs, exposed vs unexposed)	age $\geq 35$ yr -130 g (-236 to -23)	YOB and sex
			SGA associated with exposure status among women age $\geq 35$ yr (odds ratios and 90% CIs for exposed vs unexposed)	age $< 35$ yr 1.1 (0.9-1.2)  age $\geq 35$ yr 2.1 (0.9-4.9)	Previous fetal loss, primiparity, SES, maternal education, infant YOB
(Rushton 2003), UK	Review of literature on health effects of waste disposal by incineration or deposition in landfill sites	Waste disposal in landfill sites	Limited evidence for an association between low birth weight and maternal residential proximity to hazardous waste sites		
		Incineration – major toxicants include particulate matter, acidic gases and aerosols, heavy metals, dioxins/furans	The few epidemiologic studies of incinerators provide inadequate evidence for an association with low birth weight		
(Baibergenova et al. 2003), New York state	Ecologic study, 187 zip code areas with PCB-contaminated hazardous waste sites; compared low (1500-2500g) and very low (<1500 g) birth weight rates in potentially exposed regions with those in the remainder of New York State except New York City	Residence in zip code with PCB-contaminated waste disposal site or in nearby regions	Mean birth weight was slightly lower in regions with PCB-contaminated waste disposal sites	-21.6 g (p < 0.001)	
			Low birth weight rate	1.04	Gestation length

			weakly associated with PCB-contaminated waste disposal sites (relative risk)	(CI 1.02-1.07)	
			Very low birth weight rate not associated with PCB-contaminated waste disposal sites (relative risk)	0.95 (CI 0.88-1.02)	Gestation length
(Morris et al. 2003), Scotland	Ecologic study, adverse pregnancy outcomes, 1982-1997; 1849 stillbirths, 11,138 birth defect cases, 324,167 live births	Maternal residence proximity to one of 61 special waste disposal sites	Low birth weight (any gestation length) not associated with maternal residential proximity to hazardous waste disposal sites (relative risk <2 vs ≥2 km)	1.01 (0.96-1.07)	YOB, infant sex, SES

### Low birth weight, intrauterine growth retardation, preterm birth: summary

#### *Intrauterine growth retardation (IUGR), small for gestational age (SGA), birth weight adjusted for gestation length*

A population-based case-control study in Montreal found no association between SGA and maternal residential proximity to a large municipal solid and industrial waste disposal site (Goldberg et al. 1995). A retrospective cohort study of Camp Lejeune in North Carolina showed no overall association between SGA and maternal prenatal/preconceptual exposure to drinking water contaminated with tetrachloroethylene from a dry-cleaning operation; among offspring of women age 35 years or older, such exposure was associated with SGA and inversely with birth weight adjusted for gestation length (Sonnenfeld et al. 2001). An ecologic study in Nova Scotia (Canada) found no association between low birth weight (any gestation length) and maternal residence in region with a large hazardous waste disposal site (Dodds and Seviour 2001). An ecologic study in New York State found a weak but statistically significant association between low birth weight but not very low birth weight rates (adjusted for gestation length) and maternal residential proximity to hazardous waste disposal sites containing PCBs; the mean birth weight was about 22 g less ( $p < 0.001$ ) among offspring of women living near such sites (Baibergenova et al. 2003).

#### *Term birth weight*

A case-control study within the 1988 National Maternal and Infant Health Survey found no association between term low birth weight and maternal residential proximity to hazardous waste disposal sites (Sosniak et al. 1994). A retrospective cohort study in New Jersey found an association between term low birth weight and maternal residential proximity to a large hazardous waste disposal site; the association was stronger for women who lived downwind of the site

(Berry and Bove 1997). A retrospective cohort study in California found slightly reduced birth weight at term among infants of women living in high-odour regions near a large landfill site (Kharrazi et al. 1997).

*Low birth weight (not adjusted for gestation length)*

A literature review (Vrijheid 2000) concluded that there was limited evidence for an association between reduced birth weight and maternal residential proximity to hazardous waste disposal sites. A population-based case-control study in Montreal found no association between low birth weight or very low birth weight and maternal residential proximity to a large municipal solid and industrial waste disposal site (Goldberg et al. 1995). A retrospective cohort study in New Jersey found that average term birth weight in the region close to a large hazardous waste disposal site increased after the high-exposure period ended (Berry and Bove 1997). An ecologic study in the UK found a weak but significant association between low birth weight and maternal residential proximity to hazardous waste disposal sites (Elliott et al. 2001). An ecologic study in Nova Scotia (Canada) found no association between low birth weight (any gestation length) and maternal residence in region with a large hazardous waste disposal site (Dodds and Seviour 2001). An ecologic study in Scotland also found no association between low birth weight and maternal residential proximity to hazardous waste disposal sites (Morris et al. 2003). A recent review concluded that there is limited evidence for an association between low birth weight and maternal residential proximity to hazardous waste disposal sites but few epidemiologic studies and inadequate evidence for an association between low birth weight and maternal residential proximity to incinerators (Rushton 2003).

*Preterm birth, gestation length*

A population-based case-control study in Montreal found no association between preterm birth and maternal residential proximity to a large municipal solid and industrial waste disposal site (Goldberg et al. 1995). A retrospective cohort study in New Jersey found an association between preterm birth and maternal residential proximity downwind to a large hazardous waste disposal site (Berry and Bove 1997). A retrospective cohort study in California found slightly reduced gestational age among normal birth weight infants of women living in high-odour regions near a large landfill site (Kharrazi et al. 1997). A retrospective cohort study of Camp Lejeune in North Carolina showed that preterm birth was not associated with maternal prenatal/preconceptual exposure to drinking water contaminated with tetrachloroethylene from a dry-cleaning operation (Sonnenfeld et al. 2001). An ecologic study in Nova Scotia (Canada) found no association between preterm birth and maternal residence in region with a large hazardous waste disposal site (Dodds and Seviour 2001).

#### 4. Birth defects

Reference, location	Design	Exposure	Results	Association <sup>5</sup>	DR <sup>6</sup>	Covariates
(Elwood and Coldman 1981), Canada	Case-control study, 468 stillbirths caused by anencephaly, 4129 live birth controls, mothers resident in 142 communities population 10,000 or greater	Measured calcium, magnesium, copper, zinc, nickel, lead, selenium, mercury, chromium, silver, cobalt, cadmium and molybdenum levels in municipal water supplies; mean drinking water lead levels in case and control communities were 10.3 and 11.5 µg/L	No association between anencephaly and municipal drinking water level of lead, mercury, cadmium or any other element tested			Average family income, population, latitude, longitude, percent of married women employed
(Zierler et al. 1988), Massachusetts	Case-control study, 270 cases cardiac birth defects, 665 live birth controls	Assessed maternal exposure to lead and 10 other chemicals in municipal drinking water during pregnancy; median lead level was not detectable, 90 <sup>th</sup> percentile was 0.7 µg/L, highest level was 500 µg/L; median mercury level was 0.1 µg/L, 90 <sup>th</sup> percentile was 0.5 µg/L, highest level was 100 µg/L; median arsenic level was not detectable, 90 <sup>th</sup> percentile was 1 µg/L, highest level was 22 µg/L	Total cardiac birth defects not associated with detectable lead or arsenic in municipal drinking water (prevalence odds ratios, detectable vs non-detectable levels)	lead 1.1 (CI 0.6-2.1)  arsenic 1.0 (CI 0.6-1.6)		Other chemicals in drinking water, drinking water source, maternal education

<sup>5</sup> Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>6</sup> 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

			Borderline association between patent ductus arteriosus and detectable mercury in municipal drinking water (prevalence odds ratios, detectable vs non-detectable levels)	1.6 (CI 1.0-2.6)	As above
			Coarctation of the aorta associated with detectable arsenic in municipal drinking water (prevalence odds ratio, detectable vs non-detectable arsenic)	3.4 (CI 1.3-8.9)	As above
(Stockbauer et al. 1988), Missouri, USA	Cohort study, 402 births among women potentially exposed to TCDD, 804 infants of unexposed comparison women	9 residential areas with TCDD-contaminated soil (TCDD $\geq 1 \mu\text{g/g}$ ) and dust from roads treated with waste oil	No association between total or major birth defects and TCDD exposure (relative risk for major birth defects shown)	0.8 (CI 0.4-1.7)	Maternal education, smoking
(Goldberg et al. 1990), Tucson, Arizona	Population-based case-control study in region with known drinking water contamination, 246 cardiovascular birth defects (confirmed by pediatric cardiologists), 461 controls in 3 sets: 1) randomly selected from same region, 2) matched for telephone prefix, 3) other cases of cardiovascular birth	Parent-reported residential history during and before 1 <sup>st</sup> trimester; water supply for one region of Tucson was contaminated with trichloroethylene, dichloroethylene and chromium from about 1950 to 1981 when contaminated wells were closed	Cardiovascular birth defects associated with parental exposure to drinking water in contaminated region (odds ratio stated without supporting data or CI); no association between CVD birth defects among infants of persons moving into the formerly contaminated region	3	

	defects with no parental occupational or residential contact with contaminated water, 1969-1987		after the well was closed		
(Geschwind et al. 1992), New York State	Population-based case-control study, 9313 birth defect cases, 17802 healthy live birth controls, 1983-1984	Proximity to 590 hazardous waste sites; for each subject, calculated an exposure index based on likelihood of human exposure by inhalation, ingestion or dermal contact, residential proximity, waste site chemical toxicity	Total birth defects associated with maternal proximity to hazardous waste sites (odds ratio, <1.6 km vs ≥1.6 km) and with exposure index (odds ratio for low and high vs no exposure risk)	proximity 1.12 (1.06-1.18) exposure index 1.1 (1.0-1.2) 1.6 (1.3-2.0)	Maternal age, race, education, pregnancy complications, parity, infant sex
			CNS birth defects associated with maternal proximity to hazardous waste sites (odds ratio, <1.6 km vs ≥1.6 km) and possibly with exposure index (odds ratio for low and high vs no exposure risk)	proximity 1.3 (1.1-1.6) exposure index 1.3 (1.0-1.6) 1.5 (0.7-3.2)	As above
			Musculoskeletal birth defects associated with maternal proximity to hazardous waste sites (odds ratio, <1.6 km vs ≥1.6 km) and with exposure index (odds ratio for low and high vs no exposure risk)	proximity 1.2 (1.1-1.3) exposure index 1.1 (1.0-1.2) 1.8 (1.3-2.3)	
			Borderline associations	oral clefts	As above

			between oral cleft defects and chromosome abnormalities and maternal proximity to hazardous waste sites (odds ratio, <1.6 km vs $\geq$ 1.6 km)	1.2 (0.9-1.5)  chromosome abnormalities 1.2 (0.9-1.6)	
(Sosniak et al. 1994), National Maternal and Infant Health Survey, USA	Case-control study, 451 infants with birth defects, 5490 term live birth controls, USA, 1988	Linked subject records to 1990 EPA national priority list hazardous waste sites; 10% of subjects were exposed (defined as maternal residence $\leq$ 1.6 km from a hazardous waste site)	Total birth defects not associated with maternal proximity to a hazardous waste disposal site	1.0 (0.7-1.3)	Prenatal care, maternal age, smoking, alcohol, illicit drug use, employment, education, income, infant sex
(Croen et al. 1997), California	Two population-based case-control studies: (1) 507 live born or stillborn neural tube birth defect (NTD) cases, 517 live birth controls, (2) 201 live born or stillborn conotruncal heart birth defect cases, 439 oral cleft defect cases, 455 live birth controls; 1989-1991	Mother-reported periconceptual residential history; assessed maternal residential proximity to 764 hazardous waste disposal sites incl 105 National Priority List (NPL) sites; categorized chemicals and potential for human exposure at nearby residences	Non-significant association between NTDs and maternal residence proximity to NPL sites (odds ratios for $\leq$ 1 and <1/4 vs >1 mile)(37 and 8 exposed case mothers)	1.4 (0.8-2.4) 2.1 (0.6-7.6)	Maternal race/ethnicity, education, family income, periconceptual vitamin supplement use, neighbourhood educational attainment
			Non-significant or borderline associations between NTDs and maternal residence within 1 mile of a NPL site with known environmental media contamination (crude odds ratios for	air 1.4 (0.6-3.1) biota 1.7 (0.6-4.9) soil 1.4 (0.8-2.3) surface water 1.8 (0.8-3.8) ground water	

	contaminated vs uncontaminated media)(13, 10, 36, 17 and 26 exposed case mothers)	1.4 (0.8-2.6)	
	Non-significant or borderline associations between NTDs and maternal residence within 1 mile of a NPL site containing specific chemical toxicant categories (crude odds ratios for presence vs absence of specific categories)(13, 25, 15, 24, 33 and 15 exposed case mothers)	cyanides 2.3 (0.8-5.6) heavy metals 1.5 (0.8-2.8) inorganics 1.3 (0.6-2.8) semi-volatiles 1.8 (0.9-3.4) VOCs 1.4 (0.8-2.3) pesticides 2.2 (0.9-5.2)	
	Significant or borderline associations between NTDs and maternal residence within 1 mile of a NPL site containing specific toxicants (crude odds ratios for presence vs absence of specific toxicants)(21, 12, 10, 8 and 25 exposed case mothers)	lead 2.0 (0.9-4.1) pyrene 3.1 (1.0-8.6) PCBs 3.5 (0.9-11) DEHP 2.1 (0.6-6.3) benzene 1.9 (0.9-3.6)	PCBs = Arochlor 1254 DEHP = di(2-ethylhexyl)phthalate
	Borderline associations between conotruncal heart birth defects and maternal residence	1.8 (0.8-4.2) 4.2 (0.7-27)	Maternal alcohol, employment status, periconceptual vitamin supplement use,

	proximity to a NPL site (odds ratios for $\leq 1$ and $< 1/4$ vs $> 1$ mile)(10 and 3 exposed case mothers)	neighbourhood educational attainment, infant sex
	Non-significant or borderline associations between conotruncal heart birth defects and maternal residence within 1 mile of a NPL site containing specific chemical toxicant categories (crude odds ratios for presence vs absence of specific categories)(9, 7, 9 and 8 exposed case mothers)	heavy metals 1.7 (0.7-4.1) inorganics 2.3 (0.8-6.4) semi-volatiles 1.9 (0.8-4.5) VOCs 1.3 (0.6-3.2)
	Non-significant association between oral cleft birth defects and maternal residence proximity to a NPL site (odds ratios for $\leq 1$ and $< 1/4$ vs $> 1$ mile)(13 and 2 exposed case mothers)	Maternal race/ethnicity, smoking, periconceptual vitamin supplement use, neighbourhood educational attainment, infant sex
	No association between oral cleft birth defects and maternal residence within 1 mile of a NPL site containing specific chemical toxicant categories (crude odds ratios for presence vs absence of specific	heavy metals 0.9 (0.4-2.1) inorganics 1.3 (0.5-3.4) semi-volatiles 1.0 (0.4-2.4) VOCs 0.8 (0.4-1.8)

			categories)(11, 9, 11 and 11 exposed case mothers)		
(Marshall et al. 1997), New York State	Population-based case-control study, 473 CNS and 3,305 musculoskeletal birth defects, 12,436 normal births, 1983-1986	Defined exposure based on residence at delivery within 1 mile of hazardous waste sites; assessed potential for exposure via air, water or soil/dust to pesticides, metals and solvents based on information about each of 643 hazardous waste sites; included data on industrial air emissions and drinking water THM levels $\geq 100 \mu\text{g/L}$	CNS and musculoskeletal defects not associated with proximity to any hazardous waste site (respective odds ratios, $<1$ vs $\geq 1$ mile)	CNS 0.9 (0.8-1.1)  musculoskeletal 1.0 (0.9-1.1)	Adjusted as necessary for maternal age, race, education, population density, parity, delayed prenatal care, infant sex
			No association between CNS birth defects and likelihood of exposure to solvents from hazardous waste sites by routes other than drinking water (odds ratio, likelihood $>$ low vs low)	0.8 (0.4-1.6)	As above
			Borderline association between CNS birth defects and residential proximity to industrial facilities emitting solvents (odds ratio for distance 0.67-1.0, 0.34-0.66 and $\leq 0.33$ vs $>1$ mile)	1.1 (0.8-1.5) 1.4 (1.0-1.8) 1.4 (1.0-2.0)	As above

			Irregular association between CNS birth defects and residential proximity to industrial facilities emitting metals (odds ratio for distance 0.67-1.0, 0.34-0.66 and $\leq 0.33$ vs $>1$ mile)	1.2 (0.7-1.9) 1.6 (1.1-2.2) 1.2 (0.8-2.0)	As above
			Musculoskeletal birth defects not associated with likelihood of exposure to solvents from hazardous waste sites (odds ratio, likelihood $>low$ vs low) or proximity to industrial facilities emitting solvents (odds ratio, $\leq 1$ vs $\geq 1$ mile)	1.0 (0.8-1.3) 1.0 (0.9-1.1)	As above
			Musculoskeletal birth defects not associated with likelihood of exposure to pesticides from hazardous waste sites (odds ratio, likelihood $>low$ vs low) or residential proximity to industrial facilities emitting pesticides (odds ratio, $\leq 1$ vs $\geq 1$ mile)	0.8 (0.5-1.3) 1.1 (0.9-1.4)	As above
(Dolk et al. 1998), EUROHAZCON	Population-based case-control study, 1,089 birth	Assessed residential proximity to 21 hazardous	Birth defects (total) associated with	1.3 (CI 1.1-1.6)	Maternal age, SES

study, Belgium, Denmark, France, Italy, UK	defect cases, 2,366 controls, from start of birth defect registries in each region to 1993 or 1994; mothers resided within 7 km of a hazardous waste landfill site	waste landfill sites	maternal residence within 3 km of landfill site (odds ratio, < 3 vs 3-7 km)		
			Neural tube birth defects associated with maternal residence within 3 km of landfill site (odds ratio, < 3 vs 3-7 km)	1.9 (CI 1.2-2.8)	As above
			Cardiac septa and great artery/vein birth defects associated with maternal residence within 3 km of landfill site (respective odds ratios, < 3 vs 3-7 km)	1.5 (CI 1.1-2.0)	As above
				1.8 (CI 1.0-3.2)	
			Tracheo-esophageal birth defects associated with maternal residence within 3 km of landfill site (odds ratio, < 3 vs 3-7 km)	2.3 (CI 1.0-5.3)	As above
			Gastroschisis associated with maternal residence within 3 km of landfill site (odds ratio, < 3 vs 3-7 km)	3.2 (CI 1.0-11)	As above
			Borderline association between hypospadias	2.0 (CI 1.0-3.9)	As above

			and residence < 3 km of a landfill site		
(Vrijheid 2000), UK	Review of literature on health effects of residential proximity to hazardous waste sites, 1980-1998	Existing epidemiologic studies in this field have methodologic problems, potential biases and confounding factors	There is inadequate evidence for an association between birth defects and residential proximity to hazardous waste sites		
(Dodds and Seviour 2001), Sydney, Nova Scotia, Canada	Ecologic study, birth weight, gestation length and birth defect incidence rates in a community with a large hazardous waste site; compared rates to remainder of county and province, 1988-1998; 4128 births in Sydney, 11620 in remainder of Cape Breton and 109437 in Nova Scotia minus Cape Breton	Hazardous waste from a coke oven that operated for over 80 yr; chemicals include PAHs, PCBs, benzene, arsenic, lead, other heavy metals; also a waste incinerator in community	Major birth defect rate elevated in Sydney (relative risk, Sydney vs Nova Scotia minus Cape Breton)	1.3 (1.0-1.5)	Maternal age, smoking, parity
			NTD rate elevated in Sydney (relative risk, Sydney vs Nova Scotia minus Cape Breton)	1.8 (1.1-3.1)	As above
			Borderline increased cardiovascular birth defect rate in Sydney (relative risk, Sydney vs Nova Scotia minus Cape Breton)	1.3 (0.9-1.8)	As above
			Genitourinary, musculoskeletal and chromosomal	1.2 (0.7-2.2) 1.2 (0.8-1.7) 1.4 (0.8-2.4)	As above

			abnormality rates not elevated in Sydney (respective relative risks, Sydney vs Nova Scotia minus Cape Breton)		
(Elliott et al. 2001), UK	Ecologic study, birth defects and low birth weight, UK 1982-1997; over 8 million live births, 43,471 late fetal deaths, 124,597 birth defects	Maternal residence within 2 km of any of 9,565 landfill sites operational during 1982-1997; included 774 hazardous waste sites	Total birth defects associated with maternal residence near hazardous waste sites (odds ratio for residence <2 vs ≥2 km)	1.07 (CI 1.04-1.09)	Low income
			Cardiovascular birth defects associated with maternal residence near hazardous waste sites (odds ratio for residence <2 vs ≥2 km)	1.11 (CI 1.03-1.21)	Low income
			Hypospadias associated with maternal residence near hazardous waste sites (odds ratio for residence <2 vs ≥2 km)	1.11 (CI 1.03-1.21)	Low income
			Borderline association between NTDs and maternal residence near hazardous waste sites (odds ratio for residence <2 vs ≥2 km)	1.07 (CI 0.95-1.20)	Low income
(Vrijheid et al. 2002b), EUROHAZCON	Population-based case-control study, 1270 birth defect cases (including	Mothers resided within 7 km of one of the 20 hazardous waste landfill site in the 14	Total birth defects not associated with overall hazard of contaminated	low 1.4 (1.1-1.9) medium	Matched for YOB and residence in study regions <7 km from a

study, Denmark, UK, France, Belgium, Italy	pregnancy terminations, stillbirths and live births), 204 structural chromosomal abnormality cases, 2308 matched healthy live birth controls; from start of birth defect registries in each region to 1993 or 1994	study regions; experts categorized overall water and air emission hazard of each site as low, medium or high	water and air (odds ratios, <3 vs 3-7 km, by overall hazard of site)	1.2 (0.8-1.7) high 1.5 (1.1-2.0) p-trend=0.87	hazardous waste site; adjusted for maternal age and SES
			Total birth defects associated with waterborne contaminant hazard (odds ratios, <3 vs 3-7 km, by water emission hazard of site)	low 0.8 (0.5-1.2) medium 1.4 (1.1-1.9) high 1.6 (1.2-2.2) p-trend=0.06	(+) As above
			Total birth defects not associated with airborne contaminant hazard (odds ratios, <3 vs 3-7 km, by overall hazard of site)	low 1.0 (0.6-1.5) medium 1.5 (1.2-1.9) high 1.2 (0.8-2.0) p-trend=0.55	As above
			Borderline association between NTDs and airborne contaminant hazard (odds ratios, <3 vs 3-7 km, by overall hazard of site); no association between NTDs and waterborne hazard (results not shown)	low 0.5 (0.1-2.1) medium 1.9 (1.2-3.0) high 3.8 (1.0-14) p-trend=0.06	(+) As above
			Non-significant	low	As above

			association between cardiac septal defects and waterborne contaminant hazard (odds ratios, <3 vs 3-7 km, by overall hazard of site); no association between these defects and airborne hazard (results not shown)	1.0 (0.5-2.0) medium 1.6 (1.0-2.4) high 2.0 (1.1-3.8) p-trend=0.16	
			Chromosomal abnormalities not associated with overall water and air emission hazard (odds ratios, <3 vs 3-7 km, by overall hazard of site)	low 1.5 (0.9-2.7) medium 1.3 (0.6-2.9) high 1.7 (0.8-3.3) p-trend=0.87	As above
			Non-significant association between chromosomal abnormalities and waterborne contaminant hazard (odds ratios, <3 vs 3-7 km, by water emission hazard of site)	low 1.0 (0.3-2.8) medium 1.6 (0.9-2.6) high 1.7 (0.9-3.2) p-trend=0.22	As above
			Chromosomal abnormalities not associated with airborne contaminant hazard (odds ratios, <3 vs 3-7 km, by overall hazard of site)	low 1.1 (0.4-3.0) medium 1.5 (1.0-2.3) high 1.2 (0.4-3.6) p-trend=0.85	As above
(Vrijheid et al.	Population-based case-	Mothers resided within 7 km	Structural chromosomal	1.4 (1.0-2.0)	Matched for YOB and

2002a), EUROHAZCON study, Denmark, UK, France, Belgium, Italy	control study, 245 cases structural chromosomal abnormalities 2412 matched healthy live birth controls; from start of birth defect registries in each region to 1993 or 1994	of one of the 23 hazardous waste landfill site in the 17 study regions	abnormalities associated with maternal residential proximity to a hazardous waste site (odds ratio, <3 vs 3-7 km)	residence in study regions <7 km from a hazardous waste site; adjusted for maternal age; adjustment for SES did not shift the odds ratio point estimates	
			Down's syndrome and non-Down's syndrome chromosomal abnormalities both associated with maternal residential proximity to a hazardous waste site (odds ratio, <3 vs 3-7 km)	Down's 1.4 (0.9-2.1)  non-Down's 1.6 (0.9-3.0)	As above
(Orr et al. 2002), California [ordered]	Case-control study, 13,938 minority infants with major structural birth defects, 14,463 minority healthy infant controls, 1983-1988	Maternal residential proximity to National Priorities List hazardous waste sites in California	Weak association between total birth defects and maternal residential proximity to a hazardous waste site (odds ratio....	1.1 (1.0-1.3)	
			Borderline association between NTDs and maternal residential proximity to a hazardous waste site (odds ratio....	1.5 (0.9-2.6)	
(Dolk and Vrijheid 2003), UK, France	Review of literature on epidemiologic studies of birth defects and environmental pollution	Human exposure to toxicants in waste disposal sites may occur through contact with contaminated	Limited evidence for a weak association (odds ratio < 1.5) between birth defects and		

		air, water or soil	maternal residential proximity to hazardous waste disposal sites		
			Few epidemiologic studies of pregnancy outcomes and exposure to incinerator emissions		
(Rushton 2003), UK	Review of literature on health effects of waste disposal by incineration or deposition in landfill sites	Waste disposal in landfill sites	Inadequate evidence for an association between birth defects and maternal residential proximity to hazardous waste sites		
		Incineration – major toxicants include particulate matter, acidic gases and aerosols, heavy metals, dioxins/furans	The few epidemiologic studies of incinerators provide inadequate evidence for an association with birth defects		
(Morris et al. 2003), Scotland	Ecologic study, adverse pregnancy outcomes, 1982-1997; 1849 stillbirths, 11,138 birth defect cases, 324,167 live births	Maternal residence proximity to one of 61 special waste disposal sites	Total birth defects not associated with maternal residential proximity to hazardous waste disposal sites (relative risk <2 vs ≥2 km)	0.96 (0.89-1.02)	YOB, SES
			NTDs not associated with maternal residential proximity to hazardous waste disposal sites (relative risk <2 vs ≥2 km)	0.7 (0.4-1.4)	As above

			Cardiovascular birth defects not associated with maternal residential proximity to hazardous waste disposal sites (relative risk <2 vs ≥2 km)	1.0 (0.9-1.3)	As above
			Hypospadias not associated with maternal residential proximity to hazardous waste disposal sites (relative risk <2 vs ≥2 km)	0.8 (0.6-1.2)	As above
(Dummer et al. 2003), UK	Retrospective cohort study, 3234 stillbirths, 2663 neonatal deaths and 1569 birth defect deaths among 244,758 total births, 1956-1993	Maternal residential proximity to 4 incinerators and 3 crematoria in northwest England; birth certificate information on paternal occupation; mercury is major pollutant from crematoria; major incinerator emissions incl dioxins/furans, heavy metals, particulates, VOCs	NTDs associated with maternal residential proximity to incinerators but not crematoria; odds ratio for distance D computed as $1/(D + 0.1)^2$	incinerators 1.13 (1.04-1.23) crematoria 1.00 (0.87-1.16)	YOB, SES, birth order, multiple birth
			Cardiac birth defects associated with maternal residential proximity to incinerators but not crematoria; odds ratio for distance D computed as $1/(D + 0.1)^2$	incinerators 1.12 (1.03-1.22) crematoria 1.00 (0.77-1.31)	As above

(Kuehl and Loffredo 2003), Baltimore-Washington Infant Study	Population-based case-control study, 36 cases left transposition of great arteries, 3495 healthy live birth controls; Maryland, District of Columbia and northern Virginia, 1981-1989; assessed geographic case clustering	Maternal residential proximity to National Priority List (NPL) hazardous waste sites, maternal housing characteristics, Maryland toxic release inventory (air emissions of toxic chemicals) for 1987-1989; 2 of the NPL sites in Baltimore released large amounts of chlorinated solvents incl trichloroethene, tetrachloroethene, 1,2-dichloroethene and vinyl chloride	Two spatial clusters of cases identified (1 in Baltimore, 1 in DC); cases associated with maternal residence in either of 2 geographic clusters (odds ratio, yes vs no); the cluster areas contained 4 NPL hazardous waste sites (1 in DC, 3 in Baltimore)	13 (4.7-38)	
(Cordier et al. 2004), France	Retrospective cohort study, 94239 births (incl 1481 birth defects) in communities with solid waste incinerators, 470369 births (incl 6730 birth defects) in unexposed communities, 1988-1997; population-based birth defect registry	70 incinerators in study region; experts assessed potential for dioxin, metal and dust emissions based on capacity, continuous vs discontinuous operation, dust control, fume treatment, year operations began	NTD risk not associated with presence of solid waste incinerator in community (odds ratio, yes vs no) or expert-rated hazard of incinerator emissions (relative risks for medium and high vs low exposure)	presence 0.9 (0.6-1.2)  hazard 0.8 (0.4-1.7) 0.8 (0.4-2.0) p-trend > 0.05	YOB, maternal age, population density, avg family income
			Facial cleft risk associated with presence of solid waste incinerator in community (odds ratio, yes vs no) but not with expert-rated hazard of incinerator emissions	presence 1.3 (1.1-1.6)  hazard 0.8 (0.5-1.3) 1.0 (0.6-1.6) p-trend > 0.05	As above

	(relative risks for medium and high vs low exposure)		
	Conotruncal and other heart defect risk not associated with presence of solid waste incinerator in community (odds ratio, yes vs no) or with expert-rated hazard of incinerator emissions (relative risks for medium and high vs low exposure)	presence 1.1 (0.9-1.4)  hazard 1.0 (0.6-1.7) 1.0 (0.6-1.6) p-trend > 0.05	As above
	Limb reduction defect risk not increased in exposed communities (relative risk)	0.8 (0.5-1.2)	As above
	Renal dysplasia associated with presence of solid waste incinerator in community (odds ratio, yes vs no) but not with expert-rated hazard of incinerator emissions (relative risks for medium and high vs low exposure)	presence 1.6 (1.1-2.2)  hazard 1.1 (0.5-2.4) 1.3 (0.6-3.0) p-trend > 0.05	As above
	Borderline associations between obstructive urinary tract defects and	presence 1.2 (0.9-1.7)	(+) As above

	presence of solid waste incinerator in community (odds ratio, yes vs no) and with expert-rated hazard of incinerator emissions (relative risks for medium and high vs low exposure)	hazard 1.4 (0.7-2.9) 1.9 (0.9-3.9) p-trend=0.07	
	Hypospadias risk not associated with presence of solid waste incinerator in community (odds ratio, yes vs no) or with expert-rated hazard of incinerator emissions (relative risks for medium and high vs low exposure)	presence 0.9 (0.7-1.2)  hazard 0.6 (0.3-1.2) 1.1 (0.5-2.4) p-trend > 0.05	As above
	Borderline increased risk of megacolon in exposed communities (relative risk)	1.6 (0.9-2.9)	As above
	Chromosomal abnormality risk not increased in exposed communities (relative risk)	1.0 (0.9-1.2)	As above

**Birth defects: summary**

*Total birth defects*

A small cohort study in Missouri found no association between total birth defects and maternal residence in areas with TCDD-contaminated soil and dust (Stockbauer et al. 1988). A population-based case-control study in New York State found a weak but statistically significant association between total birth

defects and maternal residential proximity to hazardous waste disposal sites and an index of exposure likelihood (Geschwind et al. 1992). A case-control study found no association between total birth defects and maternal residential proximity to EPA National Priority List (NPL) hazardous sites (Sosniak et al. 1994). A literature review (Vrijheid 2000) concluded that there was inadequate evidence for an association between birth defects and maternal residential proximity to hazardous waste disposal sites. A population-based case-control study in five European countries found a weak association between total birth defects and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found a slightly increased risk of total birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between total birth defects and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An extension of the population-based case-control study in five European countries by Dolk et al. (1998), described above, found a borderline dose-response relationship between total birth defects and the estimated hazard from contaminants released into water but not those released into air from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002). A large case-control study found a weak association between total birth defects and maternal residential proximity to NPL hazardous waste sites in California (Orr et al. 2002). A review by Dolk and Vrijheid (2003) concluded that there is limited epidemiologic evidence for an association between birth defects and maternal residential proximity to hazardous waste disposal sites while a review by Rushton (2003) concluded that there was inadequate epidemiologic evidence; both reviews concluded that the few existing epidemiologic studies provided inadequate evidence for an association between birth defects and maternal residential proximity to incinerators. An ecologic study in Scotland found no association between total birth defects and maternal residential proximity to hazardous waste sites (Morris et al. 2003).

#### *Central nervous system (CNS) birth defects*

A case-control study of stillbirths caused by anencephaly (a severe neural tube birth defect) in Canada found no association with community water supply concentrations of lead, mercury, cadmium or other elements (Elwood and Coldman 1981). A population-based case-control study in New York State found an association between CNS birth defects and maternal residential proximity to hazardous waste disposal sites but not with an index of exposure likelihood (Geschwind et al. 1992). An enlarged population-based case-control study in New York State found no association between CNS birth defects and maternal residential proximity to hazardous waste disposal sites or with likelihood of exposure to solvents from such sites by routes other than drinking water; there were borderline associations with maternal residential proximity to industrial facilities emitting solvents or metals but irregular dose-response relationships (Marshall et al. 1997). A population-based case-control study in California found a non-significant association between NTDs and maternal residential proximity to NPL hazardous sites; there were borderline or significant associations between NTDs and proximity to sites with contaminated surface or ground water, sites containing cyanides, lead, pyrene, PCBs, benzene or pesticides (Croen et al. 1997). A population-based case-control study in five European countries found an association between NTDs and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found an increased risk of NTDs in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between NTDs and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An extension of the population-based case-control study in five European countries by Dolk et al. (1998), described above, found a borderline dose-response relationship between NTDs and the estimated hazard from contaminants released into air but not those released into water from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002b). A large case-control study found a borderline association between NTDs and maternal residential proximity to NPL hazardous waste sites in California (Orr et al. 2002). An ecologic study in Scotland found no association between NTDs and maternal residential proximity to hazardous waste sites (Morris et al. 2003). A retrospective cohort study in the UK found a weak association between NTDs and maternal residential proximity to hazardous waste sites but not to incinerators (Dummer et al. 2003). A large retrospective cohort study in France found no association between NTDs and maternal residence in a community with a solid waste incinerator or expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004).

#### *Cardiovascular birth defects*

A case-control study in Massachusetts found no association between total cardiac birth defects and detectable lead or arsenic in community drinking water; there were associations between patent ductus arteriosus and detectable mercury and between coarctation of the aorta and detectable arsenic (Zierler et al. 1988). A population-based case-control study in Tucson found an association between cardiovascular birth defects and parental residence in a region served by a drinking water well contaminated by trichloroethylene, dichloroethylene and chromium; this association was not observed after the well was closed (Goldberg et al. 1990). A population-based case-control study in California found non-significant associations between conotruncal heart birth defects and maternal residential proximity to NPL hazardous sites or to sites containing heavy metals, inorganics or semi-volatiles; there was no association with sites containing VOCs (Croen et al. 1997). A population-based case-control study in five European countries found associations between cardiac septa and great artery/vein birth defects and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found a borderline increased risk of cardiovascular birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between cardiovascular birth defects and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An extension of the population-based case-control study in five European countries by Dolk et al. (1998), described above, found a non-significant dose-response relationship between cardiac septal defects and the estimated hazard from contaminants released into water but not those released into air from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002b). An ecologic study in Scotland found no association between cardiovascular birth defects and maternal residential proximity to hazardous waste sites (Morris et al. 2003). A retrospective cohort study in the UK found a weak association between cardiac birth defects and maternal residential proximity to hazardous waste sites but not to incinerators (Dummer et al. 2003). A population-based case-control study in Maryland and northern Virginia found an association between l-transposition of great arteries and maternal residential proximity to four NPL hazardous waste disposal sites, including two sites that released large amounts of chlorinated solvents into air (Kuehl and Loffredo 2003). A large retrospective cohort study in France found no association between cardiac birth defects and maternal residence in a community with a solid waste incinerator or expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004).

#### *Orofacial birth defects*

A population-based case-control study in New York State found a borderline association between oral cleft birth defects and maternal residential proximity to hazardous waste disposal sites (Geschwind et al. 1992). A population-based case-control study in California found no associations between oral cleft birth defects and maternal residential proximity to NPL hazardous sites or to sites containing heavy metals, inorganics, semi-volatiles or VOCs (Croen et al. 1997). A large retrospective cohort study in France found a weak association between facial clefts and maternal residence in a community with a solid waste incinerator but no association with expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004).

#### *Musculoskeletal birth defects*

A population-based case-control study in New York State found a weak but statistically significant association between musculoskeletal birth defects and maternal residential proximity to hazardous waste disposal sites and an index of exposure likelihood (Geschwind et al. 1992). An enlarged population-based case-control study in New York State found no associations between musculoskeletal birth defects and maternal residential proximity to any hazardous waste disposal site or to industrial facilities releasing solvents or pesticides; there was also no association with the likelihood of exposure to solvents or pesticides from waste disposal sites (Marshall et al. 1997). A population-based case-control study in five European countries found an association between gastroschisis and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found no increased risk of musculoskeletal birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). A large retrospective cohort

study in France found no association between limb reduction birth defects and maternal residence in a community with a solid waste incinerator (Cordier et al. 2004).

#### *Genitourinary birth defects*

A population-based case-control study in five European countries found a borderline association between hypospadias and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). An ecologic study in Sydney, Nova Scotia (Canada) found no increased risk of genitourinary birth defects in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An ecologic study in the UK found a weak association between hypospadias and maternal residential proximity to hazardous waste sites (Elliott et al. 2001). An ecologic study in Scotland found no association between hypospadias and maternal residential proximity to hazardous waste sites (Morris et al. 2003). A large retrospective cohort study in France found an association between renal dysplasia and maternal residence in a community with a solid waste incinerator but not with expert-rated potential for exposure to dioxin, metal or dust emissions (Cordier et al. 2004). The latter study found a borderline association between obstructive urinary tract birth defects and maternal residence in a community with a solid waste incinerator and no association between hypospadias and such exposure.

#### *Gastrointestinal birth defects*

A population-based case-control study in five European countries found an association between tracheo-esophageal birth defects and maternal residential proximity to hazardous waste disposal sites (Dolk et al. 1998). A large retrospective cohort study in France found a borderline association between megacolon and maternal residence in a community with a solid waste incinerator (Cordier et al. 2004).

#### *Chromosomal abnormalities (structural)*

A population-based case-control study in New York State found a borderline association between chromosomal abnormalities and maternal residential proximity to hazardous waste disposal sites (Geschwind et al. 1992). An ecologic study in Sydney, Nova Scotia (Canada) found a slight and non-significantly increased risk of chromosomal abnormalities in a community with extensive hazardous wastes and an incinerator (Dodds and Seviour 2001). An extension of the population-based case-control study in five European countries by Dolk et al. (1998), described above, found a borderline dose-response relationship between chromosomal abnormalities and the estimated hazard from contaminants released into water but not those released into air from hazardous waste disposal sites near maternal residences (Vrijheid et al. 2002b). The latter authors also found borderline associations between both Down's syndrome and non-Down's syndrome chromosomal abnormalities and maternal residential proximity to hazardous waste disposal sites (Vrijheid et al. 2002a). A large retrospective cohort study in France found no association between chromosomal abnormalities and maternal residence in a community with a solid waste incinerator (Cordier et al. 2004).

### 5. Childhood cancer

Reference, location	Design	Exposure	Results	Association <sup>7</sup>	DR <sup>8</sup>	Covariates
(Mulder et al. 1994), Holland	Case-control study, 7 leukemia and 7 lymphoma cases, 56 matched controls, age < 40 yr; residents of a horticultural community	Self- or parent- reported information on childhood and parental occupational exposures including swimming in a pond contaminated with petroleum products and horticultural pesticides; surface water and soil samples in and around the pond had DDT, PAH and benzene levels above acceptable limits	Leukemia/lymphoma associated with swimming in contaminated pond (odds ratio, $\geq 1$ hr/wk vs no)	5.3 (1.3-17)		Matched for age and sex
(Cohn et al. 1994), New Jersey	Ecologic study, leukemia and non-Hodgkin's lymphoma, age < 20 yr, 75 municipalities, 1979-1987	Municipal water utility measurements of THMs, trichloroethylene, tetrachloroethylene, 1,1,1-trichloroethane, 1978-1985	ALL among females age < 5 yr was associated with municipal drinking water trichloroethylene levels ( $\geq 5$ vs < 0.1 $\mu\text{g/L}$ )(5 exposed cases)  ALL among males age < 5 yr was not associated with municipal drinking water trichloroethylene levels (result stated without supporting data)	3.8 (1.2-8.8)		
(Durant et al. 1995), Woburn, Massachusetts	Cluster investigation, 28 cases childhood leukemia, 1966-1986; assessed potential exposure to	Two new wells in mid-1960's may have been contaminated by hazardous wastes including arsenic, chromium, solvents, pesticides and plasticizers; water containing arsenic (70 $\mu\text{g/L}$ ) and	The childhood leukemia rate in Woburn during 1966-1986 was about four times the national average	SIR = 4.7 (p < 0.05)		

<sup>7</sup> Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>8</sup> 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

	contaminated drinking water	chromium (240 µg/L); no direct exposure measurements or estimates for individual cases			
(Knox 2000), UK	Ecologic study, 9224 childhood cancer deaths (1953-1980), no controls	Assessed migration between birth and death toward or away from municipal waste incinerators and toxic waste landfill sites; note – interpretation of these ratios is not clear	More children dying of cancer had moved away from than toward municipal waste incinerators within 3 km of either address (ratio); author's note – this is an obscure measure of risk	1.3 (p < 0.001)	
			Similar numbers of children dying of cancer had moved toward or away from toxic waste landfill sites within 3 km of either address (ratio)	1.0	
(Jarup et al. 2002), UK	Ecologic study, childhood leukemia, 3973 cases, 1983-1997	Residential proximity to 9565 waste disposal sites including 774 hazardous waste disposal sites	Childhood leukemia not associated with residential proximity to waste disposal sites (odds ratio and 99% CI, <2 vs ≥2 km)	0.96 (0.91-1.00)	Age, sex, year, region, SES
			Childhood leukemia not associated with residential proximity to hazardous waste disposal sites (odds ratio and 99% CI, <2 vs ≥2 km)	0.93 (0.81-1.06)	As above
(Costas et al. 2002), Woburn, Massachusetts	Case-control study, 19 cases leukemia, age 0-18 yr, 37 controls, 1969-1989	Potential for exposure to public water supply contaminated with trichloroethylene and other solvents from two wells	Borderline association between childhood leukemia and ever-exposure to Woburn's public drinking water supply (odds ratio, yes vs no)(15 exposed cases)	3.0 (0.8-11)	

		Association between childhood leukemia and exposure to Woburn's public drinking water supply stronger for prenatal than childhood exposure (respective odds ratios, yes vs no)	prenatal 8.3 (0.7-95)  childhood 1.2 (0.3-5.1)	Composite covariate for SES, maternal age, prenatal smoking and breast-feeding
(Rushton 2003), UK	Review of literature on health effects of waste disposal by incineration or deposition in landfill sites	The few epidemiologic studies provide inadequate evidence for an association with childhood cancer		

### Childhood cancer: summary

#### *All childhood cancers*

An ecologic study in the UK found a possible association between childhood cancer and early life residential proximity to municipal waste incinerators but not hazardous waste landfill sites (Knox 2000). A review by Rushton (2003) concluded that the few epidemiologic studies provide inadequate evidence for an association between childhood cancer and waste disposal by incineration or deposition in landfill sites.

#### *Leukemia*

A very small case-control study in Holland found an association between childhood leukemia/lymphoma and swimming in a pond contaminated by DDT, PAH and benzene and subject to runoff from intensive horticultural pesticide use (Mulder et al. 1994). An ecologic study of childhood leukemia in New Jersey found an association between leukemia in young girls but not boys and municipal drinking water trichloroethylene levels (Cohn et al. 1994). The childhood leukemia incidence rate in Woburn (Massachusetts) during 1966-1986 was elevated almost 5-fold (Durant et al. 1995). A subsequent case-control study in Woburn found a borderline association between childhood leukemia and likelihood of exposure to drinking water contaminated by trichloroethylene and other solvents; there was some evidence that the association was greater for prenatal compared to childhood exposure (Costas et al. 2002). An ecologic study in the UK found no association between leukemia and residential proximity to general or hazardous waste disposal sites (Jarup et al. 2002).

#### *Lymphoma*

A very small case-control study in Holland found an association between childhood leukemia/lymphoma and swimming in a pond contaminated by DDT, PAH and benzene and subject to runoff from intensive horticultural pesticide use (Mulder et al. 1994).

## 6. Reproductive system development

Reference, location	Design	Exposure	Results	Association <sup>9</sup>	DR <sup>10</sup>	Covariates
(Staessen et al. 2001), Antwerp, Belgium	Cross-sectional study, 200 adolescents, mean age 17 yr, life-long residents of two areas with known lead and dioxin contamination from lead, waste incineration, and other industries and controls from a non-contaminated area; physician-assessed sexual maturation stage including testicular volume; measured serum and urinary biomarkers of renal function	Measured PCBs, and dioxin-like compounds (calux <i>in vitro</i> assay of AhR activation); GM blood lead levels were 1.5 and 1.8-2.7 µg/dL in control and exposed regions	Testicular volume significantly lower in contaminated regions; did not assess association between testicular volume and blood lead levels in individuals	+		Age
			Borderline association between less than adult genital development in boys and serum PCBs (relative risk for a doubling of serum PCBs)	3.8 (CI 0.9-8.0)	(+)	
			Less than adult breast development in girls associated with serum TCDD -like activity level (relative risk for a doubling of serum dioxin activity)	2.3 (CI 1.2-4.5)	+	
(Den Hond et al. 2002),	Cross-sectional study, 200 youth age 15-19 yr, life-long residents of two areas near	Measured serum levels of PCBs (138, 153, 180)	Boys – reduced testicular volume among those in	47 vs 42-43 ml		Age, BMI, parental social

<sup>9</sup> Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>10</sup> 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

Belgium	lead and other industries or a control area; physician-assessed pubertal development	and TCDD -like compounds (chemically activated luciferase expression (CALUX) assay)	exposed regions (total testicular volumes for rural vs 2 urban regions)	(p < 0.005)	class
			No association between testicular volume and serum levels of TCDD-like organochlorine compounds		As above
			Boys – delayed genital development associated with doubling of serum PCBs but not serum TCDD-like activity (odds ratio for doubling of serum PCBs)	3.8 (p= 0.06)	As above
			Boys – reduced pubic hair growth associated with doubling of PCBs but not serum TCDD-like activity (odds ratio for doubling of serum PCBs)	2.7 (p=0.06)	As above
			Girls – delayed breast development associated with doubling of serum TCDD-like activity but not with serum PCBs (odds ratio for doubling of serum TCDD-like activity)	2.3 (p=0.02)	Age, BMI, oral contraceptive use, parental social class

**Reproductive system development: summary**

A cross-sectional study of youth in Belgium found no association between testicular volume and serum dioxin-like compounds (Staessen et al. 2001, Den Hond et al. 2002). This study found associations between delayed male genital development and reduced pubic hair growth and serum PCB but not dioxin-like compounds. Delayed breast development in girls was associated with serum dioxin-like compounds but not PCBs.

### 7. Other health effects

Reference, location	Design	Exposure	Results	Association <sup>11</sup>	DR <sup>12</sup>	Covariates
(Osius et al. 1999), Germany	Cross-sectional study, 671 children age 7-10 yr (complete data for 320 children); from region potentially exposed to PCBs, lead, cadmium and mercury from a toxic waste incinerator and two comparison regions; measured serum thyroid-stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3)	Measured blood lead (GM 2.7, range 0.5-11.4 µg/dL), cadmium (GM 0.2, range ND-1.8 µg/L) and PCBs (118, 138, 153, 170, 180, 183 and 187) (GM 0.5, range 0.1-4.5 µg/L) and 24-hr urinary mercury (GM 0.15, range ND 12.3 µg/L)	Blood TSH level associated with PCB congener 118 (a dioxin-like congener)	$\beta = 7.1$ ( $p = 0.04$ )	+	Sex, age, environmental tobacco smoke, fish consumption, blood cadmium and lead, 24-hr urinary mercury
			Blood FT3 level inversely associated with PCB congener 138, 153, 180, 183 and 187 levels ( $\beta$ for PCB-138)	$\beta = -1.0$ ( $p = 0.02$ )	+	
			FT3 inversely associated with sum of 7 PCBs	$\beta = -0.25$ ( $p = 0.02$ )	+	As above
			TSH not associated with sum of 7 PCBs	$\beta = 0.04$ ( $p = 0.79$ )		
			No association	$\beta = 0.11,$		As above but

<sup>11</sup> Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>12</sup> 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

			between blood lead and TSH, FT3 or FT4 levels (respective $\beta$ coefficients)	0.08, -0.13 (p for each 0.4-0.5)		excluding blood lead
			Blood cadmium associated with TSH and inversely with FT4 (respective $\beta$ coefficients)	$\beta = 0.71$ (p = 0.003) $\beta = -0.51$ (p = 0.04)	+	As above but excluding blood cadmium
			Thyroid hormone levels not associated with 24-hr urine mercury	$\beta = 0.18$ (p = 0.17)		As above but excluding urinary mercury
(Staessen et al. 2001), Antwerp, Belgium	Cross-sectional study, 200 adolescents, mean age 17 yr, life-long residents of two areas with known lead and dioxin contamination from lead, waste incineration, and other industries and controls from a non-contaminated area; physician-assessed sexual maturation stage including testicular volume; measured serum and urinary biomarkers of renal function	Measured PCBs, and dioxin-like compounds (calux <i>in vitro</i> assay of AhR activation); GM blood lead levels were 1.5 and 1.8-2.7 $\mu\text{g/dL}$ in control and exposed regions	Serum cystatin-C levels associated with blood lead (relative risk for a doubling of blood lead level)	3.6 (CI 1.5-5.7)	+	Sex and smoking
			Urinary $\beta_2$ -microglobulin levels associated with blood lead (relative risk for a doubling of blood lead level)	16 (CI 2.7-31)	+	As above

### Other health effects: summary

#### Thyroid function

A cross-sectional study of German children living near a toxic waste incinerator showed dose-response relationships between increased blood TSH and decreased blood FT3 levels and blood levels of cadmium and certain PCB congeners; there were no associations with blood lead or urinary mercury levels (Osius et al. 1999).

*Kidney function*

A cross-sectional study of youth in Belgium living near lead, waste incineration and other industries found dose-response relationships between serum cystatin-C and urinary  $\beta$ 2-microglobulin levels (biomarkers of reduced renal filtration rates and renal tubular damage) and blood lead levels (Staessen et al. 2001).

**8. General**

Reference, location	Design	Exposure	Results	Association <sup>13</sup>	DR <sup>14</sup>	Covariates
(Miller 1996), Canada	Review of literature on community-based studies of health effects of hazardous wastes	Water is the key medium for human exposure for most hazardous waste sites				
(Johnson and DeRosa 1997), USA	Overview of chemicals released from hazardous waste sites and public health hazard of chemical mixtures released from such sites	About 40,000 uncontrolled waste sites in EPA inventory; 1,300 of these sites comprise the National Priorities List (NPL), i.e., those sites posing the greatest public health and ecologic risks and eligible for remediation; 39% of NPL sites have known routes of human exposure – among these, 91% involve contaminated ground water and 46% contaminated soil	Data for 1992-1996 indicate that 46% of sites pose public health hazards; 30 substances are found at 6% or more of sites and incl 18 known or probable human carcinogens and many with systemic toxicity; uncontrolled hazardous waste sites are a major environmental threat to human health			
		Most frequent toxicants cited in public health assessments incl VOCs, inorganic substances, halogenated pesticides, PAHs, phenols/phenoxy acids, phthalates, nitrosamines/ethers/alcohols, organophosphates	ATSDR and EPA maintain a list (the CERCLA <sup>15</sup> list) of 275 priority substances that pose the greatest threat to human health; the top 10 in 1994 were lead, arsenic, metallic mercury, vinyl chloride, benzene, cadmium, PCBs, chloroform,			

<sup>13</sup> Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>14</sup> 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

<sup>15</sup> CERCLA is the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (Superfund)

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			benzo[a]pyrene and trichloroethylene
(Landrigan et al. 1999), USA	Review of university-based research in pediatric environmental health financially supported by the Superfund	3-4 million US children live <1 mile from a NPL hazardous waste site	
(National Academy of Sciences 1999), USA	Expert panel review of waste incineration and public health	Incinerator emissions with greatest potential for adverse health effects include particulate matter, lead, mercury and dioxins/furans	Inadequate evidence for health effects (few epidemiologic studies, methodologic shortcomings)

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