Objective 1: Overview of risks to human health posed by contaminated land

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6. References
1. Introduction

The potential impacts of contaminated land on human health were presented by the Royal Commission on Environmental Pollution (e.g. vitality, general health, bodily pain, physical and social functioning, mental health, RCEP, 1996) and the review paper by Kibble and Saunders (2001). The RCEP (1996) reported that it was not aware of any study that provided firm evidence of adverse effects of contaminated land on health. Kibble and Saunders (2001) noted a similar paucity of evidence. Evaluations of increased incidence of cancer associated with residential proximity to contaminated sites are inconsistent, whereas Kibble and Saunders (2001) considered that there is a stronger link between landfill sites and/or contaminated land and reproductive effects (primary congenital anomalies and low birth weight).

The present review focuses on the papers published since 2000 (although important papers published prior to 2000 are also referred to). It aims at bringing these analyses up to date and determining whether or not the weight of evidence shows that contaminated land may have detrimental effects on human health.

First, a brief outline of the key issues related to the study of health impact of contaminated land is presented. It includes the main exposure pathways, the difficulty in defining exposure, populations potentially most at risk and a brief description of the different types of epidemiological studies available. The recent literature is then reviewed for evidence of associations and possible causal relationships between exposure to contaminated land and health impact. Results are categorised into main types of health outcome including minor (e.g. self reported symptoms, blood pressure) and major impacts (e.g. renal dysfunction, cancers and reproductive effects).

Relevant papers were found through literature searches on ISI Web of Science from 1990 through to 2009. Keywords used are given in the Appendix A. In addition, articles were traced through references listed in previous reviews and cross-references.

Investigations of the health risks due to occupational exposure were not included in this review. Studies linking potential exposure to level of contaminants in blood or urine were not considered either, as they generally do not demonstrate an adverse health effect but only the level of exposure.

Several recent articles present human risk assessment based on soils concentration, likely exposure and toxicological values measured on surrogate organisms. These types of studies were not included in the present review as they do not demonstrate evidence for adverse effects, but only an exploration of the risk.

2. Key issues for the study of impacts of contaminated land on human health

2.1. Study of landfill sites vs. general land contamination

Very many studies focus on potential impacts of landfill on human health. The reason for a focus on landfill may relate to the potential for high levels of contamination at the site, presence of mixtures of contaminants, accessibility of information on the location and nature of landfill sites (e.g. domestic, commercial or special waste sites) and the high levels of public concern associated with landfills. Whilst landfill sites will frequently be defined as potentially contaminated, they are unlikely to be representation of the full spectrum of land contamination. For example, modern landfills are lined and capped thus restricting potential for exposure. Where exposure does occur, it is most likely to occur via inhalation or contamination of controlled waters; in contrast, dermal and/or dietary exposure may be a greater concern where
homes are built on historic industrial land. Several studies mix active and closed landfills in their analysis, with the former have potential for emissions from, for example, dust caused by vehicle movement that will not arise with contaminated land. Finally, there are frequently socio-economic differences in populations living close to landfill compared to those living further away. The review addresses studies that consider landfill as well as those on general land contamination, but results should be considered in the light of the greater volume of work on the former.

2.2. Different types of epidemiological studies

Potential effects of soil exposure on human health can be studied following two main approaches:

1. In aggregate-level approaches, the incidence of a disease outcome across a geographical area is related statistically to selected soil characteristics or indirect measures of exposure. These ecological level studies are often described as being hypothesis-forming because they can show that there is an association between a health effect and the exposure of interest but they cannot show that this association is causal i.e. that the exposure caused the effect. This is because there may be other exposures and confounding factors which influence the results which the study design cannot take into account. Such studies have the advantage of being relatively quick (and inexpensive) and provide indications of where research efforts should be focused (Hough, 2007). Their disadvantage is that they cannot prove causality.

2. The individual approach attempts to relate a health outcome to the exposure at an individual level and over time. There are two main types of study design: case-control studies and cohort studies, and they may be prospective or retrospective. Prospective studies are very expensive and time consuming. Many studies therefore opt for a retrospective approach, with the case-control design considered the most robust approach.

Single site studies investigate communities near one specific site. The main disadvantage of this kind of investigation is that they often involve low subject numbers leading to low statistical power. On the other hand, a better exposure assessment is generally possible. In geographical comparison (or ecological studies) however, a health effect is assessed in regions defined as exposed or unexposed (or categories of exposure based on e.g. distance of residence from a contaminated site), without attention to variations in exposure imposed by individual lifestyles. The types of study that can be undertaken when studying a single site are (i) cross-sectional, (ii) cohort, and (iii) case-control.

Multiple sites studies address the risks of living near contaminated sites, independent of whether the sites caused concern, by *a priori* specifying a number of sites for study. The great advantage of these investigations is that they involve larger numbers of the population, including disease / health cases of interest and hence have a greater statistical power to detect lower levels of excess risk. Multiple site studies are essential for rarer but severe adverse health outcomes such as congenital anomalies. However, they generally are able to conduct less extensive exposure assessment and misclassification of exposure tends to dilute estimates of relative risk.

The kind of study design used for multiple site investigations includes (i) case control, (ii) geographical comparison, and (iii) cluster analysis. A general problem in the interpretation of cluster investigations is that localized areas of high disease density may occur even as part of a random pattern of disease. It is difficult to distinguish clusters derived from this random pattern from those where there is a common
underlying local cause (Vrijheid, 2000). Also, areas with higher disease densities, although part of the random pattern of disease, may be selectively picked for study.

2.3. Significance

The significance of an association between exposure to contaminated land and health outcome for a case-control study is generally reported with the odds ratio (OR), which is the ratio of the probability of being exposed and developing the health outcome, to the probability of being non-exposed and developing the health outcome. The OR thus represents a relative scale where values exceeding unity indicate an elevated risk. Confidence in the estimation of OR is usually expressed by 95% confidence intervals (95%CI). The wider the confidence intervals, the less certain is the estimate of OR. The association is considered not statistically significant (p>0.05) if the confidence interval spans 1.00. In cohort studies, significance is generally quantified in terms of rate ratios (RR: ratio of the incidence rate of disease in the exposed group on the incidence rate in the non-exposed group). Incidence rates are generally normalized by person years. Therefore, RR can be considered equivalent to OR when considering rare outcomes. When a disease is not rare, RR tends to be greater than OR (Hough, 2007).

Causal interpretation can be greatly strengthened by showing a dose–response effect either within sites or between sites of differing hazard potential (Vrijheid et al., 2002b, Dolk et al., 1998, Geschwind et al., 1992), but this presumes an accurate relative assessment of the overall hazard of complex exposure which is generally difficult to achieve. The opposite can also apply in that if the exposure estimate is reliable and there is no, or even a negative, dose-response relationship, this may greatly weaken or even disprove a proposed causal relationship.

2.4. Exposure pathways

Humans can be exposed to soil contaminants through several potential routes and the significance of each of these routes will vary depending on the contaminant involved, the geological characteristic of the soil, the type of receptor, the site location and the proposed end use of the site. The three main pathways of exposure are (i) intake of soil, food and water, (ii) inhalation of soil particles and vapours, and (iii) dermal contact (including puncture). Estimates suggest that geophagic children (who have a desire to eat soil) may ingest anywhere from 1-8 g of soil per day and in extreme cases as much as 25-60 g per day (Calabrese et al., 1997). Contaminant intake from soil ingestion on residential sites may thus exceed intakes from all other pathways combined (Kibble and Saunders, 2001).

2.5. Difficulties in assessing exposure

The exposure levels associated with contaminated land are complex and difficult to define. They may involve several media (air, water, soil and food) and pathways (inhalation, ingestion and dermal contact). Exposure to contaminated land such as landfills is particularly difficult to define as many chemicals with different known toxicities and adverse effects usually coexist. In addition, contamination of many sites is poorly documented and no information is available when contamination results from illegal practices.

Analysis of tissues and body fluids for chemicals and their metabolites, enzymes and other biological substances can provide evidence for exposure. Such biomarkers of exposure might include, for example, measurement of cadmium concentrations in
urine. However, resources are rarely available to carry out extensive exposure assessment and most epidemiologic studies are based on surrogate measures of exposure.

Distance of residence to the contaminated site is by far the most common indirect method to estimate exposure. The advantage of this approach is ease and consistency of measurement, but it can be a very crude proxy for exposure. For example, it does not account for spatial variation in contaminant concentrations or the effect that lifestyle will have on exposure. Several single-site studies on residential proximity to landfills have also used odour complaints as a proxy for exposure (Shusterman et al., 1991, Lipscomb et al., 1991, Kharrazi et al., 1997).

Some multiple site studies attempted to classify level of exposure based on hazard categories of sites (e.g. Croen et al., 1997, Shaw et al., 1992), exposure indices incorporating hazard scores (e.g. Geschwind et al., 1992), or scoring methods based on expert judgment (e.g. Vrijheid et al., 2002b). The use of modelling techniques (Deloraine et al., 1995, Thomas et al., 2009) including prevailing wind direction, landscape and other parameters have also shown their potential in improving exposure assessment. However, the use of such indirect exposure measurements can lead to a misclassification of exposure that decreases the potential of a study to find a true effect.

Finally, exposure to contaminated land generally involves low level of exposure to mixtures of chemicals over long periods of time and is rarely high enough to cause acute health effects. Low-dose exposures are generally expected to generate small increases in relative risks (from cohort studies) or odds ratios (from case-control studies) that will be difficult to distinguish from “noise effects” caused by confounding factors and biases.

2.6. Who is at risk?

Although most studies consider the potential effect of contaminated land on the general population, some categories of the population are considered to be more at risk than others. Children are believed to be the most sensitive category. This is because their body is undergoing developmental changes (e.g. development of the nervous system) and they consume proportionately more food and drink and breathe more air per kg of body weight than adults. Children are also more likely to be exposed to contaminants present in soils because they spend a greater proportion of their time outdoors, have a poorer concept of hygiene than adults, and often adopt behaviours that increases their exposure (e.g. crawling activities, geophagia).

Categories of adults more at risk include workers employed during remediation of contaminated sites and gardeners, particularly allotment owners. Exposure via dermal contact, accidental soil ingestion or the food chain may be important (especially when home-grown produce makes a significant contribution to their diet; Kibble and Saunders, 2001).

3. Minor human health effects

A body of literature relates to “self reported” symptoms such as headache, fatigue, skin irritation, respiratory problems and psychological problems. By necessity, these are single-site studies where the population can be interviewed and given medical examinations. Such studies generally suffer from interpretational problems, as it is often not clear whether subjective symptoms are the result of a direct toxicological effect, or due to increased perception and recall (see Objective 6 for more detailed analysis). Most studies examining minor effects on human health have been
published in the 1990’s and only few studies were published since the review by Kibble and Saunders (2001). As a general rule, studies that report these non-specific symptoms are frequently confounded by possible impacts from other environmental factors and so cannot provide reliable evidence of a verifiable effect (Spurgeon et al., 1996). The following section provides examples of this situation.

3.1. Stress, anxiety and psychiatric disorders

The existence of concern itself is known to exacerbate community anxiety but it is often difficult to determine whether symptoms are related to a direct toxicological effect or to stress or worry. For instance, Baker et al. (1988) studied a community living near a hazardous waste site in California (2,039 subjects in 606 households) and found high level of stress and anxiety whereas no evidence of elevated levels of any serious physical disease were observed (including cancer incidence, mortality and pregnancy outcome).

Fleming et al. (1991) reported that subjects living near a landfill with hazardous waste in the USA (n=27) were concerned about the hazard, reported more symptom distress and performed more poorly on a task requiring concentration and motivation than did control subjects (n=27). Similarly, Deloraine et al. (1995) reported that chronic psychiatric disorders were more frequent among the most exposed residents around a recently closed landfill for industrial toxic waste (OR: 2.1, 95%CI: 1.0-4.4 and OR: 2.5, 95%CI: 1.2-5.3 for medium and high exposure groups, respectively, 432 cases and 384 controls). These results may be related to negative perception of the site rather than a true toxicological mechanism.

Odours may serve as sensory cues for the development of stress-related illnesses or lead to heightened awareness of underlying symptoms. The interaction between symptom prevalence and odour worry has been examined in retrospective follow-up of epidemiological studies. Shustermann et al. (1991) observed significant and positive associations between the prevalence of headache and nausea and both frequency of odour perception and degree of worry for residents living near three hazardous waste sites in California (based on odour perception: headache: OR: 5.0, 95%CI: 3.3-7.7; nausea: OR: 5.2, 95%CI: 2.9-9.4, n=2,000 adults). Relationships were strongest for worry rather than odour and the authors concluded that worry and odour perception had a potential role in the development of symptoms near hazardous waste sites. Limpscumb et al. (1991) compared the health of a community (n=193) after interim clean-up measures of the landfill were introduced, with past results on the health of the same community. The authors concluded that while the exposed population continued to experience and/or report significantly more symptoms than a comparison area, symptom reporting was clearly associated with perceived environmental risk rather than a causal mechanism between exposure and symptoms.

3.2. Throat, eye, skin irritations and other self-reported symptoms

Short-term respiratory responses have been observed for several communities living near landfills. Shusterman et al. (1991) observed significant relationships between the prevalence of eye and throat irritation and both frequency of odour perception and degree of worry (throat irritation OR: 4.3, 95%CI: 2.8-6.7 and eye irritation: OR: 4.6, 95%CI: 3.2-6.5 using odour complaint as an exposure proxy). Najem et al. (1994) reported a significantly higher prevalence of respiratory diseases (RR: 1.9, 95%CI: 1.1-3.3) and seizures (RR: 4.3, CI: 1.1, 13.9) among people who had resided in the vicinity of a Superfund hazardous chemical waste disposal site (USA, based on 358 households, 1,454 people). Deloraine et al. (1995) found that non-specific
symptoms of respiratory irritation were more frequent among people most exposed to emissions of a recently closed landfill for industrial toxic wastes (432 cases and 384 controls). After adjustment for confounding factors (age, alcohol and tobacco consumption, date of move), there was a positive trend across three groupings of exposure intensity based on modelling of airborne toxicants and time-activity patterns of the subjects throughout the study area (OR: 1.54, 95%CI: 0.69-3.41; OR: 2.09, 95%CI:1.0-4.38, for medium and high exposure groups, respectively). Berger et al. (2000) observed a higher proportion of eye, nose and throat irritations in the community living near the largest landfill in the USA compared to 7 miles away (541 residents in the landfill community, 289 residents 7 miles away). For both studies however, it is not clear whether sufficient allowance was made for socio-economic difference within the area around the site.

Zejda et al. (2000) described the results of a health survey performed in the vicinity of the largest municipal waste site in Poland (581 participants, 393 adults and 188 children). Three estimates of exposure were used: geographical location, distance and intensity of traffic transporting waste material in the vicinity of the subject’s house. Subjects’ own opinion regarding health status (poor, good or very good) was similar across the different zones of potential exposure and no significant difference was found for self-reported symptoms (including headaches, sleep/concentration disturbance, skin rashes, chronic cough) or blood and urine analyses. Although results of the questionnaire for children was more consistent with the hypothesis that exposure from the landfill may affect the health status of residents, significant difference was only observed for headache. Physical examination of the children did not show any difference across the exposure classification zones. In addition to the difficulties related to self-reported symptoms, the design of the study had weaknesses that impact on the significance of the findings (e.g. no control, voluntary participation).

Baker et al. (1988) reported the results of a health survey for a community living near a landfill in California (n=2,039). Prevalence OR were significantly greater for the hazardous landfill community, compared to a control population, for 10 out of the 23 self-reported symptoms considered (highest significance was observed for pain in the ears, nausea and dizziness).

Other studies examining communities living in the vicinity of landfills did not find any relationship with drug usage (prescription drugs to treat respiratory, ophthalmological, dermatological, gastrointestinal or neurological conditions near an industrial toxic waste landfill, Zmirou et al., 1994), an index of “self reported” health (e.g. vitality, general health, bodily pain, physical and social functioning, mental health, McCarron et al., 2000) or indices of health (e.g. mortality, rates of hospital admission and measures of reproductive health, Fielder et al., 2000).

Environmental pollution is not known as one of the risk factors for asthma although asthma symptoms can be aggravated by pollution (Holgate, 1995). Berger et al. (2000) found that asthma had a higher proportion in the community living seven miles away compared to the landfill community. However asthmatic symptoms may be aggravated by pollution and Pukkala and Ponka (2001) have shown that the incidence of asthma was significantly increased for residents of blockhouses built on a former landfill that received household and industrial wastes between 1954 and 1962 in Helsinki (60% excess in comparison with the average Helsinki population based on 2,000 subjects who had ever lived in the houses). There was no increase in the relative risk with years lived in the area and data were not adjusted for smoking or alcohol consumption. However, residents living on the former landfill had very similar lifestyles to the reference population and the authors considered it possible that part of the excess in asthma could be attributed to waste toxicants (e.g. volatile organic compounds).
3.3. Blood pressure

Hypertension has been associated with long-term exposure to high levels of cadmium in animals and occupational studies (Mitchell Perry and Kopp, 1983). However, conflicting results have been reported for the general population and no link between hypertension and exposure to contaminated land has been demonstrated so far.

Ewers et al. (1985) measured the level of cadmium in blood and urine of 286 women (aged 65-66; selected to control for confounding factors) who had spent at least 20 years in two cadmium-contaminated areas of Germany and compared results to a control population. Neither the prevalence of clinically confirmed hypertension nor the relative frequency of hypertension differed significantly among the three study groups.

Strehlow and Bärntrop (1988) studied the community of Shipham (Somerset, UK) where cadmium in locally grown vegetables typically ranged from 5 to 20 times above normal levels. No difference in blood pressure was observed when compared to the control community. Similarly, no difference for anaemia, hypertension and osteoporosis could be demonstrated for a Chinese population exposed to high level of cadmium (367-382 μg/day, n=433) for more than 25 years compared to a control population (54-70 μg/day, Cai et al., 1990). No link was found between environmental exposure to cadmium and blood pressure (Staessen et al., 1991) or hypertension (Staessen et al., 1996) for a Belgian population exposed to relatively high cadmium contamination (n=2,327).

In contrast to these negative results, Eum et al. (2008) have recently shown that blood cadmium level was significantly higher among Korean subjects with hypertension than those without. After adjusting for covariates, the odds ratio of hypertension comparing the highest to the lowest tertile of cadmium in blood was 1.51 (95%CI: 1.13-2.05), and a dose-response relationship was observed. However, no detail on the source of exposure is provided and a link with exposure to contaminated land cannot be inferred.

4. Major effects on human health

4.1. Renal dysfunction and bone damage

Cadmium has a very long biological half-life (decades, WHO, 1992) and accumulates mainly in the liver and the kidneys. Renal tubular dysfunction develops when cadmium content in the kidney cortex exceeds the critical concentration (concentration in an organ at the time any of its cells reaches a concentration at which adverse functional changes occur in the cell; varies at individual level, WHO, 1992). The early signs of the health effects include low-molecular weight proteinuria and enzymuria, characterized by an increased urinary excretion of β2-microglobulin and N-acetyl-β-d-glucosaminidase. The levels of these biomarkers of effect (characteristic biological properties that can be measured to indicate diseased/impaired processes in the body) are thus frequently used in epidemiological studies to indicate renal dysfunction. Studies frequently use multiple biomarkers to increase confidence in results.

The most severe stage of chronic cadmium intoxication occurred in Japan where a number of river basins had been heavily contaminated with cadmium after the Second World War. Rice crops have an unusual ability to accumulate cadmium in grains and cadmium intake (mainly from the consumption of locally grown rice) was estimated to be more than 10 times the maximum tolerable daily intake (WHO, 1992). Local populations were consequently affected by itai-itai disease (severe bone
and renal damage). Smelter activities contaminated rice paddies in a similar way in some parts of China. Many studies followed these populations and demonstrated a dose-response relationship between the level of biomarkers and indicators of exposure to cadmium (e.g. concentrations in blood, urine, soil, rice and other vegetables; Cai et al., 1990, Nordberg et al., 1997, Suwazono et al., 2000, Osawa et al., 2001, Jin et al., 2002, Watanabe et al., 2002). The development of severe renal dysfunctions as a consequence of exposure to cadmium from contaminated land is therefore well established. Cui et al. (2005) showed that the dose–response curve was somewhat altered by the mixed contamination of cadmium and lead as well as the intake of other minerals (n=158 exposed subjects). Follow-up studies have shown that the inhabitants living in the cadmium-polluted area in Japan and who had been identified for having high level of biomarkers, had an increased mortality compared to subjects with lower levels of biomarkers (Nishijo et al., 2006, Matsuda et al., 2002, Nishijo et al., 2004, Nakagawa et al., 2006). For instance, Nishijo et al. (2004) showed that for the most affected subjects (concentration of urinary β2- microglobulin ≥ 1,000 μg/g creatinine, n=534), mortality risk ratios were 2.71 (95%CI: 1.98–3.70) and 2.43 (95%CI: 1.71–3.47) for men and women, respectively. When the subjects were divided into four categories according to the level of urinary β2- microglobulin (<300, 300–1,000, 1,000–10,000, ≥ 10,000 μg/g creatinine), the mortality risk ratios increased proportionally to the level of biomarker in both sexes.

Nishijo et al. (2006) further investigated the causes of death for the subjects having the highest level of biomarker (n=534). The greatest increase in mortality was observed for kidney/urinary diseases and nephritis/nephrosis with a Standardised Mortality Ratio (SMR) of 3.57 (95%CI: 1.02–6.12) and 4.20 (95%CI: 1.60–6.81) when compared to subjects with lower levels of biomarkers (n=2,644).

The results of the 15-year follow-up survey by Nakagawa et al. (2006) also suggest a causal association between cadmium body burden and mortality among a Japanese population living in the cadmium-polluted river basin. Subjects (n=3,119) were divided into five groups according to their level of urinary cadmium (0-3, 3–5, 5–10, 10–20, >20 mg/g creatinine). After adjustment for age, results showed that mortality risk tends to increase with increasing concentration of cadmium in urine. For instance, women with urinary cadmium in the range 3–5 mg/g creatinine had a SMR of 2.03 (95%CI: 1.23–3.35) whilst levels of urinary cadmium >20 mg/g creatinine yielded a SMR of 3.11 (95%CI: 1.71–6.53). The authors further investigated specific causes of death for subjects with urinary cadmium > 10 mg/g creatinine. Significant excesses were observed for heart failure (SMR:1.97, 95%CI:1.06, 3.66) and renal diseases (SMR:3.89, 95%CI:1.13-13.4). Considering that heart failure was often diagnosed during this period in Japan for death without a clear cause, the authors concluded that renal disease was the only cause of death induced by cadmium exposure.

Arizawa et al. (2007a) showed that the association between exposure and mortality is weakening over time, probably because of the selective loss of advanced cases and reduced exposure after the restoration of cadmium-polluted paddy fields in the 1980’s (n=604).

Zhu et al. (2004) investigated the possible link between environmental exposure to cadmium and low bone mass in a population living near a smelter in southeast China. It was estimated that about 100,000 tons of industrial wastewater was discharged every year to a river used by locals to irrigate their fields from 1961 to 1995. In 1995, the average cadmium concentration of locally-produced rice was 3.7 mg/kg compared to the state standard of 0.2 mg/kg. Levels of cadmium in urine and forearm bone densities were measured in subjects who lived in the contaminated
area and consumed locally grown rice for their entire lifetime as well as a control population located 40 km away from the smelter (total number of participants was 790; control site selected based on pilot study showing low cadmium concentration in rice). Urinary cadmium concentrations of the exposed population were significantly higher than those in the control population (11.18 and 1.83 μg/g creatinine, respectively; P value not stated), supporting the use of a 40-km distance to define exposed population. Forearm bone densities were negatively correlated with urinary cadmium excretion (p<0.001) and forearm bone density decreased linearly with age (p<0.001) and urinary cadmium (p<0.01) suggesting a dose-effect relationship between cadmium dose and bone mineral density. The prevalence of osteoporosis in women over 50 years old was significantly higher in the polluted area compared to the control (OR: 2.09, 95%CI: 1.1-4.0). There was also a marked increase in the prevalence of fracture in the contaminated area for subjects over 40 years old (after standardization for age, RR: 4.1, 95%CI: 1.6-6.6 and RR: 2.5, 95%CI: 1.4-3.5 for men and women, respectively).

Belgium is one of the principal cadmium producers in Europe. Past emissions of several smelters have contaminated areas with cadmium and several studies have evaluated the impact on population health. A significant association was demonstrated between biomarkers of renal dysfunction (24-hour urinary excretion of β2-microglobulin, retinol-binding-protein, and N-acetyl-β-glucosaminidase) and several indices of environmental exposure to cadmium (based on distance to smelter and concentrations of cadmium in soils and locally grown vegetables, n=703, Staessen et al., 1994). Exposure to lead and zinc were also associated with alterations of the renal function (Staessen et al., 1996). Cadmium excretion in districts near smelters was 23% higher than in other districts in Belgium. The relative risk associated with doubled urinary cadmium was 1.73 (95% CI 1.16–2.57; p=0.007) for fractures in post-menopausal women (n=1,014, Staessen et al., 1999).

A follow up study of the exposed Belgian cohort reported that over 5 years, blood cadmium fell by 30% and urinary cadmium by 15% in the population exposed and thus confirm the efficacy of preventive measures put in place to reduce cadmium uptake (e.g. drinking water from the tap rather than from wells, liming soil of kitchen gardens and not growing leafy vegetables, Staessen et al., 2000). Nawrot et al. (2008) studied concentration of cadmium in blood and urine and mortality from 1985 to 2007 in an exposed cohort in Belgium (480 exposed and 476 control subjects). During this period, cadmium emissions ceased, but the soil remained contaminated with cadmium. Mortality clustered around the industrial settlements and it was associated with higher cadmium body burden. The results show that environmental exposure to cadmium increases total and non-cardiovascular mortality in a continuous fashion without threshold. The relative risk associated with a doubling of baseline urinary cadmium were 1.20 (95% CI 1.04–1.39, p=0.014) and 1.44 (95% CI 1.16-1.79, p<0.001 for total and non-cardiovascular mortality and 1.25 (95%CI 1.04-1.50) and 1.33 (95% CI 1.01-1.75) for a doubling of blood cadmium.

The results of Ezaki et al. (2003) indicated the absence of a threshold level for observing dose-response relationship between urinary levels of cadmium and β2-microglobulin (based on more than 10,000 middle-aged Japanese women). Similarly, several recent studies suggest an effect of chronic cadmium exposure even at very low concentration. Near a former battery plant, Jarup et al. (2000) showed that people with cadmium in urine of around 1 μg/g creatinine (which is in the upper part of the normal range) had a threefold increase in risk of having tubular proteinuria (early sign of renal dysfunction). Thomas et al. (2009) recently studied the population living near the Avonmouth zinc smelter (UK) that has been exposed to cadmium and other heavy metals for many decades (n=180). A dose-response relationship of borderline significance was observed between very low levels of cadmium in urine.
and prevalence of a biomarker for renal dysfunction (for urinary cadmium of 0.3-0.5 μg/g creatinine: OR: 2.64; 95%CI: 0.70–9.97 and for levels ≥0.5 μg/g creatinine: OR: 3.64; 95%CI: 0.98–13.5; p for trend = 0.045).

The studies described above indicate a strong link between cadmium exposure and biomarkers of renal or bone dysfunctions, even at very low levels of exposure. Conversely, there have been several cases of apparently high exposures to cadmium without accompanying health effects in Germany (Ewers et al., 1993), the UK (Wood, 1996, Strehlow and Barltrop, 1988, Elliott et al., 2000), France (de Burbure et al., 2003), Jamaica (Barton et al., 2004, Lalor, 2008) and Korea (Kim et al., 2008).

Ewers et al. (1993) measured the level of cadmium in blood and urine of 90 gardeners in a lead/zinc smelter area of Germany and compared results to a control population. Despite relatively high concentrations of cadmium in garden soils (up to 49 mg/kg, average of 13 mg/kg) and vegetables in the area (up to 2.79 mg/kg in celery), blood and urinary cadmium levels were not elevated in the gardeners compared to a reference group of subjects from the same area who did not consume home-grown fruit and vegetables (mean concentration in urine was 0.41 and 0.51 μg/g creatinine, respectively, Ewers et al., 1993).

Wood (1996) showed that despite high concentrations of cadmium in garden soils near a battery factory in Worcestershire (7.6–78.7 mg/kg), the levels in blood and urine of local residents (n=39) was considered not significantly elevated compared to a control population. Mean concentrations in urine in the study group were 0.21 and 0.32 μg/g creatinine for men and women, respectively, compared to 0.14 and 0.05 μg/g creatinine for the control men and women, respectively. Both the study and control group included smokers and the length of residence in the contaminated area was not taken into account. A logistic regression analysis showed that current smoking and age were of borderline significance in relation to having a urine cadmium level greater than 0.5 μg/g creatinine. After adjusting for other factors, only current smoking remained a significant risk factor for having a blood concentration > 1 μg/g creatinine.

In the UK, a national survey of stream sediments in 1978 revealed extremely high levels of cadmium, lead and zinc in Shiphm, Somerset, where zinc and lead mining had been carried out in the 19th century (cadmium concentration up to 360 mg/kg in surface garden soils, Thornton, 1988). Analysis of locally grown vegetables found that cadmium levels were also elevated and ranged from 5 up to 20 times above normal levels. There were small but measurable increases in cadmium levels in urine and blood samples compared with a control population. Small excesses of borderline significance for some cadmium-related disorders were identified (gouty arthritis, nephritis and cardiovascular disease), but the study concluded that if cadmium did have an effect on mortality it was slight (Strehlow and Barltrop, 1988). The mean urinary cadmium excretion was similar in the Shiphm and Belgian population studied (0.83 and 0.84 μg/24h, respectively, Staessen et al., 1999). The lower level of health effect observed in Shiphm compared to Belgium can be partly attributed to the fact that the Shiphm cohort consisted of volunteers who may not have been representative of the exposed village as a whole (response rate fell with age and length of residence in the contaminated area). Elliott et al. (2000) presented a follow up of the population of Shiphm and noticed an excess of borderline significance of mortality from hypertension, cerebrovascular disease, and nephritis and nephrosis (SMR 1.28, 95%CI 0.99-1.62) compared to a nearby village without cadmium contamination. All cause mortality and cancer incidence were not affected.

De Burbure et al. (2003) assessed renal parameters in children and adults living in an area of northern France known for its past heavy metal contamination around two non ferrous smelters. Concentrations in soils were relatively high for lead (100 up to
1700 mg/kg) and cadmium (0.7 up to 233 mg/kg) and blood levels of lead and cadmium were significantly higher compared to the control population. However, none of the renal parameters studied showed a significant difference between control and exposed groups (seven biomarkers were considered, including \( \beta_2 \)-microglobulin and \( N \)-acetyl-\( \beta \)-d-glucosaminidase). The influence of heavy metals on renal parameters was further assessed by stepwise multiple regression including potential confounding factors (e.g., age, gender, body mass index (BMI), smoking habits). The only positive correlation was found between the urinary excretion of \( N \)-acetyl-\( \beta \)-d-glucosaminidase (standardized for BMI and urinary creatinine) and level of cadmium in blood when considering all children in the population. Although this result indicates that even low cadmium burdens may affect the proximal tubule in children (duct system of the nephron, which is a structural and functional unit of the kidney), the absence of other positive correlation indicates a minimal renal impact of living in this area contaminated by former smelter activities.

The bauxite soils in Jamaica naturally contain high concentrations of cadmium (up to 931 mg/kg). Lalor (2008) recently reviewed the literature and examined the potential relationship between the geographical distribution of cadmium in soils and the incidence of renal diseases, cancers and mortality. Although high cadmium intake was confirmed by high cadmium content in blood and urine, the authors concluded that there is no evidence of cadmium related human distress to date for the Jamaican population. For instance, a survey of 605 patients with chronic renal failure/end stage renal disease found that the prevalence of chronic renal failure was not increased in areas known to have high soil cadmium levels (Barton et al., 2004).

Kim et al. (2008) studied a population living near an abandoned metal mine in Korea. Levels of metals in soils sampled in the study area were significantly higher than the control area and mean concentrations of cadmium and copper in rice and barley were also significantly higher than those of the control area (p<0.05). Conversely, there was no difference in metal concentrations in groundwater and air between the study and control area. Geometric means of blood and urine cadmium in the study area were significantly higher than those in the control area (urinary cadmium was 1.53 and 1.20 \( \mu \)g/g creatinine for the exposed and control population, respectively). However, there were no differences in the levels of urinary biomarkers indicating early kidney dysfunction or bone mineral density.

Severe renal and bone diseases induced by cadmium pollution seem to have occurred mainly in Asia where it is linked to a staple diet of rice (Tsukahara et al., 2003) grown on soils without extremely high levels of cadmium (up to 1.49 mg/kg, Cai et al., 1990). Soil has an unusually high ability to take up cadmium from soil and this is exacerbated by the agronomic and soil pH conditions associated with rice cultivation. The high cadmium uptake of rice accompanied by low levels of calcium, iron, and especially zinc has been suggested as a strong contributing factor that influences the absorption of cadmium and its distribution in organs and tissues.

For instance, Andersen et al. (2004) showed that dietary deficiency might increase intestinal cadmium uptake by up to 8 times. There are other confounding factors that might explain differences in health effects observed between populations. They include differences in cadmium bioavailability among foods, the level of absorption of dietary cadmium, genetics, lifestyle, diet, and antagonistic or synergistic exposures to other elements.

It is important to note that levels of cadmium exposure differ greatly between the studies carried out in Japan, Belgium and the UK (Table 1.1). The median urinary cadmium level in the exposed Japanese population was 7.0 \( \mu \)g/g creatinine (Arisawa et al., 2007). Such high levels result from a diet almost exclusively based on contaminated rice and can explain the increase in mortality observed in the Japanese
population. By comparison, Nawrot et al. (2008) reported a median urinary cadmium at baseline (1985–1989) of 0.74 μg/g and 1.03 μg/g creatinine, in the low and highly exposed districts of Belgium, respectively. Across ten Belgian districts studied by Staessen et al. (1999), mean cadmium concentration in soil ranged from 0.8 to 14.7 mg/kg in participants’ gardens and significant correlations were observed between concentrations in soil and locally grown vegetables (e.g. p=0.003 for leek and p<0.001 for celery).

Finally, Thomas et al. (2009) reported median urinary cadmium concentrations in a population living near the Avonmouth zinc smelter (UK) of 0.22 and 0.34 μg/g creatinine for men and women, respectively. Median urinary cadmium concentrations varied with history of smoking (non-smoking 0.18/smoking 0.40 μg/g creatinine for men; non-smoking 0.31/smoking 0.46 μg/g creatinine for women). Thomas et al. (2009) reported an effect of cadmium exposure on biomarkers at levels as low as 0.3 μg/g creatinine. The presence of biomarkers does not necessarily mean that an individual will suffer an adverse health effect, but Thomas et al. (2009) questioned policy on concentrations of soil cadmium considered to pose a hazard.

Development of renal dysfunctions is not restricted to areas contaminated with cadmium. Hall et al. (1996) found associations between end-stage renal disease and estimated exposure to contaminants from a landfill, based on residential proximity, number of years lived in proximity to a site and a medium or high probability of exposure (n=216 cases). For instance, elevated OR of borderline significance for end-stage renal disease was calculated for people having lived within one-mile radius of a site (OR: 1.40, 95%CI: 0.92-2.11).

Major chemical industries have operated in the county of Cheshire (UK) for over a century and ground investigations revealed that vapour transport of volatile chemicals was occurring in the vicinity of the village of Weston. In 2000, analysis of indoor air quality revealed the presence of hexachlorobutadiene (HCBD) in 20 homes at levels up to 6.8 μg/m³. The local health authority advised that exposure to HCBD should be kept below the reference value produced by the Department of Health (0.6 μg/m³) and since remediation of the houses was impossible, most residents decided to leave their homes. Staples et al. (2003) presented the results of the health authority’s investigations. Forty-seven residents underwent a health check within two months of cessation of long-term exposure to HCBD and again at least 10 months after exposure ceased. In the first round of tests 20 subjects (54%) had at least one abnormal result regarding biomarkers of renal dysfunction and six (16%) had two or more raised values compared to a reference population. At follow up, the number of subjects with at least one abnormal result had reduced to seven (19%). The results therefore support the hypothesis that exposure to the local environment induced a renal effect which improved when subjects left their homes. Although the results are consistent with the predicted toxicological effects of HCBD from animal studies, it cannot be excluded that exposure to other toxicants may have induced or contributed to the renal effects observed.

Many studies have established a link between cadmium exposure and biomarkers of renal and bone dysfunctions. Strong dose-response relationships have been observed, even at very low levels of exposure. For the studies taking place in areas without extreme cadmium contamination, the part of cadmium burden that is due to direct exposure to contaminated land is generally not known (e.g. the studies by Akesson and others in Sweden). It is important to note that the presence of biomarkers does not necessarily mean that an individual will suffer an adverse health effect. However, impact of cadmium exposure on the incidence of severe renal dysfunctions and mortality has been demonstrated in Japan as well as in Belgium. Temporality of the effect of cadmium exposure was demonstrated when contamination was reduced in Japan and when preventive measures were put in
place in Belgium. However, the long half-life of cadmium in body organs (particularly the kidney and liver) needs to be considered in relation to the expectation of reduced body burden following any exposure reduction after remedial action.

Soil concentrations are not a direct surrogate for exposure and there are examples where residents in locations with very large concentrations of cadmium in soil did not appear to suffer serious health consequences; this finding is attributed to specificities of exposure, particularly differences in uptake of cadmium into different crop species and the more diversified diets prevalent in Western Europe.

Overall, high dietary exposure to cadmium has been shown to cause renal dysfunction and bone damage. Evidence for effects from lower exposures is contradictory and/or based on biomarker responses rather than clinical health effects.
Table 1.1. Concentration levels in soils and residents exposed. Background concentrations in the UK for cadmium in soil are typically <1 mg/kg.

<table>
<thead>
<tr>
<th>Study area</th>
<th>Urinary level of cadmium in exposed population (µg/g creatinine)</th>
<th>Concentration in soil (mg/kg)</th>
<th>Other concentrations</th>
<th>Type of effect observed</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK (Avonmouth)</td>
<td>0.2-0.3</td>
<td>n/a</td>
<td>n/a</td>
<td>Biomarkers of renal dysfunction (borderline significance)</td>
<td>Thomas et al., 2009</td>
</tr>
<tr>
<td>UK (Worcestershire)</td>
<td>0.3</td>
<td>7.6–78.7</td>
<td>n/a</td>
<td>None (blood/urine concentration similar to control)</td>
<td>Wood, 1996</td>
</tr>
<tr>
<td>Germany</td>
<td>0.4; range: &lt;0.1-4 (control: 0.51; range: &lt;0.1-2.4)</td>
<td>13 (up to 49)</td>
<td>up to 2.79 mg/kg in celery</td>
<td>None (similar blood/urine between exposed and control population of women 65-66 years old)</td>
<td>Ewers et al., 1993</td>
</tr>
<tr>
<td>UK (Shipham)</td>
<td>0.7 (control: 0.6)</td>
<td>97 (2-360, garden soil)</td>
<td>5 up to 20 times above normal levels in vegetables</td>
<td>Small excesses of borderline significance for blood pressure, genitourinary disease, nephritis, cardiovascular disease. Any excess in mortality considered to be slight and of borderline significance</td>
<td>Strehlow and Barltrop, 1988; Elliott et al., 2000</td>
</tr>
<tr>
<td>Sweden (not necessarily linked to contaminated land)</td>
<td>0.7</td>
<td>n/a</td>
<td>n/a</td>
<td>Biomarkers of renal dysfunction</td>
<td>Jarup et al., 2000 Akesson et al., 2005; Akesson et al., 2006</td>
</tr>
<tr>
<td>Belgium</td>
<td>1.0 (control: 0.63)</td>
<td>0.8-17 (garden soil)</td>
<td>0.1 to 4.0 mg/kg dry weight in vegetables</td>
<td>Biomarkers of renal dysfunction Fracture (post-menopausal women) Cancer (especially lung)</td>
<td>Nawrot et al., 2006, 2008 Staessen et al., 1994, 1996, 1999, 2000</td>
</tr>
<tr>
<td>Japan (non-polluted)</td>
<td>1.5-2.4</td>
<td>n/a</td>
<td>n/a</td>
<td>Biomarkers of renal dysfunction</td>
<td>Suwazono et al., 2000</td>
</tr>
<tr>
<td>Korea</td>
<td>2.9 (control: 1.5)</td>
<td>0.36 (control : 0.18)</td>
<td>0.049 mg/kg (control:0.025) in rice</td>
<td>None (biomarkers of renal/bone dysfunction)</td>
<td>Kim et al., 2008</td>
</tr>
<tr>
<td>Japan (Jinzu basin)</td>
<td>n/a</td>
<td>n/a</td>
<td>0.06-1.06 mg/kg rice (1971-1996)</td>
<td>Biomarkers of renal dysfunction Mortality</td>
<td>Mastuda et al., 2002; Watanabe et al., 2002</td>
</tr>
<tr>
<td>Japan (Kakehashi basin)</td>
<td>5.9 (0.3-57.5; 1981-82)</td>
<td>1 (paddy soil)</td>
<td>&gt; 0.4mg/kg rice</td>
<td>Biomarkers of renal dysfunction Preterm delivery Mortality (due to kidney/urinary diseases and nephritis/nephrosis)</td>
<td>Nishijo et al., 2004, 2002; 2006; Nakagawa et al., 2006</td>
</tr>
<tr>
<td>Japan (Nagasaki and Akita Prefectures)</td>
<td>9.6 (2.0-50.8, 1982)</td>
<td>&gt;1.0 (paddy soil)</td>
<td>&gt;0.4 mg/kg rice</td>
<td>Biomarkers of renal dysfunction Mortality (total and kidney/urinary diseases and nephritis/nephrosis; association between exposure and mortality weakening over time)</td>
<td>Arizawa et al., 2001, 2007a,b</td>
</tr>
<tr>
<td>China (Dayu county)</td>
<td>11.27  (control: 3.03)</td>
<td>0.89-1.49</td>
<td>0.05 mg/L irrigation water</td>
<td>Biomarkers of renal dysfunction</td>
<td>Cai et al., 1990</td>
</tr>
<tr>
<td>China (Zhejiang)</td>
<td>11.18 (control: 1.83)</td>
<td>0.87 (control: 0.04)</td>
<td>2.4-3.7mg/kg in rice (control: 0.072-0.05)</td>
<td>Biomarkers of renal dysfunction Low bone mass, prevalence of fracture for &gt; 50 years old</td>
<td>Nordberg et al., 1997; Jin et al., 2002; Zhu et al., 2004</td>
</tr>
<tr>
<td>France</td>
<td>n/a. Significantly higher than control population</td>
<td>0.7 - 233</td>
<td>Blood concentration ≤0.52 and ≤0.86 µg/L in children and adults, respectively</td>
<td>No effect on levels of renal biomarkers</td>
<td>de Burbure et al., 2003</td>
</tr>
<tr>
<td>Jamaica</td>
<td>n/a</td>
<td>Maximum 931</td>
<td>Up to 144 mg/kg in the renal cortex of adults; mean 0.4 mg/kg in vegetables with maximum 6.5 mg/kg</td>
<td>No clear evidence of cadmium-related human disorders</td>
<td>Barton et al., 2004; Lalor, 2008</td>
</tr>
</tbody>
</table>

n/a: no value is reported
4.2. Cancer

Chemically-induced cancers are generally characterised by long latency periods, often of several decades. It is therefore very difficult to establish whether a population that has developed cancers has been or is actually being exposed to carcinogenic chemicals originating from contaminated land. Using residence location as a proxy for exposure is difficult when individuals migrate out and may be living in a different location when any cancer is diagnosed. Conversely, individuals might migrate into an area of concern but having had a carcinogenic exposure elsewhere. Epidemiological studies of cancer related to contaminated land and landfills are thus problematical and must take into account a wide range of design factors which, if not addressed, can preclude a clear interpretation.

4.2.1. Landfills

Most studies investigating the possible link between contaminated land and cancer incidence/mortality focused on residential proximity to landfills or sites of illegal waste dumping. One of the main difficulties related to the study of landfills is the definition of exposure due to complex mixtures of chemicals where documentation on contamination is generally poor and measurement of individual exposure virtually impossible. Single site studies are more likely to succeed in demonstrating a link as a better exposure assessment can be achieved compared to multiple site studies. However, low numbers decrease the statistical power to demonstrate any significant associations, increasing the likelihood of false negatives and false positives.

Several reported single and multiple-site studies have failed to demonstrate any excess in risk of developing cancer for residents near landfills. One of the most notable examples is the Love Canal site in Niagara Falls (New York State, USA). The site was used as a dumping ground for a range of extremely toxic wastes before being converted into a residential neighbourhood. Site investigation confirmed excessive chemical contamination, including known or strongly suspected carcinogens (e.g. benzene, lindane, dioxins). Janerich et al. (1981) reported a detailed study of cancer incidence around the site. The authors did not, with the exception of elevated respiratory cancers, identify any evidence of excess cancers in “exposed” communities. While rates for respiratory cancers were significantly higher, a more detailed analysis demonstrated that these rates were not statistically different from those reported in other areas of Niagara Falls which were not influenced by the site.

Residents near a landfill site in Walsall (UK) reported a cluster of childhood cancer. The community was considered potentially exposed to airborne pollutants and from possible underground seepage of toxic wastes. However, comparison of observed cancer rates did not show any excess when compared to expected rates based on regional statistics (Muir et al., 1990).

Williams and Jalaludin (1998) examined cancer incidence and mortality in the area around a regional waste disposal landfill that had received over one million tonnes of liquid waste and an unspecified range of solid domestic, industrial and hazardous waste since 1974 (New South Wales, Australia). The study considered age/sex standardised ratios in areas within 3 km of the site and no excess cancer or mortality rates were found. The authors suggested that the negative results may be explained by limitations due to the small size of the area included within the data analysis.

Similarly, four of the five cancer types evaluated by the Massachusetts Department of Public Health (2003, based on 37,258 residents) were near or below expected
rates based on state-wide rates for resident near a landfill (including residential, commercial and industrial wastes).

Two multiple site studies investigated the possible link between residence near a landfill and childhood cancer. Considering several sites at a time involves more cases (which increases statistical power) and the latency period for childhood cancer is shorter than for adults. These two studies therefore reduced two of the most limiting factors related to studies on cancer. White and Aldrich (1999) studied residence near 22 high priority landfills in the USA (238 cases of pediatric cancer) and Knox (2000) considered 460 toxic waste landfills in the UK (including migration patterns around the site and 22,450 cancer deaths occurring before the 16th birthday between 1953 and 1980). However, neither study found significant association between childhood cancer and residence near landfill sites.

Jarup et al. (2002) presented a large nationwide analysis of cancers of the bladder and brain, hepatobiliary cancer and leukaemia in Great Britain. The base population comprised people living within 2 km of more than 9000 landfill sites, whilst population living more than 2 km away from a landfill served as the reference population. Overall, 341,856,640 person-years for the adult cancers and 113,631,443 person-years for childhood leukaemia were included in the study. In spite of the very large scale of this national study, no excess risks of cancers of the bladder and brain, hepatobiliary cancer or leukaemia was found in populations living within 2 km of landfill sites. Results were similar even when the analysis was restricted to landfill sites licensed to carry special (hazardous) waste. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) considered that this finding of no excess risk for those living within 2 km of a landfill site for each of the cancers considered provided a degree of reassurance (COT, 2001). However, they noted that the lag times used in the study (1 year for childhood cancers and 5 years for adult cancers) were relatively short and had been pragmatically selected to increase the number of years in the analysis and minimise dilution through migration.

Some studies have reported an increased risk of cancer for populations living near landfill sites. However, most of these include important limitations, such as a limited control for confounding factors, no accurate measurement of exposure and/or multiple testing, which generally results in relatively low weight of evidence.

Widespread contamination of groundwater, soil, and surface water with organic and inorganic compounds occurred at the Drake Superfund Site, an industrial chemical landfill in Pennsylvania (USA). Since the air monitoring near the site only identified a small number of organic compounds, the main exposure route was thought to be direct contact with surface waters and soil in recreational areas near the site. Budnick et al. (1984) found an increase in mortality from bladder cancer among white males in one of the counties surrounding the waste site (+110% between 1950 and 1970 based on 23 deaths, while national rate remained the same). Bladder cancer in females did not show such an effect. Information concerning bladder cancer risk indicator was not available (e.g. occupation, duration of residence and employment, smoking) and it is believed that an occupational effect for males working in the Drake chemical plant may explain the excess of cancer observed.

Goldberg et al., (1995a) examined cancer rates in communities around an actively gassing municipal solid waste landfill site in Montreal, Quebec (total population of 1,000,000). The composition of gas produced by this landfill site included a range of volatile compounds including recognised carcinogens such as benzene and vinyl chloride. Cancer rates were compared with non-exposed reference areas in Montreal, which were similar to the exposed areas in terms of several key socio-demographic factors. Some significantly elevated risk ratios were identified but there was no evidence of a dose-response effect and these findings could thus have been
as a result of multiple testing (148 statistical tests). Goldberg et al. (1999) further investigated the site and conducted a case-control study (n=2,928). The area surrounding the site was divided into four exposure zones. In the exposure zone nearest to the site, elevated risks were found for cancers of the pancreas (OR:1.4; CI:0.8-2.6); liver (OR:1.8; CI:0.8-4.3) and prostate (OR:1.5; CI:1.0-2.1). In a sub-exposure zone approximately downwind from the site, high risks were also found for pancreatic cancer (OR: 1.7; CI:0.9, 3.5) and non-Hodgkin's lymphomas (OR:1.5; CI: 0.8-2.6). When distance from the site was used as an indirect measure of exposure, higher-than-expected risks were found for pancreatic cancer (OR<1.25km: 2.2; CI: 1.0-4.6); liver cancer (OR<1.5km: 2.1; CI: 0.8-5.3); kidney cancer (OR<2 km: 1.4; CI: 0.9-2.3) and non-Hodgkin's lymphomas (OR<1km: 2.0; CI: 1.0-4.0). The main limitations of the study were the absence of complete lifetime residential histories, the relatively short period from first exposure (1968) to cancer onset (1979-1985) and the use of geographic measures of proximity to estimate exposure.

Griffith et al. (1989) identified 593 hazardous waste landfills in the USA with analytical evidence of contaminated groundwater providing a sole source of drinking water supply. Significant association between excess deaths and all counties with hazardous waste sites (HWS) were shown for several cancers when compared to non-HWS counties (p<0.002). However, there was no exposure assessment and age was the only confounding factors considered.

Similarly, cancer maps from 1950 though 1979 revealed areas of high mortality from bladder cancer in Illinois counties (USA). High risk ratios for bladder cancer (1.7 for male and 2.6 for female, p<0.005 and 0.001, respectively, based on 725 cases) were identified for a particular town (Mallin, 1990). Further investigation revealed that one of four public drinking water wells in this town had been closed due to contamination; two wells were within half a mile of a landfill containing hazardous waste that had ceased operating in 1972.

Lewis-Michl et al. (1998) investigated incidence of cancer diagnosed over a ten-year period (1980-1989) near 38 municipal landfills with soil gas migration conditions in New York State (USA, n=9,020 cases). Elevated risk ratio for bladder cancer (4.1) and leukaemia (4.8) were observed for women likely to have been exposed (assessed through residency within a distance of 76-305 m of the landfill, depending on landfill characteristics). However, no difference was observed for men and other cancer types (leukaemia, non-Hodgkin's lymphoma, liver, lung, kidney, bladder and brain cancer) and important factors to assess exposure were not considered (such as length of residence within the area potentially exposed). Lewis-Michl et al. (1998) pointed out that exposure to landfill gases mainly occurred in the 1960s and 1970s. They considered that clean-up activities (e.g. capping) and landfill closures have since changed the conditions in proximity to the 38 landfills considered and that the study did not necessarily provide information about health risks related to living near landfills today.

Twelve blockhouses were built in Helsinki in the 1970s on a former landfill area containing industrial and household waste. Pukkala and Ponka (2001) investigated whether the exposure to landfill caused cancer or other chronic diseases in the inhabitants of these houses (based on 2,000 people who had lived in these houses at some time). Significant elevated risk of all cancers combined was observed for the residents of the houses built on the former landfill area compared to reference houses (relative risk: 1.50; 95% CI: 1.08-2.09). The excess was almost entirely attributable to males (relative risk 1.61; 95% CI, 1.11-2.24). Males showed an excess of cancers of the pancreas (relative risk 5.05; 95% CI, 1.38-12.9), and in skin (relative risk for melanoma and non-melanoma combined 4.03; 95% CI, 1.31-9.41), while there were no cases of these cancers among women. Although the data were not adjusted for important confounding factors such as smoking or alcohol...
consumptions, residents living on the former landfill area had very similar lifestyle habits compared with the reference cohort. In addition, there was a lag of several years after moving to the area before the excess started to appear and a slight dose-response effect with years lived in the area was observed. Because the houses in the area had municipal tap water, the area has no rivers or lakes and no edible plants had been grown in the area, exposure was considered to occur via dust, ambient air, and indoor air. Soil samples and interstitial soil gas were analysed for a range of contaminants. Soil samples contained high concentrations of polynuclear aromatic hydrocarbons (PAHs), polychlorinated biphenyls, cyanides, and some heavy metals (Finnish guidelines were exceeded more than 100-fold in several samples). In interstitial soil gas samples, concentrations of volatile organic compounds and hydrogen sulphide were also high. Indoor air was also analysed for a range of contaminants, but concentrations were similar to those found earlier in other blockhouse apartments in Helsinki. Whilst noting weaknesses in the study, Pukkala and Ponka (2001) suggested that the lag in excess cancer risk after moving to the area and slight dose-response relationship in terms of years lived at the site were supportive of a causal relationship between toxicants deriving from the landfill around the blockhouses and cancer risk.

4.2.2. Sites of illegal waste dumping

For more than a decade, wastes in the region of Campania, in southern Italy, have been poorly managed and the area has been described as the “Triangle of death” because of the widespread uncontrolled waste dumping (Bianchi et al., 2004, Senior and Mazza, 2004) The health impact of waste is still unclear, although several studies have claimed that the large excesses in mortality and morbidity observed in the region are attributable to exposure to waste (Fazzo et al., 2008, Altavista et al., 2004, Comba et al., 2006).

Altavista et al. (2004) mapped the spatial distribution of waste disposal sites and toxic waste dumping grounds in the region of Campania using GIS. Mortality between 1986 and 2000 was studied in an area with very high density of dumping sites (39 waste sites, 27 of which are likely to contain toxic wastes, 150,000 inhabitants). Cancer mortality (especially lung, pleura, larynx, bladder, liver and brain) and incidence of circulatory diseases were significantly increased compared to statistics for the whole region of Campania.

The same year, the World Health Organization acting at the request of the Italian authorities, examined the health implications of widespread uncontrolled waste dumping and toxic waste burning. The provinces of Naples and Caserta (within Campania region, 196 municipalities, around 4 million inhabitants) were characterised with regard to 20 causes of death (all cause, all cancer mortality and specific cancer causes) and 11 congenital malformations for the period 1994–2002. The results showed that the two provinces are more at risk for several cancers compared to statistics for the whole region (Comba et al., 2006). The highest risks were observed for cancer of the pleura (standardized mortality ratio of 1.33 and 1.26 for men and women respectively), cancer of the esophagus (SMR of 1.27 for women) and cancer of the trachea, bronchus and lung (SMR 1.14 for men). A group of about 40 municipalities had consistent, repeated and significant excess for several of the health outcomes considered (including cancer of the stomach, kidney, liver and lung and for urogenital and cardiovascular congenital malformations). Most of the excesses were observed in an area between the two provinces, where most of the illegal waste treatment activities were known to have taken place.

Fazzo et al. (2008) applied a cluster analysis approach in order to evaluate the geographical distribution of municipalities where significant increases of cancer and
congenital malformations are observed. A deprivation index was estimated for each municipality in order to account for the possible confounding effect of socioeconomic deprivation. The results showed a tendency towards clustering of mortality from several cancer types (lung: RR: 1.15-1.30, p< 0.03; liver: RR: 1.40-2.04, p<0.009; gastric: RR: 1.33, p<0.0003; kidney: RR: 1.70, p<0.016 and bladder: RR: 1.44-1.45, p<0.014) in a fairly well defined area that corresponds to the area defined in Comba et al. (2006). A causal relationship based on these reported associations cannot be inferred from these studies, as the level of exposure due to waste disposal remains unknown (lack of measurements and the presence of confounding sources of exposure due to industrial activities).

Greiser et al. (1991) studied a population living near an illegal industrial wastes site in Germany (282,588 inhabitants, 215 cases of leukaemia, 28 deaths from leukaemia, 68 of multiple myeloma and 157 of malignant lymphoma). Only one community, nearest to the waste site, showed a significantly elevated standardised morbidity ratio for leukaemia (1.60). Simple regression of community incidence rates with community distance to the site weighted for population size showed negative coefficients for leukaemia (r=-0.74, p=0.0092) and leukaemia, multiple myeloma and malignant lymphoma combined (r=-0.74, p=0.0094). However, it is not clear whether any confounding factors were considered.

4.2.3. Other contaminated land

Cancer incidence has also been investigated for populations living nearby contaminated land other than landfills. In some cases, high concentrations of known carcinogenic chemicals (such as asbestos, dioxins but also relatively low concentration of cadmium) were shown to have effects on cancer incidence that were large enough to be detected (as discussed in Section 4.2.1.2). On the other hand, some studies that focused on exposure to a known carcinogenic chemical (e.g. hexavalent chromium, TNT) have failed to demonstrate a clear effect on cancer incidence (Section 4.2.1.1).

Elliott et al. (2000) presented a follow-up study of the cohort living in Shipham (UK) for mortality from 1939 to 1997 (cancer incidence was analysed for 1971-1992). This study found that all cause cohort mortality in both Shipham (n=351) and the comparison population in the village of Hutton (n=260) were lower than expected (using the South West region as a whole). This study found some excess of prostate cancers in the Shipham cohort but numbers involved were too low to have any statistical power. The lack of evidence of adverse health effects in Shipham has been ascribed to the fact that locally grown vegetables would form only a low percentage of the diet. The research by Elliott et al. (2000) concluded that no clear evidence of health effects was present despite the extremely high concentrations of cadmium in the soil.

Eizaguirre-Garcia et al. (1999) studied leukaemia incidence in an area near Glasgow contaminated by the former activities of a chromium-processing factory, which had been operating from the mid-19th century until its closure in 1967. Concentrations of chromium VI in soil on the factory site were very high (900 mg/kg and around 450 mg/kg 2-3 km away). A circle of 10km radius and centred on factory site was considered in the analysis (873,643 people with 1,205 leukaemia cases). However, no relationship was found between cases of leukaemia and distance of residence to the contaminated site.

A descriptive study showed a near 10-fold increased risk of chronic myeloid leukaemia among males living in a locality of Germany known for its contamination from armament wastes containing toluene-derivatives (Kolb et al., 1993). Killian et al.
(2001) worked at the same location to carry out a case-control study within the cluster (43 cases, 123 controls) to test the hypothesis that contamination of soil and water related to trinitrotoluene (TNT) production might be responsible for cluster of leukaemia observed by Kolb et al. (1993). Although, an increased odds ratio was observed for a small group living in a particular site, estimated exposure to TNT could not explain the large majority of cases that occurred in the area in the 1980s.

Local populations of some parts of central and eastern Turkey are exposed to naturally-occurring asbestos fibres. The fibres are either tremolite (silicate mineral) asbestos or erionite which is a naturally occurring zeolite with asbestos-like properties (Dumortier et al., 1998). Baris et al. (1996, cited in Kibble and Saunders, 2001) have demonstrated a very strong association between residence in this area and respiratory cancer (especially pleural mesothelioma) with the main exposure route being inhalation of fibres from soil. Hasanoglu et al. (2006) showed that incidence of lung cancer was up to fourfold higher in zones with known tremolite asbestos contamination compared to the general population of Turkey.

Magnani et al. (2001) demonstrated an association of pleural malignant mesothelioma (cancer of the protective layer that covers most of the body’s internal organs) and environmental asbestos exposure originating from an asbestos cement factory active from 1907 to 1985 (Casale, Italy, 160 cases and 330 controls). Living in Casale was associated with a very high risk for pleural malignant mesothelioma (after discarding former workers: OR: 20.6; 95%CI: 6.2-68.6). Controlling for other sources of asbestos exposure, the results suggest that environmental exposure caused a greater risk than domestic exposure (assessed through a questionnaire on the presence of asbestos containing items indoor or in very close proximity to the house).

The Seveso accident occurred in 1976 in a small chemical manufacturing plant in the Lombardy region in Italy. A chemical cloud was released causing a large populated area north of Milan to be contaminated by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) This event gave rise to numerous scientific studies and standardised industrial safety regulations. Consonni et al. (2008) reported the results of a mortality follow-up of a cohort exposed for 1997–2001. The study cohort included 278,108 subjects resident at the time of the accident or immigrating/born in the 10 years thereafter in three contaminated zones with decreasing TCDD soil levels (zone A: 15.5-580.4, zone B: 1.7-4.3; zone R: 0.9-1.4 μg/m²) and in a reference territory comprising surrounding, non-contaminated municipalities. Results confirmed previous findings of excesses of lymphatic and hematopoietic tissue neoplasms (abnormal mass of tissue) in the zones with very high and high concentrations of TCDD in soils (RR: 2.23, 95%CI: 1.00, 4.97) and B (RR: 1.59, 95%CI: 1.09, 2.33). This study thus supports a toxic and carcinogenic risk to humans after significant exposure to TCDD from the soil, although the initial exposure was from an aerial release.

Nawrot et al. (2006) studied a population living in an area of Belgium contaminated with cadmium from former smelting activities (521 exposed and 473 control subjects). The cadmium concentration in soil sampled in gardens of the exposed area ranged from 0.8 to 17 mg/kg. The urinary cadmium excretion was shown to be significantly linked with the incidence of lung cancer. Adjusted hazard ratio was 1.70 (95%CI:1.13–2.57, p=0.011) for a doubling of urinary cadmium excretion, 4.17 (95%CI:1.21–14.4, p=0.024) for residence in the high exposure area versus the low-exposure area, and 1.57 (95%CI:1.11–2.24, p=0.012) for a doubling of cadmium concentration in soil.

On the other hand, results of follow-up studies of the Japanese populations exposed to high levels of cadmium did not show consistent results on cancer incidence and mortality (Arisawa et al., 2001, 2007b). Although, a significant association between
biomarker level and cancer mortality (RR: 2.58, 95% CI:1.25–5.36, n=275) was observed by Arizawa et al. (2007b), there was no significant increase of standardised incidence ratio of cancer, nor significant relationship between biomarker level and cancer incidence.

4.2.4. Conclusion

Most studies investigating cancer incidence and mortality were carried out on populations living in the vicinity of landfills. Several studies have suggested associations between residence near landfills containing hazardous waste and cancer (for example, leukaemia and cancer of the bladder). However, several other studies did not observe such a link and there is thus a general lack of consistency in the results obtained for landfills.

Other studies have investigated land contaminated with high concentrations of known specific carcinogenic chemicals. Exposure to asbestos, erionite and dioxins were shown to have effects on cancer incidence that were large enough to be detected. However, conflicting results were observed for cadmium and no increase in cancer incidence was observed for populations potentially exposed to high levels of hexavalent chromium and TNT (also known carcinogenic chemicals).

Russi et al. (2008) noted that if there is a cancer risk to populations living in the vicinity of toxic waste sites, it is likely to be of a magnitude not detectable via methodologies utilized to date. Without individual-level data on specific chemical exposures and competing risk factors over long latency periods, the significant associations seen to date are more likely due to multiple comparisons and presence of competing risk factors than a true exposure effect. Lack of a consistently occurring risk for some specific tumour across multiple studies further supports this suggestion.

4.3. Birth outcomes, developmental and reproductive effects

Studies examining developmental and reproductive effects tend to be inherently stronger than cancer studies because they avoid the major uncertainty associated with long latency between exposure and the onset of disease. Although many studies have been inconclusive or shown no reproductive effects (as described in Section 4.3.1), the larger and better-conducted studies generally have identified some cause of concern.

4.3.1. Congenital anomalies

Most single-site studies failed to demonstrate a link between contaminated land and congenital anomalies (Section 4.3.1.1). The major methodological issue with single-site studies is the low number of cases of congenital anomalies and therefore the low statistical power. For this reason, negative studies for this kind of investigation do not always provide reassurance.

A further concern associated with Love Canal was the possibility that chemicals within this site may have caused chromosomal damage. A study commissioned by the USEPA in 1980 appeared to demonstrate abnormally high chromosomal aberrations in local residents. The study was later reviewed by the USA Department of Health and Human Services who showed no significant differences from the control data (Wolff, 1984). Because the results failed to reassure residents, a further study was commissioned and focused on residents who were considered to have been maximally exposed (Heath et al., 1984). The results showed no increase in the frequency of chromosomal aberrations among Love Canal residents (n=46). In
another study however, children born in the Love Canal neighbourhood were shown to have a significantly increased risk of birth defects when compared to unexposed children (home owners and renters: OR: 1.95 (CI: 1.03-3.72) and 2.87 (1.15-7.18), respectively, Goldman et al., 1985). It is acknowledged that the statistical power of these two studies is very limited because of the difficulty in assessing the residents’ past exposure and the small sample size (239 children exposed during gestational life, Goldman et al., 1985).

Although Budnick et al. (1984) found an increase in mortality from bladder cancer in the male population of one of the counties surrounding an industrial chemical landfill in Pennsylvania compared to average mortality rates in the entire state and the USA, no excess in risk of birth defects was found (based on 3,098 births and 34 birth defect cases).

Fielder et al. (2000) compared indices of health (e.g. mortality, rates of hospital admission and measures of reproductive health) in a population living near a landfill site in Wales (Nant-y-Gwyddon, household, commercial, and industrial waste), with a control population matched for socioeconomic status. The study found no consistent differences in mortality, rates of hospital admissions or proportion of low birth-weight infants between the two populations. A significant increase in maternal risk of having a baby with a congenital abnormality was observed for residents near the site both before and after its opening. Roberts et al. (2000) reported that a former municipal waste incinerator located about 2 km southeast of the exposed area, operated from 1974 until 1987 (the study by Fielder et al. (2000) showed a peak in rates of congenital anomaly in 1988 and 1989 in the exposed wards). In addition, an older combustion plant had operated at roughly the same location since 1916. The more recent incinerator handled the area's municipal waste before the opening of the Nant-y-Gwyddon landfill site and was apparently closed because of local complaints, poor performance, and air pollution. The incinerator was located in a steep north-westerly valley running through the exposed wards, and atmospheric emissions probably extended into the study area.

The prevalence of congenital malformations at birth was increased in the vicinity of another landfill in Wales that had received domestic, commercial as well as special wastes including industrial filter cakes, fragmented industrial and metalliferous waste, contaminated soils, oily wastes and sewage screenings (OR: 1.9, CI: 1.3–2.9, Fielder et al., 2001). However, the authors could not exclude a possible artefact resulting from differences in reporting practices between hospitals.

Stockbauer et al. (1988) studied a range of reproductive outcomes (foetal death, low birth weight and birth defects) in an area of Missouri, USA where dust emission was controlled with a mixture that contained waste oil and dioxin (410 birth matched with 820 unexposed births). No significant excess was observed in any of the reproductive outcomes considered.

Despite very high soil concentration of hexavalent chromium at a site near Glasgow (UK, 900 mg/kg and around 450 mg/kg 2-3 km away), no relationship was found between congenital malformations and distance of residence from the contaminated site (Eizaguirre-Garcia et al., 2000, 2,678 cases along with the corresponding 81,057 births).

Morris et al. (2003) applied a large scale approach similarly to Elliot et al. (2001) and studied adverse birth outcomes in populations living near 61 hazardous waste landfill sites in Scotland. Relative risk of living within 2 km of a site were computed for all congenital anomalies combined, some specific anomalies and prevalence of still birth and low birth weight. None of the outcomes showed an excess risk compared to populations living more than 2 km away from a site.
Boyle et al. (2004) studied 83 landfills in Ireland using geographical and case-control approaches. No association was found with residential location relative to landfill sites for cases of congenital anomalies (2,136 cases in total).

Shaw et al. (1992) conducted a study on the risk of congenital malformations and low birth-weight in the San Francisco Bay (USA) considering different sources of environmental exposure (including landfills, chemical disposal sites, industrial sites, and hazardous treatment and storage facilities). Census tracts were classified into three categories according to estimated exposure based on existing sources of information. A small increase (1.5-fold) in risk was found for heart and circulatory malformations in the areas with potential human exposure but none of the other outcomes were significantly increased (based on 214,499 births including 5,617 congenital malformation cases). Results were adjusted for some potential risk factors (maternal age, race, sex of child, birth order) but not for socioeconomic status. No trend could be identified according to chemical classes and exposure routes.

Jarup et al. (2007) analyzed the risk of giving birth to a child with Down syndrome, associated with residence near 6,289 landfill sites (processing special, non-special and unknown waste type) in England and Wales. A large scale approach similarly to the study by Elliott et al. (2001) was used. Postcodes of maternal residence within 2 km of a landfill were classified as exposed while people living beyond 2 km comprised the reference population (n=4,640 cases within 2 km of landfill). No excess risk of Down syndrome related to landfill sites was found and adjustment for socioeconomic status did not influence the estimates. No differences in risk between hazardous waste sites and other landfill sites were found.

Zejda et al. (2000) described the results of a health survey performed in the vicinity of the largest municipal waste site in Poland. Three estimates of exposure were used: geographical location, distance and intensity of waste vehicle traffic. Based on the result of a questionnaire, occurrence of spontaneous abortion (miscarriage) seemed higher in women living closer to the site and congenital malformations were less prevalent in children born to women living closer to the site. However, it is not clear how confounding factors were included in the analysis and results showed a general lack of consistency between the three estimates of exposure.

Geschwind et al. (1992, cited in Kibble and Saunders, 2001) showed a small but significant additional risk of giving birth to a child with a congenital anomaly in mothers living closer to a hazardous waste site (OR = 1.12, CI: 1.06-1.18). The study was based on over 9000 congenital malformations and 17000 healthy controls living in the vicinity of 590 hazardous waste sites in the USA. Higher malformation rates were associated with both a higher exposure risk (no exposure risk: OR = 1.00; low exposure risk: OR =1.09, CI: 1.04-1.15; high exposure risk: OR = 1.63, 95% CI: 1.34-1.99) and documentation of off-site chemical leaks (not exposed: OR = 1.00; exposed, but no leaks at site: OR = 1.08, 95% CI 1.02-1.15; exposed, and leaks found at site: OR = 1.17, 95% CI 1.08-1.27). The dose-response relationship observed (higher risks with higher exposure) adds support to a possible causal relationship.

A study by Croen et al. (1997) based exposure measurement on both residence in a census tract containing a waste site and distance of residence from a site. A total of 764 hazardous waste sites in California (USA) were included and no increase in the risk for birth defects (neural tube, heart or oral defect) was found, using either measure of exposure. When only considering the sites appearing in the National Priority List (managed by the US-EPA, the NPL prioritises contaminated sites for cleanup, n=105), significantly elevated risks for neural tube defects and heart defects were observed for maternal residence within 0.25 mile. However, only 0.6% of the
(randomly-selected) control lived within 0.25 mile of a priority site and the authors acknowledge that this would result in imprecision in the estimate of risk.

The EUROHAZCON study was a multiple site case–control study, which used data from seven existing regional, population based congenital malformation registers in five European countries (Belgium, Denmark, France, Italy, and the UK, 21 sites with hazardous waste of non-domestic origin). Residence within 3 km of a landfill site was associated with a significant increase in the risk of congenital abnormalities (non chromosomal anomalies OR: 1.33; 95% CI: 1.11–1.59, 1,089 cases and 2,366 controls, Dolk et al., 1998; chromosomal anomalies OR=1.39, CI=0.88-2.17, 245 cases and 2,412 controls, Vrijheid et al., 2002a). Particularly large increases were found for neural-tube defects (OR: 1.86, 95%CI: 1.24–2.79), malformations of the cardiac septa (OR: 1.49, 95%CI: 1.09–2.04) and anomalies of great arteries and veins (OR: 1.81, 95%CI: 1.02–3.20; Dolk et al., 1998). There was also a fairly consistent decrease in risk of congenital anomalies with increasing distance from the hazardous waste sites in both studies. However, when each study area was examined separately, this association was not consistently found and many study areas reported no excess risk. This is not surprising as each landfill site will be different in terms of composition, topography, engineering and management and these factors greatly influence the potential for exposure to hazardous materials. Vrijheid et al. (2002b) developed and evaluated an expert panel scoring method for the hazard potential of EUROHAZCON landfill sites to investigate whether sites classified as posing a greater potential hazard were those with a greater risk of congenital anomaly among nearby residents relative to more distant residents. There was little evidence for a relation between risk of congenital anomaly relative to distant zones and hazard potential of landfill sites as classified by the expert panel. However, agreement between experts measured by intra-class correlation coefficients was relatively low and external validation of the hazard potential scoring method interpretation is difficult. Potential misclassification of sites may have reduced the ability to detect any true dose-response effect as agreement between experts when scoring the site was relatively low.

Elliott et al. (2001) presented the largest study to date on the possible association between residence near landfill and health outcomes. The health status of the population in Great Britain living within 2 km from landfill was assessed using congenital anomalies registrations, birth registrations, cancer registrations as well as hospital discharge data. The area within 2 km from landfill included 80% of the national population and more than 9000 sites were included in the study (81% non-special waste and 19% special waste sites). After adjustment for confounding factors, relative risks for congenital anomalies within 2 km of landfills were in slight excess (RR:1.01 99%CI: 1.01-1.02 for all anomalies combined; 1.05 (1.01-1.09) for neural tube defects, 0.96 (0.93-0.99) for cardiovascular defects, 1.07 (1.04-1.10) for hypospadias (male birth defect of the urethra) and epispadias (malformation of the penis) and 1.08 (1.01-1.15) for abdominal wall defects). No causal mechanisms are available to explain these findings at present. The dataset was thoroughly analyzed and the authors also found an apparent risk of congenital anomalies before landfill opened, which supports the hypothesis that the excess observed results from data artefacts and residual confounding factors. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment noted this lack of temporality for congenital anomalies and that the risk ratios were close to unity (COT, 2001). However, it also commented that the finding of a risk ratio of 1.07 for congenital anomalies overall for populations living around special waste landfill sites, whether or not it was related to the presence of the landfill sites, merited further investigation. Whilst risk ratios were higher for low and very low birth weight after landfill opening, COT considered that residual confounding might account, at least in part, for the differences in birth weight between study and reference populations (COT, 2001).
Elliott et al. (2009) presented a further analysis of the dataset. A total of 8,804 landfill sites were included in the analysis and were separated into two categories: landfill sites handling special wastes and sites handling non-special or unknown wastes. These were intersected with postcode coordinates of over 10 million births (136,821 with congenital anomalies). A landfill exposure index was calculated to represent the geographic density of landfill sites within 2 km of births for each 5x5 km grid square. For the two categories of landfill sites, the index was classified into four categories of intensity. Risks for the second, third and top categories were compared to the bottom category, comprising areas with no such landfill sites within 2 km (index of zero). For special waste sites, adjusted OR were significant for the third category of the landfill exposure index for all anomalies combined and cardiovascular defects (OR: 1.08, 95%CI: 1.02-1.13 and 1.16, 95%CI: 1.00-1.33, respectively) and for hypospadias and epispadias for the third and top categories (OR: 1.11, 95%CI: 1.02-1.21 and OR:1.12, 95%CI: 1.02-1.22, respectively). After adjustment, there were no excess risks in relation to sites handling non-special or unknown waste types.

Orr et al. (2002) focused on racial / ethnic minority infants in California. Women who lived in the same census tract as hazardous waste sites appearing on the National Priority List of the US-EPA (n=84) had a slight increased risk for giving birth to an infant with birth defects (OR:1.19, 95%CI: 0.98-1.27). The greatest association was for neural tube defects (OR:1.54, CI:0.93-2.55), particularly anencephaly (a disorder that results in the absence of a major part of the brain, skull and scalp; OR:1.85, CI:0.91-3.75). The strongest association was between potential exposure and birth defect among American Indians/Alaska natives (OR: 1.19, CI: 0.62-2.27)

Kuehl and Loffredo (2003) studied an uncommon congenital cardiovascular malformation (L transposition of the great arteries) in Baltimore children (USA). Extensive personal and occupational exposure data from parental interviews were available for all subjects (n=33). A GIS was used to identify potential environmental exposures. Over 75% of all cases occurred in two regions characterized by release of toxic chemicals into air and by hazardous waste sites (within these regions, the case-control OR was: 13.4, 95%CI, 4.7-37.8). Parental exposures to hair dye, smoking and laboratory chemicals were also associated with case status.

The epidemiological studies carried out in the region of Campania (Italy, described in the cancer section) also investigated the possible consequences of widespread uncontrolled waste dumping on the occurrence of congenital malformation. The first study by Comba et al. (2006) evaluated eleven types of congenital malformation across 196 municipalities (around 4 million people between 1994 and 2002). Two sets of municipalities with significant excesses in the total of congenital malformations and on some specific groups were identified (urogenital malformations and cardiovascular malformations). The area where municipalities exhibited higher risk of mortality and aggregate congenital malformations overlapped with the area where most illegal dumping of toxic wastes took place. Fazzo et al. (2008) further investigated the issue with a cluster analysis approach of congenital malformations at municipality level. Clusters with significant excess of total congenital malformations (RR 1.28-5.85, p <0.016) and malformations of limb (RR 1.3, p< 0.022), cardiovascular (RR 1.54-2.04, p<0.001) and urogenital system (RR 2.38-4.29, p<0.002) were observed after standardization by socioeconomic deprivation index. The clusters were concentrated in a sub-area where most of the illegal practice of dumping toxic waste had taken place. However, the level of exposure due to waste disposal remains unknown and a causal relationship cannot be inferred from this study (the area includes other environmental stressors due to intensive agriculture, industrial activities, and high population density).

Malik et al., (2004) reported a 20% increased risk of congenital heart disease for the children of mothers who lived within a mile of hazardous waste landfills in Texas,
USA (OR=1.2, CI: 1.1−1.4, 276 hazardous landfills considered, 1,283 cases and a random sample of 2,292 controls). The number of cases and controls living within 0.25 mile of a landfill was too small to support a dose-response relationship.

In Wales, Palmer et al. (2005) pooled data from populations living within 2 km of 24 landfill sites licensed to receive domestic, commercial and industrial wastes and that opened from 1983 through to 1997. They found that the ratio of observed to expected rates of congenital anomalies (n=2,633 cases) increased by about 40% after opening (standardized RR: 1.39; 95%CI:1.12−1.72). However, this increase did not persist in data collected between 1998 and 2000 (standardized RR: 1.04; 95%CI:0.88−1.21). Causal inferences are difficult because of possible biases from incomplete case ascertainment, lack of data on individual-level exposures, and other socioeconomic and lifestyle factors that may confound a relationship with area of residence.

Kuehn et al. (2007) studied more than 900 hazardous waste sites in Washington State (USA). Residential proximity to both low and high priority sites according to the US-EPA National Priority List was associated with increased risk of malformation that decreased with distance of residence from sites (n=63,006 cases). Relative to living more than five miles away from a site, living less than 5 miles away was associated with increased risk of any malformations in offspring (for 2<d<5 miles: OR 1.15; 95%CI: 1.10-1.21; 1<d<2 miles: OR 1.26, 95%CI: 1.20-1.32; 0.5<d<1 mile: OR 1.28, 95%CI: 1.22-1.35; for d<0.5 miles: OR 1.33, 95%CI: 1.27-1.40.). Although some confounding factors were accounted for (e.g. employment, marital status, education and medical insurance status; none of which changed the associations), the authors admit that the ability to measure socio-economic status is still restricted and that this limits the ability to control for any related confounding influences.

No single-site studies could unequivocally demonstrate a link between land contamination and congenital anomalies. The statistical power of single site studies to detect an effect is limited because of the difficulty in assessing the residents’ past exposure and the small sample size (as for the studies with hexavalent chromium, Eizaguirre-Garcia et al., 1999 and dioxins, Stockbauer et al., 1988).

Most multiple site studies demonstrated a link between residence near landfills and birth defects. It must be acknowledged that the number of anomalies included in the analysis may result as an artefact of multiple testing. Nevertheless, several recent multiple site studies (Orr et al., 2002, Comba et al., 2006, Malik et al., 2004, Palmer et al., 2005, Kuehn et al., 2007) support the results of previously well conducted studies (e.g. Geshwind et al., 1992, Elliott et al., 2001) that residence near hazardous waste sites may be associated with increased risk of congenital anomalies. Some studies have shown important relationships supporting a causal relationship such as association with exposure through time (increased risk after opening of the site, Palmer et al., 2005) or with decreasing distance of residence to landfills (Kuehn et al., 2007) or intensity of exposure (higher risk where most illegal dumping occurred Fazzo et al., 2008).

4.3.2. Low birth weight/preterm deliveries

Although most epidemiological studies carried out on the residents of the Love Canal site showed no evidence of a higher incidence of cancer or congenital anomalies, results of Vianna and Polan (1984) and Goldman et al. (1985) suggest a possible link between exposure to waste and incidence of low birth weight. Vianna and Polan (1984) studied the incidence of low birth weight among the resident of the Love Canal from 1940 through to 1978. Significant excess was found in the historic swale area from 1940 through 1953, the period when various chemicals were dumped in this disposal site (compared to upstate New York, p <0.0001). Potential confounding
factors (e.g. smoking, education, maternal age) did not appear to account for this observation. Rates were comparable to those of upstate New York from 1954 through 1978, the period when there was no deposition of chemical wastes. In addition to the excess in birth defects, (Goldman et al., 1985) also showed that children born to homeowners in the Love Canal neighbourhood had an average decrease in birth weight of 50 g and a higher prevalence of low birth weight (OR = 3.0, CI 1.7-7) when compared to unexposed children.

Several other single site studies have demonstrated excess risks for low birth weight for resident near landfills. Kharrazi et al. (1997) investigated adverse pregnancy outcomes for the population living near a hazardous waste landfill in California (n=25,216 births). Three indirect methods were used to estimate exposure and odour complaints seemed to be a better indicator for exposure than distance to the landfill or census tract of residence. Adjusted risk ratios showed no effect on birth outcome for 1978-1986. However, for 1981-1984, the period of highest estimated exposure, low birth weight and gestational age were significantly reduced (p=0.02 and 0.05, respectively).

Goldberg et al. (1995b) demonstrated excess risks for low birth weight (adjusted OR: 1.20; 95%CI: 1.04-1.39) and small size for gestational age (adjusted OR: 1.09; 95%CI: 0.96-1.24) in the residents of the exposure zone proximal to an actively gassing municipal solid waste landfill in Montreal (Quebec, domestic, commercial and industrial wastes). No excess was observed for very low birth-weight and preterm birth (based on 12,665 births, 7,977 cases and 7,856 controls).

Berry and Bove (1997) studied birth-weight at a site for municipal and industrial waste in New Jersey (USA). The site closed in 1971 after complaints of residents, but the heaviest exposure to toxic waste was estimated to have occurred during the late 1960s to the mid-1970s due to runoff and air emissions into the neighbouring community and contamination of a local lake. From 1971 to 1975, full term births to parents living within a radius of 1 km to the landfill (n=6,600) had a significant higher proportion of low birth-weight (<2500 g, OR: 5.1; CI: 2.1-12.3) than a control population (n=30,000; 11,579 births were included overall). Similarly, infants had twice the risk of prematurity (OR:2.1; CI:1.0-4.4) during 1971-75 compared to the control group. Although information on some confounding factors was not available, mothers in the exposed area appeared to be of higher socioeconomic status (indicated by better prenatal care and a higher level of maternal education). If the result was confounded by socioeconomic status and lifestyle factors, the bias would likely be towards the null. In addition, birth weights were higher in the area closer to the site than in the control area before and after the period with greatest off-site pollution (late 1960s to mid-1970s). This supports the hypothesis that low birth-weights in the community close to the waste site during the period of maximum potential exposure may have been related to pollution from the site.

Baibergenova et al. (2003) evaluated the consequences of living near a PCB hazardous waste site or near a body of water contaminated with PCBs in New York State (USA, total number of births = 945,077). The birth weight in the PCB postcodes was on average 21.6 g less than in other postcodes (p<0.001) and there was still a statistically-significant increased risk of 6% after adjustment for confounding factors.

Finally, prevalence of preterm deliveries has also been linked to exposure to high concentrations of cadmium. Nishijo et al. (2002) showed that the rate of preterm deliveries was significantly higher for mothers with higher urinary cadmium for a population of Japanese women (n=57) living in the Jinzu river basin, historically contaminated with very high concentrations of cadmium (p<0.01 after adjusting for maternal and gestational age). A significant and positive correlation was found between maternal urinary cadmium and cadmium in breast milk. The lack of
relationship between maternal exposure to cadmium and level in breast milk previously reported by studies carried out in Europe can probably be explained by a much lower concentration of cadmium in breast milk in European countries (<0.9 nmol/L, Schramel et al., 1988; Oskarsson et al., 1998) compared to the Japanese studies (average 4.6 nmol/L, Nishijo et al., 2002).

Morgan et al. (2004) investigated the risk of low birth-weight near 10 English hazardous waste landfill sites included in the EUROHAZCON study (of 205,227 babies, 11,465 (5.6%) had a birth weight <2500g). A small increase in risk of borderline significance was found within 3 km of hazardous waste landfill sites compared with 3-7 km zones (OR: 1.03, 95%CI: 0.98-1.08). This was substantially smaller than excess risk of congenital malformation near the same sites calculated from EUROHAZCON data (Dolk et al., 1998; Vrijheid et al., 2002a).

Elliott et al. (2001) also assessed possible consequence of living near landfill in Great Britain on birth-weight (n>9,000 landfills). Slight excess risks for low birth weight were observed (low birth-weight RR: 1.05, 99%CI: 1.05-1.06; very low birth weight RR: 1.04, 99%CI: 1.03-1.05). Unlike the study by Morgan et al. (2004), these slight excesses were significant in the Elliot et al. (2001) study and this may have been due to the greater statistical power that was achieved by including the whole population of Great Britain (based on the birth registrations of England, Wales and Scotland 1983-1998).

Despite a relatively low statistical power, several single site studies have demonstrated a significant link between residence in the vicinity of landfills and the prevalence of low birth weight and/or preterm delivery. Low birth weight and preterm deliveries are much more frequent than congenital anomalies. In the study by Elliott et al. (2001) for instance, the occurrence of low birth weight cases was four times more frequent than all congenital anomalies together when considering the entire population of Great Britain. A difference between exposed and non-exposed population is therefore easier to demonstrate compared to rarer outcomes. Results on low birth weight and preterm deliveries are relatively consistent and temporality was demonstrated on several occasions (Kharrazi et al. (1997; Berry and Bove (1997). Literature thus provides an overall good weight of evidence supporting a link between low birth weight and residence in the proximity of landfill sites.

### 4.3.3. Foetal death/still birth/infant death

In comparison to the great number of studies which have addressed the risk of congenital anomaly or low birth weight in relation to proximity to landfill sites, only a few considered the risk of still birth or neonatal death. Results from these investigations do not suggest a link between residence near landfill sites and foetal death (Elliott et al., 2001, Dummer et al., 2003). On the other hand, a link to specific foeto-toxic chemicals is suggested by the results of Mueller et al. (2007).

In their very large-scale study considering the entire British population, Elliott et al. (2001) did not find excess risk of stillbirth for maternal residence nearby a landfill. Dummer et al. (2003) examined all causes of stillbirth and infant death in Cumbria (UK) between 1950 and 1993 (4,325 stillbirths, 3,430 neonatal death and 1,569 lethal congenital anomalies that occurred among 287,993 births). Deaths from congenital anomalies were grouped into five classes according to the anomaly. Overall, results do not suggest an increased risk of still birth or neonatal death with proximity to landfill sites. Although a small but significant increased risk of death from “other congenital anomalies of nervous system” was associated with household and putrescible waste landfill sites, no data on exposure level or chemical are available. A
causal effect cannot thus be inferred and there is a possibility for a chance finding in view of multiple testing.

Mueller et al. (2007) showed that foetal deaths for women residing near hazardous waste sites in the USA (n=939 landfills) were not associated with the distance of residence to the site. However, an association was observed among women residing less than one mile from pesticide–containing sites. When distance to the site was used as a continuous variable, a 1% decrease in the odds ratio with each additional mile of distance was observed (p < 0.05).

4.3.4. Mental retardation

Aelion et al. (2008) identified an area in South Carolina, USA with a significantly higher prevalence of mental retardation and developmental delay (MR/DD) in children compared to the state-wide average. After matching for an area without prevalence of MR/DD, these two areas were mapped and surface soil samples were collected (0–5 cm depths) and analyzed for arsenic, barium, beryllium, chromium, copper, lead, manganese, nickel and mercury. All metal concentrations in the MR/DD cluster area were significantly greater than those in the area with no excess (the origin of the metals was not elucidated). A further analysis of the data showed that association between metal concentrations and MR/DD could be made in the urban area, but not in the rural area studied (Aelion et al., 2009). Exposure levels were not assessed and together with the findings of the latter study, results do not support a direct causation between environmental soil metal concentrations and MR/DD.

4.3.5. Semen parameters

Differences in semen parameters have been described between two regions in Flanders, Belgium with a suspected difference in environmental exposure (mainly due to cadmium contamination). Dhooge et al. (2007) investigated whether these differences were associated with lifestyle or environmental factors. Men consuming locally-produced vegetables (n=37 out of 94) but not fruit had significantly lower serum-free testosterone and luteinizing hormone (p=0.04). No relationship was found with lifelong exposure to cadmium (as reflected by urinary concentration of cadmium). The surprisingly strong impact of self-grown vegetable consumption did not seem to be related to soil contamination by cadmium. The study authors inferred pesticide exposure by inappropriate application or other factors such as nutritional deficiency, physical activity, or stress as possible alternative explanations for difference in semen parameters.

4.3.6. Conclusion

No single-site studies could unequivocally demonstrate a link between contaminated land and congenital anomalies. This can be partly explained by the low statistical power of such studies investigating rare health outcomes. On the other hand, several recent multiple-site studies support the results of previously well conducted studies that residence near hazardous waste sites may be associated with increased risk of congenital anomalies. In addition, some studies demonstrated causal relationships such as an increased risk after opening of the site, with decreasing distance of residence to landfills or intensity of estimated exposure

In spite of a relatively low statistical power, several single site studies have demonstrated a significant link between residence in the vicinity of landfills and the
prevalence of low birth weight and/or preterm delivery. Results are relatively consistent and temporality was demonstrated in several occasions.

In comparison to the great number of studies which have addressed the risk of congenital anomaly or low birth weight in relation to proximity to landfill sites, only a few considered the risk of still birth or neonatal death. Although a link to specific foeto-toxic chemicals has been suggested, results from these investigations generally do not support a link between residence nearby landfill sites and foetal death.

Other developmental and reproductive outcomes such as mental retardation or semen parameters have been investigated. However, the number of studies is very restricted and results were generally inconclusive.

4.4. Physical effects

Contaminated land can represent a physical hazard to site users. Landfill gas can cause explosion and fire. Explosions have occurred under houses built near to former landfill sites in Loscoe (Derbyshire) in 1986 and Kenilworth (Warwickshire) in 1989 (Kibble and Saunders, 2001).

Sites may also present physical dangers such as shafts, holes, tanks, tunnels, dilapidated structures and subsidence due to collapse of underground workings. The colliery spoil slide at Aberfan in 1966 killed 144 people including 116 school children (Kibble and Saunders, 2001).

Generally, the controls on such physical effects have improved markedly over time, partly in response to the events mentioned above. No evidence for more recent impacts of physical effects on human health was found in the review.

4.5. Grey literature

Whilst the primary focus of this review was on scientific investigations into impacts of contaminated land on human health, the grey literature was also searched for specific instances where linkages were reported. The search included web sites and the press and specifically excluded journal articles, conference proceedings, research and policy reports that are cited in the remainder of the review. It was restricted to reports where documented ill health was linked to a specific site in the UK that was known to have contaminants present. Many media reports address potential impacts of land (particularly land used for housing) that has either been declared contaminated or is under investigation as potentially contaminated. Such reports rightly identify significant concerns on the part of the public, but they were excluded if actual harm to health had not been recorded. Reports in the grey literature to instances such as Shipham that are covered within peer-reviewed work were excluded. The results of the review of the grey literature are given in Table 1.2.
Table 1.2. Summary of grey literature that links contaminated land and impacts on human health

<table>
<thead>
<tr>
<th>Date</th>
<th>Location</th>
<th>Site details</th>
<th>Incident</th>
<th>Impact</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1986</td>
<td>Loscoe, Derbyshire</td>
<td>Infilled quarry adjacent to brickworks</td>
<td>Explosion due to methane &amp; large fall in barometric pressure</td>
<td>One bungalow destroyed. No injuries</td>
<td>Near miss</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1984</td>
<td>Abbeystead, Cumbria</td>
<td>Valve house</td>
<td>Explosion due to methane gas</td>
<td>16 killed</td>
<td>Methane thought to have been from natural sources</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2004/05</td>
<td>Leftwich, Cheshire</td>
<td>Residential estate</td>
<td>Benzene contamination</td>
<td>Two toddlers die from rare from of leukaemia (acute myeloid leukaemia)</td>
<td>Health Protection Agency investigation says no evidence of health risk; families rehoused on compassionate grounds</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1985-1999</td>
<td>Corby steelworks</td>
<td>Ex-steelworks that was demolished, excavated and redeveloped</td>
<td>Removal of waste of unknown composition to allow redevelopment</td>
<td>Sixteen cases of children born with birth defects (deformed limbs; two further cases rejected by High Court Judge)</td>
<td>Corby Borough Council appealing a recent High Court ruling in favour of families involved</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>Stratford, London</td>
<td>Former paint factory</td>
<td>Leakage of naphthalene</td>
<td>BBC’s Watchdog programme reported that health of residence was adversely affected</td>
<td>No further details on nature of impacts found</td>
</tr>
</tbody>
</table>

The instances reported in Table 1.2 are of great concern to local residents. Investigations into the Leftwich case failed to find a link between the low-level presence of benzene and the death of two (biologically unrelated) young girls from leukaemia. There has been a long-running court case related to waste disposal from the Corby steelworks that has recently found in favour of the defendants who claim a link between remediation works and the birth defects (although no causal link has been established). It is possible that some additional cases have been missed within the grey literature, either because material is not available in electronic form or because the search terms for such material are so disparate that exhaustive search is extremely difficult. Nevertheless, it is notable that there are very few instances of health impacts that are directly linked to contaminated land within the grey literature.
The instances at Leftwich and Corby do not conflict with the known literature in that expert review has found no link for the leukaemia cases but sufficient evidence to satisfy the Courts of a plausible link in the Corby case. The BBC’s Watchdog programme reported in 2006 that the health of residents in Stratford, London was “impacted” by exposure to naphthalene released from a former paint factory. No further details on the nature of these impacts were found in the literature. The UK does not have a large number of cases where links between contaminated land and impacts on human health have been postulated within the grey literature but not yet investigated in peer-reviewed works.

5. Overall conclusion

As noted by previous reviews of this topic, the available literature has several important shortcomings that are imposed by the nature of the impacts under investigation, by lack of consistency in methodological approach and, sometimes, by shortcomings in study design. Nevertheless, it is important to draw out such information as is available from the literature. These aspects are dealt with in turn below.

5.1. Shortcomings in available studies

Failure to properly characterise exposure is a major shortcoming across the available literature for impacts of contaminated land on human health. The great majority of studies considering hazardous waste sites make no attempt to characterise the contaminants that are present at a particular location. Direct exposure measurements are almost never available and most studies rely on residential distance from the site as a surrogate measure of exposure or occasionally use exposure modelling. Kibble and Saunders (2001) are critical of the “many studies [that] are undertaken where there is little or no evidence of any viable route of exposure”. Distance of residence from contaminated land is a poor surrogate for exposure to contaminants via the atmosphere and does not adequately represent exposure via a source of drinking water, food or contact with soil. Characterisation of exposure has been particularly challenging when investigating potential to cause cancer due to the long gestation period for the disease, extensive imm- and em-igration from study areas and the large number of confounding factors that potentially contribute to the disease.

Studies on health impacts associated with land contaminated with cadmium demonstrate the importance of properly characterising exposure. Clear causality was established for exposure of Japanese populations through eating rice grown on contaminated land, leading to itai-itai disease (severe renal/bone disease). The Shipham case study in the UK involved soil residues of cadmium that were up to 10 times larger than those in Japan. Despite this, there is no consistent evidence for long-term health impacts at Shipham and this is attributed to a much smaller reliance of the local population on locally-grown produce (Elliot et al., 2000).

Several authors including Vrijheid (2000) and WHO (2007) cite the treatment of confounding factors and bias as further reasons for lack of definitive evidence for or against impacts on health. There is no consistent approach in controlling for confounding factors and different studies will control for different factors according to study-specific decisions made by the researchers and presumably influenced by the availability/ease of collection of data on different factors. Socio-economic status is a key determinant for health, but methodologies to characterise deprivation are under-developed (WHO, 2007).
Several studies in the literature test for multiple effects, thus greatly increasing the chance of a Type 1 error (false positive; WHO, 2007). Single-site studies offer the opportunity for analysis based on detailed case-histories and more robust exposure assessment. However, such studies generally lack sufficient sample size to detect changes in health outcomes that are likely to be rather small overall (relative risks where calculated are generally between 1 and 2 and only in a very small number of instances exceed 4). Investigations considering multiple sites can better address the challenges of sample size, but mostly do so at the expense of proper characterisation of exposure and control of confounding factors.

5.2. Overall state of knowledge on impacts of land contamination on human health

Russi et al. (2008) conclude that progress in determining any impact of contaminants in hazardous waste sites on cancer risk will require “assembly of a massive collection of individual-level exposure data to toxic waste site chemicals over long periods of time and a detailed individual-level assessment of competing cancer risk factors. The likelihood is low that so detailed an assessment will ever be undertaken.” Whilst study of diseases with shorter latency period is more tractable, it seems reasonable to suggest that definitive studies to demonstrate whether or not land contamination in general impacts on human health are equally distant at present. However, despite the methodological limitations, the scientific literature does contain evidence for impacts of contaminated land on specific aspects of health.

The largest volume of work into health impacts from contaminated land has considered various effects associated with potential exposure to chemicals from hazardous waste disposal sites. A workshop was organised in 2007 by the Regional Office for Europe of the World Health Organisation (WHO, 2007). Available evidence on the health effects of environmental exposures from landfills (and waste incinerators) was reviewed and discussed by a group of international experts in epidemiology, environmental science, public health and economics. Results of the analysis were compiled in a report (WHO, 2007) and are summarised in Table 1.3.

The scale against which the evidence was assessed was developed by Wigle (2003):

1. **Sufficient evidence** is based on peer-reviewed reports of expert groups or authoritative reviews.

2. **Limited evidence** includes relationships for which several epidemiological studies (including at least one case-control or cohort study) showed fairly consistent associations and evidence of exposure-risk relationship after control for potential confounders.

3. **Inadequate evidence** is used for a relationship for which epidemiological studies were limited in number and quality (for example, small studies, ecologic studies, limited control of potential confounders), had inconsistent results, or showed little or no evidence of exposure-risk relationships.
Table 1.3. Summary of epidemiological evidence for health effects associated with exposure to contaminants from hazardous waste disposal sites (WHO, 2007)

<table>
<thead>
<tr>
<th>Health effect</th>
<th>Level of evidence</th>
<th>Health effect</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early foetal deaths</td>
<td>Inadequate</td>
<td>Oro-facial birth defects</td>
<td>Inadequate</td>
</tr>
<tr>
<td>(spontaneous abortion)</td>
<td></td>
<td>Musculoskeletal birth defects</td>
<td>Inadequate</td>
</tr>
<tr>
<td>Late foetal deaths (stillbirths)</td>
<td>Inadequate</td>
<td>Genitourinary birth defects</td>
<td>Limited</td>
</tr>
<tr>
<td>Intrauterine growth</td>
<td>Inadequate</td>
<td>Musculoskeletal birth defects</td>
<td>Inadequate</td>
</tr>
<tr>
<td>retardation</td>
<td></td>
<td>Genitourinary birth defects</td>
<td>Limited</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>Inadequate</td>
<td>Gastrointestinal birth defects</td>
<td>Inadequate</td>
</tr>
<tr>
<td>Birth weight adjusted for</td>
<td>Inadequate</td>
<td>Chromosomal abnormalities</td>
<td>Inadequate</td>
</tr>
<tr>
<td>gestation length</td>
<td></td>
<td>(structural)</td>
<td></td>
</tr>
<tr>
<td>Term birth weight</td>
<td>Inadequate</td>
<td>All childhood cancers</td>
<td>Inadequate</td>
</tr>
<tr>
<td>Low birth weight (not adjusted for gestation</td>
<td>Limited</td>
<td>Leukaemia</td>
<td>Inadequate</td>
</tr>
<tr>
<td>period)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm birth, gestation length</td>
<td>Inadequate</td>
<td>Lymphoma</td>
<td>Inadequate</td>
</tr>
<tr>
<td>Total birth defects</td>
<td>Limited</td>
<td>Reproductive system development</td>
<td>Inadequate</td>
</tr>
<tr>
<td>Central nervous system birth defects</td>
<td>Limited</td>
<td>Thyroid function</td>
<td>Inadequate</td>
</tr>
<tr>
<td>Cardiovascular birth defects</td>
<td>Limited</td>
<td>Kidney function</td>
<td>Inadequate</td>
</tr>
</tbody>
</table>

The conclusion reached by WHO (2007) is consistent with earlier statements by Kibble and Saunders (2001) that (i) evaluations of increased incidence of cancer associated with residential proximity to contaminated sites are inconsistent, and (ii) there is a stronger link between landfill sites and/or contaminated land and reproductive effects (primary congenital anomalies and low birth weight).

Within the current review, the other extensive body of evidence that emerges is that for impacts of land contaminated with cadmium on human health. Clear causality has been established for severe renal and bone disorders under conditions of high dietary exposure to cadmium (e.g. exposure via a diet dominated by locally-grown rice in parts of Japan and China; rice has an unusual ability to accumulate cadmium in the grains). At much lower exposures, links have been established between cadmium exposure and biomarkers of renal or bone dysfunctions; at these lower exposures, the link to health impacts per se is not generally established. Soil concentrations are not a direct surrogate for exposure and there are examples where residents in locations with very large concentrations of cadmium in soil did not appear to suffer serious health consequences; this finding is attributed to specificities of exposure, particularly differences in diet.

The scale developed by Wigle (2003) and subsequently deployed by WHO (2007) provides a useful framework to summarise the findings of this review, albeit that it draws on a much narrower pool of expertise than WHO can deploy. Table 1.4 presents a perspective on extent of evidence for impacts for contaminated land in general rather than just for hazardous waste sites.
Table 1.4. Summary of epidemiological evidence for health effects associated with exposure to contaminants from contaminated land (top-level conclusions from the current review)

<table>
<thead>
<tr>
<th>Health effect</th>
<th>Level of evidence</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress, anxiety, psychiatric disorders</td>
<td>Sufficient</td>
<td>Evidence primarily relates to hazardous waste sites, but likely to be a more generalised phenomenon</td>
</tr>
<tr>
<td>Throat, eye, skin irritations</td>
<td>Inadequate</td>
<td>Studies are largely confounded by potential reporting bias</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Inadequate</td>
<td>No evidence so far</td>
</tr>
<tr>
<td>Renal dysfunction and bone damage</td>
<td>Limited</td>
<td>Causality has been established under conditions of high exposure to cadmium due to dietary intake; evidence for effects under lower exposure situations is contradictory and/or based on biomarker responses rather than health impacts.</td>
</tr>
<tr>
<td>Cancer</td>
<td>Inadequate</td>
<td>Evidence is inconsistent and exposure is inadequately characterised. Some specific links have been established (naturally-occurring asbestos, sites significantly contaminated with dioxins)</td>
</tr>
<tr>
<td>Birth defects</td>
<td>Limited</td>
<td>Evidence from multiple site studies is relatively consistent and causality was established with proxies of exposure from hazardous waste sites</td>
</tr>
<tr>
<td>Low birth weight / preterm deliveries</td>
<td>Limited</td>
<td>Studies are largely related to landfill sites. Evidence is relatively consistent and temporality was demonstrated on several occasions</td>
</tr>
<tr>
<td>Foetal death / stillbirth / infant death</td>
<td>Inadequate</td>
<td>The few studies investigating this outcome do not support an effect</td>
</tr>
</tbody>
</table>

Bradford-Hill’s criteria (1965) can be used in the assessment of evidence for causation of health impacts by exposure to contaminated land:

1. Strength: most additional risk factors are relatively small, though this does not mean that there is not a causal effect.
2. Consistency: findings regarding reproductive effects from potential exposure to landfill sites are relatively consistent as are health impacts at high exposure (e.g. the link between cadmium and renal disorders); consistency is missing for most other associations.
3. Specificity: this has proved very difficult to demonstrate for all but a few impacts at high exposure.
4. Temporality: almost all studies are retrospective, but some studies do report temporality (e.g. congenital anomalies Palmer et al., 2005; birth weight: Vianna and Polan, 1984; Kharrazi et al., 1997; Berry and Bove, 1997; mortality in Japan: Arizawa et al., 2007a; biomarkers in Belgium: Staessen et al., 2000).
5. Biological gradient: relationships between dose and biomarker responses have been demonstrated for exposure to cadmium; gradients for exposure surrogates have also been demonstrated for some studies linking reproductive effects with proximity of mother’s residence to landfill sites.
6. Plausibility: the potential for health impacts is generally biologically plausible although plausible routes of exposure are not always defined (Kibble and Saunders, 2001).

7. Coherence: generally coherence between epidemiological and laboratory findings has not been an objective of study; those studies that link exposure to health-related biomarkers generally fall short of looking at health impacts and vice versa.

8. Experiment: not relevant in the current context.

9. Analogy: some analogy with worker exposure is drawn within the literature, but this fails to address the extrapolation step between high and low exposures.

The top-level conclusions provided in Table 1.3 should be considered within the context of two important points. The first is that a lack of evidence does not mean that there is no effect. The absence of an established link between contaminated land and health in the UK may also be partly the result of limitations in risk assessment and epidemiological techniques (Kibble and Saunders, 2001).

Secondly, the assessment of risks to health contained within the literature refers to the potential for impacts under the conditions that were pertaining at the time considered by the study. Much of the literature refers to potential exposure occurring over the last 30-40 years. There have been significant improvements in our understanding and management of potentially contaminated land during this period that are likely to lead to significantly lower exposures today than would have occurred in the 1970s, for example. Set against this, pressure for land continues to expand the stock of potentially contaminated land that is released for housing or other uses where the public may come into contact with contaminants. Overall, it seems unlikely that the potential for widespread impacts of contaminated land on health are increasing over time.

5.3. Suggestions for further work

The review demonstrates that causal inferences are difficult because of possible biases from incomplete case ascertainment, lack of data on individual-level exposures, and other socioeconomic and lifestyle factors that may confound a relationship with area of residence (Palmer et al., 2005). This suggests, as noted earlier in this report, that the study design most likely to provide interpretable information for all the health outcomes discussed in this report are likely to be prospective investigation of sufficient statistical power and well-collected and relevant exposure data. Conversely, further studies of a cross-sectional nature are unlikely to be helpful.

Several authors have noted the prohibitive nature of studies that would be required to provide definitive evidence for or against cause-and-effect for those health impacts such as cancers that have long gestation period. Nevertheless, these authors call for continued surveillance for potential impacts to provide the necessary safeguards and alert to specific issues for intensive study (Russi et al., 2008).

Further insights on health effects of contaminated land are likely to be gained from studies that consider exposure pathways and biomarkers of exposure and effect, and compare waste-related exposures with those due to other sources of pollution. (WHO, 2007). Biomarkers for both exposure and effect have been deployed with some success in investigating impacts of cadmium on human health. Extension of such approaches to other common contaminants should add greatly to the current knowledge bank.
6. References


International Archives of Occupational and Environmental Health, 55, 217-239.


WATANABE, Y., KOBAYASHI, E., OKUBO, Y., SUWAZONO, Y., KIDO, T. & NOGAWA, K. 2002. Relationship between cadmium concentration in rice and...


APPENDIX A

The database ISI web of Science was searched for references. However, considering the wide variety of keywords involved in the theme, most papers were identified by cross reference.

Search keywords in the database ISI web of Science were as follow:

1. by contaminants (917 titles found)
   human health and soil and
   metal or cd or cadmium or Ni or nickel or Co or cobalt or Pb or lead or As or arsenic or phenol or cyanid or sulfite or sulfide or sulphate or wood or pentachlorophenol or PAH or benzene or benzo[a]pyrene or benzo-[a]-pyrene or perchloroethylene

2. by contaminated land type (828 titles found)
   human health and soil and
   contaminated land or landfill or waste or smelter or plant

3. by health effect (1080 titles found)
   soil and human and
   mortality or cancer or leukaemia or stress or anxiety or self reported or urinary or renal or disorders or respiratory or developmental or reproductive or congenital or birth weight