Performance of several decision support tools for determining the need for systematic screening of childhood lead poisoning around industrial sites

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Background: Living around industrial sites may expose young children to lead and cause elevated blood lead levels (BLLs). Systematic screening for childhood lead poisoning is necessarily invasive but may be appropriate, depending on children's exposure levels. Our objective was to assess the performance of several decision support tools for determining the need for systematic BLL screening in children around industrial sites. Method: We used several exposure models to predict BLLs: the pharmacokinetic model IEUBK, the InVS dose model, and an empirical relation (Lewin, 1999) between soil concentrations and BLLs. We tested the BLLs (percentage of children with a BLL >100 μg/l) that they predicted as well as threshold levels of soil pollution (200, 400, 500 ppm) for 71 situations for which the literature reports both environmental soil concentrations and BLLs in children aged 0–6 years. The tools' performance (sensitivity and specificity) was assessed by the rate of 'correct' (mass screening or not) decisions, judged retrospectively on the basis of measured BLLs, for different tolerated percentages of children with elevated BLLs. Results: Decision support systems based on soil pollution levels were not adequately protective. The IEUBK and (updated) InVS mechanistic exposure models were the most effective in this setting. Conclusion: Exposure models may provide decision support if sufficient data about environmental contamination and dietary intake are available. Absolute performance measurement nonetheless remains difficult, in view of the limitations of the input data.

Keywords: blood lead screening, environmental exposure, lead exposure, lead exposure modelling, lead poisoning, soil pollution

Introduction

Lead is a cumulative toxic pollutant that is absorbed by the pulmonary and gastrointestinal routes and causes neurobehavioural problems, learning disabilities, and mental retardation in children. Because of their behaviour, especially their hand-to-mouth activity, young children (0–6 years) are particularly exposed to lead dust, both in dwellings with old lead paint and around industrial sites with past or ongoing lead emissions. The impact of industrial lead sources, especially smelters, on the blood lead level (BLL) of children living nearby, was first noticed a century ago and has been widely documented since the 1970s. The influence of emissions persists long after they are noticed, which is usually defined by a BLL >100 μg/l, although this cut-off point is somewhat arbitrary today, given recent findings about the effects of low doses of blood lead poisoning that necessitates individual management. Because of the test's invasiveness (blood sample required) and the alarm that mass screening may cause in a community, such programmes are recommended only for populations selected according to criteria for possible lead exposure. The United States has recommended targeted screening rather than universal screening since 1997. In 2003, a consensus conference on lead poisoning among children and pregnant women in France concluded that BLL screening should consider children living near industrial sites to be a priority. Public health authorities in the many countries where industrial sites do or did emit lead must make decisions about such screening.

Once a decision is made to screen for elevated BLLs around targeted industrial sites, it becomes essential to define the criteria that determine its relevance at a particular site. The presence of a lead source alone is not a sufficient criterion since lead emissions do not necessarily indicate significant overexposure of children. It has been suggested that soil lead levels may serve as a sensitive and robust environmental diagnostic tool to predict areas where children will have elevated BLLs.

We propose here to examine and compare the usefulness of several decision support tools that use environmental information to predict overexposure of a population of children. These diagnostic tools are intended to provide guidance for decisions that must also include social and political aspects, which are not considered here. The objective of this study is to compare their ability to make the 'correct' decision about whether or not to set up systematic screening. The tools tested here are based solely on environmental information (thresholds based on soil contamination levels) or on exposure assessed by either a mechanistic model (predicting external and/or internal doses) or an empirical relationship based on soil lead concentrations.

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Material and methods

Decision support tools tested

Several decision support tools were compared by retrospective application to industrial sites for which levels of both environmental contamination and blood lead in young children (0–6 years) are known. The criterion for implementing mass screening was the proportion of children with BLLs >100 μg/l; we assumed that above a given level (and we tested several), systematic screening was appropriate. In populations where BLLs were measured in unbiased samples, we know whether systematic screening was appropriate. In populations where we assumed that above a given level (and we tested several), the percentage depends on the situation and involves a policy choice: we therefore compared these tools for several different proportions of children with BLLs >100 μg/l: 1, 2, 4, 6, 8, 10, and 20%. This study tested the following tools:

- Comparison of (measured) soil contamination with cut-off points (200, 400, or 500 ppm). Such values are frequently cited in the literature as a basis for determining the appropriateness of a health risk assessment or remediation for a given site.12,13
- Comparison of predicted BLLs (geometric mean and percentage of children with BLLs >100 μg/l) with given cut-off points. In practice, this involves modelling BLLs from environmental concentrations. We compared the following models:
  
  - The pharmacokinetic IEUBK model (Integrated Exposure Uptake Biokinetic Model for Lead in Children), developed by the US Environmental Protection Agency to furnish plausible estimates of BLLs in children as a function of their multimedia exposure to lead. This model is fully described by White et al.14
  - The ad hoc model developed15 in France by the Institute for Public Health Surveillance (InVS). BLLs are estimated by modelling the external dose from the lead concentrations in the environment, human exposure factors, and a linear dose-to-BLL model from WHO:16 1.6 μg(Pb)/l (blood) per μg(Pb)/day ingested (diet, water or dust and soil) + 19.2 μg(Pb)/l (blood) per μg(Pb)/l (air). This model, initially constructed with intentionally overestimated exposure indicators, was designed to be associated with a recommendation for systematic screening if the BLL predicted for an average individual is greater than the intervention threshold of 100 μg/l, or the cut-off point of 250 μg/l for a particularly exposed individual (because of unfavourable behaviour or environment). We tested both this original model (InVS_original) and an updated version (InVS_updated), which does not overestimate the exposure indicators. The distribution around the mean BLL was estimated by considering a geometric standard deviation of 1.6. Details: InVS_original is adapted for 0–6 year olds: averaged indicators (dietary intake, water consumption water) from 2 to 6 years. The ‘high value’ of soil and dust concentrations are calculated as the geometric means ×2GSD, with GSD = 1.6. Quantity of soil and dust ingested: 100 mg/d (60% dust, 40% soil, x4 for ‘unfavourable’ behaviour). Soil bioavailability (compared with food) = 1. In VS updated (InVS_updated): idem, with updated exposure parameters from recent data: dietary intake,17 water consumption,18 and lead soil bioavailability 3/5 relative to food.
  - Levin’s empirical model,18 which predicts mean BLLs based on soil lead concentrations. It is based on observations around industrial sites and is near the median (+50 μg/l for +1000 p.p.m.) of the other models:19

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\text{Ln}(\text{BLL}) = 0.2758 + 0.2438 \text{Ln} (\text{Soil lead level})
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The distribution around this mean BLL was estimated by considering a geometric standard deviation of 1.6.

We used Excel® to run all models except IEUBK, the software available from the US Environmental Protection Agency website.

This study is not a standard comparison of models, although we did test several lead exposure models: our aim was to assess their suggested decision (whether to implement systematic blood testing or not), which might well be adequate even though the BLL forecast may be imprecise.

Study selection

These tools were tested on sites identified by a search for the literature in the Medline database according to the following criteria: (title word = lead and title word = dust) OR (title word = lead and keyword = dust) OR (keyword = lead and keyword = dust or soil).

This literature search was completed by a search for unpublished work by contacting the authors of the articles identified by the Medline search and institutions working in the field of environmental health.

The inclusion criteria were as follows:

- Publication after 1975
- Site with industrial lead source, located in North America, Australia, or Europe
- BLLs tested in children aged 6 months to 6 years
- Availability of BLL results and lead content (expressed in p.p.m.) in soils and/or dust and in the air for operating sites
- BLL tested in a representative population sample (we excluded intervention studies in targeted populations)
- Absence of work-related exposure (by workers bringing home dust from operational industrial sites) or with indoor dust measurements—and therefore possible quantification of this exposure pathway.

A total of 71 situations (references available on request) were identified (one paper might describe several places or periods) describing population BLLs and environmental contamination. Twenty-nine involved (mainly) mining sites; 45 came from North America (42 from the United States) and 26 from Europe; 44 were conducted between 1990 and 2005.

Data collection

For each situation, we recorded the identification of the study (author, year of publication, place, date), type of environmental setting (industrial, mining, etc.), BLLs, and environmental data, as follows.

BLLs: Geometric means of BLLs, and percentage of BLLs >100 μg/l, in children aged 6 months to 6 years (if not available, calculated by a transformation of the median or arithmetic mean assuming a lognormal distribution and a geometric standard deviation of 1.6 if the specific standard deviation was not known).

Environmental data: Lead concentrations in environmental media were recorded as geometric means. When the dust lead concentration was not indicated, it was assumed to equal 0.7 × (soil concentration in μg/g) + 100 (μg/g / μg/m³) × Cw (μg/m³) (default estimate in IEUBK). When not reported, concentration in water was assumed to be 4 μg/l (default estimate in IEUBK). Food values were generally not reported; the default values (μg/d) we used gradually decline from 60 in 1975 to 3 in 2000 (North America, Northern Europe), 10 in 2000 (Western Europe, Oceania), and 40 in 1995.
Air concentration was either the level reported in the study or a default value ranging from 1.1 (1978) to 0.02 (2000) in North America (US: EPA Air Trends. Lead http://www.epa.gov/airtrends/lead.html) and from 1.1 (1986) to 0.02 (2002) in Europe.23

Criteria for comparison of decision support tools

The decision (whether or not to conduct mass screening for elevated BLLs in a given area) requires being able to distinguish the sites around which systematic screening is (relevant according to the criteria mentioned above) from others for which it is not; the aim is to identify the sites where children’s BLLs should be tested. The ability of the systems tested here to suggest the ‘correct’ decision is determined by measuring their sensitivity (Se) and specificity (Sp), the standard criteria for diagnostic tests. They were assessed for different acceptable proportions (AP) of elevated BLLs: 1, 2, 4, 6, 8, 10, and 20% of BLLs >100 mg/l.

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Se = \frac{TP}{TP + FN}, Sp = \frac{TN}{TN + FP}
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where TP is the number of true positives, i.e. (PP > AP) and (PO > AP); decision = ‘correct decision’ = Yes; TN is the number of true negatives, i.e. (PP < AP) and (PO < AP); decision = ‘correct decision’ = No; FP is the number of false positives, i.e. (PP > AP) and (PO < AP); decision = Yes and ‘correct decision’ = No; FN is the number of false negatives, i.e. (PP < AP) and (PO > AP); decision = No and ‘correct decision’ = Yes. With PP as the predicted percentage of BLLs >100 µg/l; PO as the observed percentage of BLLs >100 µg/l (measured or calculated from information about distribution); and AP as the acceptable proportion of elevated BLLs.

We also estimated the differences between measured and predicted (by the IEUBK, InVS, and Lewin models) geometric means of BLLs [(predicted BLL—measured BLL)/(measured BLL)] to assess the differences in model performance.

Results

Sensitivity and specificity of the decision support tools for determining relevance of systematic BLL screening are presented in Figure 1. If we consider, for example, that systematic screening should be conducted around a site where 2% of the children have a BLL >100 µg/l, the IEUBK model has a sensitivity of 0.96 and a specificity of 0.54. There is thus a probability of 0.96 of identifying a site where systematic screening would be useful. The probability of identifying a site where screening is not useful is 54%.

Depending on the acceptable percentages of elevated BLLs, the sensitivity of the different tools ranged from 0.27 to 1, and the specificity from 0 to 0.98. Soil pollution levels alone were quite insensitive (Se was ~0.7 for the 200 p.p.m. cut-off and <0.5 for the 400 and 500 p.p.m. cut-offs) for deciding on systematic screening. On the other hand, thresholds of 400 and 500 were always more specific. The InVSoriginal model was often as specific, but with better sensitivity. The regression model proposed by Lewin offered good sensitivity at the thresholds of 1 and 2% but minimal specificity. Its performance was poorer than the other tools for the other acceptable percentages of elevated BLLs. The IEUBK (especially) and InVSupdated models were most sensitive (Se > 0.9) regardless of the cut-off points. Their specificities were ~0.6–0.7 for the thresholds of 4% and above, lower below (except for InVSupdated at 2%).

Discussion

Using soil concentrations cut offs alone is unsatisfactory for judging the appropriateness of systematic screening because the sensitivity of this tool is insufficiently protective of population

Figure 1 Sensitivity and specificity of tools for identifying sites as a function of the acceptable percentage of elevated BLLs
health. Globally, the IEUBK and InVS\textsubscript{updated} models performed similarly and can be considered the most effective. IEUBK was slightly more sensitive and InVS slightly more specific.

Figure 2 presents the differences between predicted and measured BLLs for all and more recent (post-1990) studies. Predictions are slightly better for the more recent studies. In any case, they appear more reliable, given the improvement in sampling and analytic techniques, which reduces the imprecision associated with measurement errors, as well as our better knowledge of dietary lead intake and the reduction in air pollution—difficult to estimate because of its variability. In 26 and 25 of 44 recent cases, the InVS\textsubscript{updated} and IEUBK models, respectively, predicted a mean BLL with an error of <40%. Lewin’s model was better with 31/44 but had more underestimated BLLs and thus lower sensitivity. Examination of the BLLs predicted by this model (data not shown) suggests that it attributes less importance to the soil exposure pathway and therefore predicts a smaller range of BLLs for sites with often substantial soil pollution. The InVS\textsubscript{original} model appears to overestimate BLLs when soil contamination is high. This may be due to the linear relation between external dose and BLL in this model, which does not take into account the toxicokinetic phenomena of saturation. The overestimation does not appear with the InVS\textsubscript{updated} model, which considers the lower bioavailability of soil and thus accords less importance to this medium.

Comparison between measured and modelled data requires representative measurements of both exposure media and BLLs.\cite{LoefflerB2006} However, as Lorenzana\cite{LoefflerB2006} points out, measuring the association between environmental lead contamination and BLL requires strict epidemiologic protocols, which are not generally enforced around polluted soils because population health requires screening rather than study. Moreover, all useful environmental information is not always available. In some cases therefore we had to use default values, especially for dietary intake. We used national estimates and presumed that the study and national populations had similar dietary habits and that local contamination does not substantially affect lead intake from food. This assumption has been verified recently in Germany,\cite{LoefflerB2006} perhaps explained by the slight lead absorption by vegetables, the food most likely to be local in origin.

Air lead concentrations were not always reported: when they were not for an operating industrial site, this site was excluded. Default values for atmospheric lead concentration were used only in situations where the air was not the dominant lead source. Lead concentrations in the public water supply are rarely measured; those nonetheless generally play only a marginal role as long as there are other important sources, such as the soil, around industrial sites: results were relatively insensitive to the choice of default value for water (4 μg/l), in the range of other frequently encountered values (0–10 μg/l).

Though all the studies we selected included soil concentration measurements, only some measured home dust levels. When the lead in home dust might have been transferred from operating plants by employees, the site was excluded; in the other cases concentrations were estimated from the soil and air levels. The use of different methods for sampling soil and dust can cause considerable measurement errors.\cite{LoefflerB2006} Given the large number of situations to be analysed, optimal data were not always available for the models, especially those requiring the most data (IEUBK and InVS). Accordingly we underestimate these models’ performance, compared with how they work in real situations, where the required data can be collected. This is especially true for the mining sites, where the soil lead is least bioavailable\cite{LoefflerB2006} and where sometimes simple knowledge of the mineral can very substantially reduce the uncertainty associated with exposure estimate.\cite{LoefflerB2006} Figure 3 illustrates this greater overestimation of predicted BLLs when the lead source is a mining site with no other industry. Estimation of BLLs is also subject to imprecision,\cite{LoefflerB2006} especially when few subjects are tested. From these limitations, we can state that the performance of the tools tested here is globally underestimated because of the quality of the available data.

Judging the absolute usefulness of a decision support tool is difficult because it requires assigning a relative weight to
different ‘wrong decisions’; one may for example, consider false negatives more important than false positives. For 44 recent studies (BLLs measured from 1990 onward) and at a threshold of 2%, the IEUBK model

- compared with systematic screening; avoids 7 futile screening (7 TN), but leads to two incorrect decisions against screening (2 FN);
- compared with decision not to conduct mass screening, regardless of the situation: recommends 29 useful screenings (29 TP) and 6 futile screenings (6 FP).

In other terms, the positive predictive value \([TP/(TP+FP)]\) is 0.83 and the negative predictive value \([TN/(TN+FN)]\) is 0.78 for these sites. We must recall nonetheless (cf. above) that the performance, therefore the usefulness, of these tools is underestimated here because of the data quality and in particular the failure to take bioavailability into account. When Hogan compared the IEUBK model’s prediction and measurements for three datasets, he found close agreement when the environmental data were representative of the population exposure.

Our sample of situations is not representative of those for which decisions about systematic screening are required today, if only because of an inclusion bias in the study; situations where BLLs were not measured (i.e. screening was determined not to be necessary) are excluded by definition. There is also a possible publication bias, which tends to favour situations where pollution and/or BLLs are highest.

Our results support the use of these decision support tools to decide about implementation of systematic screening of elevated BLLs in children around industrial sites. The IEUBK and InVS updated models performed best for this use, but require more input data. Appropriate use of these models assumes

- acquisition of site-specific environmental data, especially for soils and dust, that must be representative of the concentrations of children’s exposure. This supposes a local level investigation to identify, sample, and analyse relevant exposure media;
- consideration of the lower bioavailability of mining soils; and
- use of recent default data, especially for dietary intake (e.g. Total Diet studies) to take into account the decrease in diet contamination after lead was banned in gasoline.

Another factor to be taken into account is the tool’s acceptability, by the population (transparency, in favour of simple tools), users (ergonomics, ease of use, that is true of all the tools tested here), and policy-makers.

Finally, we must point out that primary prevention must continue, separately from BLL screening activities, because there is no known safe lead level in children’s blood.

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