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Exposure assessment for a population-based case-control study combining a job-exposure matrix with interview data

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Objectives A system that combines the ease of use of a job-exposure matrix while taking into account job-specific data is needed. This study aimed to produce a detailed method for combining interview data with expert assessments for a large population-based case-control study of Parkinson's disease.

Method An interview-administered core questionnaire with a series of questions that triggers substance-specific questionnaires to gather information on key parameters is administered. Using a job-exposure matrix to generate base estimates, assessors can modify this estimate of exposure intensity using worker-specific data such as the use of control measures, reports of substance-specific acute symptoms, and the quantity of material being processed. Detailed guidance for making adjustments to exposure estimates for these modifiers is presented.

Results The method has been partially validated through the use of a comparison of estimates for a separate cohort with previously validated exposure reconstructions. Agreement was high, with a Spearman's rho of 0.89 ($P < 0.01$). The results from a quality assurance system employed as part of the methodology show a high degree of repeatability in generated exposure values both over time (Spearman's rho 0.98, $P < 0.01$) and between different assessors (Spearman's rho 0.88, $P < 0.01$).

Conclusions The method provides detailed quantitative exposure indices for occupational epidemiology. It has particular strengths both in terms of ease and speed of use. It is hoped that it will provide a useful structure for future epidemiologic work.

Key terms expert systems, exposure assessment, job-specific questionnaires, occupational, Parkinson's disease.

The identification of associations between exposure and ill health is central to occupational epidemiology. The ability to establish exposure–response gradients is dependent on the accurate assignment of participants' exposure levels. Exposure misclassification can have the effect of overestimating risk (1) or, more commonly, reducing the likelihood of identifying a statistically significant relationship between exposure and disease (2).

Exposure classification can be achieved by a range of methods dependent on the complexity of the information available. Where daily personal exposure measurements

have been made, the accurate classification of a worker's exposure is relatively straightforward. It is extremely unusual to have such data, and in the more usual scenario, in which few or no measurements of exposure exist, the classification of exposure is more difficult. A lack of measurement data is often the case when participants are drawn from a subset of the population rather than from a specific workplace.

Subjective exposure estimation techniques, pioneered by exposure modelers such as Fidler et al (3) and Cherrie et al (4), can be employed to assess exposure

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retrospectively when measurement records do not exist. These techniques use deterministic methods to identify factors likely to influence the level of exposure. Values for these parameters are then modified depending on the information available on the exposure scenario. They can be combined to reflect differences in tasks and differences between workers. For example, Glass and her co-workers (5) used deterministic modeling in the retrospective assessment of benzene exposures. Base estimates were generated from measured concentration levels and then modified using information on technological changes and changes in the product over time.

A simplified system for utilizing "expert judgment" is the concept underlying the job-exposure matrix. This procedure involves creating a two-dimensional grid on which some value of exposure is entered for each job title or industrial grouping. Job-exposure matrices can be established to estimate just one type of exposure, such as chlorinated aliphatic hydrocarbons (6), or a range of chemical exposures (7–8). The inherent weakness of this approach is that people with the same job title but different work conditions may be wrongly classified as having the same exposure. Kromhout and his co-workers (9) have demonstrated large differences in personal exposure levels between individual workers carrying out the same job.

An alternative approach is to employ experts to assess exposure levels. This method can be time-consuming and costly, particularly in large population-based studies with many different occupations. Furthermore, the quality of expert-assessed exposure levels has been shown to be highly dependent on the amount of detail available regarding the jobs being assessed (10–11). Job-specific questionnaires have also been used as a means of gathering information on the work environment, sources of exposure, and behavioral parameters linked to exposure levels (12). A job-specific questionnaire provides the assessor with details that allow the use of subjective modeling techniques to reflect inter-worker variability in personal exposure levels and to capture the influence of historical changes in work practices on assigned exposure levels.

A method is needed that utilizes the benefits of job-exposure matrices in terms of simplicity and the ability to process large numbers of job titles and marries the obtained data with the extra information gained on modifiers of exposure in job-specific questionnaires. The process of combining a job-exposure matrix and information from worker interviews could be undertaken by an occupational hygienist or a similarly skilled individual on review of the questionnaire. This paper describes such a new quantitative exposure assessment method. It was developed for a range of substance types employed in a large population-based multicenter case-control study.

Methods

The method included the development of a suitable questionnaire for data collection, a job-exposure matrix, and primary exposure modifiers identified as likely to influence exposure levels. It also involved partial validation of the generated estimates and quality assurance procedures to confirm the repeatability of the reconstructed exposures.

The "Geoparkinson study" for which the method was developed is a European multicenter study that is aiming at investigating the genetic, environmental, and occupational risk factors associated with the development of Parkinson's disease. Parkinson's disease is a neurodegenerative disorder characterized by tremor, rigidity, and bradykinesia. Little is known as to the cause(s) of most cases of the disease, but laboratory and epidemiologic investigations have suggested that solvents (13–14), pesticides (15–16), and the metals iron (17), copper and manganese (18) may be risk factors.

Development of the questionnaire

A questionnaire was developed to enable data collection relating to occupational and nonoccupational exposure to solvents, pesticides, copper, manganese, and iron. Because evidence indicates that postal questionnaires can introduce a high degree of exposure misclassification (19), we decided to use an interviewer-administered form of questionnaire.

The questionnaire collected demographic information and data relating to lifestyle factors such as use of certain medications, alcohol consumption, and tobacco use. The core questionnaire gathered a full occupational history from the participant. Information on every job lasting longer than 6 months was collected. This included the job title and both the start and end dates for the job. A broad classification of the type of industry (based on the Standard Industrial Classification of Economic Activities, 1992) was recorded (20). For each job there was a series of questions regarding exposure to each of the target agents (solvents, pesticides, and metals). The trigger of these questions prompted the administration of additional exposure-specific questionnaires to gather more-detailed data on work conditions, symptoms, and possible exposure concentrations. The same process was carried out for nonoccupational exposures. Exposure-specific questionnaires aim to gather data relevant to the tasks in which exposure to the substance or chemical of interest takes place, whereas job-specific questionnaires collect information on the entire job process.

The questionnaire was piloted in a small group of 10 participants recruited from a respiratory medicine clinic at a university teaching hospital in Aberdeen. Difficulties with the administration of the questionnaire, the wording

of certain questions, and the understanding of a variety of expressions were identified and corrected at this stage.

The Geoparkinson study involved four centers across Europe, based in Scotland, Italy, Sweden, and Romania. The finalized questionnaires were translated from the English original into each national language. To insure consistency of administration and data entry, a 1-day training session for all those involved in carrying out the subject interviews was undertaken.

The purpose of the exposure-specific questionnaires was to gather additional data about the job title to assist in exposure reconstruction. The questionnaires were constructed using our previous experience of collecting lifetime occupational data in a case-control study of painters reporting neuropsychological symptoms (21). In addition, we referred to the job-specific questionnaires employed by previous studies (12). The finalized exposure-specific questionnaires aimed at gathering the following information: (i) a brief description of the tasks and work methods involved in the job, (ii) an average duration of exposure to the material in terms of hours per day, (iii) an average frequency of contact with the material in terms of days per year, (iv) an indication of the quantity of the material used (for solvents and pesticides only), (v) any acute health effects suffered as a result of working with that material.

Taken together with the job title, the country, and the time period of the employment, the information gained was deemed sufficient for estimating exposure levels.

Job-exposure matrix

A selection of questionnaires from all four countries was examined to identify the common job titles. A list of 60 common job titles was then used as the basis for the job-exposure matrix. Five occupational hygienists from the United Kingdom with experience in exposure measurement, modeling, and assessment techniques classified the exposure to solvents, pesticides, and the three target metals for each of the job titles into one of the following four categories: none, low, medium, or high exposure. The exposure intensity was evaluated in terms of the three primary occupational exposure routes (inhalation, dermal, and ingestion), where applicable. In addition, each member of the expert panel was asked to provide a quantitative exposure value for each of the three categories (low, medium, or high). This quantitative exposure value was provided in relation to the current occupational exposure limit in force in the United Kingdom (22) for each of the substance groups being assessed (mixed solvents, copper, manganese, iron, and a pesticide typical of the task being assessed). For example, where an expert classified the job title "joiner" as having low exposure to mixed solvents, the expert may then have classified the term "low" as 5% of the

current occupational exposure limit for mixed solvents. This method allowed the generated exposure indices to be easily converted to airborne concentrations in parts per million or milligrams per cubic meter.

To generate the job-exposure matrix, we assigned the median exposure classification from the five occupational hygienists to each job title. No job title had an assessed exposure intensity spanning more than two classification groups (ie, zero-low, low-medium, and medium-high were the only discrepancies between the five hygienists). The substance exposure level (relative to the appropriate occupational exposure limit) for each of the "low", "medium", and "high" categories, as assigned by the five experts, was determined using the median value assigned to each category by the five assessors. From the results of this exercise, the intensity of these classifications was found to be close to a ratio of 100 (high):40 (medium):5 (low) with the "high" category corresponding to a figure close to the occupational exposure limit for all five chemical groups.

Exposure modifiers

The interviewers were instructed to encourage workers to describe the work process and the use of any equipment in the location where the work was carried out, the use of ventilation to reduce airborne concentrations, the use of personal protective equipment, and any visible signs of exposure such as fumes, mists, and surface contamination. In relation to solvent and pesticide use, data on the amount of skin contact and the use of gloves and overalls were also sought. This information was used to modify the basic exposure category derived from the job-exposure matrix.

Information on historical work practices and health and safety policies within each country was gathered through discussion with occupational health or hygiene professionals and a review of the literature. Our discussions suggested that the use of solvents in coating applications was generally reduced at a much earlier date in Sweden than in the other three nations involved in the Geoparkinson study. Similarly the use of copper sulfate as a pesticide in agriculture was reported for a higher proportion of farm-related workers in Italy than elsewhere. The provision of respiratory protective equipment was good in Sweden and (slightly later) in the United Kingdom, whereas Romania reported only occasional use of respirators or masks. The effect of these national and era-specific differences in work practices on the exposure to solvents, pesticides, iron, copper, and manganese was incorporated into the comprehensive guidance document that was used to modify the reconstructed exposure levels.

The influence of the exposure modifiers on the intensity of the exposure value was based on the results

of previous studies, for example, Cherrie's examination of the effect of ventilation and room volume on exposure (23) and discussions with a range of occupational hygienists. Typical modifying guidance notes are shown in table 1. Similar guidance material was developed for the metal and pesticide questionnaires.

Exposure metrics

Three exposure indices were generated from the questionnaire data. The first metric was the total number of years of exposure to each of the materials in question. This metric was produced by summing the number of years from each job title that was assigned a positive exposure. The second metric was cumulative exposure. This metric was derived by multiplying the estimated exposure intensity, the exposure frequency (number of days per year), a frequency adjustment to take into account the number of hours per day of exposure, and the exposure duration (number of years of contact within that job). This total exposure figure for each job was then expressed in terms of the occupational exposure level times years (OEL $\times$ years), where 1 OEL $\times$ year is equivalent to exposure at the current OEL airborne concentrations in the United Kingdom for 8 hours a day for 240 workdays a year. The cumulative exposure was simply the sum of the calculated total exposure values from each job title.

The third metric was the average annual intensity of exposure. This figure reflects the average level of exposure across one or more jobs. It is produced by dividing the cumulative exposure by the number of years of exposure to that material. It is expressed as a fraction of the occupational exposure limit and indicates the equivalent average daily exposure level for a worker during employment involving exposure.

Exposure reconstructions

The basic job-exposure matrices, the guidance material for interpreting the questionnaire responses, and two worked examples are available at <http://www.abdn.ac.uk/deom/ssempole>.

The completed questionnaires were first examined to determine if they contained exposure-specific questionnaires for the subject in question. Where exposure-specific questions had been completed, the subject's questionnaire was then fully assessed by the primary assessor (SS). Subjects who had no exposure-specific questionnaires were deemed as having no occupational or nonoccupational exposures and were assigned zero exposure values for all the chemical exposure metrics. Exposure assessment was carried out blind to the case-control status of the person with questions relating to medication and history of Parkinson's disease removed from the questionnaire prior to the assessment procedure.

Job titles with positive reported exposures but not included in the job-exposure matrices were found to contribute approximately 15% of the total of those requiring assessment. These "nonjob-exposure matrix" titles were assessed by matching the job title to the closest job type within the matrix and using the descriptive material to confirm the assigned category. For example, an operator who worked producing Wellington boots was classified as likely to have "medium" solvent exposure similar to the job task described in the matrix as "an assembly line process using solvents or adhesives".

Validation dataset

In order to partially validate the methodology reported in this paper, we tested the method on a random selection of 20 men from a previously described case-control study (21). We had collected detailed occupational histories from these men and were able to extract data from these histories that were similar to those collected in the questionnaires for the current Geoparkinson study. Values for lifetime cumulative solvent exposure had been previously generated and validated for this group as part of an earlier study (24) using subjective exposure reconstruction methods for inhalation exposure (25) and dermal exposure (26). Values were generated for lifetime cumulative solvent exposure using the current method; they were then compared with the previous estimates.

Table 1. Sample guidance for modification of the exposure intensity value generated by the job-exposure matrix (JEM).

Parameter description	Guidance for modifying exposure intensity
Symptoms reported while working with solvents	Headaches—not relevant; dizzy spells generally indicative of values greater than the occupational exposure limit (OEL) (150%); unconsciousness representative of values >2.5 OEL (250%).
Ventilation and engineering controls	Report of particularly poor ventilation indicative of a 50% (approximately) increase in the JEM value; description of very effective ventilation system or control measure indicative of a 50% decrease.
Use of respiratory protective equipment (RPE)	Report of frequent use of cartridge-type indicative of a 50% reduction in the JEM value; frequent use of air-fed apparatus indicative of a 50% reduction.
Work location	Report of working in small confined spaces such as tanks or small sealed rooms indicative of increase to at least 100% of the OEL; description of outside work would tend to reduce the exposure level by a category (high to medium; medium to low).
Quantity of solvent used	Reported use of less than 50 ml indicative of a probable exposure level no more than 20% of the OEL and generally closer to 5%; greater than 2 l of use per day suggestive of medium-to-high (40–100%) exposure levels.

Quality assurance procedures

Quality assurance checks on the assessment process involved two procedures to establish interobserver and intraobserver repeatability of the estimates, respectively. The first involved internal validation, with a second assessor (FD) checking a proportion of the assessments performed by the primary assessor (SS). This procedure was carried out for approximately 10% (N=119) of the questionnaires that required assessment, chosen at random from all four countries. These assessments were completed with the assessor blind to the results of the primary assessor's estimates. The second quality control procedure was achieved by the primary assessor repeating his assessment of a random 5% (N=59) selection of the completed questionnaires covering a wide range of job titles and substance groups. This procedure was again carried out with the assessor blind to the initial assessment, and it was conducted at the conclusion of the assessments to insure that recall was minimized.

Results

Validation dataset

The correlation between the nontransformed estimates produced for cumulative exposure to mixed solvents in the previously validated method (24) and the current method was very strong (Spearman's rho 0.89) and significant at $P < 0.01$. Figure 1 shows the near linear relationship on a log-log graph between the two methods; the data indicate a high level of agreement.

Quality assurance procedures

The assessments carried out by both the primary and secondary assessors produced agreement, in terms of ever-never exposed, for a total of 548 of a possible 595 lifetime chemical exposure combinations (agreement for 92% of the combinations). Of these 548 agreements, 191 were for positive exposures and 357 were for zero-assigned exposures.

Where the assessors agreed that there had been exposure in an individual's lifetime (N=191), the Spearman's rho correlation coefficient for the magnitude of the cumulative exposure estimates was 0.88 ($P < 0.01$). The differences in the assessed exposure intensities tended to be for job titles that were not included in the job-exposure matrices but had reported positive exposure.

Figure 2 shows the high level of agreement for cumulative exposure estimates between the primary and secondary assessor. The data are presented on a log-log scale. There was no bias between the two assessors. When the scenarios in which one or both of the assessors

reported zero exposures were excluded, the median ratio of the cumulative exposure estimates (secondary and primary assessor) was 1.0. Of the 47 (8%) scenarios in which the assessors did not agree on whether exposure had taken place, most (N=36) of the differences stemmed from the secondary assessor reporting zero exposure in cases in which the primary assessor identified exposure. By category, the disagreement can be broken down as 5 for solvents, 5 for pesticides, 4 for iron, 10 for copper, and 12 for manganese.

There was a small number of the positive exposure scenarios (19 of a total of 191) in which the agreement between the primary and secondary assessor was poor and bias spanned an order of magnitude or greater. An analysis showed that most of these large differences occurred for pesticide and copper exposures, and the differences resulted from different interpretations of non-occupational data describing persons who had tended small vineyards or crops for home use (applying pesticides including copper sulfate). Where data on frequency of use were sparse or lacking, the two assessors may have selected different figures for both the number of

Figure 1. Graph of lifetime solvent-exposure estimates from a previously validated method (dockyard method) versus the current method. (CE = cumulative exposure, OEL = occupational exposure limit)

Figure 2. Estimated cumulative exposure (CE) levels from primary and secondary assessors (47 scenarios in which a zero value was reported by one or the other assessor are excluded). [Note that for the cumulative exposure estimates $100 = 1 \text{ OEL} \times \text{year}$] (OEL = occupational exposure limit)

days spent applying pesticides per day and the number of hours spent applying pesticides per day. When we identified these differences, we updated the guidance material to ensure that standard values were applied where full descriptions of exposure frequencies and durations of use were lacking.

Approximately one-quarter of the positive assessments of exposure provided perfect agreement between the primary and secondary assessors. This result indicated that the guidance enables users to select the same exposure level for 25% of the job titles (67% if we include the zero exposure occupations). As 60% of the primary-secondary assessment pairs had a bias between 0.5 and 2.0, we can also state that the guidance produces excellent agreement for most of the job titles. Most of the points on the 1:1 line are from well-defined job titles that appear in the job-exposure matrix and have descriptive data of good quality that details the work conditions, use of control measures, and protective equipment. In this respect the supplied guidance material would clearly lead the assessor to assign particular values to the exposure level. Points showing large deviations from the 1:1 line tend to be unusual occupations or cases in which the provided job description was poor and required that the assessor use some degree of interpretation to categorize the likely exposure level.

The second quality assurance procedure involved the primary assessor repeating 5% (N=59) of all assessments blind to the initial assessments. This exercise allowed the reproducibility of the procedure to be examined. There was agreement on the presence or absence of exposure in 98% of all possible combinations, and the Spearman's rho correlation coefficient for the repeated versus initial cumulative exposure estimates was 0.98 ($P<0.01$). Figure 3 shows the agreement between the initial and repeated estimates of cumulative exposure. The data are again presented on a log-log scale.

Figure 3. Graph of initial and repeated cumulative exposure (CE) estimates for a 5% selection of questionnaires. [Note that for cumulative exposure estimates $100=1 \text{ OEL} \times \text{year}$] (OEL = occupational exposure limit)

Discussion

The range of processes available for exposure assessment in population-based epidemiologic studies has been reviewed by Stewart (27). This commentary highlighted the usefulness of job-specific data with respect to exposure determinants and simple deterministic models to reconstruct past exposures. The importance of detailed guidance material for parameters involved in any exposure reconstruction process has been emphasized by Cherrie & Schneider (25).

Stengel and his colleagues (28) compared the sensitivity and specificity of a job-exposure matrix and an expert assessment procedure. The simple job-exposure matrix was generally poor at identifying positive exposure as defined by the expert assessment (sensitivity 23–63%), but good at rejecting false positives (specificity 87–98%). The work by Stengel and his colleagues suggested that the use of a simple job-exposure matrix, when compared with that of expert assessment procedures, could lead to a loss of study power equivalent to a reduction in subject numbers by a factor of 5 to 10.

A study by Tieleman and his co-workers (29), who evaluated the effectiveness of a variety of exposure assessment methods in comparison with the results of biological monitoring showed the greatest levels of agreement between job-specific questionnaires and objective measures of exposure. Using urinary metabolites of aromatic solvents as the “gold standard” for exposure, this study found that the highest positive predictive value was achieved for a job-specific questionnaire (0.52) followed by an expert evaluation on the basis of generic occupational questionnaires (0.33). The positive predictive value for the job-exposure matrix (0.27) was considerably lower. This evidence indicates that job-specific questionnaires provide one of the best available methods of identifying positive exposure in retrospective studies.

The population-based nature of the Geoparkinson study means that there are no “gold standards” of exposure with which to compare the performance of this method. We believe that the process of indirectly validating the method for the solvent exposure reconstruction against previously validated exposure reconstruction methodology provides evidence that the approach is defensible.

The primary assessor (SS) was involved in a previous dockyard study (21), and it is possible that this could have introduced recall bias into the validation process. We think any such effect was likely to have been small, as the time elapsed between the assessments for the dockyard and the Geoparkinson studies was in excess of two years. In carrying out the 20 random reassessments, the assessor had no personal identifying information.

Validation work for the pesticide and metal exposure levels was not possible due to a lack of preexisting measurements. Estimates for these chemicals are based on scientific principles similar to those applied to the validated solvent assessments, but we acknowledge that the validity of the method for other substance groups could be lower. Additional validation of this method, particularly in relation to exposure scenarios involving metals or pesticides, is required.

We are aware that bias may have been introduced into the data collection as the interviewers were not blind to the case-control status of the participants. We attempted to minimize any bias by highlighting this possibility for the interviewers in the training session and asking them to use the uniform questionnaire and guidance sheets when administering the questionnaires. We also insured that the exposure assessor was blind to the case-control status of the persons involved. All information pertaining to the health status of a person was removed from the questionnaires prior to delivery to the exposure assessor.

The participants' recall of the names of pesticides used was uniformly poor and, as a result, we were unable to generate exposure estimates for particular pesticides. To address this problem, we estimated exposure in terms of the typical pesticides used for the agricultural class or activity described. For example, we used paraquat dichloride (OEL 0.1 mg/m³ for 8-hour time-weighted average exposure) for weedkilling tasks in gardening hobbies or jobs. We acknowledge that many pesticides do not have occupational exposure limits in the United Kingdom and that our method of using a generic "pesticide" metric to describe exposure to a diverse range of chemicals is based on the assumption that all pesticides act in an additive manner. While we accept the limitations of this approach, we believe that the quantitative values assigned to lifetime pesticide exposure is a considerable improvement over simple classification systems employing such measures as ever-never and years of exposure. For pesticide assessment the influence of dermal exposure and uptake was also evaluated in deterministic modeling (26).

The questionnaire's reliance on self-reports to trigger exposure-specific questionnaires may have resulted in some differences in ascertainment between countries. Perceived "exposure" or "use of chemicals" may be influenced by intensity. For example, when workers are aware that others in their factory have become intoxicated from solvent vapors after using paints to spray confined spaces, they may consider their own small-scale use of degreasants on worktools as insignificant and respond negatively to the trigger question. Similarly, the greater the emphasis of a workplace on control and health and safety training, the more likely it is that the worker will have recognized exposure to sources of

chemicals even if the exposure was actually very low. It is conceivable that some of those working in the most poorly controlled environments were also the most likely to report no exposure incorrectly for that job. To check for this potential bias, we examined a random selection of questionnaires from all four countries to determine if there was a greater frequency of negative exposure reports for job titles that were classified in the job-exposure matrix as having high exposure for a particular substance group (industrial spray painters, farmers, welders). Only a small proportion of questionnaires (5–10%) with these job titles had responded negatively to the trigger question, and there was no evidence of differences in this fraction between countries. Nevertheless, we would recommend that any future system have a predefined job-exposure matrix for each substance under study and that a report of a job title rated as positive in the job-exposure matrix would automatically result in the administration of the exposure-specific questionnaire without respect to whether the person reported having worked with the material.

As discussed previously, the provision of high-quality guidance material for exposure reconstructions is essential. Detailed descriptions of industries and tasks are required, and an understanding of historical changes in work practices is necessary. One of the key points highlighted in Stewart's commentary (27) is the need for epidemiologic studies to provide detailed documentation of their assessments to assist others carrying out similar studies and to prevent investigators continually "re-inventing the wheel". For multicenter epidemiologic studies the production of an international "library" of exposure assessment methods and appropriate guidance material would prove useful when retrospective exposure assessments are performed. Details of common process methods, likely changes over time, and the use of control measures would all help in the assessment process. An on-line resource tool that is searchable by industry, chemical, or task and that hygienists and epidemiologists could contribute to would be particularly beneficial.

We believe that our expert-based system, used to modify simple job-exposure matrix categorization, can provide improved exposure reconstructions for population-based studies. The method, developed for use in the Geoparkinson study, draws on many recent advances in the field of exposure assessment. It provides detailed quantitative exposure indices for use in determining associations between ill health and occupational and environmental exposures to solvents, pesticides, and a variety of metals. It has particular strengths in terms of ease and speed of use and repeatability across assessors. It is hoped that it will provide a useful structure for other exposure reconstruction methodologies in future epidemiologic work.

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