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Assessing Occupational Exposure to Chemicals in an International Epidemiological Study of Brain Tumours

MARTIE VAN TONGEREN[1]*, LAUREL KINCL[2,3], LESLEY RICHARDSON[4], GEZA BENKE[5], JORDI FIGUEROLA[2], TIMO KAUPPINEN[6], RAMZAN LAKHANI[4], JÉRÔME LAVOUÉ[4], DAVE MCLEAN[7], NILS PLATO[8] and ELISABETH CARDIS[2] FOR THE INTEROCC STUDY GROUP**

[1]Centre for Human Exposure Science, Institute of Occupational Medicine (IOM), Research Avenue North, Riccarton, Edinburgh EH14 4AP, UK; [2]Center for Research on Environmental Epidemiology (CREAL), Barcelona, Spain; [3]Oregon State University, Corvallis, USA; [4]University of Montreal Hospital Research Center (CRCHUM), Montreal, Canada; [5]Monash University, Melbourne, Australia; [6]Finnish Institute of Occupational Health (FIOH), Helsinki, Finland; [7]Massey University, Wellington, New Zealand; [8]Karolinska Institute, Stockholm, Sweden

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The INTEROCC project is a multi-centre case–control study investigating the risk of developing brain cancer due to occupational chemical and electromagnetic field exposures. To estimate chemical exposures, the Finnish Job Exposure Matrix (FINJEM) was modified to improve its performance in the INTEROCC study and to address some of its limitations, resulting in the development of the INTEROCC JEM. An international team of occupational hygienists developed a crosswalk between the Finnish occupational codes used in FINJEM and the International Standard Classification of Occupations 1968 (ISCO68). For ISCO68 codes linked to multiple Finnish codes, weighted means of the exposure estimates were calculated. Similarly, multiple ISCO68 codes linked to a single Finnish code with evidence of heterogeneous exposure were refined. One of the key time periods in FINJEM (1960–1984) was split into two periods (1960–1974 and 1975–1984). Benzene exposure estimates in early periods were modified upwards. The internal consistency of hydrocarbon exposures and exposures to engine exhaust fumes was improved. Finally, exposure to polycyclic aromatic hydrocarbon and benzo(a)pyrene was modified to include the contribution from second-hand smoke. The crosswalk ensured that the FINJEM exposure estimates could be applied to the INTEROCC study subjects. The modifications generally resulted in an increased prevalence of exposure to chemical agents. This increased prevalence of exposure was not restricted to the lowest categories of cumulative exposure, but was seen across all levels for some agents. Although this work has produced a JEM with important improvements compared to FINJEM, further improvements are possible with the expansion of agents and additional external data.

Keywords: cancer epidemiology; case–control; job-exposure matrix

*Author to whom correspondence should be addressed. Tel: +44-131-449-8097; Fax: +131-449-8084; e-mail: martie.van.tongeren@iom-world.org
**INTEROCC Study group members: Canada—Daniel Krewski, University of Ottawa; Jack Siemiatycki, University of Montreal Hospital Research Centre; Marie-Elise Parent, INRS-Institut Armand-Frappier; France—Martine Hours, IFSTTAR; Germany—Brigitte Schlehofer and Klaus Schlefer, DFKZ; Israel—Siegal Sadetzki, Gertner Institute, Chaim Shiva Medical Center and Tel Aviv University; UK—Sarah Fleming, University of Leeds.

BACKGROUND

The occupational environment provides a particularly fruitful arena for investigating causes of cancer. A large fraction of known human carcinogens were discovered through studies in the workplace (Siemiatycki *et al.*, 2004). Two distinct epidemiological approaches to occupational cancer risk have been used: industry-cohort and community-based case–control studies. The cohort study approach is a powerful tool for studying exposure–disease relationships, but it has several potential limitations, including problems in gaining access to industries, difficulty in obtaining information for potential confounders, limited information on disease status, and loss to follow-up. Another limitation of the cohort study is that it is difficult to study rare disease, such as brain cancers (Breslow and Day, 1987). The community-based case–control study approach, which can overcome some of the limitations of cohort studies, must rely on more tenuous methods for assessing occupational exposure (Siemiatycki, 1996).

Methods used in occupational cancer community-based case–control studies include job or industry-title analyses, self-reports of exposure, job exposure matrices (JEMs), and expert evaluation (Siemiatycki, 1996). Some researchers have developed approaches that combine some of these methods (Stewart *et al.*, 1996), allowing for more specific questions to be targeted at subjects likely to have been exposed to the exposures of interest. A more recent approach uses expert systems, job-specific modules, and computer-assisted personal interviews (CAPI) called OccIDEAS (Fritschi *et al.*, 2012). These approaches have advantages and disadvantages, with some trade-off between cost and validity.

The INTERPHONE study was set up in 2000 to evaluate possible risk of glioma, meningioma, acoustic neuroma, and malignant parotid gland tumours in relation to mobile phone use and to other potential risk factors [ionizing radiation, occupational exposure to electromagnetic fields (EMFs), and the subject's personal and familial medical history] (Cardis *et al.*, 2007; The INTERPHONE Study Group, 2010, 2011). An important component was the collection of an occupational history from each subject and information about occupational sources of exposure to EMFs. Subsequently, data from 7 countries (Australia, Canada, France, Germany, Israel, New Zealand, and the UK) out of the 13 countries that participated in the INTERPHONE study were included in the INTEROCC study to investigate the possible interaction between exposure to EMF and chemicals in the workplace on the risk of brain cancer. These seven countries were selected based on the following criteria: (i) the core occupational calendar was well conducted and reflects a complete work history; (ii) the local principal investigator (PI) was committed to participating in this study; and (iii) the local PI had access to expertise in occupational exposure assessment. The INTEROCC study includes 2054 glioma, 1924 meningioma, and 695 acoustic neuroma cases, and 5601 population-based controls.

To investigate the effect of exposure to a wide range of chemicals on the risk of brain tumours, it was necessary to relate the occupational history information to quantitative exposure estimates. Given the large number of subjects and the lack of details about each job held, a JEM approach was the only feasible approach. It was decided to use the Finnish job exposure matrix (FINJEM) (Kauppinen *et al.*, 1998), the largest available population-based JEM, as modified during the Nordic Occupational Cancer study (NOCCA) (Kauppinen *et al.*, 2009). The FINJEM covers major occupational exposures occurring in Finland since 1945 and has been successfully applied in a number of studies in Scandinavia and other countries (Dryver *et al.*, 2004; Karipidis *et al.*, 2007).

It was not possible to apply FINJEM directly to the occupational histories of the INTEROCC study population, as the International Standard Classification of Occupations 1968 (ISCO68) was used to code occupational histories in the INTEROCC project, while FINJEM uses the Finnish occupational coding system. Furthermore, following an initial review of the FINJEM exposure estimates and comparison of these estimates with estimates from a population-based case–control study of lung cancer in Canada (Lavoué *et al.*, 2012), it was decided to modify some of the FINJEM estimates to deal with some of the observed discrepancies. This paper describes the methods used to modify the FINJEM for application to the INTEROCC study to assess occupational exposure to a selected group of chemicals and presents a comparison of the modified and original FINJEM exposure estimates. Results of the epidemiological analyses investigating the relationship between exposure to chemicals in the workplace and risk of developing glioma and meningioma will be presented elsewhere.

METHODS

Selection of chemical agents

A number of chemical agents were selected for inclusion in the INTEROCC study, based on a review of the literature in relation to brain tumours and possible occupational risk factors (Table 1). Not all substances posited in the literature were included in this study. Pesticide exposures were not included as the prevalence of exposure was expected to be low and it would not be feasible to attain the necessary level of specificity in terms of exposure to active ingredients, based on the information provided in the work histories.

Coding of occupational histories

Within the INTERPHONE study, eligible cases and controls had been interviewed using a CAPI, which included detailed questions on mobile phone use and potential sources of EMF exposure at the workplace and elsewhere (Cardis *et al.*, 2007). In addition, participants provided a complete occupational history of all jobs held for more than 6 months. Occupational information requested included (i) job title, (ii) description of tasks, (iii) company name, (iv) description of activities of the company, and (v) the start and end year for each job.

Occupational histories were coded in each centre using the ISCO68 codes according to common guidelines developed for this project. Inter-rater trials were carried out to determine the reliability of the coding between different countries, which showed that the reliability was moderately increased following an initial coding trial that included a discussion of results (McLean *et al.*, 2011).

Table 1. INTEROCC agents of interest with FINJEM acronym and units of measurement.

Agent grouping	Agent	FINJEM acronym	Units
Solvents	Chlorinated hydrocarbon solvents	CHC	ppm
	Perchloroethylene	PER	ppm
	Trichloroethylene	TRI	ppm
	1,1,1-Trichloroethane	TCE	ppm
	Methylene chloride	MCH	ppm
	Aromatic hydrocarbon solvents	ARHC	ppm
	Toluene	TOLU	ppm
	Benzene	BENZ	ppm
	Aliphatic and alicyclic hydrocarbon solvents	ALHC	ppm
	Gasoline	GASO	ppm
	Other organic solvents	OSOL	ppm
Combustion products	Diesel exhaust emissions	DEEX	mg m^{-3}
	Gasoline exhaust emissions	GEEX	mg m^{-3}
	Bitumen fumes	BITU	mg m^{-3}
	Benzo(a)pyrene	BAP	µg m^{-3}
	Polycyclic aromatic hydrocarbons	PAH	µg m^{-3}
	Welding fumes	WELD	mg m^{-3}
Metals	Cadmium	CD	µg m^{-3}
	Chromium	CR	µg m^{-3}
	Iron	FE	mg m^{-3}
	Nickel	NI	µg m^{-3}
	Lead	PB	µmol l^{-1} blood
Dusts	Animal dust	ANIM	mg m^{-3}
	Asbestos	ASB	f cm^{-3}
	Quartz	QUAR	mg m^{-3}
	Wood dust	WOOD	mg m^{-3}
Others	Formaldehyde	FORM	ppm
	Oil mist	OIL	mg m^{-3}
	Sulphur dioxide	SO2	ppm

Military work was coded, when possible, to the appropriate ISCO68 occupation code. Thus, for drivers, cooks, office workers, pilots, etc. in the military, the ISCO68 codes most closely related to their activities was used. Subjects reporting vocational training were handled in a similar manner, i.e. coded for the occupation most closely related to activities in the training and for the education industry.

The Finnish job exposure matrix

FINJEM was developed by scientists at the Finnish Institute of Occupational Health (FIOH). A detailed description of the original FINJEM is provided by Kauppinen *et al.* (1998). Agents, occupational codes, and calendar time (periods from 1945 to 2009) are the basic dimensions on which exposure is assessed. Exposure to each agent is characterized by the proportion (*P*) of workers exposed in a given job category and the mean level of exposure (*L*) among the exposed by time period. The threshold used to assign non-null quantitative exposure is $P > 5\%$. The original FINJEM exposure estimates were based on the judgment of about 20 experts at the FIOH and supported by the extensive FIOH measurement and survey database. For 16 substances, revised exposure estimates were available for the period 1960–1974 and 1975–1984 from the NOCCA project, during which the FINJEM was adapted to reflect differences in exposures in five different Scandinavian countries (Kauppinen *et al.*, 2009).

Linking FINJEM to ISCO68

A crosswalk was developed between the ISCO68 five-digit codes and the Finnish three-digit codes. This was undertaken independently by four exposure experts and the results were subsequently compared and reconciled. Unfortunately, it was not possible to create one-to-one links between the Finnish and ISCO68 classifications and therefore the crosswalk includes some multiple links, i.e. where one Finnish code was linked to several ISCO68 codes and *vice versa*. The crosswalk, which is available as supplementary data at *Annals of Occupational Hygiene* online, was reviewed by the exposure assessment team, including two experts of the Finnish coding system.

Several other minor modifications to the FINJEM–ISCO68 linkage were carried out. For example, ISCO68 does not contain a specific code for petrol service station attendants, who are included within the large retail sales group in ISCO68 (groups 4–51). It was decided that this was an important omission, particularly for exposure to engine exhaust fumes, and a specific code was added to the ISCO68 coding system. This code was subsequently linked to the Finnish code for the petrol station attendants and cashiers.

Modification of FINJEM exposure estimates

Methods were developed and applied to the FINJEM in order to deal with a number of its limitations. The following sections describe the methods used to modify FINJEM exposure estimates for the INTEROCC study.

Linkage of several Finnish codes to one ISCO68 code. When multiple FINJEM codes were linked to one ISCO68 code, a weighted mean was calculated for the proportion exposed (*P*) and the level of exposure (*L*) for each agent assigned among the FINJEM codes. The weighting was taken from the number of workers in each occupational code provided by FINJEM (i.e. based on the Finnish rather than the INTEROCC population).

Linkage of several ISCO68 codes to one Finnish code. As there are 311 three-digit Finnish codes and over 1500 five-digit codes in ISCO68, it was inevitable that many of the Finnish codes were linked to several ISCO68 five-digit codes. This could lead to important lack of specificity in the exposure assignments. The impact of this lack of specificity was estimated by comparing the FINJEM exposure estimates with estimates from a large lung cancer case–control study in Montreal, Canada (Siemiatycki, 1991). The exposure estimates in this study were based on expert assessments following a review of detailed occupational histories, in which exposure to a list of nearly 300 substances was assessed for each subject. These assessments were subsequently summarized by ISCO68 code (Lavoué *et al.*, 2012), thereby allowing comparison with the FINJEM estimates (using the crosswalk between FINJEM and ISCO68).

The Montreal study assigned an exposure level to each job held by subjects as 0 (no exposure) to 3 (high exposure) (Lavoué *et al.*, 2012). In order to permit averaging exposure ratings within ISCO68 codes, the Montreal exposure intensity scale was modified by applying a weight of 1, 5, and 25 to the low-, medium-, and high-exposure categories, respectively (based on a consensus scheme adopted by Montreal experts), and by adjusting the exposure estimate for the fraction of the working time that exposure was reported to occur.

The FINJEM–Montreal comparison, described in detail elsewhere (Lavoué *et al.*, 2012), allowed us to identify a number of ISCO68 groups, each group linked to a single Finnish code, with potential heterogeneous exposure based on Montreal exposure estimates. For example, there is only one FINJEM code for all types of mechanics, whereas there are 21 separate five-digit ISCO68 codes for the different types of mechanics, including motor vehicle mechanics, aircraft engine mechanics, machine fitters, machine assemblers, and precision instrument makers. A 2-fold difference between the minimum and maximum Montreal exposure level assigned to the ISCO68 codes linked to a single FINJEM code was adopted as an arbitrary threshold for deciding if heterogeneity occurred. In these cases, we carried out the following calibration procedure. We assumed that the initial FINJEM estimate L for a particular FINJEM code should be the arithmetic mean of the actual exposure estimates for the ISCO68 codes linked to that FINJEM code:

$$L_i = L \times \frac{M_i}{\bar{M}} \quad (1)$$

where L_i is the calibrated estimate for the exposure intensity for ISCO68 code = i; L is the original FINJEM estimate for the FINJEM code, which is linked to ISCO codes i–n; M_i is the exposure estimate from the Montreal study for ISCO68 code = i; and $\bar{M}$ is the arithmetic average of M_i values. Results of the calibration were peer reviewed, which resulted in some modifications when the calibrations were carried out based on limited number of observations in the Montreal study. For example, the internal calibration of the ISCO68 codes linked to 'Machine and engine mechanics' resulted in relatively high exposures to aromatic hydrocarbons for the ISCO68 code 'Office machine mechanic', which were in the same order of magnitude as mechanics of heavy and transport machinery. It was decided that this was not realistic and exposure to aromatic hydrocarbons was reduced for this occupational group.

Wide period covered by a critical time window (1960–1984) in FINJEM. FINJEM provides estimates of exposure for several time periods (1945–1959, 1960–1984, 1985–1994, 1995–1997, 1998–2000, 2001–2003, and 2004–2006) and within each period, exposure is assumed to have remained constant. It was felt that the time period 1960–1984 was too wide, especially as it covered an important transition period in the early 1970s in which exposure to many substances was significantly reduced due to a combination of technological change and increased regulation (Kauppinen *et al.*, 2012). For 16 substances, revised exposure estimates were available for the periods 1960–1974 and 1975–1984 from the NOCCA project (Kauppinen *et al.*, 2009). For the remaining 12 agents of interest included in the INTEROCC study, we split the time window. The exposure estimates for the time window 1960–1974 were estimated as the average of the original estimates for time periods 1945–1959 and 1960–1984, while for the time window 1974–1984, this was based on the average estimates from the original 1960–1984 and 1985–1994 time windows.

Inconsistencies of estimates for solvent exposure. FINJEM provides estimates for four broad groups of solvents (aliphatic and alicyclic hydrocarbons, aromatic hydrocarbons, chlorinated hydrocarbons, and other organic solvents) as well as seven individual solvents (e.g. benzene, toluene, trichloroethylene) (Table 1). Since the exposure assessments for the development of the FINJEM were carried out independently, agent by agent, some inconsistencies exist in the assignment of exposure estimates between some individual substances and the solvent groups they belong to. For example, FINJEM code 652 (machine and engine mechanics) was assigned exposure to toluene and benzene but not to aromatic hydrocarbons. In order to make these solvent assignments more consistent for a given occupation, the estimates for a solvent group were modified to at least the level of the highest individual solvent exposure within the group (in terms of the product of $P \times L$).

Inconsistencies in exposure estimates for diesel and gasoline exhaust fumes. Inconsistencies existed with diesel exhaust (DEEX) and gasoline exhaust (GEEX) in FINJEM exposure estimates across various occupational groups. For example, service station attendants were assigned DEEX but not GEEX exposure, while labourers were assigned exposure to GEEX but not to DEEX. Since FINJEM assigned both DEEX and GEEX to motor vehicle and tram drivers (FINJEM code 540), the time period specific ratio of the DEEX to the GEEX exposure intensities (L) for this occupation was used to impute missing DEEX or GEEX exposure intensities for occupations involving road transport. For asphalt workers, who had a higher DEEX exposure level than the other transport occupations, the DEEX/GEEX ratio from FINJEM code 552 (road and tram service personnel) was used as we felt that this was a more representative reference. The prevalence of the missing DEEX or GEEX exposure was set at the prevalence level for the exhaust exposure already assigned for the same occupational code.

Low exposure estimates for benzene prior to 1974 in FINJEM. There was a consensus in the exposure assessment group that benzene use was widespread prior to 1974 and that benzene exposure occurred simultaneously with exposure to other solvents, whereas FINJEM only assigned benzene exposure sporadically. FINJEM occupational codes (pre-1974) were reviewed to identify those with no benzene exposure that did have exposure to another indicator solvent for both time periods prior to 1974. The solvent used as an indicator of benzene exposure for a given occupation code was selected in hierarchical order as follows: aromatic hydrocarbon solvents, chlorinated hydrocarbon solvents, aliphatic hydrocarbon solvents, other organic solvents, toluene, and trichloroethylene. The average ratio of the benzene level to the indicator solvent level was calculated across FINJEM occupations for each time period (1945–1959 and 1960–1974), where the benzene and indicator solvent exposure was non-null. This ratio was applied to the level of the indicator solvent for that occupation to estimate the benzene level. The prevalence for the created benzene level was copied from the indicator solvent. Estimates of benzene exposure after 1974 were not modified.

No code for supervisors and foremen in FINJEM. Within ISCO68, there are specific codes for supervisors/foremen in different occupations or industries (ISCO68 group 7-00). However, no equivalent codes are available in the Finnish system, therefore no exposure estimate existed. It was, therefore, decided to link the ISCO68 codes for supervisors to the most appropriate Finnish code (based on the occupation and industry) and arbitrarily reduce the exposure intensity by 25% to account for the fact that the supervisors/foremen have generally lower exposures than workers they supervise.

Underestimation of exposure to polycyclic aromatic hydrocarbons and benzo(a)pyrene. The estimates of exposure for polycyclic aromatic hydrocarbon (PAH) and benzo(a)pyrene (B[a]P) in FINJEM ignored the contribution to these agents from exposure to environmental tobacco smoke (ETS). Even though the exposure to PAHs and B[a]P from ETS is likely to be relatively low compared to industrial sources, it was decided to include this source due to the widespread exposure to ETS in the past. Exposure to ETS is assigned by FINJEM as a proportion of the working hours exposed from 1985 to 1994 onwards (although for some occupations, estimates were only available from 1998 to 2000 onwards). Estimates from 1985 to 1994 or 1998 to 2000 were copied into the earlier time periods, assuming exposure to tobacco smoke would have been at least as much in earlier time periods. To estimate exposure to PAH and B[a]P from ETS, data were used from Castro *et al.* (2011), who observed B[a]P and PAH levels in respirable particulate matter ($PM_{2.5}$) from tobacco smoke of 0.046 ng B[a]P per microgram of $PM_{2.5}$ and 0.474 ng all PAHs microgram of $PM_{2.5}$, respectively. Next, we used data from several studies in the UK (Semple *et al.*, 2007, 2010; Gotz *et al.*, 2008) to determine the $PM_{2.5}$ levels in bars and restaurants. A weighted geometric mean level of $PM_{2.5}$ of 139 µg m^{-3} was obtained from these studies. By combining these data, exposure estimates for bar and restaurant staff of 65.9 ng m^{-3} for PAH and 6.4 ng m^{-3} for B[a]P were calculated.

To extrapolate and obtain estimates of PAH and B[a]P exposure levels for all FINJEM codes, the ratio of the ETS exposure for the occupational code and the ETS exposure for waiters in bars and restaurants (FINJEM code 821) was multiplied by the PAH- and B[a]P-derived estimates obtained for bar and restaurant staff. The prevalence estimates for ETS were used for the derived PAH and B[a]P. If FINJEM already assigned an estimate for PAH and B[a]P, then this estimate was overwritten only if the derived level from ETS exposure ($P \times L$) was higher than the original estimate.

Peer review of all modifications to FINJEM for use in INTEROCC

The chemical exposure assessment team (M.v.T., L.K., L.R., T.K., N.P., G.B., D.M., J.L., and D.K.) reviewed each modification to the FINJEM as it was implemented. The final results after implementation of all modifications were again reviewed for coherence and consistency and those retained are described in this paper.

Comparison of FINJEM and INTEROCC JEM estimates

To evaluate the impact of the modifications made to the exposure estimates when developing the INTEROCC JEM, we compared the results of the exposure assessment when applying the two JEMs on the INTEROCC study population. First, we compared the proportion of exposed INTEROCC study subjects as estimated by FINJEM and INTEROCC JEM for each agent by time period. In this comparison, a subject was considered exposed if the proportion of exposed individuals within an ISCO68 category was greater than or equal to 5%. Next, we compared the results after calculating cumulative exposure for all study subjects for each agent across the entire occupational history. The cumulative exposure estimate was calculated as the sum of the product of the probability of exposure *P*, the level of exposure *L*, and the duration for each job held by a subject. Again, a subject was considered exposed if employed in a job that had been coded to an ISCO68 code with a proportion of exposed individuals greater than or equal to 5%. Cumulative exposure categories were then developed as follows: never exposed, low exposed: bottom 30% of the cumulative exposure distribution, medium exposed 30–60%, high exposed 60–90%, and very high exposed: top 10%. It should be emphasized that the cumulative exposure estimates shown in this article are developed to allow comparison between the FINJEM and INTEROCC JEM. In future papers of the INTEROCC study investigating the association between estimates of occupational exposure and risk of brain tumours, different exposure definitions and cumulative exposure categories may be used. In particular, a higher threshold might be selected for the exposed status.

RESULTS

There were over 35 000 jobs coded in the seven participating INTEROCC countries. As expected, the majority of occupations were in the professional, clerical, sales, and service sectors. The largest professional group consisted of managers and administrators with groups such as health professionals (physicians and nurses), teachers, accountants, and social workers making up the bulk of the other professionals. Clerical workers were by far the most prevalent group followed by occupations in sales. Detailed analyses of occupation and industry distributions and of their association with brain tumour risk will be published elsewhere.

The outcome of all the modifications resulted in considerably more occupations being 'exposed' (i.e. with a job code for which it is estimated that at least 5% of workers in this occupation are exposed to the chemicals of interest) in the INTEROCC JEM than in FINJEM for most time periods. Table 2 shows, by agent, the number of occupations (ISCO68 codes) linked to exposure and the mean $P \times L$ exposure for the INTEROCC JEM and FINJEM. Notably, as a result of the modifications, the number of occupations considered as exposed for the solvent groups increased considerably, while for individual solvents, it remained largely unchanged, except for benzene prior to 1974, which increased. Also the number exposed to B[a]P and PAH was drastically increased.

Heterogeneity of exposures resulting from differences in occupations grouped into one Finnish occupational code (see section Linkage of Several ISCO68 Codes to One Finnish Code)

FINJEM-based exposure estimates for groups of ISCO68 codes that were linked to single Finnish occupational codes in the crosswalk were compared with estimates for the same ISCO68 codes based on expert judgements in Montreal (Lavoué *et al.*, 2012) to determine if important differences in exposure occurred within these groups of ISCO68 codes. Based on this comparison, exposure estimates for six agents (aromatic hydrocarbons, iron, gasoline exhaust, other organic solvents, lead, and welding fumes) for a total of 123 ISCO68 codes were modified. Table 3 shows selected examples of these modifications, while supplementary data at *Annals of Occupational Hygiene* online provide details of all these modifications. Exposure to aromatic hydrocarbons for painters showed the most dramatic differences with an 8-fold difference between building painters at the lowest end and spray painters at the highest end. Taxi drivers have three times the estimated exposure to gasoline exhaust than other motor vehicle drivers, with levels for tram and bus drivers in between. The new levels of blood lead assigned to the different groups of mechanics range from no exposure for mechanics not working with motor vehicles (such as office machine mechanics) to levels of 112 µmol l^{-1} for those repairing automobiles and 119 µmol l^{-1} for motorcycle mechanics.

Impact of the modifications on prevalence and exposure in the INTEROCC study population

Table 4 shows the prevalence of INTEROCC study subjects exposed to each agent in each time period for FINJEM and the INTEROCC JEM. Due to the modifications, there are significant differences in numbers exposed for the three solvent groups as well as benzene, B[a]P, PAH, and gasoline engine emissions across all time periods.

Table 5 shows the distribution of the number of INTEROCC subjects by category of cumulative exposure for each agent as assigned by each JEM.

Table 2. Comparison of the number of ISCO68 occupational codes that are considered to be exposed and the estimated mean exposure for the exposed ISCO68 codes when using FINJEM and the INTEROCC JEM.

Agent	1945–1959				1960–1974				1975–1984				1985–1994				1995–1997			
	FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM	
	n	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean
Solvents																				
CHC (ppm)	108	1.4	219	2.7	92	1.1	225	1.4	92	1.1	198	1.1	90	1.1	215	0.7	90	0.8	125	0.7
PER (ppm)	31	1	31	1	44	1	35	1.5	44	1	44	0.8	42	0.4	44	0.5	42	0.3	44	0.4
TRI (ppm)	132	3.8	132	3.8	118	1	131	1.3	118	1	110	0.6	26	0.4	26	0.4	26	0.4	26	0.4
TCE (ppm)		—		—	34	1.7	34	1.7	34	1.7	160	0.8	173	0.3	173	0.3	5	0.3	5	0.3
MCH (ppm)	16	2.5	16	2.5	99	1	78	1.4	99	1	99	0.7	99	0.3	99	0.3	99	0.3	99	0.3
ARHC (ppm)	112	4.4	312	7.6	115	3.2	289	8.3	115	3.2	150	4.3	115	4.4	140	3.7	115	3.6	140	3.1
TOLU (ppm)	132	10.1	131	10.1	130	5.5	131	10	130	5.5	124	2.2	105	0.9	105	0.9	105	0.9	105	0.9
BENZ (ppm)	151	0.5	308	0.9	123	0.1	274	0.7	123	0.1	67	0	32	0	32	0	9	0	9	0
ALHC (ppm)	99	4.7	101	4.6	127	4.3	129	4.6	127	4.3	129	4.1	93	3.9	95	3.8	93	2.7	95	2.6
GASO (ppm)	36	0.2	36	0.2	25	0.1	26	0.2	25	0.1	25	0	25	0	25	0	25	0	25	0
OSOL (ppm)	117	3.3	116	3.3	107	4.9	107	5	107	4.9	101	4.9	86	6.5	86	6.4	86	7.6	86	7.5
Combustion products																				
DEEX (mg m^{-3})	120	0	108	0	137	0.1	113	0.1	137	0.1	125	0.1	119	0.1	108	0.1	115	0.1	104	0.1
GEEX (mg m^{-3})	54	8.2	82	6	63	5	88	5.6	63	5	87	4.1	53	4.2	63	4.3	53	4.1	63	4.3
BITU (mg m^{-3})	44	0.1	44	0.1	51	0.1	51	0.1	51	0.1	51	0.1	51	0.1	51	0.1	44	0.1	44	0.1
B[a]P (μg m^{-3})	164	0.3	1349	0	164	0.1	1349	0	164	0.1	1349	0	155	0.1	1367	0	148	0.1	1105	0
PAH (μg m^{-3})	126	2.8	1334	0.3	131	2.5	1334	0.3	131	2.5	1334	0.2	129	2.1	1352	0.2	122	2.2	1090	0.3

Table 2. *Continued*

Agent	1945–1959				1960–1974				1975–1984				1985–1994				1995–1997			
	FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM		FINJEM		INTEROCC JEM	
	n	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean	*n*	Mean
WELD (mg m^{-3})	198	1	198	1	196	0.9	198	1.1	196	0.9	198	0.7	200	0.6	198	0.6	201	0.5	198	0.5
Metals																				
CD (μg m^{-3})	96	0.4	96	0.4	83	0.4	83	0.4	83	0.4	83	0.4	83	0.3	82	0.3	83	0.3	82	0.3
CR (μg m^{-3})	211	1.6	211	1.6	242	3.3	242	2.7	242	3.3	244	3.6	246	3.5	243	3.5	235	3.5	234	3.5
FE (mg m^{-3})	202	0.6	201	0.6	202	0.4	201	0.5	202	0.4	201	0.3	202	0.3	202	0.3	202	0.2	202	0.2
NI (μg m^{-3})	269	0.9	269	0.9	276	1.5	276	1.1	276	1.5	276	1.5	279	1.3	276	1.2	279	1.3	278	1.2
PB (μmol l^{-1} blood)	361	0.3	351	0.3	345	0.2	345	0.3	345	0.2	307	0.2	272	0.1	262	0.2	261	0.1	249	0.1
Dusts																				
ANIM (mg m^{-3})	84	0.1	84	0.1	84	0.1	84	0.1	84	0.1	84	0.1	84	0.1	84	0.1	86	0.1	86	0.1
ASB (f cm^{-3})	261	0.2	261	0.2	304	0.2	304	0.2	304	0.2	287	0.1	137	0	137	0	93	0	93	0
QUAR (mg m^{-3})	218	0.2	218	0.2	218	0.1	218	0.2	218	0.1	218	0.1	218	0.1	218	0.1	218	0.1	218	0.1
WOOD (mg m^{-3})	61	0.8	62	0.8	62	0.8	62	0.7	62	0.8	62	0.7	62	0.6	62	0.6	63	0.6	62	0.6
Others																				
FORM (ppm)	124	0	128	0	203	0.1	206	0.1	203	0.1	205	0.1	203	0	207	0	195	0	199	0
OIL (mg m^{-3})	123	1	123	1	130	0.6	130	0.8	130	0.6	130	0.6	130	0.6	130	0.6	130	0.6	130	0.6
SO_2 (ppm)	61	0.4	61	0.4	61	0.3	61	0.4	61	0.3	61	0.3	61	0.3	61	0.3	54	0.3	54	0.3

n = number of ISCO68 occupational categories with proportion of exposed workers greater than or equal to 5%; mean = estimated mean exposure across all the exposed ISCO68 occupations calculated by $P \times L$.

Table 3. Examples of exposure ($P \times L$) to selected agents for FINJEM occupations linked to multiple ISCO68 codes, judged to be heterogeneous in exposure: exposure by FINJEM and separately for each ISCO68 code in the INTEROCC JEM.

Exposures	Occupation code/source	Description	$P \times L$ by time period				
			1945–1959	1960–1974	1975–1984	1985–1994	1995–1997
ARHC (ppm)	FINJEM 680	Painters, lacquerers, and floor layers	8.0	5.6	5.6	14.4	5.0
	ISCO 9-31.20	Building painter	4.2	5.0	1.7	3.0	1.0
	ISCO 9-31.30	Structural steel and ship painter	20.2	24.3	8.1	14.6	5.1
	ISCO 9-39.30	Spray painter (except construction)	36.3	43.6	14.5	26.2	9.1
GEEX (mg m^{-3})	FINJEM 540	Motor vehicle and tram drivers	3.2	2.3	2.3	1.4	1.4
	ISCO 9-85.20	Tram driver	3.2	2.8	1.8	1.4	1.4
	ISCO 9-85.30	Taxi driver	5.2	4.5	3.0	2.2	2.2
	ISCO 9-85.40	Motor bus driver	2.7	2.3	1.6	1.2	1.1
	ISCO 9-85.90	Other motor vehicle drivers	1.7	1.5	1.0	0.7	0.7
PB (μmol l^{-1} blood)	FINJEM 652	Machine and engine mechanics	0.3	0.2	0.2	0.1	0.1
	ISCO 8-43.20	Automobile	1.1	0.9	0.9	0.8	0.8
	ISCO 8-43.40	Motor cycle	1.2	1.0	1.0	0.8	0.8
	ISCO 8-49.20	Diesel engine (except motor vehicle)	0.6	0.5	0.5	0.4	0.4
	ISCO 8-49.65	Office machines	0.0	0.0	0.0	0.0	0.0

Five cumulative exposure categories were derived from the distribution in the INTEROCC study: (i) not exposed (not shown in Table 5), (ii) low exposure (first 30% of exposed), (iii) medium exposed (30–60% of exposed), (iv) high exposed (60–90% of exposed), and (v) very high exposed (top 10% of exposed). The numbers increased most in the lower tertiles of exposure for 19 agents, including PAH and B[a]P. However, for the remaining agents, the change in numbers exposed is distributed across categories and for trichloroethylene, methylene chloride, benzene, and formaldehyde, increased numbers were found in the higher categories.

DISCUSSION

One of the major challenges to studies of occupational risk factors for disease is the difficulty of assessing exposure. Various approaches have been developed based on detailed occupational histories (Siemiatycki *et al.*, 1991; Fritschi *et al.*, 2012). These are, however, costly and lengthy enterprises. A useful alternative is to use a JEM, particularly when the only information available is a crude occupational history. The FINJEM covers major occupational exposures since 1945 and it is the only national community-based effort of its kind. However, the relevance of the FINJEM estimates of exposure to other countries is not given and the occupational codes used are Finnish. We, therefore, undertook a multistep process, addressing specific weaknesses identified by an international group of occupational hygienists, using approaches agreed upon by the said group, and with an ultimate check in a peer review of the final modified exposure estimates, in order to better reflect prevailing exposure patterns in the seven participating countries and render them more consistent.

INTEROCC used a large population-based JEM (FINJEM) to assign exposure to the 29 chemical agents of interest. The ISCO68 classification was chosen for INTEROCC because it contains a larger number of five-digit codes that are more detailed than any subsequent version of the international classification system. Therefore, the first hurdle was to create a link between the ISCO68 classification system and the Finnish codes. We successfully created such a link (provided in supplementary data at *Annals of Occupational Hygiene* online), which is available

Table 4. Proportion (%) of exposed subjects in the INTEROCC study population by agent and time period comparing the FINJEM and INTEROCC JEM.

Agent	1945–1959		1960–1974		1975–1984		1985–1994		1995–1997	
	FINJEM	INTEROCC JEM	FINJEM	INTEROCC JEM	FINJEM	INTEROCC JEM	FINJEM	INTEROCC JEM	FINJEM	INTEROCC JEM
Solvents										
CHC	3	10	4	16	4	11	3	8	2	3
PER	1	1	2	2	2	2	2	2	1	1
TRI	7	7	6	7	6	5	1	1	1	1
TCE			2	2	2	8	7	7	0	0
MCH	1	1	6	6	6	5	5	5	3	3
ARHC	4	18	4	15	4	8	3	9	2	3
TOLU	6	8	6	12	6	7	4	8	3	3
BENZ	7	12	7	13	7	6	2	2	0	0
ALHC	3	11	5	17	5	11	4	11	3	4
GASO	3	3	3	3	3	3	2	2	1	1
OSOL	3	3	3	4	3	3	2	2	1	4
Combustion products										
DEEX	14	14	12	14	12	12	8	8	6	6
GEEX	6	13	7	11	7	9	6	7	5	7
B[a]P	8	80	7	82	7	81	5	83	3	51
BITU	0	0	1	1	1	1	1	1	0	0
PAH	8	80	6	81	6	80	4	82	3	51
WELD	11	11	9	11	9	8	6	6	5	5
Metals										
CD	2	2	2	2	2	1	1	1	1	1
CR	12	12	10	12	10	9	8	8	5	5
FE	11	11	9	11	9	9	6	6	5	5
NI	11	11	9	10	9	8	7	7	5	5
PB	14	14	14	16	14	12	10	10	8	7
Dusts										
ANIM	9	9	4	4	4	3	2	2	2	2
ASB	21	21	17	19	17	15	9	9	4	4
QUAR	11	11	7	8	7	6	5	5	4	4
WOOD	4	4	2	2	2	2	2	2	1	1
Others										
FORM	7	8	8	11	8	8	6	8	4	5
OIL	9	9	5	7	5	4	3	3	2	2
SO_2	1	1	1	1	1	0	0	0	0	0

Note: Study subjects were considered to be exposed if they had ever worked in an occupation with a assigned proportion of exposed workers greater than or equal to 5%.

to other researchers with the caveat that the current crosswalk concerns only the occupations held by INTEROCC study subjects. However, there are only 311 occupation codes in FINJEM, while there are over 1500 five-digit codes in ISCO68. Inevitably, the crosswalk linked some FINJEM codes to many ISCO68 codes, thereby assigning identical exposure estimates to these ISCO68 codes, where in reality exposure may differ greatly.

The relevance of FINJEM exposure estimates to other countries is not clear. FINJEM has been applied in various studies in different countries (Dryver *et al.*, 2004; Karipidis *et al.*, 2007), but a comprehensive evaluation of the relevance of the estimates of prevalence and level for other countries has, to our knowledge, not been carried out. Unfortunately, it was also not feasible to include such an evaluation by comparing FINJEM estimates with local exposure estimates, due to lack of resources and because estimates were generally not readily available in the same format. A comparison was carried out for the Nordic countries involved in the NOCCA study (Kauppinen *et al.*, 2009). Most exposures were considered

Table 5. Distribution of numbers of subjects in the INTEROCC study population derived from FINJEM and INTEROCC JEM, by lifetime cumulative exposure category (excluding the never exposed category) for each agent.

Group of agents	Agent	Exposure category	FINJEM, n^a	INTEROCC JEM, n^b	Difference, n^c
Solvents	CHC	>0 to ≤2.44 ppm-years	148	343	195
		2.45–8.91 ppm-years	149	422	273
		8.92–27.72 ppm-years	151	369	218
		>27.73 ppm-years (top 10%)	50	140	90
	PER	>0 to ≤0.70 ppm-years	77	80	3
		0.71–1.88 ppm-years	75	76	1
		1.89–8.74 ppm-years	84	77	−7
		>8.74 ppm-years (top 10%)	27	29	2
	TRI	>0 to ≤2.48 ppm-years	207	243	36
		>2.48–7.18 ppm-years	222	199	−23
		7.19–20.21 ppm-years	212	195	−17
		>20.21 ppm-years (top 10%)	74	84	10
	TCE	>0 to ≤1.13 ppm-years	197	179	−18
		1.13–2.50 ppm-years	180	181	1
		2.50–9.75 ppm-years	228	319	91
		>9.75 ppm-years (top 10%)	69	139	70
	MCH	>0 to ≤2.00 ppm-years	204	183	−21
		2.00–6.00 ppm-years	210	207	−3
		6.01–18.38 ppm-years	213	204	−9
		>18.38 ppm-years (top 10%)	70	65	−5
	ARHC	>0 to ≤5.20 ppm-years	150	500	350
		>5.20–32.29 ppm-years	150	234	84
		32.30–184.50 ppm-years	150	308	158
		>184.50 ppm-years (top 10%)	51	126	75
	TOLU	>0 to ≤5.00 ppm-years	203	225	22
		5.00–20.25 ppm-years	203	182	−21
		20.26–151.75 ppm-years	204	200	−4
		>151.75 ppm-years (top 10%)	68	63	−5
	BENZ	>0 to ≤0.30 ppm-years	206	258	58
		0.30–0.86 ppm-years	220	207	−23
		0.87–2.84 ppm-years	213	320	120
		>2.84 ppm-years (top 10%)	72	201	124
	ALHC	>0 to ≤4.59 ppm-years	178	217	39
		4.59–14.65 ppm-years	191	193	2
		14.66–115.72 ppm-years	185	190	5
		>115.72 ppm-years (top 10%)	62	59	−3
	GASO	>0 to ≤0.16 ppm-years	106	126	20
		0.16–0.47 ppm-years	102	98	−4
		0.48–1.36 ppm-years	114	88	−26
		>1.36 ppm-years (top 10%)	36	46	10
	OSOL	>0 to ≤16.12 ppm-years	97	118	21
		16.12–64.02 ppm-years	98	113	15
		64.03–234.00 ppm-years	97	63	−34
		>234.00 ppm-years (top 10%)	33	30	−3
Combustion products	DEEX	>0 to ≤0.04 mg m^{-3}-years	429	377	−52
		0.04–0.26 mg m^{-3}-years	430	438	8
		0.27–1.18 mg m^{-3}-years	429	367	−62
		>1.18 mg m^{-3}-years (top 10%)	144	190	46

Table 5. *Continued*

Group of agents	Agent	Exposure category	FINJEM, n^a	INTEROCC JEM, n^b	Difference, n^c
	GEEX	>0 to ≤11.79 mg m^{-3}-years	244	370	126
		11.79–40.00 mg m^{-3}-years	245	195	−50
		40.01–132.40 mg m^{-3}-years	244	214	−30
		>132.40 mg m^{-3}-years (top 10%)	83	140	57
	BITU	>0 to ≤0.12 mg m^{-3}-years	27	30	3
		0.13–0.32 mg m^{-3}-years	27	26	−1
		0.33–1.28 mg m^{-3}-years	28	28	0
		>1.28 mg m^{-3}-years (top 10%)	10	8	−2
	B[a]P	>0 to ≤0.02 μg m^{-3}-years	222	5845	5623
		0.02–0.06 μg m^{-3}-years	223	1813	1590
		0.07–0.28 μg m^{-3}-years	222	401	179
		>0.28 μg m^{-3}-years (top 10%)	75	76	1
	PAH	>0 to ≤0.30 μg m^{-3}-years	210	6718	6508
		0.31–1.05 μg m^{-3}-years	210	1013	803
		1.06–4.35 μg m^{-3}-years	215	281	66
		>4.35 μg m^{-3}-years (top 10%)	71	92	21
	WELD	>0 to ≤0.66 mg m^{-3}-years	299	297	−2
		0.66–2.70 mg m^{-3}-years	299	300	1
		2.71–29.75 mg m^{-3}-years	300	304	4
		>29.75 mg m^{-3}-years (top 10%)	100	95	−5
Metals	CD	>0 to ≤0.36 μg m^{-3}-years	69	71	2
		0.36–1.67 μg m^{-3}-years	72	70	−2
		1.68–6.90 μg m^{-3}-years	71	72	1
		>6.90 μg m^{-3}-years (top 10%)	24	23	−1
	CR	>0 to ≤1.82 μg m^{-3}–years	336	353	17
		1.82–9.37 μg m^{-3}-years	340	337	−3
		9.38–114.27 μg m^{-3}-years	339	330	−9
		>114.27 μg m^{-3}-years (top 10%)	113	108	−5
	FE	>0 to ≤0.64 mg m^{-3}-years	299	323	24
		0.64–2.17 mg m^{-3}-years	299	298	−1
		2.18–11.73 mg m^{-3}-years	300	279	−21
		>11.73 mg m^{-3}-years (top 10%)	100	98	−2
	NI	>0 to ≤2.18 μg m^{-3}-years	308	312	4
		2.18–7.89 μg m^{-3}-years	311	329	18
		7.90–30.79 μg m^{-3}-years	310	299	−11
		>30.79 μg m^{-3}-years (top 10%)	104	93	−11
	PB	>0 to ≤0.45 mg m^{-3}-years	475	499	24
		0.45–1.40 mg m^{-3}-years	476	412	−64
		1.41–4.83 mg m^{-3}-years	476	401	−75
		>4.84 mg m^{-3}-years (top 10%)	159	246	87
Dusts	ANIM	>0 to ≤0.06 mg m^{-3}-years	137	151	14
		0.06–0.15 mg m^{-3}-years	140	142	2
		0.16–0.51 mg m^{-3}-years	138	139	1
		>0.51 mg m^{-3}-years (top 10%)	47	30	−17
	ASB	>0 to <0.14 f cm^{-3}-years	534	608	74
		0.14–0.67 f cm^{-3}-years	537	494	−43
		0.68–3.36 f cm^{-3}-years	536	483	−53
		>3.36 f cm^{-3}-years (top 10%)	179	191	12

Table 5. *Continued*

Group of agents	Agent	Exposure category	FINJEM, n^a	INTEROCC JEM, n^b	Difference, n^c
	QUAR	>0 to ≤0.13 mg m^{-3}-years	263	274	11
		0.13–0.55 mg m^{-3}-years	263	272	9
		0.56–2.21 mg m^{-3}-years	263	249	−14
		>2.21 mg m^{-3}-years (top 10%)	88	82	−6
	WOOD	>0 to ≤1.31 mg m^{-3}-years	78	86	8
		1.31–4.98 mg m^{-3}-years	79	68	−11
		4.98 to 19.00 mg m^{-3}-years	78	79	1
		>19.00 mg m^{-3}-years (top 10%)	27	26	−1
Others	FORM	>0 to ≤0.02 ppm-years	293	192	−101
		0.02–0.08 ppm-years	294	240	−54
		0.09–0.79 ppm-years	294	415	121
		>0.79 ppm-years (top 10%)	98	135	37
	OIL	>0 to ≤0.25 mg m^{-3}-years	184	166	−18
		0.25–2.40 mg m^{-3}-years	184	200	16
		2.41–30.60 mg m^{-3}-years	185	184	−1
		>30.60 mg m^{-3}-years (top 10%)	63	66	3
	SO2	>0 to ≤0.68 ppm-years	21	20	−1
		0.68–2.71 ppm-years	21	23	2
		2.72–13.45 ppm-years	21	21	0
		>13.45 ppm-years (top 10%)	7	6	−1

Note: Study subjects were considered to be exposed if they had ever worked in an occupation with a assigned proportion of exposed workers greater than or equal to 5%. Categories derived from distribution of lifetime cumulative exposure (low exposed: bottom 30% of the cumulative exposure distribution, medium exposed: 30–60%, high exposed: 60–90%, and very high exposed: top 10%).

[a]*n* refers to the number of INTEROCC study subjects categorized in each cumulative exposure category when using the original FINJEM.

[b]*n* refers to the number of INTEROCC study subjects categorized in each cumulative exposure category when using the INTEROCC JEM.

[c]*n* refers to the difference in the number of INTEROCC study subjects included in each cumulative exposure category based on the original FINJEM and INTEROCC JEM.

to be fairly similar between the Nordic countries, with only a few major differences identified (Kauppinen *et al.*, 2009). Furthermore, a comparison was carried out of FINJEM estimates with exposure estimates obtained from expert assessments from a large case–control study of lung cancer in Montreal, Canada (Lavoué *et al.*, 2012). The results of this comparison suggested that for some exposure, there were substantial differences between FINJEM estimates and the estimates obtained from the Canadian study, although for exposure to metals, the assessments appear to be reasonably comparable (Lavoué *et al.*, 2012).

A group of exposure assessment experts undertook a review of FINJEM and its relevance to an international study and a range of modifications were developed and implemented. Expanding on the work undertaken for the NOCCA study (Kauppinen *et al.*, 2009), splitting the time period 1960–1984 into pre- and post-1974, more accurately reflects the changes in exposure levels to many substances from the earlier to the later period. This was a time of increasing regulation in industry, and although changes were not implemented uniformly across countries, the trend was similar in most of the INTEROCC countries. It remains an important issue for future work to resolve more precisely when and to what extent the changes in use patterns occurred in each country. For example, the timing for a decrease in asbestos and benzene exposure differs considerably from one country to another.

Assessments for the grouped and individual solvents included in FINJEM were carried out independently and were not previously verified for consistency. In this study, we tried to ensure that the assessments for individual solvents were taken into account for the group solvents. It should be noted that not all individual solvents are included in FINJEM and this could be addressed in future work. The expert group was also struck by the lack of benzene attribution when other solvents had been assigned in FINJEM for the period prior to 1974. This may relate to the more limited use of benzene in Finland than in many other countries. The modifications resulted in a considerable increase in the prevalence of exposure to benzene in the earlier periods. Similar inconsistencies existed in FINJEM for gasoline and diesel emission exposure assignments. Thus, the assessments for motor transport and road maintenance and repair workers led to an overall increase in numbers of subjects exposed to both diesel and gasoline emissions.

Further, the assessment of exposure to B[a]P and PAH did not reflect occupational exposure to ETS. An innovative approach was developed resulting in a significant increase in the prevalence of exposure to both. Although the mean cumulative exposure decreased significantly because of the addition of low values, those occupations such as furnace men and foundry workers, where exposure to B[a]P and PAH is the highest, remain the highest exposed occupations. It is worth noting that while the modifications to B[a]P and PAH resulted in more subjects exposed in the lowest exposure category, this did not hold for the modifications to other substances. For all the other agents, the increase in numbers of occupations can be observed across all levels of exposure.

The fewer the occupation codes used for exposure assessment, the more likely it is that greater misclassification will occur because of heterogeneity of exposure across the subgroups linked to a given code. We attempted to resolve this issue by comparing the FINJEM exposure assessments with individual expert assessment for multiple ISCO68 five-digit codes linked to one Finnish code. This was limited to occupations for which we had sufficient data in the Montreal study to compare the expert assessments. In addition, this was only possible for ISCO68 codes linked to a FINJEM code for which an exposure was assigned. We have shown that calibrating the FINJEM estimates to account for these differences in exposure is feasible and important for reducing misclassification. This is an important area for future work to render population-based JEMs more accurate in their assessments. However, it should also be noted that this problem is closely related to the system of occupational codes used in constructing a JEM, which are generally not specifically designed for epidemiological studies ('t Mannetje and Kromhout, 2003).

In summary, several important modifications to the exposure estimates for the 28 agents of interest were implemented, addressing among others some heterogeneity of exposure within FINJEM, the wide time period covered by a critical time window (1960–1984) and inconsistencies within FINJEM for some solvent exposures and diesel and gasoline engine exhaust exposures. Although the work undertaken within the INTEROCC project has produced some important improvements for researchers using the FINJEM, there remain many areas to be explored further. In addition, the modifications undertaken within INTEROCC were focussed on the particular *a priori* group of agents selected for analysis of risk of brain cancer. We did not address issues related to the other chemical or physical agents available in FINJEM, or those agents of interest with very low population prevalence such as mercury or arsenic.

A link between exposure to pesticides and increased risk of brain tumours has been hypothesized (Khuder *et al.*, 1998; Lee *et al.*, 2005; Provost *et al.*, 2007). Pesticide exposure was not included in the INTEROCC study as FINJEM only provides exposure estimates for fungicides, herbicides, and insecticides rather than (categories of) active ingredients. The use of the active ingredients can vary widely across and within countries and over time. Information on historical use of pesticides on crops is available in various countries and could perhaps be used to develop a country-/region-specific exposure matrix for farmers (Dick *et al.*, 2010).

Biocides are a good example of agents where inter-country differences in exposure may be large. Other similar agents are asbestos and silica, where differences have been noticed to occur between Nordic countries (Kauppinen *et al.*, 2009). Furthermore, the nature and level of exposure for chemical and metal workers will depend to a large extent on the chemical and metal industry present in each country.

The comparison of exposure by expert judgement in Montreal with FINJEM estimates revealed several circumstances where exposure was null in FINJEM but not in Montreal and we believe that there are several occupational groups for which the FINJEM exposure assessment needs to be reviewed. We explored different approaches to resolving these differences. However, due to the lack of an appropriate basis for estimating occupation-specific prevalence on the one hand and the lack of the data necessary to establish a reasonable estimate for level of exposure on the other, it was agreed that further work would be required to address this question. It would be extremely valuable to explore other sources of exposure data such as CAREX (Kauppinen *et al.*, 2000) and the SYNERGY JEM (Peters *et al.*, 2012) to fill these potentials gaps in FINJEM.

Both FINJEM and the INTEROCC JEM use the *P* equal to or greater than 5% as a threshold to assign exposure. For example, if in a given occupational code fewer than 5% of the workers are exposed to an agent, then that occupation is considered unexposed. However, it should be noted that different definitions of exposure can be derived from the estimates of *P* for risk analyses. Theoretical calculations indicate that high specificity (i.e. avoiding false positive exposure assignments) is important in reducing the misclassification bias when the prevalence of exposure is low (Flegal *et al.*, 1986). As the FINJEM and INTEROCC JEM have assigned both a *P* (proportion of workers exposed) and *I* (intensity of exposure), the sensitivity and specificity can be modified by using different exposure cut-off points. For example, by using *P* as a means of defining exposure, a higher specificity can be achieved by assigning exposure only to those occupations where *P* is high (e.g. 50%). In addition, a recent paper by Burstyn *et al.* (2012) refers to aggregation bias when using JEMs that provide a proportion of exposed workers as well as an intensity (as is the case in FINJEM and INTEROCC JEM). The aggregation bias is caused by the fact that each occupational code includes both exposed and non-exposed workers. Simulations demonstrated that under certain conditions, bias in odds ratios away from the null is possible (Burstyn *et al.*, 2012). The advantage of both the FINJEM and INTEROCC JEM is that these JEMs can be applied in a flexible manner with different cut-off points for *P* to define the exposed category to try to minimize bias.

Finally, although the ISCO68 occupational classification system remains one of the best available international systems for occupational epidemiological studies, despite its limitations compared to more detailed systems such as the two versions of the Dictionary of Occupational Titles used in Canada and the USA from the 1970s, it is becoming out of date. There is an urgent need to develop an updated international classification of occupations, which is appropriate for use in cancer epidemiological studies.

SUPPLEMENTARY DATA

Supplementary data can be found at http://annhyg.oxfordjournals.org/.

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