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Estimating Exposures in the Asphalt Industry for an International Epidemiological Cohort Study of Cancer Risk

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Background *An exposure matrix (EM) for known and suspected carcinogens was required for a multicenter international cohort study of cancer risk and bitumen among asphalt workers.*

Methods *Production characteristics in companies enrolled in the study were ascertained through use of a company questionnaire (CQ). Exposures to coal tar, bitumen fume, organic vapor, polycyclic aromatic hydrocarbons, diesel fume, silica, and asbestos were assessed semi-quantitatively using information from CQs, expert judgment, and statistical models. Exposures of road paving workers to bitumen fume, organic vapor, and benzo(a)pyrene were estimated quantitatively by applying regression models, based on monitoring data, to exposure scenarios identified by the CQs.*

Results *Exposures estimates were derived for 217 companies enrolled in the cohort, plus the Swedish asphalt paving industry in general. Most companies were engaged in road paving and asphalt mixing, but some also participated in general construction and roofing. Coal tar use was most common in Denmark and The Netherlands, but the practice is now obsolete. Quantitative estimates of exposure to bitumen fume, organic vapor, and benzo(a)pyrene for pavers, and semi-quantitative estimates of exposure to these agents among all subjects were strongly correlated. Semi-quantitative estimates of exposure to bitumen fume and coal tar exposures were only moderately correlated. EM assessed non-monotonic historical decrease in exposures to all agents assessed except silica and diesel exhaust.*

Conclusions *We produced a data-driven EM using methodology that can be adapted for other multicenter studies.* Am. J. Ind. Med. 43:3–17, 2003. *© 2003 Wiley-Liss, Inc.*

KEY WORDS: bitumen; tar; exposure matrix

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INTRODUCTION

The International Agency for Research on Cancer (IARC) has assembled a cohort of asphalt workers from eight countries (Denmark, Finland, France, Germany, The Netherlands, Norway, Sweden, and Israel). In the context of the study, asphalt workers were defined as individuals involved in handling of asphalt from its manufacture at asphalt plants to its application in paving, roofing, or waterproofing. Some of the employees in the companies of interest were also employed in building and ground construction. Employees of oil refineries who are, strictly speaking, part of the asphalt industry were excluded from the study. Throughout this discussion, we will use the European convention of referring to the binder used in asphalt mixes as 'bitumen.' In North America, the binder is referred to as 'asphalt.' The study was prompted by an ongoing controversy about possible carcinogenicity of emissions derived from bitumen, the binder used in the asphalt mix [IARC, 1985, 1987; Hansen, 1989a,b, 1991, 1992; Wong et al., 1992; Partanen and Boffetta, 1994; Cole et al., 1999]. The primary concern was whether lung cancer was associated with bitumen fume exposure. Thus, inhalation of other known and suspected lung carcinogens that are likely to have occurred in the study population, such as coal tar, polycyclic aromatic hydrocarbons (PAH), silica dust, diesel fume, and asbestos, also had to be assessed. Exposure assessment was designed to be specific for country, time period, company, and job class, since we anticipated that production characteristics nested within these categories affected exposure pattern. Table I defines the agents that were assessed. The objective of this report is to describe the development of an exposure intensity matrix for the IARC multicenter international cohort study of cancer risk among European asphalt workers.

MATERIALS AND METHODS

Exposure Measurements and Supplementary Data

To facilitate the assessment of the intensity of exposure in a cohort of asphalt workers we created a database of exposure measurements. The database has been extensively described elsewhere [Burstyn et al., 2000a] and only its principal features are highlighted below. The Asphalt Worker Exposure (AWE) database was developed in order to standardize the compilation of exposure data. The exposure data was comprised of measurements of exposure levels for a variety of agents among asphalt workers, plus supplementary information. The exposure data was entered into the AWE database from the original measurement reports and field observation records. The supplementary information was analogous to collected data from a company questionnaire (CQ) on production characteristics in companies enrolled in the study, ensuring that AWE data can be linked directly to other data used in the exposure assessment. Most of the available exposure data was collected in the participating countries as of February 1999 ($N = 2,007$). The major contributors (70% of samples) were four Nordic countries, with 35% of samples originating from Norway. The earliest collected samples originated from the late 1960s, but the majority of samples were collected in the late 1970s and between 1985 and 1997. The data set was judged to be sufficiently comprehensive and balanced to permit statistical modeling of the intensity of exposure to bitumen fume, organic vapor, and PAH in paving operations.

Principal outcomes of the analyses of individual exposure measurements from paving workers collected by the AWE database workers [Burstyn et al., 2000b] are summarized below. Bitumen fume and organic vapor levels did not

TABLE I. Definitions of Agents to be Assessed

Agent	Definition	Assessment type[a]
Bitumen fume	Occupational exposure to solid-phase inhalable organic matter of bitumen origin	SQ + Q
Organic vapor	Occupational exposure to gas-phase inhalable organic matter (of bitumen or solvent origin)	SQ + Q
PAH[b]	Occupational exposure to inhalable 4-6 ring polycyclic aromatic hydrocarbons (PAH) emitted from bitumen- and tar-containing materials, excluding those originating from diesel exhaust	SQ + Q
Diesel exhaust	Occupational exposure to inhalable diesel exhaust	SQ
Asbestos	Occupational exposure to inhalable asbestos fibers	SQ
Silica	Occupational exposure to respirable crystalline silica	SQ
Coal tar	Occupational exposure to coal tar	SQ

[a]SQ, semi-quantitative; Q, quantitative.
[b]Benzo(a)pyrene was used as a representative of PAH exposure in quantitative exposure assessment.

display any consistent correlation patterns between each other. Benzo(a)pyrene exposure level appeared to act as an appropriate indicator of exposure to 4-6 ring PAH. Full-shift exposures to bitumen fume, organic vapor, and benzo(a)pyrene steadily declined over the last 20 years at a rate of 6–14% per year. Mastic laying and re-paving were associated with elevated bitumen fume exposures compared to hot mix paving. Surface dressing, oil gravel paving, and elevated asphalt temperature led to higher organic vapor exposures. Increased benzo(a)pyrene exposure levels were principally attributed to the use of coal tar in paving (a practice currently discontinued in Western Europe). In general, it was concluded that (a) bitumen fume, organic vapor, and PAH have somewhat different determinants of exposure and (b) for road paving workers, exposure intensity can be assessed on the basis of time period and production characteristics. Statistical models that support the above conclusions are summarized in Table II.

Information About Workplaces

We gathered information about companies enrolled in the study through a CQ aimed to ascertain temporal changes in production characteristics and work organization. The questionnaire was developed in close collaboration with the asphalt industry and was based on a questionnaire originally applied in a study of the Finnish asphalt industry. The summary of the information sought through the CQs is presented in Table III. The questionnaires were administered to a knowledgeable company representative or a group of representatives either through a personal semi-structured interview or by mail. Prior to being assembled into a common database, all CQs were checked for errors, omissions, and inconsistencies. The data gathered was compared with information about production characteristics derived from the exposure measurement reports (AWE data). Lastly, information gathered by CQs and any additional information

TABLE II. Predictive Models ($\log_e(\text{Exposure}) = \Sigma_{\text{all } j}(\beta_j \times \text{Determinant of Exposure } j) + \text{Intercept}$) of Bitumen Fume, Organic Vapor, and Benzo(a)pyrene Exposures, Adjusted for Sampling Strategy and Analytical Methods (Adapted From Burstyn et al. [2000a] with permission)

	Estimates of models' parameters					
	Bitumen fume (mg/m^3)		Organic vapor (mg/m^3)		Total benzo(a)pyrene (ng/m^3)	
Determinant of exposure	ß[e]	M[f]	ß[e]	M[f]	ß[f]	M[f]
Mastic laying	0.88	2.4	0.78	2.2	1.27	3.6
Mastic laying × worst case[a]	1.71	13	1.70	12	3.07	80
Recycling	0.89	2.4	NS[c]		1.51	4.5
Recycling × worst case[a]	1.67	12	NP[d]		NP	
Surface dressing	NS		1.88	6.6	0.38	1.5
Oil gravel	−1.51	0.2	0.48	1.6	−0.65	0.5
Tar use[b]	NS		NS		1.68	5.4
Years before 1997	0.062	1.06	0.135	1.14	0.107	1.11
Application temperature in non-mastic paving (°C)	NS		0.009	1.009	NS	
Intercept (associated exposure)	−2.10	(0.12 mg/m^3)[i]	−1.19	(0.30 mg/m^3)[j]	0.91	(2.5 ng/m^3)[k]
% variance explained	41		36		43	
$_{BW}\hat{S}^2$[g]	0.99		1.16		0.43	
$_{WW}\hat{S}^2$[h]	1.08		1.26		1.71	

[a]Symbol "×" denotes multiplicative interaction terms in a model.
[b]Tar use variable was not initially offered into bitumen fume and vapor models, however, when added to the final form of the models it was not statistically significant.
[c]Variable is not statistically significant and therefore, is not included in the model or did not improve model fit upon inclusion in the model (assume regression coefficient of zero).
[d]Not possible to estimate.
[e]Regression coefficient.
[f]Multiplicative factor, $M = e^{\beta + \text{interaction term}}$ (interaction term is needed only to estimate exposures during worst case scenarios for mastic laying and recycling), it can be used to infer exposure level by multiplying exposure associated with intercept by M-value: for example, bitumen fume exposure during mastic laying in 1997 is $2.4 \times 0.12\ mg/m^3 = 0.29\ mg/m^3$.
[g]Variance of the distribution of logarithmic means of individual's exposures (between-worker).
[h]Variance of the distribution of logarithmic means of exposure from day to day for an individual (within-worker).
[i]As measured by extracting organic matter (indifferent method and solvent) collected onto particulate filters of 37 mm open-face cassette, 25 mm closed face cassette (Millipore), or PAS6 sampler.
[j]Organic matter collected by XAD2 sorbent from gas phase of asphalt emissions.
[k]Any sampling and analytical method.

TABLE III. Type of Information Gathered by Company Questionnaires (CQs) as Well as in Consultations With Industry Representatives and Industrial Hygienists From the National Centers, Collected for Each one of the Following Time Intervals: Before 1960, 1960–1964, 1965–1969, 1970–1974, 1975–1979, 1980–1984, 1985–1989, 1990–1996

Job class	Type of information gathered
All	Average duration of work shift (hours), average duration of annual work season (months), employment pattern in winter (off season)
Road paving	*Frequencies* of mastic laying (indoors and outdoors), surface dressing, oil gravel paving, recycling/re-paving (hot vs. cold), paving with coal tar, paving asbestos-containing mixes, pouring cement; year when coal tar and asbestos were last applied; type of fuel used in machines and trucks (diesel or petrol); application temperatures
Asphalt mixing	Type of plant: batch or continuous processes installation year of cyclones and baghouse filters, other control measures; frequencies of making mixes with coal tar or asbestos; *frequency of* being exposed to respirable silica dust; year when coal tar and asbestos were last used; use of the following mixes and agents (yes/no): hot mixes, cold mixes, recycled asphalt, coal tar pitch, quartz containing aggregates, limestone
Waterproofing and roofing	Indoor or outdoor work; products used (yes/no): hot bitumen, bitumen felts, bitumen solution, bitumen emulsion, coal tar pitch; *frequencies of* making using coal tar or asbestos products; year when coal tar and asbestos were last used
Building and ground construction	*Frequencies of* working with specific products or being exposed to: asbestos, diesel exhaust, quartz dust, coal tar/coal tar pitch containing products, bitumen containing products

required for application of the exposure assessment algorithm were re-evaluated and supplemented at a joint meeting of industrial hygiene and industry experts from each country.

Building a Study-Specific Exposure Matrix (EM)

The Road Construction Workers' Exposure Matrix (ROCEM) was developed on the basis of CQs, analysis of the AWE database, and expert judgments. Each cell of the exposure matrix was defined by a unique combination of country, company, job class, time period, and agent. Applying regression models to CQ data produced quantitative exposure estimates. Semi-quantitative exposure estimates were based on (a) country-specific expert evaluation of relative exposure intensities between different working conditions and (b) CQ data.

Quantitative exposure intensity estimates

Quantitative exposure assessment was carried out only for paving workers since it was not possible to obtain sufficient data to construct predictive models of exposure for other job classes. Furthermore, for paving, quantitative exposure assessment was possible only for bitumen fume, organic vapor, and benzo(a)pyrene (proxy of 4-6 ring PAH). Regression models described in Table II were directly applied to predict a person's full-shift time-weighted average exposure. In order to translate these predictions into a mean exposure intensity for a given 5-year interval (as was demanded by the exposure matrix), we had to take into account day-to-day and person-to-person variability in work performed over that time interval. Thus, we calculated mean exposure (M_j) for a given group of workers who experienced N exposure *scenarios* ($S_{1j}, S_{2j}, \ldots S_{ij} \ldots S_{Nj}$) in a given time interval j according to the following formula:

$$M_j = \sum \{X_{ij} \times f(S_{ij})\} \text{ for all } S_{ij}\text{'s that fall into time interval } j, \quad (1)$$

where X_{ij} represented the median value of the long-term means of individual exposures of a group of workers who have experienced exposure scenario S_{ij} in a given time interval j (i.e., prediction of the multiple linear regression model), and $f(S_{ij})$ was the frequency of scenario i during time interval j, such that $\Sigma\, f(S_{ij}) = 1$ for a given j.

Frequencies of some scenarios (mastic paving, surface dressing, and utilizing coal tar containing mixes and products) were estimated directly from CQs, however, they did not contain information on the frequency of "worst case" situations and on the frequency of two conditions that appear to be important determinants of exposure: oil gravel paving and recycling operations. Experts from each country assessed the frequency of these events. The worst case scenario in mastic laying corresponded to indoor work. The worst case scenario in recycling corresponded to hot in situ re-paving, an operation in which asphalt is heated with a propane burner before removal/re-paving. We assumed that oil gravel paving was carried out only in Nordic countries.

The X_{ij} was calculated using information provided in Table II, according to the following formula: [Tornero-Velez et al., 1997]

$$X_{ij} = \exp\left(m_{ij} + 1/2\,{}_{WW}\hat{S}^2\right) \quad (2)$$

where m_{ij} was the logarithmic mean of a worker who has experienced exposure scenario S_{ij} and ${}_{WW}\hat{S}^2$ was an estimate of logarithmic within-worker variance. The values of m_{ij}

were directly calculated using regression equations, and $_{ww}\hat{S}^2$ values were parameters for each exposure model (Table II).

Time intervals *j* were defined by CQ as finite time intervals. It was assumed a priori that production conditions have remained constant over 5-year intervals. For the purposes of predicting exposure levels we used the time difference between 1997 and the midpoint of the time interval *j* as a value of time-related variable. Furthermore, due to scarcity of data for pre-1970 time period, we assumed that there was no time trend in the exposures before 1970. Deviation from the above patterns will occur in the assessment of benzo(a)pyrene exposures. Thus, if coal tar use had been discontinued part way through a time period *j*, separate assessments were performed for years before and after coal use was discontinued.

Some companies have indicated that road paving workers took part in laying concrete. We assumed that bitumen fume, organic vapor, and benzo(a)pyrene exposure were zero during handling of concrete. It was also assumed that when coal tar was used in the past, it was always used in combination with bitumen (as an additive to alter binder's properties).

Our earlier work indicated that there were no significant differences in exposure to bitumen fume and benzo(a)pyrene among persons performing different tasks within a paving crew [Burstyn and Kromhout, 2000]. Consequently, no attempts were made to take into account tasks within a paving crew (e.g., paver operator, screedman, roller driver) in exposure assessment.

Semi-quantitative estimates of exposure intensity for bitumen fume, organic vapor, and PAH in road paving, asphalt mixing, waterproofing/roofing, ground construction and building construction

Assessing differences in exposure intensities within a job class. We made the following assumptions about relative magnitudes of bitumen fume, organic vapor, and 4-6 ring PAH exposure exposures in different scenarios:

1. a three-fold difference between indoor and outdoor exposures to all three agents;
2. a two-fold difference between bitumen fume/organic vapor exposures during mastic laying outdoors and corresponding exposures during other paving (based on regression models (Table II) and expert judgment);
3. indoor mastic laying was associated with a four-fold increase in PAH exposure compared to outdoor mastic laying (based on regression models (Table II) and expert judgment);
4. PAH exposure was five times higher when coal tar was used than when bitumen alone was used. (On the basis of the results of laboratory experiments, PAH content of tar can be assessed to be 100 or even 1,000 times higher than that of bitumen [Lindstedt and Sollenberg, 1982; Brandt et al., 1985; Darby et al., 1986; Machado et al., 1993]. Our estimate of a five-fold difference was made on the basis of multiple regression models (Table II) of benzo(a)pyrene exposure among pavers ($e^{1.68} = 5.4$) in order to keep the relative effect of tar use on PAH levels consistent between quantitative and semi-quantitative exposure assessment procedures.);
5. in absence of coal tar and bitumen there was no PAH exposure (above some general background in the environment) among asphalt workers (based on expert judgment). The PAH that derived from diesel exhaust are 'counted' as part of diesel exhaust exposure (see below).
6. Time trend in bitumen fume, organic vapor, and PAH levels were assumed to be the same for all job classes (road paving, asphalt mixing, waterproofing/roofing, ground construction, and building construction). This assumption enabled us to calculate time period correction factors on the basis of regression models described in Table II. We also assumed that there was no time trend before 1970. Only in Finland was a separate time trend for bitumen fume in waterproofing/roofing estimated: exposure intensity was assumed to be three before 1985, two for 1985–1989 time period, and 0.5 for 1990–1996 time period on a semi-quantitative scale.

Once the presence of the relevant exposure scenarios was enumerated for each company, time period, and job, we calculated summary indices for each cell of the ROCEM. This was performed in a manner analogous to quantitative exposure assessment, i.e., by computing a frequency-weighted sum of exposure indices that were assigned to scenarios present in each cell of the ROCEM.

Assessing differences in exposure intensities between job classes. Semi-quantitative exposure estimates also reflected differences between job classes. Semi-quantitative exposure estimates described in this paper thus far do not take this into account, since they are expressed as multiples of some unknown exposure level in a job class-specific scenario. In order to correct for these differences, a set of multipliers was developed. These multipliers reflect relative exposure intensity of exposure in a given job class to exposure intensity in road paving. Values of multipliers for asphalt mixing were derived from the AWE database. The comparison between exposures in road paving and asphalt mixing was restricted to seven surveys in which both job classes were sampled (Table IV). Logarithms of exposure levels were compared with corrections made in multiple regression models for survey code (surrogate for sampling strategy, analytical methods, time, and country) and sample

TABLE IV. Comparison of Exposure Levels in Paving and Asphalt Mixing in Seven Surveys That Monitored Exposures in Both Job Classes (Extracted From AWE Database)

	Bitumen fume (mg/m^3)		Organic vapor (mg/m^3)		Benzo(a)pyrene (ng/m^3)	
Job class	**GM (n)**	**95% CI$_g$**	**GM (n)**	**95% CI$_g$**	**GM (n)**	**95% CI$_g$**
Paving	0.15 (557)	0.13–0.18	1.84 (303)	1.45–2.33	1.98 (320)	1.56–2.46
Asphalt mixing	0.12 (64)	0.07–0.20	2.31 (47)	1.27–4.22	2.41 (51)	1.33–4.00

GM, geometric mean; n, sample size, 95% CI$_g$, 95% geometric confidence interval.

positioning (personal vs. area samples). According to these models (not shown), for all three exposure measures there were no differences in exposure levels between road paving and asphalt mixing. The probability of the median exposure levels between the two job classes being different never approached statistical significance of 5%. On the basis of these results, we conclude that there are no large systematic differences between bitumen fume, organic vapor, and PAH exposure between road paving and asphalt mixing.

The AWE database did not contain sufficient information to compare bitumen fume and organic vapor exposure for waterproofs and roofers to other job classes. The industrial hygiene subgroup of the study (Timo Kauppinen, Pirjo Heikkilä, Hans Kromhout, Igor Burstyn) reached a consensus that the following assumptions are reasonable: (a) bitumen fume and PAH exposures are two times higher during waterproofing and roofing than during paving; (b) organic vapor exposure intensities are similar in waterproofing/roofing and paving.

The industrial hygiene subgroup of the study also deemed that for building and ground construction, job class-specific, or country-specific corrections for exposure intensity estimation were not needed.

Semi-quantitative assessment of exposure intensity for diesel exhaust, asbestos, silica, and coal tar

Exposures to diesel exhaust, asbestos, and silica were assessed on the basis of presence or absence of contact with the material that can give rise to the exposure as reported in the CQs. If contact with the source of exposure was absent, an exposure intensity of ‘‘zero’’ was assigned. If there was contact with the agent, an exposure intensity of ‘‘one’’ was assigned. We also assumed that (a) workers in waterproofing and roofing were not exposed to diesel exhaust and silica, (b) all asphalt mixing workers were always exposed to diesel exhaust to a similar extent, (c) paving workers were not exposed to silica, (d) silica-containing materials were always used at asphalt plants, since sand and gravel are essential ingredients in asphalt mixes.

Reference exposure level for silica was assumed to be that occurring in ground construction (intensity = 1). Silica exposure intensity at asphalt plants was assessed to be twice (intensity = 2) as high as that arising during ground construction (intensity = 1). Silica exposure intensity at asphalt plants was corrected for the presence of exposure control measures. The industrial hygiene subgroup has reached a consensus on the following assumptions: (a) cyclones reduce exposure by a half, and (b) bag-house filters reduce exposure by a factor of four. We estimated relative exposure intensities between job classes for each country. In these corrections, building construction workers were generally assigned silica and asbestos exposures that were twice the intensity of those observed in ground construction.

Exposure intensity estimated in accordance with the above procedure was further multiplied by fraction of work time that the material was used (obtained from CQs). It was also assumed that (a) diesel engines were always used when diesel-powered trucks were in use, (b) diesel engines were used 50% of the time when both diesel- and petrol-powered trucks were used.

Exposure to coal tar was assumed to have the same intensity in all job classes. It was estimated as frequency of coal tar use, derived directly from the CQs.

Semi-quantitative exposure assessment for other job classes

Once semi-quantitative exposure indices had been assigned to paving, asphalt mixing, waterproofing and roofing, ground construction and building construction, we proceeded with estimating exposures for the remaining job classes. In subsequent discussion ‘exposure’ refers to semi-quantitative exposure estimates. The approach we adopted below is analogous to the one employed by Macaluso et al. [1996] in assessing exposures for jobs which were ‘‘poorly specified’’ in a cohort study of synthetic rubber workers. The overall procedure for these jobs typically involved reconstructing their exposure as a weighted average of exposures for cells in the exposure matrix that were based on primary data. The country-specific exposure assessment algorithm for job classes discussed in this section is summarized in Table V. We also assumed that office administration and management personnel were not exposed to any agent of interest (exposure intensity of *zero* for all agents).

TABLE V. Country-Specific Definitions of Exposures in Selected Job Classes

Country	Job class (definition and assumptions about exposure profile): Unspecified road paving or asphalt mixing worker	Unspecified other bitumen worker	Unspecified blue collar worker	Unspecified road construction worker	Unknown job
France	Does not exist	Laboratory technicians: exposure to bitumen is 50% of road paving workers; silica exposure intensity = 0.5	Surveyors and site managers (spent 40% of their time driving and the rest as either administrators or foremen at paving site): 20% of exposure of road paving	50% in road paving; 50% in ground construction	Equally likely to be in road paving, asphalt mixing, and ground construction
Norway	Weighted average: 5 (road paving): 1 (asphalt mixing)	Laboratory workers (see France)	Exposed to diesel exhaust and silica only	Does not exist	Does not exist
Sweden	Weighted average: 5 (road paving): 1 (asphalt mixing)	Does not exist	Assumed to be similar to road paving, but it is unclear how these people came in contact with asphalt emissions	Not included in the cohort	Mean of other job classes: road paving, asphalt mixing, roofing, building construction, ground construction
Israel	Inspectors, supervisors, and technicians, exposure 10% of paving	Laboratory workers (see France)	Unexposed to all agents of interest	Does not exist	Unexposed to all agents of interest
The Netherlands	Weighted average: 5 (road paving): 1 (asphalt mixing)	Laboratory workers (see France)	Workers with possible asphalt exposure (20% of pavers' exposure, see France)	50% in road paving; 50% in ground construction	Does not exist
Finland	Does not exist	Company-specific adjustments[a]	Does not exist	Does not exist	Does not exist
Denmark	Weighted average: 5 (road paving): 1 (asphalt mixing)	Equally likely to belong to road paving, asphalt mixing, and roofing	Equally likely to belong to all job classes, except office staff	Does not exist	Mean of all other job classes
Germany	Weighted average: 5 (road paving): 1 (asphalt mixing)	Laboratory workers (see France)	Any manual work, but not in paving, ground construction, or building construction	50% in road paving; 50% in ground construction	Mean of all other job classes

[a]Laboratory workers in two companies (see other countries); electricians (one company, same as office workers); bitumen felt production plant (unique to Finnish cohort: assume to be like road paving in bitumen and PAH exposure and like building construction in terms of asbestos and silica exposure).

Work-shift duration adjustments

To account for differences in work-shift duration between companies and time periods, the estimates of exposure intensity were first standardized to 8-hr work-shifts. These ‘duration adjusted’ indices were calculated for each company and time period according to the following formulas:

$$_{\mathrm{D}}\mathrm{M}_j = \mathrm{M}_j \times (\mathrm{W}_j/8) \tag{3}$$

$$_{\mathrm{D}}\mathrm{SQ}_j = \mathrm{SQ}_j \times (\mathrm{W}_j/8) \tag{4}$$

where W_j, average work-shift duration in time period j in a given company (in hours); M, quantitative exposure intensity estimate; and SQ, semi-quantitative exposure intensity estimate. W_j values were estimated on the basis of information gathered by CQs. For job classes not covered by CQs, estimates of W_j were based on evaluation by a panel of experts and were judged to have been similar to the estimates for job classes covered by the CQs.

Missing Values

Missing values in the exposure matrix arose due to missing CQ input from which they ought to have been derived. In these cases, country-, job class-, agent-, and time-period specific averages replaced missing values in the final version of the matrix applied to cohort analysis. If that was not possible (as in the case of one company per country in France and Israel, and one CQ representing all Swedish firms), averages over all countries, i.e., job class-, agent-, and time-period specific averages were used. This last set of values was also used in cases where job histories in the cohort contained situations for which there were no corresponding cells in exposure matrix (due to missing or inadequate CQs). The rationale for this procedure in replacing the missing values was based on the assumption that the missing values occurred at random with respect to true exposure levels within country-, job class-, agent-, and time-period specific strata. Exposure estimates only in Norway, Finland, The Netherlands, and Germany used replacement values. For semi-quantitative exposure assessment, the following percentage of all exposed person-years used replacement values: bitumen fume, organic vapor, and asbestos—2.7% each, coal tar—3.6%, silica—1.7%, PAH—2.8%, and diesel exhaust—1.4%. In quantitative exposure assessment (bitumen fume, organic vapor, and benzo(a)pyrene exposure among pavers) only 2.6% of person-pears used replacement values.

Examining Content of the Exposure Matrix

We calculated arithmetic means standard deviations and ranges for quantitative exposure estimates.

Semi-quantitative exposure scores were examined graphically by job class and agent. For this purpose, exposure scores were represented as relative scores (ratios of arithmetic means to the respective minimum value) because absolute values of exposure scores are meaningless. Rank correlations (Spearman) between estimates for different agents for each cell of exposure matrix were examined. Any correlation of greater than 0.70 that had at most 5% probability of being equal to zero due to chance was considered biologically and statistically significant; it was examined graphically in more detail. Assessed historical exposure patterns were also examined graphically for each agent and type of exposure measure.

Statistical analyses were carried out in SAS version 6.12 (SAS Institute, Cary, NC). Microsoft Access 2.0 (Microsoft Corporation, Seattle, WA) facilitated data management and database application development. Graphs were prepared in Sigma Plot 4.01 (SPSS, Inc., Chicago, IL).

RESULTS

Workplaces

Only one firm was recruited from France and Israel, but these enterprises were the largest in their countries and their operations covered the entire countries. One CQ was obtained from each, even though it was recognized that there may have been important differences in work practices between different sub-divisions of the firms. The Swedish sub-cohort originated from numerous companies, but it was not possible to trace individual firms due to numerous mergers in the industry. Therefore, only one questionnaire was complied for Sweden. It represented average changes in production characteristics in Sweden. From the other five countries we were able to obtain CQs for each firm enrolled in the cohort (typically a small-to-medium size enterprise). In Germany and Norway, questionnaires from sub-divisions and individual asphalt plants within some large companies were also available. Thus, Denmark contributed six CQs, Finland—six, The Netherlands—six, Germany—138, and Norway—59. Most of the firms enrolled in the cohort paved (51%) and manufactured (94%) asphalt. However, some companies were also engaged in ground construction (27%), building construction (6%), and waterproofing/roofing (6%).

Coal Tar Use

Coal tar use declined dramatically from early 1960s to mid-1970s in the cohort. The steepest average decline in coal tar use was observed in Denmark (from almost universal use to complete discontinuance of the practice). In the Dutch firms, only 40% of person-hours were devoted to work with coal tar in paving prior to 1974 at which point coal tar use dropped to 20% of person-hours until it was discontinued in the 1990s. Germany and Sweden reported that at its peak in 1960s coal tar use accounted on average for approximately 20% of person-hours. The practice was progressively discontinued, ending in Sweden around 1974, but persisting in Germany, with less than 1% average frequency, until 1996. Coal tar use in road construction in France appeared to have been limited to less than 1% of person-hours and continued till 1996 in specialized surface dressing operations. In Finland, there was limited coal tar use in paving prior to 1960 (1% of person-hours). In Norway, on average coal tar was used has been limited to 3% of person-hours prior to 1960s, discontinuing in 1984, at which point its use was limited to only 0.1% of person-hours. In Israel, the recruited company never used coal tar in paving. Coal tar use in other segments of the recruited asphalt companies reportedly followed the same pattern.

Exposures Assessed

Quantitative exposure estimates for bitumen fume, organic vapor, and benzo(a)pyrene among pavers are summarized in Table VI. Modeled time trends in these exposures are illustrated in Figures 1–3. Semi-quantitative exposure estimates showed the pattern that was governed by assumptions made during estimation procedure. Waterproofing and roofing operations were assessed, on average, to have been associated with the highest bitumen fume, organic vapor, and PAH exposures, exceeding those occurring in paving by a factor of 1.5–3. Estimated exposures in paving and asphalt mixing were similar for most agents, except that (a) asphalt

TABLE VI. Descriptive Statistics for Quantitative Exposure Estimates for Paving Activities

Agent	Time period	N[a]	AM[b]	SD[c]	CV[d]	Min[e]	Max[f]
Bitumen fume (mg/m^3)	All	611	0.99	0.72	73	0.06	6.99
	< 1960	46	1.47	0.57	39	0.23	3.71
	1960–1964	61	1.33	0.66	50	0.21	3.42
	1965–1969	70	1.30	0.61	47	0.21	3.42
	1970–1974	77	1.46	1.04	71	0.21	6.99
	1975–1979	86	1.04	0.66	63	0.15	5.12
	1980–1984	87	0.80	0.49	61	0.50	3.96
	1985–1989	91	0.59	0.38	64	0.34	2.90
	1990–1996	93	0.44	0.28	64	0.06	2.24
Organic vapor (mg/m^3)	All	573	59	86	146	1	827
	< 1960	42	107	131	122	18	827
	1960–1964	58	112	119	106	19	827
	1965–1969	66	106	101	95	19	827
	1970–1974	71	105	97	92	17	827
	1975–1979	81	54	50	93	9	421
	1980–1984	82	27	25	93	4	214
	1985–1989	86	13	13	100	2	109
	1990–1996	87	6	4	67	1	31
Benzo(a)pyrene (ng/m^3)	All	573	146	262	179	5	3,079
	< 1960	42	322	298	93	47	1,387
	1960–1964	58	274	295	108	41	1,193
	1965–1969	66	229	261	114	41	1,144
	1970–1974	71	246	434	176	41	3,079
	1975–1979	81	124	239	193	24	1,803
	1980–1984	82	71	138	194	29	1,120
	1985–1989	86	39	75	192	15	651
	1990–1996	87	24	46	192	5	403

[a]Number of cells in ROCEM with CQ inputs.
[b]Arithmetic mean.
[c]Standard deviation.
[d]Coefficient of variation in %.
[e]Minimum value.
[f]Maximum value.

plants were associated with silica exposure, while paving was not and (b) tar use seemed to have been more prevalent at the paving sites. Overall, paving and asphalt mixing was associated with higher exposures than building and ground construction, except that their diesel exhaust exposures were estimated to have been similar. In order to illustrate time trends in all agents of interest, irrespective of actual scale for each agent, average exposure estimates have been expressed relative to average estimates for each agent in 1990–1996 time period and plotted versus time periods (Fig. 4). It is clear that the EM assessed a decline in exposure to most agents. The steepest decline was observed for tar exposure: a factor of 200 from pre-1960 time period to 1990–1996. However, exposures to silica and diesel exhaust remained virtually unchanged. Slight increase in diesel exhaust exposures in the 1960s can be attributed to substitution, in paving operations, of petrol-powered machines with diesel-powered ones.

The procedure employed in constructing the EM resulted in only weak-to-moderate correlation between tar use and all other agents except for silica (Table VII). The correlation between bitumen fume exposure and tar use has been assessed to be stronger in the past, but the maximum correlation was moderate: 0.47 (for pre-1960 time period). Quantitative exposure estimates for pavers were strongly correlated among themselves (N = 572, all $P = 0.0001$) with rank correlation ranging from 0.78 (bitumen fume and organic vapor) to 0.93 (bitumen fume and benzo(a)pyrene). Strong rank correlation among semi-quantitative estimates of PAH, bitumen fume, and organic vapor was not due to extreme values (examined graphically, results not shown).

DISCUSSION

Estimated Quantitative Exposure Intensities

Quantitative estimates of exposure intensity among pavers (Table VI) decreased in time, as can be expected from the statistical models, but the decrease was not monotonic due to temporal variability of the distribution of determinants. Also the variability of exposure estimates steadily decreased from 1970–1974 to 1990–1996. This may be a sign of convergence and standardization of work practices since changes in variability must derive from the distribution of production conditions reported in CQs. An alternative explanation is that recall of working conditions more remote

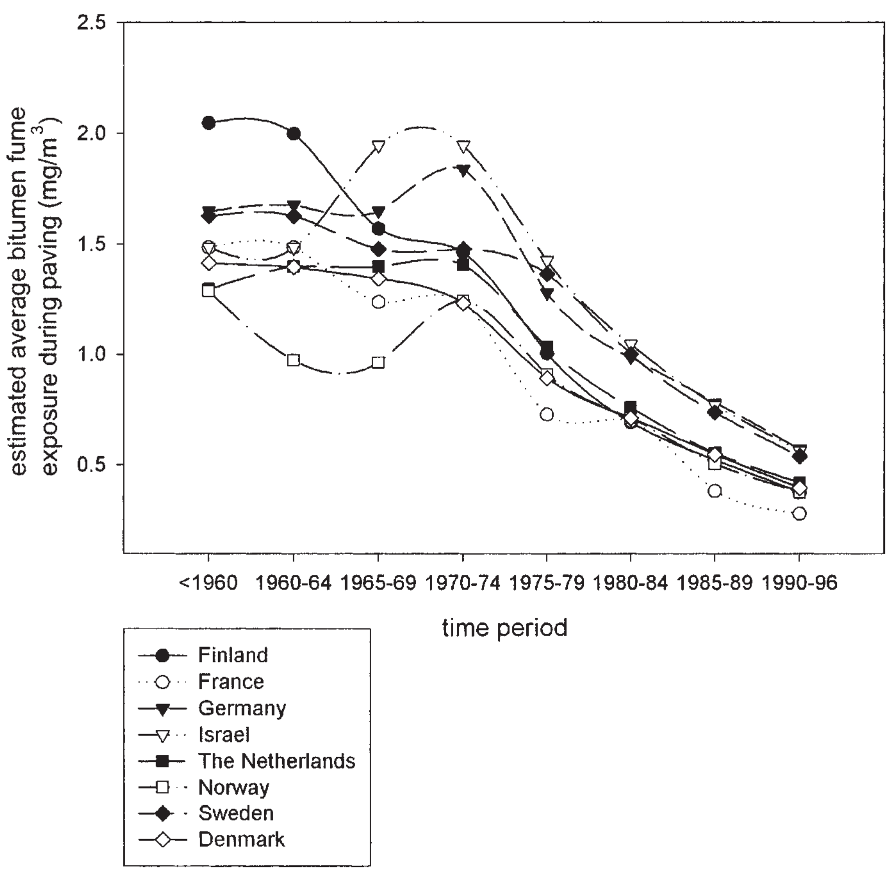

FIGURE 1. Assessed time trend in average bitumen fume exposure (pavers only).

TABLE VII. Pair-Wise Rank (Spearman) Correlation Between Semi-Quantitative Exposure Scores to Different Agents in the Exposure Matrix (EM) (Correlation Coefficient, (Number of Pairs)); all $P = 0.0001$, Unless Otherwise Noted

Agents	Bitumen fume	Organic vapor	Diesel exhaust	PAH	Silica	Coal tar
Asbestos	0.14 (3,986)	0.13 (3,987)	0.07 (5,035)	0.17 (3,975)	0.04 (4,952)[a]	0.30 (4,390)
Bitumen fume		0.98 (4,089)	0.44 (4,063)	0.96 (4,069)	0.05 (3,972)[b]	0.34 (3,900)
Organic vapor			0.38 (4,064)	0.97 (4,069)	0.04 (3,973)[c]	0.37 (3,900)
Diesel exhaust				0.35 (4,054)	0.16 (5,031)	0.20 (4,469)
PAH					0.03 (3,971)[d]	0.46 (3,902)
Silica						−0.06 (4,386)[e]

[a] $P = 0.01$.
[b] $P = 0.001$.
[c] $P = 0.005$.
[d] $P = 0.07$.
[e] $P = 0.0002$.

in time was subject to a greater error. However, if this latter effect was present, it did not operate strongly in the pre-1960–1969 time period due to absence of time trend in exposure variability. In the pre-1960–1969 time period variability of exposure estimates was on the same order or smaller than in 1970–1974, suggesting that either (a) the uncertainty about characterization/recall of production conditions 30 or more years in the past was substantial, leading to absence of attempts to describe them very precisely or (b) there was little evolution in paving practices in the 1960s. In relative terms, variability over time was estimated to have been less pronounced for bitumen fume and organic vapor. Relative variability in benzo(a)pyrene exposure estimates increased in time, probably due to different times of cessation

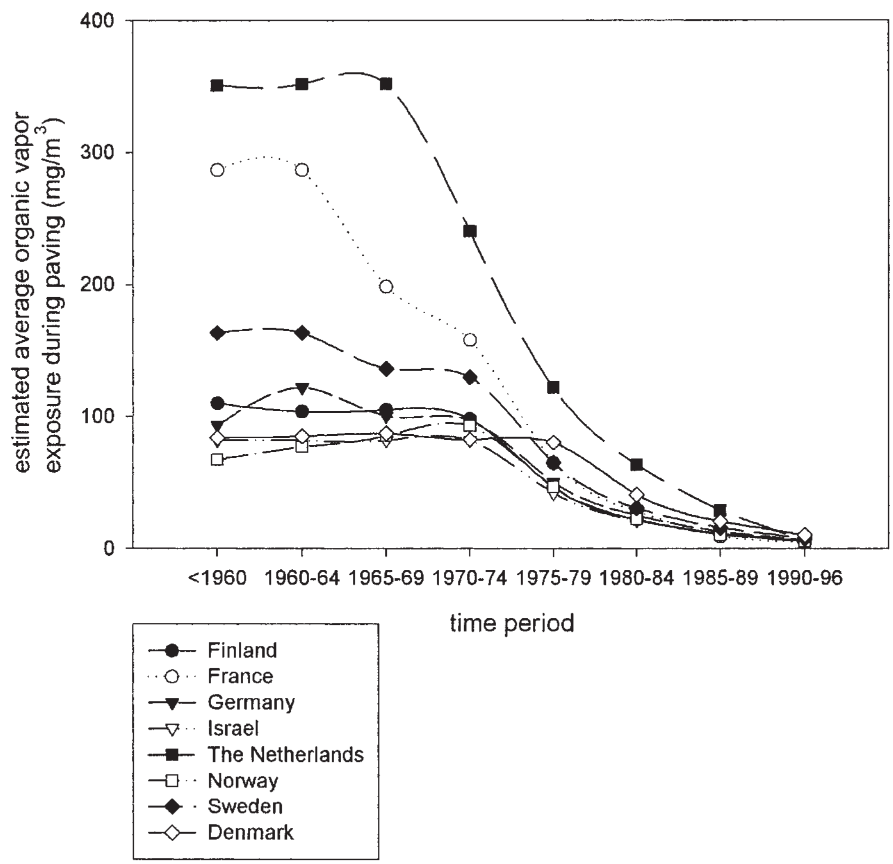

FIGURE 2. Assessed time trend in average organic vapor exposure (pavers only).

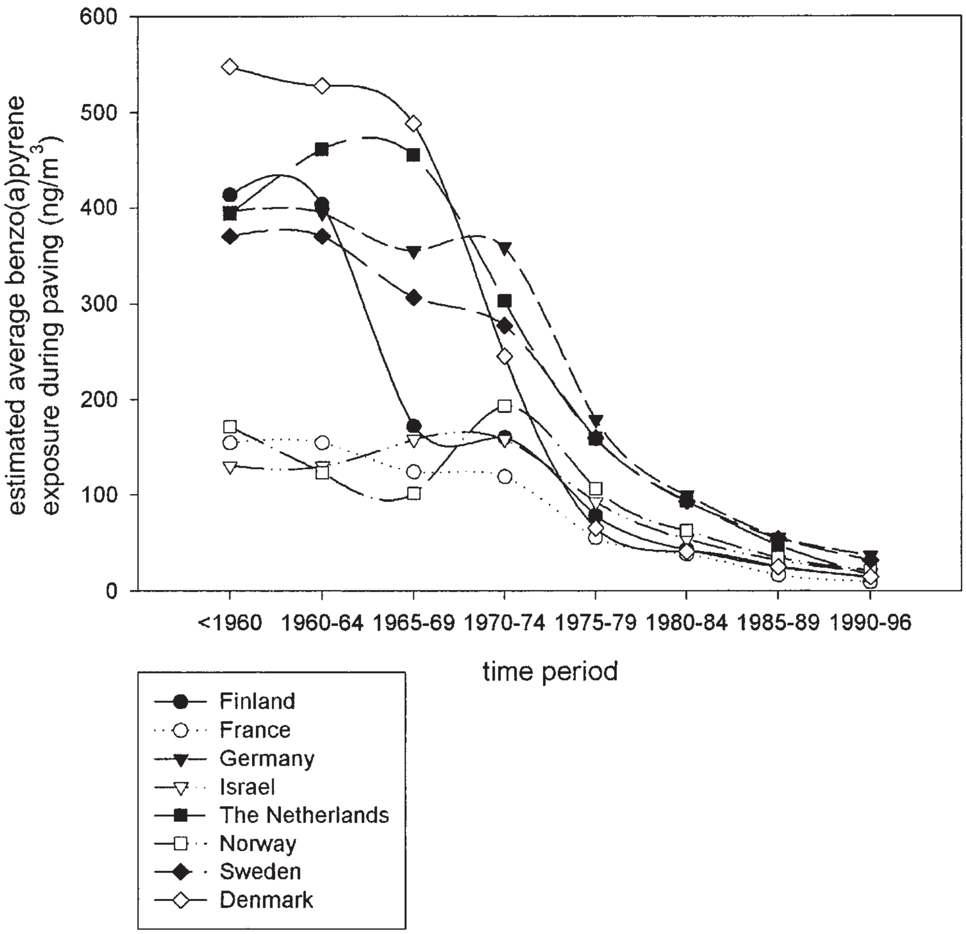

FIGURE 3. Assessed time trend in average benzo(a)pyrene exposure (pavers only).

of coal tar use among firms. It should be also noted that the presented estimates of variability are not of actual exposures, but of exposure matrix estimates. These estimates lack natural variability of exposure levels since they were derived in a deterministic, rather than stochastic process.

Historical Exposure Patterns in Quantitative Exposures Estimates for Pavers

Figures 1–3 present estimated patterns in average country-specific quantitative exposure estimates for pavers. Statistical exposure models that these estimates were based on did not detect any country-specific effect and did not use them in estimating exposure intensities for different scenarios. Therefore, the observed differences between countries (and thus companies) must be attributed to responses to the CQs. It is quite clear that the assessed patterns of exposure are not monotonic in time. For example, average bitumen fume and benzo(a)pyrene exposures in Norway first declined from pre-1960 to 1964, then rose again in 1970–1974 to pre-1960 levels and only after that started to decline again. The pattern for organic vapor in Norway is different in that exposures steadily increased until the middle of 1970s. The pattern for organic vapor is probably due to discontinuation of oil gravel paving in favor of surface dressing, with the latter producing higher organic vapor exposures. The trend of bitumen fume and benzo(a)pyrene is harder to interpret but it is probably linked to both discontinuation of oil gravel paving (associated with "low" exposure for the two agents) and introduction of recycling operations (associated with "high" exposure for the two agents). The elevated organic vapor exposures among pavers in France and The Netherlands arose from higher application temperatures and frequency of surface dressing relative to other countries. Similar explanations can be devised for all the observed patterns since they were assessed on the basis of a deterministic procedure consisting of simple arithmetic operations.

The complexity of the assessed patterns should be noted that ought to invoke the notion of complexity of exposure patterns that can be anticipated of industry consisting of small-to-medium size enterprises spread over vast a geographical area. It is doubtful whether such a complex picture could have been reproduced with any degree of

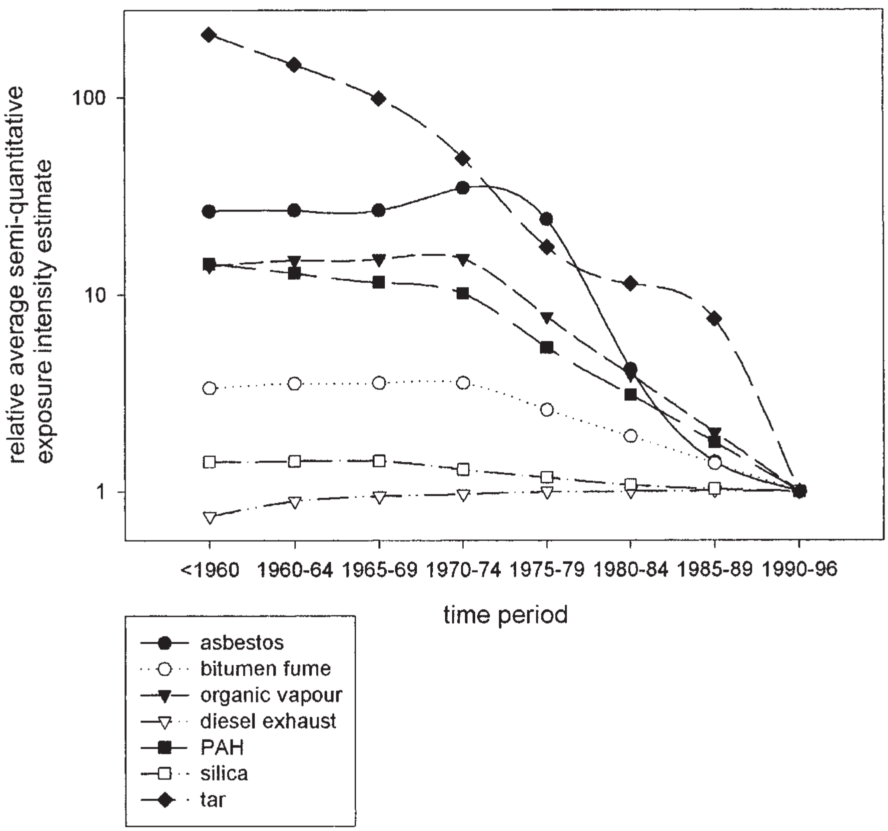

FIGURE 4. Time trends in semi-quantitative exposure scores.

certainty (and surely not in a reproducible manner, with all assumptions explicitly stated) in a procedure that was not data driven (i.e., based on expert evaluation of CQs alone).

Implication for Epidemiological Analysis of Correlation Between Exposure Intensities

Absence of strong correlation between PAH exposure and tar use was likely due to discontinuance of the use of tar in more recent years, leading to bitumen fume being the primary source of PAH exposure (excluding those that originate from diesel exhaust). Moderate rank correlation between bitumen fume and diesel exhaust was also noted. It probably arose from virtually exclusive use of diesel engines in road paving.

Strong correlation among PAH (not of diesel exhaust origin), organic vapor, and bitumen fume indicates that it will be very difficult, if not impossible, to distinguish between their effects in analysis of relationship between exposures and health risks in the IARC cohort analyses. This suggests that we may be left with the ability to assess the health effects of asphalt emissions, rather than bitumen fume. However, correction for tar use should be possible to achieve because the lack of a strong correlation between tar use and bitumen fume suggests that tar use may not confound associations due to asphalt emissions. Furthermore, relatively low prevalence of coal tar use in most countries and especially in recent decades raises hope that we may have a tar-free sub-cohort of sufficient size to conduct a meaningful analysis.

Validity of Exposure Matrix

The validity of the present EM depends on presence of errors and biases in a chain of efforts that led to its creation. Quantitative exposure estimates were based on examination of exposure measurements gathered into AWE database. The majority of measurements in the database were judged to be free of any obvious biases with respect to typical full-shift exposure levels [Burstyn et al., 2000a]. The validity of models based on that data and used in quantitative exposure intensity estimation has already been assessed as satisfactory [Burstyn et al., 2002]. Predicted bitumen fume exposures tended to be lower than concentrations found during paving in the USA. This apparent bias might be attributed to differences between Western European and USA paving practices. Evaluation of external validity of the benzo(a)pyrene exposure model revealed that the model produced unbiased exposure estimates for re-paving operations and underestimated exposures during the use of coal tar in asphalt. Overall, benzo(a)pyrene models underestimated exposures by 51%.

In semi-quantitative exposure estimation, the AWE data was relied upon as much as possible, ensuring that they were defensible and reproducible. However, sparse exposure monitoring data forced us also to make assessments based exclusively on professional judgment of occupational hygienists. Challenging these assumptions about relative intensities of exposure can make further improvements to the validity of the exposure matrix. This is possible because the assumptions made in semi-quantitative estimation were explicitly stated.

CQs were the driving force in between-company and country differences, and their quality was the key to validity of the exposure matrix. Individuals of varying degree of experience, knowledge of past working conditions, and motivation, filled out CQs. Consequently, it was not possible to standardize responses to CQs among companies and countries enrolled in the study. An effort was made to control the quality of the questionnaires by resolving obvious logical inconsistencies and resorting to opinions of groups of national experts. Nonetheless, it would have been desirable (although impractical in a cohort design due to the large number of small firms) to corroborate the questionnaire information with production records. A more thorough and valid information about past production conditions might be obtainable in nested case-control study design that focuses on fewer persons (e.g., lung cancer cases and controls) and firms that are most informative for estimation of relative risks. Thus, EM presented in this article may be further improved if case-control study nested in the cohort of asphalt workers were to be carried out. The deterministic nature of EM allows it to be re-calculated with relative ease. Sensitivity analysis of associations seen in epidemiological analysis can be carried out through such challenges.

CONCLUSION

We have demonstrated that quantitative exposure assessment is possible in multicenter occupational cohort studies if sufficient occupational hygiene monitoring data can be recovered and subjected to statistical modeling. We have also developed a paradigm for reproducible semi-quantitative assessment of exposures on the basis of small number of explicitly stated assumptions. Complex exposure patterns assessed by the EM could not have been developed with any degree of certainty by relying exclusively on ‘‘expert evaluation’’ methodology. In applying the EM to epidemiological analyses, we cannot distinguish among health risks associated with bitumen fume, organic vapor and PAH exposures. Adjustment of risk estimates for coal tar exposure should be possible. Our approach produced an EM that can be challenged in future studies and easily re-estimated, if necessary. Methodology that we employed can be adapted for other mutlicenter studies.

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