Exposure assessment for a multicentric cohort study of cancer risk among European asphalt workers

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Utrecht University

Exposure assessment for a multicentric cohort study of cancer risk among European asphalt workers

Karakterisering van beroepsmatige blootstelling voor een multicentrum cohortonderzoek naar kankerrisico bij Europese asfaltwerkers

(met een samenvatting in het Nederlands)

by

Igor Burstyn

born on April 22, 1971 in Kiev, the USSR.

Proefschrift

Proefschrift ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de Rector Magnificus, Prof. dr. W.H. Gispen, ingevolge het besluit van het College voor Promoties in het openbaar te verdedigen op donderdag 17 mai 2001 des middags te 12.45 uur door.

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Dedicated to all my fellow travelers:

past, present and future.

Table of Contents

Chapter 1: Introduction.

Background and objectives of the study

Bitumen, derived from crude oil or naturally occurring, has been used by humans since antiquity (1) and according to some evidence played a role as waterproofing and binding material in construction of the Tower of Babel and the Hanging Gardens. Chemically, bitumen is a complex mixture of hydrocarbons soluble in chloroform and consisting of both aliphatic and aromatic compounds, some of which bear nitrogen, oxygen or sulfur functional groups (2). Forgotten for several millennia, this material started to serve humans again since the advent of industrial revolution (1). In early 18th century, Erinys d'Erinys described natural bitumen deposits in Germany, France and Switzerland. However, the first bituminous road was built almost a century later, in 1810, in Lyon, France. Large-scale industrial use of bitumen started with exploitation of natural bitumen deposits in Trinidad, with first commercial shipment arriving in England in 1840's. Bitumen's main use, in terms of volume, has been in paving, as a binder for inorganic fillers in asphalt mixes. According to European Asphalt Pavement Association,[1] there are at present approximately 4000 asphalt mixing plants in Western Europe. A typical mixing plant employs 5 to 10 individuals. These plants produce annually approximately 275 million tones of hot and 10 million tones of cold asphalt. These asphalt mixes are applied to road surfaces and by approximately 100,000 members of paving crews across Western Europe.

Recent review and meta-analysis reported an by aggregated relative risk of 1.2 for lung cancer among asphalt workers (3). Elevated cancer risks for other cancers, such as stomach, bladder, skin, and leukemia, were also reported. The review also reported the risk varied between different type of work in asphalt industry: roofing work had consistently higher risk than road construction and maintenance.

Uncertainty about bitumen toxicity motivated this study, when International Agency for Research on Cancer (IARC) concluded in 1987 that the evidence for bitumen carcinogenicity to humans was inadequate (4). The main uncertainty in the evaluation arose because it was not possible to exclude the possibility of confounding of available epidemiological studies by concurrent use by pavers and roofers/waterproofers of coal tar, a recognized carcinogen, and bitumen (3,4). With the coal tar use voluntarily discontinued by the asphalt industry in Western Europe, industry, regulators, scientists and government agencies received an opportunity to learn whether it is likely that bitumen exposure *per se* is carcinogenic (5). To address this question a historical cohort of asphalt workers was assembled in eight countries (Denmark, Finland, France, Germany, the Netherlands, Norway, Sweden and Israel) by IARC in order to obtain diverse exposure profiles and sufficient numbers of the main health outcome of interest (lung cancer). This cohort, unlike other multicentric cohorts, consisted primarily of small-to-medium sized firms, creating additional challenges in cohort assemble and exposure assessment. Assessment of historical exposures to known and suspected carcinogens in the cohort became the main objective of this dissertation. An integral part of this research was also to evaluate how different methodological aspects of exposure assessment could have influenced epidemiological analyses of exposure-response associations in the cohort.

[1] P.O. BOX 175, 3620 AD Breukelen, the Netherlands, e-mail at EAPA@wbinet.nl, web-site: www.eapa.org.

Structure and content of this thesis

> I will try to make my explanation briefly and plainly, and to keep it free from professional obscurities and technicalities. The matter is of utmost importance.
>
> "The Woman in White" by William Wilkie.

In chapter 2, I will further introduce the asphalt industry and summaries our knowledge about exposures in the industry at the onset of this project. Description of one of the key exposure assessment tools, database of exposure measurements in asphalt firms, will occupy chapter 3. This methodological presentation is followed, in chapter 4, by the analysis of an elaborated database of exposure measurements from the participating countries with a goal of developing empirical models for assessing exposures of road pavers in the epidemiological study. Chapter 5 explores alternative groupings of pavers to those derived on the basis of analysis presented in chapter 4. This is achieved by ascertaining whether we can identify a rule for assembling uniformly exposed groups for pavers. Uniformly exposed groups form ideal unit for exposure assessment and risk evaluation because all persons within a uniformly exposed group have the same exposure and can be easily contrasted with members of other uniformly exposed groups. Validation of exposure models derived in chapter 4 will be described in chapter 6. The manner in which both statistical and expert-evaluation-based models were used to construct an exposure matrix for the study of cancer risk in the European asphalt industry is the subject of chapter 7. Chapter 7 also illustrates some patterns of exposure inferred as a result of building the exposure matrix. In chapter 8 I will compare the performance of different exposure indices and latency assumption in modeling relationship between bitumen fume exposure and lung cancer mortality risk. This is the first step in exploring how different exposure assessment methods influence the outcome of the epidemiological investigation. Methodological issues and lessons derived from this entire project will be presented in chapter 9. In the appendix I will address briefly one of the newly emerging issues in asphalt industry that arose from widespread introduction of recycling[2]. Although this issue was not fully tackled in the IARC study of asphalt industry, I will attempt to show that it deserves more attention of public health researchers.

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[2] recycling of both old road surfaces and use of recycled waste as additives to asphalt

Chapter 2: A literature review of levels and determinants of exposure to potential carcinogens and other agents in the road construction industry.

Burstyn I, Kromhout H, Boffetta P: Literature review of levels and determinants of exposure to potential carcinogens and other agents in road construction industry. *American Industrial Hygiene Association Journal* 61:715-726 (2000).

Abstract

Workers in road construction industry include asphalt plant workers, ground construction workers and road paving workers. These individuals can be exposed to a wide range of potentially hazardous substances. A summary of levels of exposure to different substances measured during road construction is presented. Modern road paving workers are typically exposed to 0.1 to 2 mg/m^3 of bitumen fume which includes 10 to 200 ng/m^3 of benzo(a)pyrene. Sampling strategies and analytical methods employed in each reviewed survey are briefly described. The published reports provide some insight into identity of factors that influence exposure to bitumen among road construction workers: type of work performed, meteorological conditions, temperature of paved asphalt. However, there is a lack of (a) comprehensive and well-designed studies that evaluate determinants of exposure to bitumen in road construction, and (b) standard methods for bitumen sampling and analysis. Information on determinants of other exposures in road construction is either absent or limited. It is concluded that data available through published reports have limited value in assessing historical exposure levels in road construction industry.

Introduction

There is a long-standing controversy about the health effects of fumes and vapours generated during road paving with bitumen-based[†] materials. There is some evidence of irritant properties of such fumes (1) and it has been suggested that exposures to aliphatic amines are responsible for some of these symptoms (2). Bitumen fumes may also contribute to the development of bronchitis among highly exposed workers (3). Neurological and acute respiratory symptoms have been reported to be precipitated by bitumen exposure in road paving workers (1). However, a more recent study by Exxon Biomedical Science Inc. failed to find such an association (4). A relationship between renal disease and bitumen fume has been suggested by one report (5). Studies conducted in Turkey provide some evidence of cytogenic damage and adverse effect on immune system due to bitumen fume exposure (6)(7). However, in a Swedish study of tar-free paving it was observed that bitumen-originating polycyclic aromatic hydrocarbons did not produce genotoxic effects (8).

International Agency for Research on Cancer (IARC) has evaluated the carcinogenicity of bitumens in 1985 and 1987 (9,10). It has classified steam-refined and air-refined bitumens as possible human carcinogens (IARC Group 2B). However, evidence for the carcinogenicity of undiluted bitumens was inadequate (IARC Group 3). Animal studies with dermal application of the condensate of oxidized (roofing) bitumen demonstrated that the condensate has carcinogenic potential (11). The degree of similarity between laboratory generated fumes and those produced in laboratories remains a subject of debate. Asphalt workers have also been listed among occupations with a possible excess of cancer (12).

The following paper summarizes information available to us through reports published through the end of 1999 on levels of exposure and determinants of exposure in road construction industry. It serves as departure point for further discussions of risk evaluation and exposure assessment among asphalt workers in a multicentric IARC study of European asphalt industry (13).

Road construction industry

We have divided all road construction workers into three job classes: asphalt mixing, ground construction and road paving. The definition of job class is consistent with that adopted for the IARC study of the asphalt industry (13). We excluded from the discussion those employees in the road construction industry whose exposure to substances emitted in the course of actual road construction is either unlikely or episodic: office staff, laboratory technicians and management.

Asphalt mixing

Asphalt mixing is a process whereby bitumen is combined with mineral aggregate to produce asphalt. This takes place at asphalt mixing plants, which fall into two general categories: drum plants and batch plants. In all asphalt plants mineral aggregates are heated and dried before being mixed with bitumen in a mixing unit. The resultant asphalt mix is either transferred directly to a transport truck, which takes it to a paving site, or stored in silos prior to transport.

[†] In this article we follow the European nomenclature of bitumen for petroleum binder, which, when mixed with inorganic materials, yields asphalt. In North American nomenclature bitumen is synonymous with asphalt.

In a generic batch plant, mineral aggregates are heated in a rotary drum dryer to a temperature between 135°C and 180°C. Heated and dried mineral aggregate is placed into a pug mill mixer, where it is coated with bitumen and mineral filler. Bitumen is pumped into a pug mill mixer in discrete portions from bitumen storage tanks. Drum plants differ from batch plants in that the heating and drying of the mineral aggregate as well as the addition of bitumen and filler take place in the drum mixer in a continuous mode. A deviation from this rule is a so-called twin drum plant in which two separate drums are used: one for drying and heating of mineral aggregates and the other for mixing in bitumen and filler. The drum mixer is, in essence, a modified rotary drum dryer (employed in batch plants). It is a revolving cylindrical drum with a hot gas burner, which heats mineral aggregates delivered by hoppers and an injection system for bitumen and filler.

Most asphalt plants are stationary, but a small number of them are mobile. There is also a limited number of driving asphalt plants that can mix and lay asphalt in a continuous process at the paving site.

Ground construction

Ground construction, in the context of the road paving industry, is a set of activities that are required to prepare a road surface for paving. To prepare the road surface for application of asphalt, soil removal and shaping tasks are performed. Next, the road surface may require 'stabilization' via application of lime or cement. The application of lime or cement onto the road surface is often followed by mechanical sweeping.

Paving

This broad job class encompasses work involved in different types of road paving, surface dressing as well as indoor paving. In this section, we present a generic description of these activities and most common terminology used to describe them.

Small crews of workers (5-9 individuals) perform road paving. They can usually be separated into the following job titles: paver operator, screedman, rakerman, roller driver, transport truck driver and supervisor. Transport truck drivers deliver hot application mix from an asphalt plant to the paving site. Application mixtures are transported at temperatures that range from 140 to 200°C (14). The application mixture is transferred into a paving machine which applies it to the road surface. The paver operator is seated on top of the paving machine, between the hopper that receives hot mix from the transport truck and the screed that discharges the hot mix onto the surface being paved. The screedman controls the discharge of hot mix from the screed, and is normally located immediately above the freshly spread mix. The raker (rakerman) helps to spread the hot mixture discharged from the screed by using a hand rake or a shovel. Rollers are used to compress the application mixture once it has been applied to the paved surface. Roller drivers, who, in modern operations in Europe, are typically seated in the cabin, operate them. However, older rollers that may still be used were commonly not equipped with cabins.

Recycling/resurfacing operations are often combined with road paving. The old layer of asphalt is stripped and mixed with new asphalt, either at the asphalt plant or at the paving site, and re-applied to the road surface. Heating the old asphalt with propane burners can facilitate resurfacing (hot re-paving). Cold re-paving is can also be performed. Re-paving performed at the road construction site in conjunction with paving of a new road surface is known as *in situ* re-paving.

In surface dressing, the binding agent is applied to the road surface in order to ensure uniform application of chipping. Binding agents are kept at a temperature of at least 90°C. They include bitumen cutbacks (mixture of bitumen and solvents, such as kerosene) and bitumen emulsions (aqueous bitumen dispersions). During surface dressing, spray bar operators (sprinklers or fantail operators) control discharge of the surface dressing material onto the existing road surface. The spray bar operator stands at the back of the truck containing the application mixture and regulates the density and width of spray via a control panel. If necessary, spraying is done manually via hoses. Chipping is spread on top of the sprayed material from a separate truck, which follows the truck from which binder is sprayed. A chipping sprayer controls this process. The chipping truck is followed by rakermen who further flatten the chipping with rakes. Rollers finish the process by pressing the chipping into the layer of binder.

Mastic laying or application of mastic asphalt may be performed either indoors or outdoors. A kettle is used to heat a mixture of very fine mineral aggregate and paving/hard bitumen to about 200°C. The kettlemen are operate and control the kettles. Mastic asphalt is poured into buckets and carried by pourers to the application site. After it is poured in a desired location, troweller/mastic layer spreads mastic asphalt. Some advances towards mechanization of mastic laying have been made.

Exposure types and levels in road construction industry

The individuals employed in the road construction industry have the potential to be exposed to a vast number of hazardous substances. For each category of exposure we will present (a) the reported exposure levels and (b) briefly characterize the analytical method used to measure or 'define' the exposure.

Bitumen fumes and vapours: Bitumen-attributable organic matter and benzo(a)pyrene

Vapours and fumes originating from bitumen mixtures are primarily products of the evaporation of bitumen binder from the application mixture. Therefore, they can be expected to be chemically similar to bitumen (15), but they occur simultaneously with aggregate dust, solvents, additives, diesel and other automotive exhaust. Bitumen is the residue of a fractional distillation of crude oil. It is a complex mixture containing a high proportion paraffinic and naphthenic hydrocarbons (molecular weight: 300 to 100,000). Bitumen also contains compounds with nitrogen, oxygen and sulfur functional groups. Some of these compounds fall into the category of polycyclic aromatic compounds, which include polycyclic aromatic hydrocarbons (PAH). The exact composition of bitumen depends on the source of the crude oil and the refining process (11). Literature on the composition of commercially available bitumen is 'limited and fragmented' (16), however some information on bitumen and its derivatives used in paving is available (17).

A variety of analytical procedures have been employed to separate bitumen-derived organic matter from the inorganic materials. Some of the principal approaches to the extraction of bitumen-derived chemicals from dust- and gas-phase samples are: benzene soluble matter, cyclohexane soluble matter, carbon disulfide soluble matter, carbon tetrachloride soluble matter, chloroform soluble matter (corrected for boiling point distribution of bitumen-attributable organic matter), dichloromethane soluble matter. Bitumen-attributed emissions were quantified either gravimetrically, or by use of gas chromatography, liquid chromatography or infrared spectroscopy. Different PAH series have been assayed as indicators of bitumen exposure. When investigators sought to identify individual components of asphalt emissions, they employed chromatography, sometimes coupled with mass spectroscopy. Extensive reviews of sampling methodologies employed to measure PAH/bitumen emissions and an in-depth discussions of their limitations have been published (18)(19).

Inhalation exposure

It is apparent from the literature that bitumen constituents are divided in unequal proportions into particulate (fume) and gaseous (vapour) phases of bituminous emissions (16,18,20-22). Melting point appears to determine whether a substance appears in the vapour or particulate phase of asphalt emissions at a given temperature (21). The apportion of PAH into bitumen fume and vapour at typical paving temperatures can also be predicted on the basis of molecular weight: gaseous phase of asphalt emissions consisted mostly of PAH with molecular weight less than 228, while the particulate phase consisted mainly of heavier PAH (16,20) Most frequently, particulate matter from asphalt emissions (fume) was collected in personal exposure monitoring by means of total dust samplers. In recognition of the importance of the gas phase of asphalt emissions (vapour)(19), some investigators also collected samples of asphalt vapour, employing sorbent tubes to this purpose. Particulate and gas samples were often collected in series.

It has been reported that not all solvents used to extract organic matter from environmental samples of bitumen emissions have equal efficiency (19). For example, cyclohexane was reported to have lower ‘dissolving capacity’ than benzene (23). Therefore, in order to simplify comparison of the results of various studies, we will organize the discussion on the basis of the analytical methods used to extract asphalt emissions from sampling media. For each extraction method we will present, whenever possible, summaries of the levels of exposure to bitumen-attributable organic matter, and benzo(a)pyrene (most commonly assayed PAH). Since each study used different PAH series to define “total PAH” we will not consider this exposure measure. This decision is analogous to the one made in another review of exposure in the asphalt industry (11). The measurement of PAH alone can not be considered a valid measure of bitumen exposure, since (a) only trace amounts of PAH are present in bitumen and (b) the toxicity of bitumen emissions can not be entirely attributed to their PAH content (24). Thus at present, a bitumen-specific exposure marker is lacking. This is reflected in that there are no standard analytical methods for measuring bitumen emissions.

Exposure levels to bitumen fume and vapour reported in the literature are summarized in Table 2.1. Supplementary information on sampling strategy and measurement methods is also supplied in the Table. It would appear that most studies were rather small, collecting 20 to 40 measurements. They were conducted primarily in North America in the 1990’s. Exposure levels tended to be elevated during mastic paving indoors and in older studies. Exposures at asphalt plants appear to be of the same order of magnitude as those in most road paving operations. Benzo(a)pyrene levels are generally low, with older European studies being more likely to find detectable levels. In non-mastic applications, bitumen exposure levels were on the order of 0.1 to 2 mg/m^3 and benzo(a)pyrene exposures ranged between 10 and 200 ng/m^3. The description of sampling strategies and analytical methods was often incomplete with an exception of investigations conducted by the National Institute for Occupational Safety and Health (NIOSH) and Exxon Biomedical Science Inc.

Table 2.1: The reported levels of inhalation exposure to organic fume and vapour.

Solvent [h]	Operation(s)	Total organic matter n	Total organic matter mg/m^3	Benzo(a)pyrene n	Benzo(a)pyrene µg/m^3	Sampling strategy	Sampling media/device	Ref [i]
Benzene	paving of hot mix, resurfacing, application of dense road base asphalt	23	0.02-3.97	5[a]	$0.23*10^{-3}$[A] $(0.16-0.36)*10^{-3}$	nd	unspecified particulate sampler	(36)
	surface dressing	4	0.2[A] (0.1-0.5)			Sampling was conducted for the 'maximum time allowable by the content and pattern of the task.' Measurements were collected on either a single day or over several consecutive days.	glass fiber filter with a silver membrane filter as a backup in a closed-face 37-mm cassette	(14)
	paving of hot mix and application of bitumen cutback	7	0.2[A] (0.1-0.3)					
	mastic paving (kettlemen)	4	2.9[A] (1.8-5.0)					
	mastic paving (indoor tasks)	8	6.0-13.6					
	paving	5	0.08[G] (0.05-0.29)			nd	Unspecified	(47)
	single road construction project	7	0.42[A] (0.09-1.07)	3	0.11 to <0.22	Measured exposure during the execution of representative tasks.	PVC filters and 37-mm cassette; Teflon filter and Chromosorb 102 tube for PAH sampling	(22)
	asphalt mixing	33	0.15[Gb] (GSD=2.8)	33	<0.151	A cross-sectional survey of 'asphalt' industries. Sample industrial sites across the USA. Up to two samples per each study participant on consecutive days.	37-mm sampling cassettes with Teflon filters and XAD2 sorbent tubes	(25)
	paving	37	0.24[Gb] (GSD=3)	37	<0.151			
	road paving	?	0.47[A] (0.03-4.4)			Nd	Unspecified	(24)
	Hot mix road paving	80	Fume: 0.09[G] (GSD=2.57) Volatile hydrocarbons: 0.38[G] (GSD=4.75)			A cross-sectional survey of 'asphalt' industries, 2 consecutive days of sampling per person	Fume: modified NIOSH Method 5023; Volatile hydrocarbons: charcoal tube following particle filter	(4)

Solvent [h]	Operation(s)	Total organic matter n	Total organic matter mg/m3	Benzo(a)pyrene n	Benzo(a)pyrene μg/m3	Sampling strategy	Sampling media/device	Ref [i]
	Asphalt mixing	20	Fume: 0.06[G] (GSD=1.74) Volatile hydrocarbons: 1.06[G] (GSD=2.40)					
	Hot mix paving in a tunnel	9	0.3-1.26			nd	37 mm closed face sampler with Teflon filter, OSHA method 58	(38)
	Hot mix paving with and without crumb-rubber modified asphalt [g]	29 32 3 2 27	<0.007-0.61 0.01-0.88 <0.03-0.13 <0.1 <0.01-0.82			Representative, up to 4 consecutive sampling days with repeats for each person	NIOSH method 5042, particulate phase only	(30) (29) (31) (32) (33)
Cyclohexane	road paving	17	0.17[A]	1	0.61	nd	Unspecified particulate sampler with glass-fiber filter	(15)
	road paving application of bitumen cutback and oil gravel paving	17 6	1[A] (0.1-2.7) 0.25[A] (0.1-0.5)	13	<0.05	nd	Unspecified particulate sampler	(19)
	road paving			4	0.01-0.02	nd	37 mm closed face sampler with glass fiber filter and Tenax GC packing as backup	(48)
Carbon disulfide	road paving	79	0.36[G] (0.20-1.29)			nd	Particulate sampler with glass fiber filter; charcoal tube	(1)
Carbon tetrachloride	road paving[c]			6	2-9	nd	Particulate sampler with glass fiber filter	(49)
	indoor mastic flooring[d]	35	19.7[G] (0.5-260)	9	4		Unspecified particulate sampler	(19)
Chloroform	road paving dense and	58	1.2[Ae] (paver	15	≤ 0.007	Designed to obtain exposure measurements	Particulate sampler and XAD-	(20)

Solvent [h]	Operation(s)	Total organic matter n	mg/m^3	Benzo(a)pyrene n	µg/m^3	Sampling strategy	Sampling media/device	Ref [i]
	drainage asphalt; cold laying of recycled asphalt; gravel laying		drivers and screedmen) 0.3[Ae] (roller drivers)			during application of the most commonly used type of asphalt mixes in Sweden.[f]	2 sorbent tube	
Unspecified	Road work in Australia	?	0.4-8.9 (peak exposures 300-900 mg/m^3)			Nd	Organic matter in particle samples only	(5)

A -- arithmetic mean; G -- geometric mean; nd -- not described; a -- It is not clear from the report whether the 5 samples which were analyzed for specific PAH were representative of all the samples collected in the investigation; b -- The benzene soluble matter levels could be positively biases due to migration of the components of PTFE particulate filters used in the study, into benzene solvent employed in extraction of the organic matter. This suggestion is motivated by the observation that in 22 samples, the mass of benzene soluble matter extracted from "total" dust exceeded that detected by weighing prior to extraction. c -- No information was supplied in the original report about the type of asphalt handled by the study participants, but given the low levels of benzo(a)pyrene observed, it is not likely that coal tar was present in the application mixtures during exposure monitoring. d -- Hansen argued that the measured exposures are primarily due to bitumen exposure and not coal tar, since mastic asphalt does not contain coal tar. However, industry representatives have contradicted this statement (50). e -- corrected for boiling point distribution of bitumen-attributable organic matter; f – three worker were monitored on each sampling occasion: paver operator, screedman and roller driver; g – personal breathing zone samples only; h -- solvent used extract organic matter; i-- reference.

Dermal exposure

Bitumen condensate is a product of condensation of bitumen fume and vapour. It can be expected to precipitate both on equipment handled by road construction workers and the skin/clothes of these workers.

A US study (25) reported low PAH content in dermal wipe samples of hot mix asphalt plant workers and members of road paving crews. Skin wipe samples were analyzed for 17 PAH, though only 6 PAH were detectable in all of the analyses. Only one sample out of 25 collected at the asphalt plant had detectable PAH (3 out of possible 17 PAH). The number of dermal wipe samples with detectable PAH in road paving was not reported. However, a close examination of the reported data revealed that it is not likely that more than 5 or 6 out of 30 dermal wipe samples contained any detectable PAH.

The Chevron Research and Technology Company has conducted a laboratory study of chemical composition of bitumen asphalt (26). Benzo(a)pyrene levels in asphalt fume condensate ranged from 0.04 to 2.8 ppm. Bitumen fume condensate generated in paving asphalt mixes had a total 3- to 7-ring PAH content ranging from 4 to 16 ppm (n=18).

Coal tar and coal tar pitch

Vapours and fumes originating from coal tar- and coal tar pitch-containing mixtures are the products of the evaporation of coal tar/pitch and bitumen binders. We have already presented the types and levels of the substances that can be emitted due to the evaporation of bitumen. The present discussion focuses on airborne substances of coal tar and coal tar pitch origin. Coal tar and coal tar pitch are coal distillation products, composed mainly of highly condensed aromatic hydrocarbons, including PAH. The content of PAH in coal tar/pitch has been reported to be about 100 to 1000 times higher than that of bitumen (14,26-28).

In a Dutch study, exposures at four surface dressing sites were studied (23). A mixture of bitumen and coal tar was applied to the road surface at an application temperature of 140 to 180°C. Dust samples were collected onto 37-mm cassettes with glass fiber filters. Twenty-eight full-shift personal dust samples were collected, and their cyclohexane soluble matter content was reported to have a geometric mean of 0.2 mg/m^3. Unfortunately, no estimates of the variability in this calculation were provided. The reported exposure levels were not representative of the pattern of exposure in surface dressing, since workers actually involved in the spraying of binder and tank truck drivers were excluded from the study for logistical reasons. The study also investigated dermal exposure to asphalt emissions. Dermal deposition of pyrene was determined via skin pads (with polypropylene as absorbing material) attached to different sites on the bodies of workers. There was no significant correlation between airborne levels of cyclohexane soluble matter and dermal PAH exposure. The distribution of the relative amounts of individual PAH was different in airborne and dermal samples, indicating that fume available for inhalation and fume precipitating onto skin of workers during surface dressing with coal tar-containing mixes have different compositions.

A review article by Lindstedt and Sollenberg (1982) indicated that during asphalt paving of highways with asphalt-tar mixture, benzo(a)pyrene exposures of 50 to 350 $\mu g/m^3$ were observed. These levels are considerably higher than those observed when coal tar was not used. The same study apparently reported that there was a 'considerable skin exposure from the contaminated clothes.'

Biological monitoring of PAH exposures

A Dutch study of surface dressing with tar-containing binder investigated urinary metabolite level of PAH (1-hydroxypyrene) (23). Geometric means of the excreted PAH metabolite varied among paving sites from 0.7 to 2.8 µmol/mol creatinine. End-of-shift samples tended to have higher 1-hydroxypyrene content than the pre-shift ones. There was no significant correlation between airborne levels of cyclohexane soluble matter and 1-hydroxypyrene levels. However, the amounts of pyrene collected from different sites of the workers' bodies were correlated with urinary 1-hydroxypyrene levels ($r=0.4-0.6$, $p<0.05$).

During a study of 28 subjects in tar-free paving in Sweden(8), 1-hydroxypyrene levels in urine had geometric mean of 0.96 (range 0.04-4.0) µmol/l. Referents not employed in road paving had lower geometric mean 1-hydroxypyrene levels in urine (0.60 μmol/l, range 0.14-2.2 μmol/l, n=30). No difference between pre- and post-shift levels was observed for road pavers, but the levels dropped by an average of 0.64 μmol/l after a weekend, suggesting that the increases level of PAH metabolites was related to occupational exposure. A correlation between pyrene in the personal breathing zone and 1-hydroxypyrene levels in urine was observed (r=0.4-0.6). Road pavers did not have elevated rates of sister chromatid exchanges and micronuclei compared to referents. All subjects were non-smokers.

A study of 21 rakerman, 7 asphalt plant employees (exposed group) and 28 university/hospital staff (controls) revealed elevated 1-hydroxypyrene levels in urine of subjects exposed to bitumen fumes (6). The mean urinary 1-hydroxypyrene excretion among exposed persons was 0.78 μmol/mol creatinine versus 0.52 μmol/mol creatinine in controls. After controlling for age, sex and smoking habits, the authors concluded that bitumen fumes were associated with elevated rates of sister chromatid exchanges, micronuclei and high frequency sister chromatid exchange cells. However, 1-hydroxypyrene levels in urine and cytogenic endpoints did not correlate.

In general, it would appear that 1-hydroxypyrene levels in urine of road paving and asphalt mixing workers tend to increase if coal tar is used. They increase towards the end of work-shift and decline upon removal of bitumen exposure. The relationship among dermal deposition of organic matter, its levels in personal breathing zone and PAH metabolites in urine is poorly understood in road construction industry.

Sulfur-substituted hydrocarbons

Sulfur-substituted hydrocarbons can be emitted during road paving of crumb-rubber modified mixes (29-35). In conventional paving benzothiazole (sulfur-substituted hydrocarbon associated with vulcanized rubber) was virtually non-detectable. Other sulfur compounds were at or barely above the limit of detection. However, when crumb-rubber modified mixes were applied, benzothiazole levels ranged from 3.3 to 233 $\mu g/m^3$ and other the concentrations of sulfur compounds varied from <0.5 to 792 $\mu g/m^3$ (n=44). Sulfur-substituted compounds were collected by 37 mm stationary samplers loaded with Teflon filter and followed by ORBO 42 sorbent tubes. Organic matter was extracted from filters with hexane and assayed by gas chromatography with sulfur chemiluminescence detection. Samplers were positioned in locations were the highest asphalt emission levels were expected (screeds and hoppers of pavers).

Mineral aggregates

Mineral aggregates are the second primary component of asphalt. These commonly include gravel and sand, but asbestos and lime have also been used, albeit very infrequently. Another potential source of silica/quartz exposure is the road surface itself, which is manipulated during road construction. Results of studies that have measured total or inhalable dust, respirable dust and respirable silica exposures in the road construction industry are presented in Table 2.2. Just like in the case of studies of bitumen fume and benzo(a)pyrene exposure, most published studies were rather small in scale. The highest inhalable dust levels were reported during mastic paving. Inhalable dust exposures in other paving and asphalt mixing operations appeared to be similar to each other. Little information is available about respirable dust and

Table 2.2: The reported levels of inhalation exposure to total/inhalable and respirable dust.

Operation(s)	Sampling device	Sampling strategy	Respirable Dust				Total/Inhalable Dust			Ref [g]
			n	Mean† mg/m^3	Variability‡	$\%SiO_2$	n	Mean† Mg/m^3	Variability‡	
resurfacing operation; paving with hot rolled asphalt; paving using dense road base asphalt	unspecified	full-shift samples; repeated measurements within a person					23		0.15-5.71	(36)
surface dressing	closed-face 37-mm cassettes	task-specific sampling					4	0.6[A]	0.2-1.5	(14)
road paving using hot bitumen or paving with kerosene-based bitumen cutback							8	2.6[A]	0.2*-15.1	
mastic laying (kettlemen)							4	4.4[A]	2.9-7.7	
indoor mastic laying							8	13.3[A] to 14.2[A]	10.5-18.2	
road paving	unspecified	Unknown					3	0.34[G]	<0.02-0.59	(47)
road construction: operations involving moving soil	unspecified; two stage Marple personal cascade impactor with a PVC filter (respirable dust)	task-specific (~5.5 hours); aimed at measuring exposure during normal operating conditions	4		0.03-0.53	0-32[a]	10	0.72[A]	0.20-1.33	(22)
asphalt mixing	37-mm cassette	2 samples per study participant, industry-wide survey	6	0.24[G]	3.1 (GSD)		33	0.78[G]	2.8 (GSD)	(25)
road paving			7	0.18[G]	1.5[b] (GSD)		37	0.37[G]	1.7 (GSD)	
road paving	unspecified	Unknown		0.18	0.09-0.3		?	0.43[A]	0.11-0.86	(24)
paver operators	unspecified sampler with fiberglass filter	2-hour samples[c]					14	1.26[A]	0.15-5.61	Cited by (19)
rakermen							7	0.93[A]	0.25-3.46	
screedman							7	0.83[A]	0.33-1.47	
asphalt mixing	unspecified	Unknown					?	0.7[A]	?-1.7	Cited by (19)
road paving							287	0.5-2[A]	?-6.4	
surface dressing							9	0.8[A]	?-1.3	
paver operators	unspecified	Unknown					5	0.58[A]	0.25 (SD)	(15)

			Respirable Dust				Total/Inhalable Dust			
			n	Mean†	Variability‡	%SiO$_2$	n	Mean†	Variability‡	
screedmen							12	0.83[A]	0.63 (SD)	
sweeping unsealed road	Casella cyclone	Unknown	1	11.9		0.2	1	75		(27)
sweeping sealed road			1	1.5		24				
screedmen			4		0.2-0.9	6-18	1	7.8		
Hot mix paving in a tunnel	37 mm closed face sampler, NIOSH method 0500	Unknown					9		1.09-2.17	(38)
Hot mix paving with sulfur-extended asphalt	37 mm sampler with and without 10 mm nylon cyclone for respirable particulate	Representative, complaint-based	7	2.4[Ad]	0.2-5.1		10	3.1[Ac]	0.5-5.6	(43)
Hot mix paving with and without crumb-rubber modified asphalt	NIOSH method 5042/0500 for total particulate and Dorr-Oliver nylon cyclone for respirable particulate (NIOSH Method 0600)	Representative					29[e]		0.03-0.78	(30)
			12[f]		<0.02-9.0		32[e]		0.14-1.4	(29)
			16[f]		<0.03-0.52		44[e]		0.01-1.2	(31)
			16[f]		<0.02-3.1		29[e]		0.09-1.3	(32)
			11[f]		<0.02-0.98		27[e]		0.02-1.03	(33)
			16[f]		<0.03-0.58		29[e]		<0.02-0.67	(34)
			16[f]		<0.02-3.8		34[e]		<0.02-1.0	(35)
Hot mix road paving	NIOSH methods 0500 and 0600	A cross-sectional survey of 'asphalt' industries, 2 consecutive days of sampling per person	80	0.10[G]	2.78 (GSD)		80	0.33[G]	2.18(GSD)	(4)
Asphalt mixing			20	0.10[G]	2.53 (GSD)		20	0.45[G]	1.91(GSD)	

† -- A = arithmetic, G = geometric; ‡ -- Range in mg/m^3 unless otherwise indicated; GSD = geometric standard deviation; SD = standard deviation (in mg/m^3); a – based on analysis of silica in only 3 respirable dust samples; b – underestimate, since 6 out of 7 samples were below 0.18 mg/m^3 limit of detection; c -- it is unclear how these short periods during which exposure was measured were selected; d – 100% sulfur; e – personal breathing zone samples only; f – area samples; g -- reference.

silica exposure during road construction, but there it would seem that these exposures could be substantial during ground construction. Respirable dust levels are similar in road paving and asphalt mixing. Just as in the case of bitumen-attributable emissions, differences in methods employed by different investigators and incomplete reporting of results raise the possibility that the observed inter-study exposure patterns are confounded.

The only lime and cement dust exposure measurements in road construction industry, reported in the scientific literature, were obtained during ‘road stabilization’ work in New Zealand (27). It is not clear how common such operations are. Cement and lime dust samples were collected by open-face sampling cassettes onto cellulose acetate filters. Cement dust levels were determined gravimetrically. Lime dust levels was assayed for calcium using atomic absorption spectroscopy (NIOSH Method). The reported lime dust exposures ranged from 0.5 to 78.5 mg/m^3. Five cement dust exposure measurements ranged from 17500 mg/m^3 (in bag breaking and emptying) to 0.6 mg/m^3 (in rotary mixer driving).

Solvents

One can reasonably expect that solvents used in the road construction industry are similar to those used in other industries. rganic solvents can be used directly (e.g. to clean equipment), and can form a part of application mixes. In one Dutch study (36), the use of gas oil to clean paving equipment was observed. Another study (14) reported kerosene use to clean equipment. Norseth et al. (1991) observed acute symptoms, such as ‘abnormal fatigue’ and ‘reduced appetite’, in a group of 79 road construction workers and concluded that the observed symptoms were consistent with solvent exposure. They measured mean exposures to volatile organic compounds in 77 samples to be on the order of 0.14 to 40 ppm. The authors pointed out that these solvent exposures were ‘low’ compared to those occurring in painting, dry cleaning and degreasing. This last observation seems to be corroborated by a New Zealand study (27), which reported exposures to 6 hydrocarbon solvents in road construction to be on the order of 10 to 10,000 times below the regulatory limit (unspecified). In Norway (37), the use of diesel as a solvent to clean equipment was responsible for approximately 60% (by mass) of total PAH exposure. In studies reporting solvent exposure levels, long term detection charcoal tubes were used to collect the environmental samples. Gas chromatography was employed in quantification of the hydrocarbon solvents.

Aliphatic amines

Aliphatic amines can be used as additives to bitumen emulsions, cutback bitumen and paving bitumen. Thus, amines can be potentially emitted during the application of such materials. The irritating potential of aliphatic amines has been recognized (2). Nevertheless, in a Norwegian study (1) of health effects among road paving workers, amine addition did not appear to produce an increase in acute symptoms. Unfortunately, the actual exposure levels were not measured. Aliphatic amine exposures of <0.02 to 0.5 mg/m^3 have been measured among members of 4 crews of Swedish road paving workers involved in the application of a aliphatic amine-enriched emulsion (2). Aliphatic amines were collected simultaneously from the gas and particulate phases of emissions by using the combination of XAD2 adsorbent tube and a particulate sampler (unspecified) with glass fiber filter. Both the particulate filter and adsorbent tube were coated with 1-napthylisothiourea. The monitored workers either drove ‘the slurry machine’ or raked hot bitumen emulsion after it was applied to the road surface. The bitumen emulsion used contained 4-6% bitumen, which in turn contained about 0.2% amine. Even though most measured exposures for individual amines were low (around the detection limit of 0.02 mg/m^3) the authors speculated that the additive effect of several aliphatic amines might produce irritant effects. They also pointed out that owning to the fact the emulsion applied in their study was 'a rather pure technical product,' there was a possibility 'that higher exposures will result if a wetting agent of lower purity is used.' Thus, the aliphatic amines exposure levels reported in this Swedish study cannot be considered as representative of those arising in the application of amine-enriched bitumen emulsion.

Aldehydes

Aldehydes are not components of bitumen, but it has been suggested that they may form during the laying of asphalt. In a Swedish exposure survey (20), glass fiber filters impregnated with 2,4-dinitrophenylhydrazine was used to collect aldehydes. The filter was mounted into a sampling cassette of unspecified configuration. The samples were analyzed for formaldehyde, acetaldehyde, acrolein, propanal, benzaldehyde and tolyaldehyde using high pressure liquid chromatography. Screed operators ('technicians') were monitored for aldehyde exposure, yielding 16 samples. None of the assayed aldehydes occurred in detectable quantities (limit of detection: 0.007 mg/m^3).

According to a review compiled by the European industry (11) concentrations of aldehydes detected during road paving by another Swedish investigation reached a level of 2.3 mg/m^3. It is not clear whether conditions under which these measurements were conducted were common in the industry.

Vehicle exhaust

The majority of road-paving equipment used in Europe is powered by diesel engines. Thus, one can expect European road paving workers to be exposed to diesel exhaust. Unfortunately, there are no published reports of diesel exhaust measurements during road paving in Europe. In an evaluation conducted in the US, measurement of diesel exhaust as elemental carbon during paving in a tunnel revealed that diesel exhaust made little contribution to total organic matter exposure (n=3, 0.027-0.066 mg/m^3)(38). Paving in the tunnel was conducted at night, presumably when there was little or no general traffic in the tunnel. In another US study, elemental carbon monitoring during hot mix paving in open space also indicated low diesel fume exposure (n=74, range: <0.0002 – 0.095 mg/m^3) (29,31-35).

Since most of the road paving equipment is powered by diesel engines, exposure to gasoline-powered engine exhaust in road construction must originate from the background traffic. A Norwegian survey found that the levels of exhaust gases at a paving site depend on the amount of surrounding traffic (37). In a Swedish study vehicle exhaust from surrounding traffic made significant contribution to total hydrocarbon exposure during road paving (20). However, another Swedish study concluded that vehicle exhaust is not a major source of PAH exposure in road paving (8).

Nitrogen dioxide (NO_2) and carbon monoxide exposures (CO) have been associated with engine exhaust exposures. Consequently they can originate either from background traffic or road paving machinery during road paving operations. Some of the NO_2 exposures measured during Norwegian survey of exposures among road paving workers (37) were reported to exceed 'permissible value'. The same study indicated that the measured CO exposures were 'low'. Unfortunately, neither measured levels, nor the occupational exposure limits used were reported. The analytical methods were not adequately described. Investigations by NIOSH reported full-shift time-weighted average CO concentrations between 8 and 40 ppm with peak values as high as 1000 ppm (30)(29,32). The CO and NO_2 in the air were not detected during night-time paving in a tunnel, presumably due to absence of general traffic (38).

Determinants of exposure and exposure controls

The potentially hazardous nature of road construction work raises the issue of minimizing exposure that can lead to adverse health effects. Studies of the determinants of asphalt-related exposure identified a number of factors in road construction activities that can influence exposure levels. These include job class, type of asphalt, application methods, application temperature, volatility of asphalt, meteorological conditions, tasks performed within a road paving crew, design of paving equipment, and degree of enclosure of the paving site. We will focus on summarizing the findings of those studies that relate to the identity of the determinants of exposure to bitumen fume and PAH in the industry. Data on exposure to respirable silica, asbestos, lime, vehicle exhaust, solvents, NO_2, CO, aldehydes and aliphatic amines are insufficient for the determinant of exposure analysis.

Job class

There is little information on the exposures at asphalt mixing plants and in ground construction, making it difficult to investigate the relationships between job class and exposures. A report from the USA (25) indicated that road paving crews can be more highly exposed to benzene soluble matter than employees of asphalt plants. However, the situation with total and respirable dust was reversed. The opposite trend was found in a Norwegian study (37). Exposure levels were found to be lower during road paving than among asphalt plant personnel. It would appear that the ground construction crews have little opportunity for asphalt fume/vapour/condensate exposure. However, their exposure to mineral aggregates can be substantial (27). Beyond this, the available reports do not allow comparison of exposures in this job class to road paving and asphalt mixing.

Asphalt plants

In a study of hot mix asphalt production in the USA (39), particulate samples were collected isokinetically from process effluent gas stream. Glass fiber filters were used as sample collection media. Organic matter was extracted from the filters with benzene, PAH in the organic matter were separated by chromatography and subsequently quantified by ultraviolet-visible spectrophotometry. Bitumen binder was added to the mix at 121°C. Duplicate particulate samples were simultaneously collected from gas effluents entering and exiting a water spray tower. A water spray tower was the last step in effluent de-contamination process in which emissions originating from mixer and rotary dryer were treated in a cyclone and, subsequently, a water spray tower. Benzo(a)pyrene levels in effluent prior to treatment in a water tower were on the order of 1500 $\mu g/m^3$. It appeared that PAH originated from combustion gasses emitted from the rotary spray dryer (prior to addition of bitumen to the mix). This would imply that bitumen binder is only a minor source of PAH in asphalt plant emissions. The authors of the report indicated that their results could not be considered typical, since they are based on a limited number of samples. It is also difficult to extrapolate from process effluent levels to personal exposure levels. However, the results indicate that (a) in batch asphalt plants rotary dryers can be a more important source of PAH exposure than mixers and (b) 10-to-20 fold decrease in environmental PAH emissions can be achieved by the scrubbing in a water spray tower.

In another US study (40), analysis of the available data on factors that influence environmental emissions from the drum asphalt plants was performed. The author indicated that it appears that wet scrubbers were effective in reducing the emissions. However, bag house filters, effective in reducing emissions originating from pug mill mixer plants, were ineffective in reducing emissions from drum plants. The author also reported that mix temperature, bitumen injection point in the drum mixer and coarseness of the mix appeared to influence emission levels. Elevated mix temperature was associated with higher emission rates. Increasing the distance from burner to injection point of bitumen binder appeared to lower the concentration of partially oxidized hydrocarbons in effluent. Mixing of coarser asphalt was associated with decreased particulate emission levels. It must be noted that it is not clear whether these factors affect occupational exposures of plant personnel. It is also not clear how 'grain loading' (exposure measure used by the author) relates to inhalable and respirable particle levels. Finally, the evaluation of the appropriateness of the author's conclusion is hindered by incomplete description of methods and results.

Results of a survey of US asphalt industry (4) indicate that mechanics at the asphalt plants (n=2) were more highly exposed to total and respirable particulate than other asphalt plant employees. However, the highest organic matter exposures tended to occur among supervisors/clerks (n=4) and plant operators (n=3).

Paving

Composition of asphalt

The chemical composition of emissions from application mixtures depends on a variety of factors. It can be safely assumed that the chemical composition of the application mixtures has a direct effect on the determination of the composition of asphalt emissions. The composition of the application mixtures has been modified in Western Europe in recent decades due to discontinuation of the use of coal tar and pitch as components of asphalt (13). Thus, we can conclude that time period (before or after use of coal tar in road construction) can be expected to be a significant determinant of exposure to hazardous substances in the asphalt industry. This effect can be anticipated to be country-specific, since the use of coal tar was discontinued at different times depending on the country.

Addition of rubber to hot-mix asphalt, according to experiments performed by the US EPA, 'does not have a dramatic impact on the air emissions (of particulate and PAH) generated in the paving process' (41,42). However, extensive survey conducted by NIOSH indicates that paving with crumb-rubber modified asphalt can lead to elevated bitumen fume and benzothiazole exposures (29-35). An investigation of paving with sulfur-extended asphalt in the US revealed high total and respirable sulfur particulate exposure levels which appeared to be associated with eye and respiratory tract irritation (see Table 2.2 for exposure levels) (43). It is not clear how common paving with sulfur-extended asphalt is now or was at the time of the investigation in 1982. Little additional data is available on exposure patterns during paving with rubber-modified and other modified asphalt mixes.

Application methods

Mastic asphalt paving has been reported to result in much higher asphalt fume exposure levels than other road construction activities (3,11,14). This conclusion can be equally based on both within- and between-study comparisons. Inhalable dust and PAH exposures during surface dressing appear to be similar to those arising in application of hot mixes. The need to reduce exposures that occur during surface dressing has been identified, even though the available exposure data is limited (11). Furthermore, inhalable dust levels and benzene soluble matter levels generated in rolling of hot asphalt appeared to be higher than those produced during cold resurfacing and application of dense base asphalt (36). Little information is available on exposures during re-paving operations, but high exposures, possibly due to tasks performed and heating of the old asphalt during re-paving, have been reported (11). Thus we can tentatively arrange road paving operations in the following order of decreasing (left to right) bitumen exposure levels:

mastic paving ≥ re-paving > hot asphalt, surface dressing > cold applications.

Examination of Table 2.1 confirms this ranking. The highest organic matter exposure levels were reported during mastic paving (from about 2 to 260 mg/m^3). Limited data on resurfacing (re-paving) indicates that it can be associated with organic matter exposures as high as about 4 mg/m^3. Exposures during hot mix paving and surface dressing were on average below 1 mg/m^3 and for more recent data – below 0.5 mg/m^3. Limited data on cold applications indicates that they were associated with exposure levels akin to the lower range of those observed during hot mix paving (0.1 to 0.5 mg/m^3), but given that cold applications are expected to result in lower emissions of organic matter (see section below) we felt justified in relegating them to the lowest exposure category among other road paving methods.

The type, temperature and volatility of the mixes used characterize paving methods. Consequently, differences in exposures during different road paving activities can be attributed to these properties of the application mixtures (discussed below).

Application temperatures and volatility

The quantity of bitumen fume generated appears to depend greatly on temperature of bitumen. According to the results of a laboratory study conducted by the Chevron Research and Technology Company (26), the amount of bitumen fume condensate generated at 232°C was only 2 to 12% of the condensate produced at 316°C. The degree of temperature-dependence varied with the source of the crude oil used in the manufacture of bitumen.

On the basis of a study of Norwegian asphalt workers (1), it has been recommended to keep application temperature below 150°C, which should, according to the authors, keep combined inhalable fume and vapour exposures to below 0.40 mg/m^3 (carbon disulfide soluble matter). An increase in acute symptoms, supposedly reflecting a change in exposure pattern, occurred between application temperatures of 145 and 155°C. Another Norwegian study (37) reported that the temperature of the application mix was one of the most important factors in determining asphalt fume exposure. It was observed that ‘evaporation of asphalt fumes and other volatile compounds' was 'doubled for every 15°C increase in mix temperature.' This last finding is in agreement with a Swedish report (20).

A laboratory study of emissions from two types of asphalt commonly used in California was recently conducted (16). The percentage of PAH in gaseous phase of bitumen emissions was observed to increase with temperature. The investigators reported that pattern and amount of volatile organic matter emissions depended on the type and temperature of asphalt. The temperature range used in the tests was between 150°C and 250°C. It is not clear which properties of the asphalt were responsible for the observed 'type of asphalt' effect.

An analytical model of bitumen fume exposure has been developed in laboratory studies (44), indicating that the volatility and temperature of bitumen can have a significant impact on exposure levels. The model has been validated under field conditions only to a limited extent (36).

Tasks

Tasks performed by road paving workers also appear to be related to exposure levels. The operator of the paving machine is usually more highly exposed to PAH and inhalable dust than other personnel (11,20,37) High exposures among foremen where also observed (37). Screedmen were the most highly exposed (for all agents monitored) members of road paving crews according to recent investigation of US industry (4). Exposures among roller drivers were reported to be 4 times lower than for other members of a road paving crew. In surface dressing operations, it was reported that fantail operators where more highly exposed then rakermen (23). There are also some indications that the distance between the rakerman and the paver is an important factor in determining the exposure levels of these individuals: an increase in that distance appeared to reduce personal inhalable dust exposure by a half (19). The actual difference in the distance was not mentioned.

Equipment

It has been reported that the use of some paving machines can reduce exposure levels by up to 60% (37). Features of this 'environmental paver', presumably responsible for reduction in exposure levels, included cabins with doors and windows that can be locked, as well as partial enclosure and ventilation of the screed. The importance of closing doors and windows of cabins installed on paving machines was emphasized, since leaving them open resulted in entrapment of asphalt fumes inside the cabins. The authors of the report also recommend use of special carrying baskets (not described) which would isolate foremen from the source of exposure. NIOSH has published guidelines for design of ventilation exhaust system for screed of the paving machines (45) and subsequently evaluated performance of this control measures under laboratory and field conditions, resulting in its further refinement (46).

Enclosed paving sites, weather conditions and personal respiratory protective equipment

Enclosed paving sites, such as tunnels, were associated with some of the highest reported exposure levels (37,38). During handling of mastic asphalt indoors, exposure levels were 2 to 3 times higher than for workers at the same work-site who worked outdoors (14).

Meteorological conditions, such as air temperature (37), wind speed and direction (36,37), were listed as one of the most important factors affecting exposure levels. Asphalt and bitumen type were reported to influence exposure levels, but to a lesser extent than meteorological conditions and application temperature (37). An increase in relative humidity was reported to decrease bitumen fume exposure (20).

During one hygiene survey in the USA, it was observed that dust masks, though available to road paving workers, were not worn even when emission of asphalt fumes into workers' face was visible (22). In another US study, the use of respiratory protection among workers exposed to asphalt fume was not observed (25).

Dermal exposure

According to the Centre for Research and Contract Standardization in Civil and Traffic Engineering (CROW) (11), 'there is a lack of information regarding skin exposure' to bitumen condensate. The same document speculates that 'fumes condensed onto tools or machine surfaces may be transferred to hands and clothes.' There are very few studies examining causes of skin exposure in road construction. The effect of protective clothing on dermal PAH exposure during handling of asphalt was difficult to evaluate in one study due to low overall levels of exposure detected by skin wipes (25). Not all workers were reported to wash hands prior to lunch breaks after handling asphalt (25). There appears to be no correlation between airborne asphalt fume and dermal deposition of asphalt condensate (23).

Conclusion

For the IARC historical cohort study of asphalt industry, data reported in published reports have limited value in assessing exposure levels. It can be used for very crude qualitative grouping of the road construction workers into groups that are likely to have similar exposure patterns. Road paving and asphalt mixing workers can be expected to have similar bitumen exposure which is higher than that of ground construction workers. In contrast, ground construction workers are probably a job class with elevated silica exposure. Workers engaged in mastic laying, those who paved hotter asphalt mixes and paved in enclosed spaces can be expected to have elevated bitumen fume exposure. Bitumen fume exposures at asphalt plants and outdoor hot mix paving and surface dressing can be expected to be similar. This comparison can be confounded by presence on organic matter of non-bitumen origin. Exposure to PAH can be anticipated to be elevated when coal tar is added to paving mixtures. There is also some evidence that the exposures have been higher in the past. However, misclassification of exposure in such grouping can be expected to be substantial and its magnitude and direction would be impossible to quantify. Assembling industrial hygiene measurements from various studies into a single database and obtaining access to unpublished data may help refine exposure assessment in road construction industry.

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Chapter 3: Designing an international industrial hygiene database of exposures among workers in asphalt industry.

Burstyn I, Kromhout H, Cruise P, Brennan P: Designing an industrial hygiene database of exposures among workers in asphalt industry. *Annals of Occupational Hygiene* 44(1):57-66 (2000).

Abstract

Objectives: The objective of this project was to construct a database of exposure measurements which would be used to retrospectively assess the intensity of various exposures in an epidemiological study of cancer risk among asphalt workers.

Methods: The database was developed as a stand-alone Microsoft Access 2.0 application, which could work in each of the national centers. Exposure data included in the database comprised measurements of exposure levels, plus supplementary information on production characteristics which was analogous to that used to describe companies enrolled in the study.

Results and Discussion: The database has been successfully implemented in eight countries, demonstrating the flexibility and data security features adequate to the task. The database allowed retrieval and consistent coding of 38 data sets of which 34 have never been described in peer-reviewed scientific literature. We were able to collect most of the data intended. As of February 1999 the database consisted of 2007 sets of measurements from persons or locations. The measurements appeared to be free from any obvious bias.

Conclusions: The methodology embodied in the creation of the database can be usefully employed to develop exposure assessment tools in epidemiological studies.

Introduction

The International Agency for Research on Cancer (IARC) is currently engaged in a multicentric study of cancer risk among European asphalt workers. The study design is a retrospective cohort assembled from workers in eight countries: Denmark, Finland, France, Germany, Israel, the Netherlands, Norway and Sweden. This report is concerned with the exposure assessment aspect of that study.

A number of reports of exposure measurements among European asphalt workers have been published. Measurements of inhalable dust exposures have been carried out in Denmark (1,2), Finland (3), and the Netherlands (4-6). Exposures to benzo(a)pyrene and a series of other specific PAH have been monitored in Denmark (1,2), Finland (3,7), the Netherlands (4-6), Norway (8), Germany (9-11) and Sweden (12). Levels of airborne bitumen fume and/or vapour in the asphalt industry have been measured in Finland (3,7), the Netherlands (4,6,13), Norway (8,14) and Sweden (12). An assessment of dermal exposure in the European asphalt industry was performed only in one Dutch survey (13). Information available in the scientific literature on exposures in the asphalt industry does not cover all countries, time periods and agents of interest for the epidemiological study. In an attempt to obtain data that can address these limitations, we set out to build an industrial hygiene database that would contain information on the relevant exposure measurements in the participating countries. We were particularly interested in collecting measurements of exposure to bitumen fume, bitumen vapour, inhalable dust, respirable silica, diesel exhaust, asbestos fibers and polycyclic aromatic hydrocarbons (PAH).

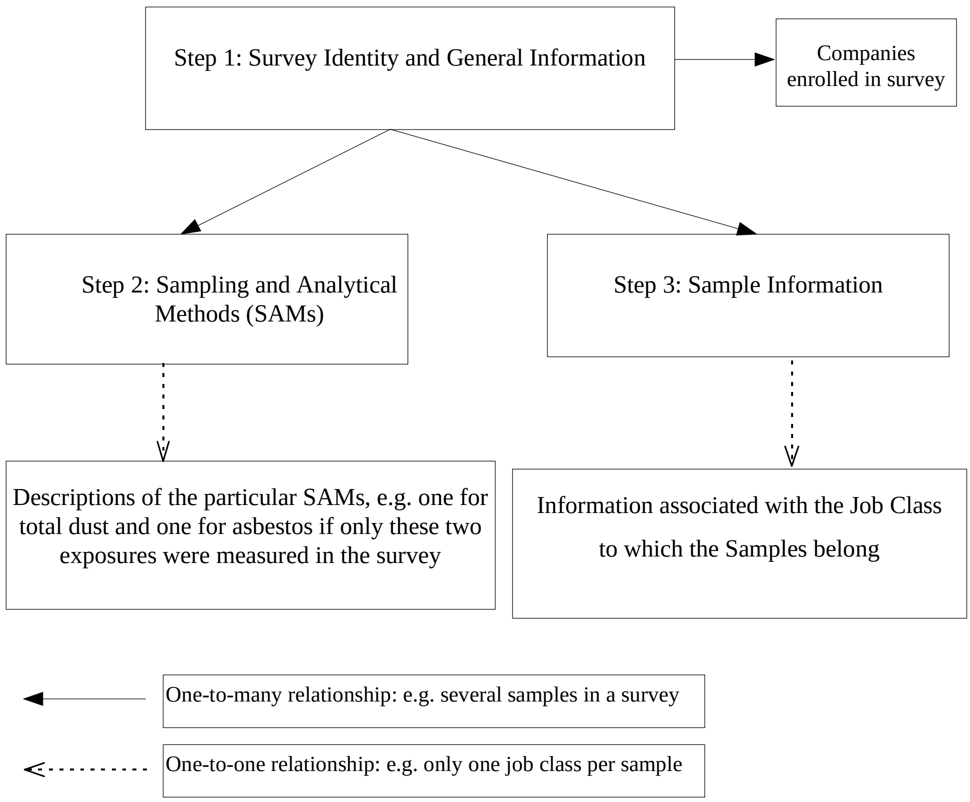
This paper describes our experience with creating an international industrial hygiene database and discusses methodological issues that arose in that process.

Methods

Structure of the industrial hygiene database

The Asphalt Worker Exposure (AWE) database, a Microsoft Access 2.0 application, was developed in order to collect exposure data in the IARC multicentric study of cancer risk among European asphalt workers. The exposure data comprised individual exposure measurements plus supplementary information on when, how, why and under what circumstances the exposure measurements were obtained. The principal rationale for retrieving individual measurements for the database, rather than relying on summary statistics, was to enable us to adequately control for differences between surveys. The appendix describes variables included in the database and, in combination with Figure 3.1, illustrates the hierarchical structure of relationships between variables in the database. The list of variables is quite extensive, and it was expected that not all data sets would contain information for every variable. Therefore, only a subset of the variables was ‘required’ in the data entry process, as indicated in the appendix. Job class-specific information was analogous to information collected using a company questionnaire about production characteristics in the companies enrolled in the cohort study. This ensured that samples entered into the AWE database could be, at least in principle, linked directly to data gathered by the company questionnaires. This linkage should allow us to study how well the information gathered by company questionnaires predicts exposure intensity. It also provides an additional source of information for validation of information retrieved by the company questionnaires. Table 3.1 contains a list of definitions and codes used to classify job titles and classes in the AWE database.

Figure 3.1: Relationships between groups of variables in the AWE database.



Data collection protocol

The collaborating centers were asked to obtain exposure data available in their jurisdiction. A user's guide to the database application was developed, which contained detailed step-by-step instructions on using the AWE database. Whenever possible, the original data sheets ('raw' data) were used to enter information into the database. Data entry was performed in the collaborating centers using a version of the AWE database (referred to as a satellite database) which was identical to the master database in all respects except one. In each satellite database the country code (part of the Survey Number) was pre-set to an appropriate constant, thus identifying all data entered at one particular center. This (a) facilitated simple appending of data from a satellite database to the master database, and (b) allowed for data entry to take place in separate locations simultaneously. Prior to being added to the master database from a satellite database, data was examined for obvious errors, and sample printouts of satellite database content were compared with source records.

The AWE database has the capacity to be adapted to needs of a particular data set. For example, because agents measured varied between surveys, data entry forms were customized to make the application easier to use, thereby reducing data entry errors. Such modifications were effected by transmitting the database via electronic mail to and from the co-ordination center.

Table 3.1: Classification and codes of job classes and titles in the AWE database.

Job Class Code	Job Title Code	Job Class/Title	Examples of jobs incorporated in this title, where provided
Road paving			
11	111	Asphalt paving worker	Paver operator, rakerman, screedman, shovller, roller driver, sprayer of bonding agent, laborer, assisting worker in paving operations, foreman
	112	Surface dressing (SD) worker	Spraybar operator, aggregate operator
	113	Mastic worker	Mastic layer, assisting worker in mastic laying
	114	Emulsion paver	
	115	Recycling worker	
	118	Other workers in road paving operation	Lorry driver transporting asphalt, not paver operator nor roller driver, traffic controller, cleaner, repairer or maintenance worker
	11	Unknown or unspecified road paving worker	
Asphalt mixing			
12	12	Unknown or unspecified asphalt mixing worker	
	121	Asphalt mixing worker	Plant operator, loader, stoker or fireman, laborer, assistant worker in asphalt mixing
	128	Other workers in asphalt mixing	Lorry driver, repairer or maintenance worker
Water proofing and roofing			
14	148	Other workers in water proofing or roofing	Warehouseman, foreman at water proofing or roofing site, insulator (not using bitumen), cleaner, lorry driver, other drivers in water proofing or roofing
	145	Assisting worker in water proofing or roofing	
	144	Mopman	
	143	Kettleman	
	142	Roofer	
	14	Unspecified water proofing or roofing worker	
	141	Waterproofer	
Building construction			
20	209	Driver	
	200	Other building construction workers	Reinforced concrete layer, stonemason, reinforcing iron worker, roofers excluding asphalt roofers, assisting worker, foreman, electrician
	201	Bricklayer, plasterer, tile setter	
	202	Concrete shutter and finisher	
	203	Construction carpenter	
	204	Painter, laquerer, floor layer	
	205	Insulation worker excluding waterproofers	
	206	Plumber	
	207	Welder	
	208	Construction cleaner	
	20	Unspecified construction worker	
Ground construction			
30	309	Other road construction workers	Foreman
	305	Drivers	
	304	Assisting worker	
	303	Brick road layer	
	302	Concrete road layer	

Job Class Code	Job Title Code	Job Class/Title	Examples of jobs incorporated in this title, where provided
	30	Unspecified ground construction worker	
	301	Charger, driller, other stone quarrying man	
Other jobs			
13	13	Unspecified road paving or asphalt mixing worker	Workers who are known to be involved in either road paving or asphalt mixing, but who cannot be specifically classified
15	151	Laboratory technician	
	152	Roofing felt manufacturing worker	
	15	Unspecified other bitumen worker	
40	40	Unspecified blue collar workers	All other manufacturing and related jobs
80	80	Office, administration and management	
99	99	Unknown job	

Note: Job classes other than those expected of asphalt paving industry have been used in the database since there was a possibility that some members of the cohort worked in these jobs for at least part of their work history. Some of these non-asphalt paving jobs may have resulted in exposure to carcinogens. Consequently, exposure information about these other job classes was also thought, albeit less actively than that which was expected to pertain to the majority of cohort members (i.e. asphalt paving and asphalt mixing workers).

Results and Discussion

Experience of creating the AWE database

Gathering data

A total of 2007 sets of measurements from persons or locations across 38 different surveys have been entered into the AWE database as of February 4, 1999. Most samples in the AWE database measured exposures to inhalable dust, bitumen fume, organic vapour and various PAHs. The data collection effort spanned a period of one year. Data originated from all eight countries participating in the epidemiological study. The earliest available data was from the late 1960's.

The creation of the AWE database gave us access to a wealth of data previously unpublished in peer-reviewed scientific journals (34 out of 38 surveys). Consultations with industry, regulatory agencies and local research groups were very fruitful in identifying unpublished data. We were able to collect most of the data identified into the AWE database. However, there were some German and Swedish measurements that we were not able to access because raw data was either impossible to obtain or no longer existed. Individual surveys, whether published in the freely available scientific literature or not, were often either too small to permit statistical modeling or were under-analyzed. Therefore, using the AWE database enabled us to access information that otherwise would not have been available to us. It would appear that in studying the asphalt industry, as in the IARC study of the pulp, paper and paper product industries (15), searching for unpublished data has proved to be a highly rewarding effort.

It was possible to obtain core information required by the AWE database for all samples. Supplementary information that was provided about the type of work performed by each member of the job class appeared to be comprehensive for the majority of samples. This provided us with an opportunity to model the effect of production characteristics on exposure levels. In general, the ability to collect complex supplementary information in a consistent manner in different countries is one of the main strengths of the AWE databases and methodology it represents.

Is the AWE data free from bias?

In assessing usefulness of the retrieved industrial hygiene data, we had to ascertain whether the measured exposures were representative of the exposures experienced by the asphalt workers. We would consider a measurement to be free of bias if it was a valid estimate of the mean long term exposure level for a given set of production conditions (e.g. full-shift time-weighted average exposure measurement). It was not possible to obtain an exact description of how companies, individuals and days of sampling were selected in different surveys. However, we were able to assess other possible sources of bias in the AWE database (Table 3.2). The majority of surveys claimed either to have used a representative sampling strategy or to have been conducted for research purposes. From this, we can derive some assurance that sampling strategy and reason for sampling were not significant sources of bias. Unfortunately, there was little consistency between reason for sampling and the ensuing sampling strategy. This result may reflect the subjective nature of defining a sampling strategy or actual inconsistencies between reasons for sampling and sampling strategies. We should also note that bias from sampling strategy or reason for sampling will only arise if we cannot account for the reason a particular circumstance was deemed to be, for example, a worst case scenario. Therefore, if the reported exposure circumstances account fully for variability in exposure (i.e. there is no variability due to sampling strategy *per se*), we can view even worst case samples as representative of the conditions under which they were collected. If the frequency of such conditions is accounted for in estimating long-term average exposure, an appropriate correction can be made.

Table 3.2: Some possible sources of bias in the AWE data (38 surveys, 2007 samples)

Source of bias	Characteristics of the AWE database	
Reason for sampling	Research Compliance testing Complaint-based Routine sampling	21(surveys) 7 3 7
Sampling strategy	Representative Task-specific Worst case Unknown	18 (surveys) 8 3 9
Sampling duration	No grab samples, average sampling duration 5 to 6 hours (minimum: 2 hours, maximum: 8 hours)	
Stationary samples	24% of overall samples	12% in road paving
Sampling method	Information on sampling heads and filter materials was collected, enabling quantification of differences between methods	
Analytical method	Information on analytical methods and extraction solvents was collected, enabling quantification of differences between methods	
Personal protective equipment	5 samples collected on persons who used respirators	

Thus, in general we did not exclude data from the AWE database on suspicion that it might be biased. Instead, we gathered information on what the source of bias might be with the intent to adjust for it in the analysis of the data. However, one Norwegian data set (unpublished) was excluded from the AWE database because there were strong reasons to believe that substantial mistakes had been made in either collection or analysis of the samples.

Challenges of creating a database of industrial hygiene measurements

Building a database application: flexibility vs. data security

The process of creating the AWE database application revealed some interesting methodological difficulties in the design of such a data collection tool. The database was created prior to the time when the data gathering effort was initiated. Thus, creating the application required an attempt to foresee what type of data would be available in the centers that performed the data entry. Since such foresight cannot be expected to be perfect, the structures of the database had to be sufficiently flexible so that they could be adapted to the needs of a particular center. However, flexibility in a database application often can only be gained at the expense of data security. Unfortunately, in trying to achieve a balance between database flexibility and data security, some of the *a priori* guesses at optimal database structure were erroneous, resulting in somewhat repetitive data entry procedures. Most importantly, an extra step in the data entry process should have been added for the description of working conditions on a day that a particular crew of workers was being monitored. Currently, the description of working conditions is being done separately for each sample. Such a system offers maximum flexibility, but it failed to anticipate that almost invariably monitoring data was grouped by days of monitoring. Therefore, in designing AWE-type applications, it would be advisable to examine the data that will be entered into the database before designing the database's basic structures.

Core vs. additional information

It has been our experience that in addition to the type of available data, the objective of a particular study defines the core data that must be entered into a database. This core data has a direct impact on the structures of the database. As a result, it might be difficult to design a database that would be applicable to all situations which call for the examination of industrial hygiene measurement data, despite efforts to establish standard guidelines for creating such databases (16). For example, in the AWE database it was sufficient to know the job class associated with each sample, but not an exact description of the task(s) performed. However, in other applications (e.g. surveillance, hazard control) more detailed information about work performed during exposure measurement is probably necessary. Nonetheless, we have made an attempt to collect as much information as possible about the circumstances under which exposures were measured. We hope that the use of the AWE database to collect the information beyond the minimal core data will prove to be beneficial, not only to the exposure assessment in the ongoing epidemiological study, but also to other investigations that may necessitate exposure assessment in the asphalt industry. For example, we were able to obtain information on repeated exposure measures within individuals as well as job titles and tasks performed by sampled workers. This information will aid us in assessing the homogeneity of exposure among various groups of asphalt workers. Even though this may not be directly applicable to the exposure assessment in the cohort study, it could provide important information for designing the exposure assessment protocol for a subsequent case-control study or a study of hazard control techniques.

Different types of information from that foreseen during database design can be incorporated by (a) the use of fields that permit one to enter free text or (b) modification of the database structure (e.g. addition of extra options in pull-down lists or creation of new variables). Our experience with relying on the first method of data acquisition has indicated that such an approach has several limitations. Even though information entered as free text was often invaluable, it was inconsistently collected by various research centers. Furthermore, free text information must be re-coded for use in data analysis, a time-consuming and subjective process in its own right. The second method has the distinct advantage of simplifying data management, but it relies on a request for changes to the database from the person performing data entry. It is difficult to assess whether these requests are made consistently between centers in an international study. Ideally, one would be able to foresee all the types of information that may be available about an exposure measurement, but this is not very likely. Therefore, an industrial hygiene database should be sufficiently flexible in order to absorb new types of information. An "ideal" industrial hygiene database should be adaptable both to theoretical developments in the field of exposure assessment and the peculiarities of a particular data set being added to it, while maintaining consistency in coding of variables common to all observations in the database.

Conclusions

Compiling an industrial hygiene database for use in a multicentric study of occupational hazards is an essential first step in creating a study-specific exposure matrix with quantitative exposure estimates. The structure of the AWE database (individual measurements alongside supplementary information) allowed empirical modeling and unraveled significant predictors of exposure levels and trends in exposure levels (see Burstyn et al. 2000, accompanying paper). The ensuing regression models and observations of relative exposure intensities will aid in making the creation of a study-specific exposure matrix a more objective process. Therefore, the methodology embodied in the creation of the database can be usefully employed to develop exposure assessment tools in epidemiological studies.

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Appendix

Description of variables included in AWE database: data entry was required for variables marked with '*'.

Variable or type of information ascertained	Description
Identification of the data source and general information (Step 1 of data entry).	
Survey Number*	Unique code identifying each survey generated by the database automatically, first two digits define country, followed by a dash and numerical survey-specific code. (stored in 'text' format)
Who conducted the survey	A group of variables that identity person who conducted the survey; name and address of the organization that performed the survey.
Reference	Where were the description and/or analysis of the data published?
Sampling strategy*	Restricted to the following list: worst case, random, representative, task-specific, unknown. The following definitions were used: 'worst case': sampling under conditions when highest exposures were anticipated; 'random': workers and or days of sampling were randomly selected for full shift monitoring; 'representative': sampling was conducted to obtain a collection of typical full shift exposures, without regard of how frequently they arise; 'task-specific': sampling for duration of specific tasks only
Reason for sampling*	Restricted to the following list: industrial hygiene research, routine follow-up, test of compliance, epidemiological study, complaint-based**,** and unknown.
Start and end date of survey	Two dates in the following format: '2 digit month code/4 digit year code.'
Companies participating in survey and Company code*	Company name, address, contact person, means of contact and comments. Company code was generated automatically by appending a number, preceded by '~', to the Survey Number.
Exposure types, sampling and analytical procedures (Step 2 of data entry).	
Type of exposure measured*	Agent measured in the survey. Restricted to the following options: inhalable dust, respirable dust, asbestos, oil mist, PAH, diesel exhaust, asphalt/bitumen fume, asphalt/bitumen vapor, CO, NO_2.
Sampling device*	Type and/or name of sampler used to collect the agent being measured
Sampling media*	Type of filter of adsorbent placed into the sampling device in order to collect the agent of interest
Mean sampling rate (units)*	Mean rate at which air was drawn through the sampler (in liters/minute).
Mean duration of sampling (units)*	Average duration of sampling in the survey (minutes).
Analytical method*	Short description of the analytical procedure (e.g. IR-spectroscopy, gravimetric, etc.). For bitumen fume, vapor, PAH and other organic compounds, extraction media also had to be specified, choosing from the following options: cycloxehane, benzene, dichloromethane, CS_2 or chloroform.

Variable or type of information ascertained	Description
Method limit of detection (units)*	Limit of detection calculated for the described method.
Definition of the method limit of detection*	Description of how the limit of detection was calculated.
Comments	Any other peculiarities of the sampling and analytical methods.
Sample information (Step 3 of data entry).	
Sample ID*	Unique identifier generated by the database by appending a dash, followed by numeric code to the Survey Number.
Original Sample ID	Code used to identify a sample in the original survey.
Worker ID	If replicate exposure measures were collected from workers in the survey, each worker was assigned a numerical 4-digit code. For example first worker in survey was usually assigned code of 0001. Worker ID was nested within survey Number, therefore Worker ID's can replicate between different surveys.
Company*	Name of company from which the sample originated. Limited to the list of companies identified as taking part in the survey on Step 1.
Exposure levels measured for the Sample ID*	Exposures measured for the given sample in pre-defined units. Exposure can be indicated a being below the limit of detection specified in Step 2 or above maximum level quoted on Step 3. Users were encouraged to enter actual sample-specific limits of detection or maximum values, were applicable. Exposure for at least one agent had to be specified, and more then one agent per sample was allowed
Location	Where was the sample collected (which province, highway, town etc.)?
Date	When was the sample collected?
Environmental conditions	Temperature (°C), % relative humidity, atmospheric pressure (mmHg), wind speed (m/s) or subjective assessment of wind strength (low wind, high wind, variable wind, no wind, unknown), wind direction (upwind, downwind, crosswind, none, unknown).
Sample type	Personal or area/stationary sample.
Comments	Any peculiarities of the samples not described by other variables.
Job Class*	One of the following options had to be selected: road paving, asphalt mixing, waterproofing/roofing, building construction, ground construction, other. The choice of a Job Class determined what type of information is subsequently requested by the database.
If 'road paving' job class was selected on Step 3:	
Job title*	A code based on the definitions developed for the epidemiological study (Table 3.1).

Variable or type of information ascertained	Description
Tasks performed	Description of dominant task performed.
Paving in tunnel	Yes/No
Exposure controls	Exposure control measures used.
Fuel type	Dominant type of fuel used to power the machinery: unknown, petrol, diesel.
Bitumen type used	If known, code for bitumen type used was entered (e.g. B180, H80/90 etc.).
Equipment	Equipment used in the road paving during exposure monitoring.
% time devoted to specific applications	Proportion of time worked on one of the following specific applications: laying mastic; surface dressing with pure bitumen; surface dressing with cutbacks, fixed bitumen, etc.; paving coal tar containing mixes; paving asbestos containing mixes.
Application temperatures	Application temperatures (in °C) for the following work performed during the exposure monitoring period: application of hot mixes, mastic paving, surface dressing, oil gravel paving, application of emulsion, other (e.g. concrete).
Volatility of asphalt	Volatility of the asphalt handled during the exposure monitoring period (in %rec450).
Types of asphalt mixtures used	Restricted to the following options: polymer modified bitumen, scrap rubber modified bitumen, fly ash modified bitumen, other modified bitumen, recycling bitumen binder, recycling coal tar containing asphalt, coal tar containing bitumen solutions, coal tar solutions, coal tar-containing emulsions, concrete, coal tar pitch containing products, asbestos-containing mixes
If 'asphalt mixing' job class was selected on Step 3:	
Job title*	A code based on the definitions developed for the epidemiological study (Table 3.1).
Type of asphalt plant	Restricted to the following options: batch, continuous: drum mixer, continuous: other, unknown.
Exposure control measures	Restricted to the following options: cyclones, wet scrubbers, bag-house filters other.
Mixes produced	Restricted to the following options: hot mixes, cold mixes, recycled asphalt, bitumen asphalt, tar-containing asphalt.
Agents used in mixtures	Restricted to the following options: coal tar as binder in mixes, coal tar as additive in bitumen binder, other use of coal tar, coal tar pitch, quartz-containing aggregates, lime-containing aggregates, asbestos.
If 'waterproofing/roofing' job class was selected on Step 3:	
Job title*	A code based on the definitions developed for the epidemiological study (Table 3.1).
Type of work done	Restricted to the following options: waterproofing indoors, waterproofing outdoors, roofing indoors, roofing outdoors, both water proofing and roofing.

Variable or type of information ascertained	**Description**
Products used in waterproofing	Restricted to the following options: hot bitumen, bitumen solutions, bitumen emulsions, coal tar containing products, coal tar pitch containing products, asbestos containing products.
Products used in roofing	Restricted to the following options: hot bitumen, bitumen felts, bitumen solutions, bitumen emulsions, coal tar containing products, coal tar pitch containing products, asbestos containing products.
If 'building construction' job class was selected on Step 3:	
Job title*	A code based on the definitions developed for the epidemiological study (Table 3.1).
Products and potential exposures	Restricted to the following options: asbestos containing products, diesel fume, quartz dust, coal tar/coal tar pitch, bitumen.
If 'ground construction' job class was selected on Step 3:	
Job title*	A code based on the definitions developed for the epidemiological study (Table 3.1).
Products and potential exposures	Restricted to the following options: asbestos containing products, diesel fume, quartz dust, coal tar/coal tar pitch, bitumen.
If 'other' job class was selected on Step 3:	
Job title*	Code for one of the following job titles or classes, based on the definitions developed for the epidemiological study (Table 3.1), had to be specified: unspecified road paving or asphalt mixing worker, unspecified bitumen worker, laboratory technician, roofing felt manufacturing worker, unspecified blue collar worker, office administration and management, unknown job.

Chapter 4: Statistical modeling of the determinants of historical exposure to bitumen and polycyclic aromatic hydrocarbons among paving workers.

Burstyn I, Kromhout H, Kauppinen T, Heikkilä P, Boffetta P: Statistical modeling of the determinants of historical exposure to bitumen and polycyclic aromatic hydrocarbons among paving workers. *Annals of Occupational Hygiene* 44(1):43-56 (2000).

Abstract

Introduction: An industrial hygiene database has been constructed for the exposure assessment in a study of cancer risk among asphalt workers.

Aim: To create models of bitumen and polycyclic aromatic hydrocarbons (PAH) exposure intensity among paving workers

*Methods***:** Individual exposure measurements from pavers (N=1581) were collected from 8 countries. Correlation patterns between exposure measures were examined and factors affecting exposure were identified using statistical modeling.

*Results***:** Inhalable dust appeared to be a good proxy of bitumen fume exposure. Bitumen fume and vapour levels were not correlated. Benzo(a)pyrene level appeared to be a good indicator of PAH exposure. All exposures steadily declined over the last 20 years. Mastic laying, re-paving, surface dressing, oil gravel paving and asphalt temperature were significant determinants of bitumen exposure. Coal tar use dictated PAH exposure levels.

Discussion: Bitumen fume, vapour and PAH have different determinants of exposure. For paving workers, exposure intensity can be assessed on the basis of time period and production characteristics.

Introduction

The International Agency for Research on Cancer (IARC) is currently engaged in a cohort study of cancer risk among European asphalt workers. The objective of the exposure assessment in the study is to estimate exposures of road paving workers to bitumen and coal tar. An investigation of the potential cancer risk due to bitumen exposure is the primary goal of the study. However, coal tar exposure is an important confounder, since it is "causally associated with cancer in humans" (1) and has been used in paving processes in the past (2). Because polycyclic aromatic hydrocarbons (PAH) are a "major component" of coal tar (1), we assumed *a priori* that PAH exposure is an appropriate measure of exposure to coal tar.

Previously published inhalable dust, bitumen and PAH exposure data for the asphalt industry have been reviewed (3-18). They revealed that in modern road paving workers are typically exposed to 0.1 to 2 mg/m^3 of bitumen fume which includes 10 to 200 ng/m^3 of benzo(a)pyrene. It was further concluded that these reports were of limited value in assessing historical exposure levels in the industry since they lack comprehensive evaluation of the determinants of exposure in road construction (19). However, the published reports could be used to create the following crude grouping of road construction workers into groups with similar exposure (in order of decreasing exposure level to both bitumen and PAHs from left to right):

mastic laying > surface dressing > hot mix paving > cold applications.

Substantial non-differential misclassification of exposure can be expected to be present in such a grouping, and the degree of this misclassification would be impossible to estimate. Therefore, given that published reports appear to be insufficient for an accurate exposure assessment in the study, a database of individual exposure measurements in the asphalt industry of participating countries (AWE database) was assembled (20). The analysis of the paving workers' exposures collected in the database is presented in this report.

The specific goals of this investigation were (a) to ascertain appropriate measures of exposure levels for use in the epidemiological study, (b) to identify factors influencing exposure intensity, and (c) to construct statistical models that can be used to infer averages of long term exposure in the past for a group of road paving workers.

Methods and materials

Description of the AWE database

A detailed description of the Asphalt Worker Exposure (AWE) database is given in the companion paper (20). However, key features of the database will also be summarized here. The objective in creating the AWE database was to construct a database of exposure measurements, which would be used to assess the intensity of exposure in a cohort of asphalt workers. The exposure data collected into the database comprised measurements of exposure levels for a variety of agents among asphalt workers, plus supplementary information. The supplementary information was analogous to collected data from a company questionnaire on production characteristics in companies enrolled in the study. This ensures that AWE data can be linked directly to other data that will be used in the exposure assessment. All available exposure data was collected in eight participating countries (N=2007). The major contributors (70% of samples) were four Scandinavian countries with 35% of samples originating from Norway. Germany was the second largest contributor of samples (20%). The remaining 10% of samples were approximately equally distributed among France and the Netherlands. A small portion of the data came from Israel. The majority of measurements were personal samples (92%) with the exception of samples collected from German asphalt plants, which were mostly stationary (273/283). Stationary samples were employed to determined vehicle exhaust emissions (CO and NO_2 monitors placed on the machines employed in road paving) as well as to measure bitumen fume/vapour emissions at different positions in asphalt plants and on road paving equipment.

The earliest collected samples originated from the late 1960's, while the majority of samples were collected in the late 1970's and between 1985 and 1997. The data set is sufficiently large to permit statistical modeling of the intensity of exposure to inhalable dust, organic matter in the dust (bitumen fume), organic matter content of gaseous emissions (bitumen vapor) and PAHs, since each agent was measured in 500 to 1000 samples. The majority of measurements were made among road paving workers (N=1581), and only a few came from asphalt plants (351) and waterproofing or roofing operations (62). The overwhelming majority of measurements have not yet been described in peer-reviewed literature. Measurements were originally collected primarily to test compliance, and for industrial hygiene research. Half of the studies claimed to have used a representative sampling strategy.

In nine data sets included in the AWE database, up to 5 repeated measurements within individuals were identified. These studies were conducted between 1977 and 1996 in France, the Netherlands, Sweden and Norway. Exposures to dust, bitumen fume, vapour, and PAH in a variety of road paving and asphalt mixing operations were measured repeatedly for individual workers. This was typically achieved by monitoring exposures of a single crew over a number of consecutive days.

Correlation between exposure measures

Prior to statistical modeling, the correlation between different exposure measures has been explored in order to establish which exposure measure would be the best available proxy of agents considered. Correlation coefficients between inhalable dust, bitumen fume and bitumen vapour exposure levels were computed. A total of 27 different PAHs were determined in some samples in the AWE database. These PAHs were often determined in both fume and vapour, resulting in up to 54 different possible PAH levels for a sample. However, in some samples only benzo(a)pyrene levels were determined. Since we were primarily interested in modeling a proxy for exposure to all PAHs (such as benzo(a)pyrene), the sum of benzo(a)pyrene levels in fume and vapour was used as a measure of benzo(a)pyrene exposure when both were available for a sample. We investigated the correlation between benzo(a)pyrene levels and bitumen fume/vapour levels. In addressing the question of whether benzo(a)pyrene levels are representative of all other PAH levels, we have resorted to principal component analysis. Principal component analysis identified groups of variables that share a common feature. Only those groups of variables which contributed substantially to explaining multiple correlation in the data where examined in detail. Each variable comprising a principal component was judged by the absolute magnitude of its eigenvector (relative to other variables) in order to see how strongly it was associated with the factor common to all variables in a given principal component.

Building predictive models of exposure

We examined the frequency distributions of exposure levels in order to determine if transformations prior to statistical modeling were warranted. Skew in the distributions signaled that logarithmic transformation was needed to satisfy the assumptions of inferential statistical analysis.

Variables used to represent determinants of exposure were defined on the basis of the company questionnaires. All company questionnaire questions had analogues in the AWE database. Their definitions can be found in Table 4.1. In addition to these variables, other variables were constructed representing workers, sampling under conditions when highest exposures were anticipated, stationary samples, type of sampling head used, and sorbent type used to collect gas-phase emissions.

Table 4.1: Definition of company questionnaire-based variables used in statistical modeling

Variable Type	Definition	Comments
Dummy	"1" if a positive answer was given to the following question, "0" otherwise	
Tar use	"Recycling tar containing asphalt" or "Application of coal tar solution" or "Application of coal tar pitch products" or "Application of coal tar containing bitumen solution" or "Application of coal tar emulsion"	In AWE data, 5 indictors of coal tar use were correlated with primary cause of coal tar use being "Application of coal tar solution"
Hot mix	"paving hot mixes"	
Surface dressing	"surface dressing"	
Oil gravel	"oil gravel paving"	
Emulsion	"application of emulsion"	
Other paving	"other paving"	
Mastic laying	"mastic paving"	
Recycling operation	recycling operation; not part of company questionnaire [A]	
Recycle bitumen	"recycling bitumen binders"	
Recycling tar	"recycling tar containing asphalt"	
Modified bitumen	polymer, scrap rubber, fly ash or other modified bitumen	
Categorical		
Country	country where survey was performed	
Continuous		
Application temperature	Application temperature in °C [B]	
Year	difference between 1997 and year of the start date of survey	Maximum duration of a survey was one year

A – considered to be a potential predictor that can be incorporated into the exposure assessment protocol; B – missing values were not uniformly distributed among job titles, therefore they were substituted with job title-specific averages.

Multiple linear models for bitumen fume and bitumen vapour were constructed in the sequential procedure described below. At each step of the model building process, all variables that were not statistically significant (0.10 level) were removed from the models.

Newly added variables were kept in the models if they were statistically significant, and if alterations in regression coefficients for other variables appeared to be interpretable. At step 1 all variables listed in Table 4.1, except for time and country related variables, were forced into each model. Patterns of correlation between variables in Table 4.1 were explored by computing correlation coefficients, and if a correlation existed ($r > 0.70$), only one of the correlates was used in further modeling. The choice of the correlate was driven by considerations of ease in interpretation, should it be included in the final form of the model. At step 2 a variable representing time trend was added to the models. At step 3 a country variable was added to the models. At step 4 variables representing sampling strategy (worst case vs. representative) and sample positioning (area vs. personal) were added to the models. At step 5 variables representing sampling methods were introduced into the models. At step 6 country-related variables were removed from the models in order to study their effect on model fit. Negligible change in model fit signaled that country-related variables could be removed without harming the predictive power of the models. The rationale for this was that country-related effects are difficult to interpret and it was considered that small losses in model fit could be compensated for by an increase in generalization of the model. Finally, at step 7 a random worker effect was introduced into the models (Proc Mixed in SAS 6.12, restricted maximum likelihood algorithm, compound symmetry covariance matrix). All effects included at step 6 were treated as fixed effects, and worker identity was introduced as a random variable. This consequently permitted the resulting within- and between-worker components of exposure variability to be quantified. These values are needed for calculation of the maximum likelihood estimates of the average of long term exposure for a group of individuals.

Models of PAH exposure were constructed by evaluating the statistical significance of significant predictors of total organic matter (i.e. bitumen fume and vapour) plus the variable representing tar use. The rationale for this approach was based on the expectation that PAHs originate from both bitumen and coal tar.

The fit of the predictive models was evaluated graphically by plotting observed versus predicted exposure levels. Residuals were analyzed by plotting predicted values against residual errors. Statistical analysis was performed using SAS 6.12 (SAS Institute Inc.), data management tasks were performed using Microsoft Access 2.0 (Microsoft Corp.) and graphs were prepared using SigmaPlot version 4.01 (SPSS Inc.).

Results

Exposure levels and correlation between exposure measures

Arithmetic and geometric summary statistics for bitumen fume, bitumen vapour and benzo(a)pyrene exposures are summarized in Table 4.2. It is apparent that the exposures cover a wide range of values and tend to be higher during mastic laying.

There was a high degree of correlation between fume and inhalable dust levels (Figure 4.1). This allowed us to construct the following regression model: (mg/m^3 bitumen fume)=0.93× (mg/m^3 inhalable dust), which accounted for 97% of variability in bitumen fume levels. The intercept of the above model was not different from zero, and was therefore excluded from the final form of the model. Thus, we have concluded that inhalable dust emitted in road paving primarily consists primarily of organic particulate matter, which we refer to as “bitumen fume.” In all subsequent analyses, when an inhalable dust level was reported for a sample but the organic matter content of that dust was not determined, we assumed that bitumen fume constituted 93% of inhalable dust and used that value in statistical modeling.

No consistent correlation between bitumen fume and bitumen vapour levels appeared to exist. Its magnitude and statistical significance varied greatly between countries (Table 4.3). Thus, we concluded that we were justified in creating separate predictive models for bitumen fume and vapour.

Not all PAHs were determined in the 415 samples for which series of PAHs were quantified, so missing values were replaced with averages of reported levels for each PAH. Furthermore, for each PAH a sum of its levels in particle and vapour phase was used as an indicator of “total” exposure. The first two principal components accounted for 50% of the multiple correlation between PAH levels in fume and vapour. The first principal component appeared to be dominant (it explained 38% of the multiple correlation). None of the PAHs contributed disproportionately to the first 2 principal components. In effect, when eigenvectors indicated that a set of PAHs was contributing to a principal component (>0.20), all eigenvectors for the set of ‘significant’ PAHs were approximately equal (0.20 to 0.44). The set of PAHs comprising the first principal component consisted of 13 out of 27 measured PAHs. The first two principal components included 18 out of 27 monitored PAHs. Benzo(a)pyrene was an important contributor only to the second principal component and has a high degree of correlation with it ($r = 0.79$, $p < 0.0001$, $n = 414$). Thus, we have concluded that total benzo(a)pyrene is a good proxy of one of the principal sources of PAH exposure. In subsequent statistical modeling we have considered both the first principal component and total benzo(a)pyrene as proxies of PAH exposure. The expression used to calculate the value of the first principal component is given below (all PAH levels were in ng/m^3):

0.28×(acenaphthene)+0.27×(acenaphthylene)+0.27×(anthanthrene)+0.26×(benzo(a)anthracene)+0.22×(benzo(a)fluorene)+0.29×(benzo(k)fluorathene+0.28×(fluoranthene)+0.30×(fluorne)+0.30×(phenanthrene)+0.26×(pyrene)+0.23×(2-methylnaphthalene)+0.29×(1-methylnaphthalene)+0.30×(biphenyl).

Table 4.2: Bitumen fume, bitumen vapour and benzo(a)pyrene exposure levels among paving workers

		All paving operations						Mastic laying only					
	non-detectable values	n	GM	GSD*	AM	SD	Range	n	GM	GSD*	AM	SD	Range
bitumen fume (mg/m^3)	184	1193	0.28	6.75	1.91	13.1	<LOD – 260	119	2.29	6.32	13.4	39.5	0.02 – 260
bitumen vapour (mg/m^3)	5	510	1.86	6.91	7.59	20.0	<LOD – 290	35	2.06	3.27	4.13	6.74	0.23 – 38.1
benzo(a)pyrene (ng/m^3)	321	487	8.58	6.82	95.8	476	<LOD – 8000	15†	61.6	8.76	715	2038	<LOD – 8000

* – unit-less; LOD – method limit of detection; n – sample size, GM – geometric mean, GSD – geometric standard deviation, AM – arithmetic mean, SD – arithmetic standard deviation; † – 2 non-detectable values.

Benzo(a)pyrene levels had a statistically significant correlation with bitumen fume ($r = 0.42$, $p < 0.0001$, $n = 419$), but bitumen fume exposures explained only 18% (0.42^2) of variability in benzo(a)pyrene levels. This moderate correlation was driven by the high correlation between benzo(a)pyrene and bitumen fume levels during mastic laying (mastic laying: $r = 0.96$, $p < 0.0001$, $n = 12$; other paving: $r = 0.32$, $p < 0.001$, $n = 407$). In general, there was no correlation between benzo(a)pyrene and bitumen vapour exposures ($r = -0.01$, $p < 0.87$, $n = 364$). However, the correlation between mastic vapour and benzo(a)pyrene was very strong ($r = 0.99$, $p <0.0001$, $n=10$). Thus, it appeared that factors other than bitumen fume and vapour levels have an important bearing on benzo(a)pyrene exposure levels. The first principal component of PAHs was not correlated with either bitumen fume or vapour.

Thus, on the basis of the correlation patterns presented above, we selected bitumen fume (n = 1193), bitumen vapour (n = 510), total benzo(a)pyrene (n = 487) and the weighted sum of PAH levels comprising the first principal (n = 414) as dependent variables in subsequent statistical models.

Figure 4.1: Correlation of bitumen fume and inhalable dust exposure among asphalt workers (bitumen fume=0.93×inhalable dust, R^2 = 0.97, n = 266).

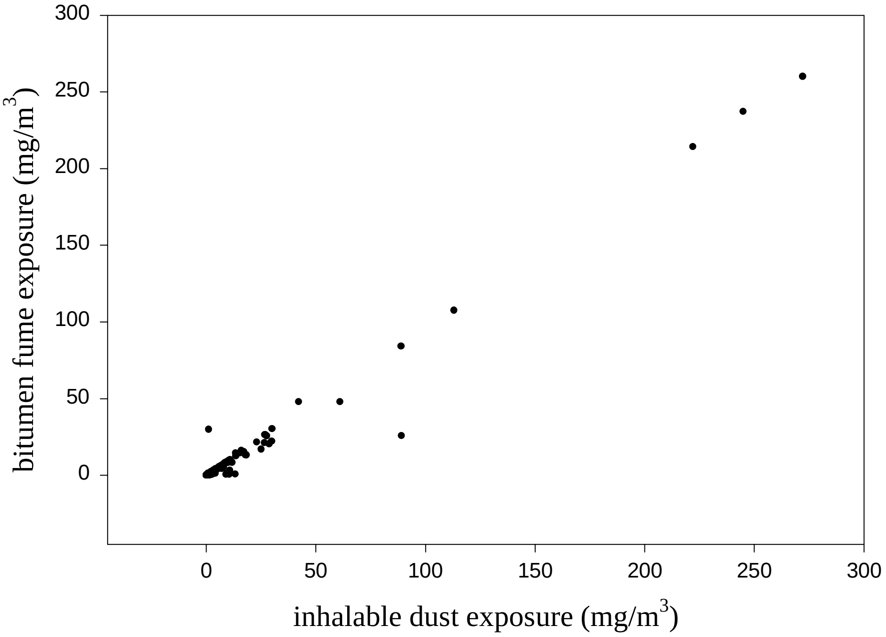


Table 4.3: Summary of the analysis of correlation between bitumen fume and vapour exposure among road paving workers

Country	Number of observations	Pearson r (p(r=0))
Finland	57	0.03 (0.8)
France	26	– 0.05 (0.8)
Germany	116	0.1 (0.3)
Norway	279	0.04 (0.5)
Sweden	23	0.95 (0.0001)
All countries	501	0.01 (0.02)

Statistical distribution of exposure levels and treatment of non-detectable values

All four measures of exposure levels followed skewed distributions, which were normalized by logarithmic transformations (base *e*). Thus, natural logarithms of exposure levels were used in the subsequent statistical modeling in order to stabilize variance. Values below the limit of detection were set to be equal to that limit. This will result in an upward bias in the absolute levels of bitumen fume and vapour. Nevertheless, this should have negligible effect on the identification of determinants of exposure, since non-detectable values represented only a small proportion of bitumen fume (184/1193) and vapour (5/510) measurements. A large proportion (321/487) of benzo(a)pyrene values appeared to be non-detectable, even if, in order to qualify as a non-detectable value, both fume and vapour PAH levels had to be reported as non-detectable. Non-detectable benzo(a)pyrene exposure levels were replaced by survey-specific limits of detection, which ranged from 1 to 50 ng/m^3. The use of the detection limit was justified because it was not possible to assess how the limit of detection was calculated in different surveys and we used the reported values as an indicator of the original investigator's best estimate of the measured values.

Predictive models of exposure

Statistical models of exposure to PAHs comprising the first principal component accounted for less than 9% of total variability and revealed no association between production factors and this measure of PAH exposure. On the other hand, statistical models of exposure to bitumen fume, bitumen vapour and benzo(a)pyrene exposure explained 36 to 43% of total variability and revealed strong associations with various production factors. They are summarized in Table 4.4. In the table, the reference category (defined by the intercept) depends on what variables were important in that model, but in all cases hot mix paving is included in the reference category. The models have the same general form:

$log_e(\text{exposure}) = \Sigma_{\text{all } i}\ \beta_i \times(\text{determinant of exposure } i) + \text{intercept} + \text{worker effect}.$

It is apparent that mastic laying was associated with elevated exposures to all three agents. Recycling operations produced elevated bitumen fume exposures, while below than average bitumen fume exposures resulted from oil gravel paving. Surface dressing, oil gravel paving and elevated application temperatures increased bitumen vapour exposures. There were no differences in the exposures to bitumen fume and bitumen vapour between countries, when adjusted for the effects of other determinants of exposure. The effect of application temperature on bitumen fume exposure in non-mastic applications, adjusted for other predictors of exposure, was the same as in an univariate analysis (Figure 4.2), but it failed to improve model fit and was thus excluded from the final form of the bitumen fume model. Bitumen vapour and benzo(a)pyrene exposures have declined from the 1970's to the 1990's (11 to 14% per year) more rapidly than bitumen fume exposures (6% per year). These time trends are illustrated in Figure 4.3. Since coal tar use is a time-dependent variable, interaction between time trend and tar use was examined in benzo(a)pyrene model, but it was found to be not statistically significant (p=0.29).

The benzo(a)pyrene model shared most determinants of exposure with the bitumen fume and vapour models, except with respect to coal tar use. Indeed, when bitumen fume levels and coal tar use were considered as the only predictors of benzo(a)pyrene exposure, the following model resulted, accounting for 32% of variability in benzo(a)pyrene exposure:

$\log_e(\text{ng/m}^3 \text{ benzo(a)pyrene}) = 0.10\times(\text{mg/m}^3 \text{ total organic fume})+2.71\times(\text{tar use: “yes”=1, “no”=0})+1.50.$

In the model, tar use *per se* accounted for 20% of variability in benzo(a)pyrene exposure.

Examination of the residuals of the three models revealed no substantial deviations from the assumption of homoscedasticity.

Table 4.4: Statistical models of log_e(mg/m^3 bitumen fume), log_e(mg/m^3 bitumen vapour) and log_e(ng/m^3 benzo(a)pyrene)

Variable	**bitumen fume**		**bitumen vapour**		**benzo(a)pyrene**	
	ß	SE	**ß**	SE	**ß**	SE
Mastic laying	**0.88**	0.22	**0.78**	0.47	**1.27**	0.47
Mastic laying × worst case (indoors) [A]	**1.71**	0.29	**1.70**	0.70	**3.07**	0.84
Recycling	**0.89**	0.25	**NS**		**1.51**	0.28
Recycling × worst case [A]	**1.67**	0.37	**NP**		**NS**	
Surface dressing	**NS**		**1.88**	0.24	**0.38**	0.20
Oil gravel	**-1.51**	0.28	**0.48**	0.47	**-0.65**	0.38
Tar use	**NS**		**NS**		**1.68**	0.28
Years before 1997	**0.062**	0.008	**0.135**	0.034	**0.107**	0.022
Application temperature in non-mastic paving(°C)	**NS**		**0.009**	0.003	**NS**	
Area sample (yes/no)	**NS**		**2.26**	0.37	**NS**	
Sorbent type [B]						
Silica	**NA**		**-2.74**	0.24	**NS**	
Charcoal	**NA**		**-0.95**	0.37	**NS**	
Sampling head [C]						
37 mm closed face	**-1.32**	0.15	**NA**		**NS**	
GGP	**1.20**	0.16	**NA**		**NP**	
Intercept	**-2.09**	0.11	**-1.19**	0.42	**0.91**	0.16
% variance explained by fixed effect	41		36		43	
number of observations	1193		510		487	
${}_{BW}S^2_y$ (${}_{B}R_{0.95}$)	0.99 (49)	**0.20**[D]	1.16 (68)	**0.31**[D]	0.43 (13)	**0.28**[D]
${}_{WW}S^2_y$ (${}_{W}R_{0.95}$)	1.08 (59)	**0.22**[D]	1.26 (81)	**0.27**[D]	1.71 (168)	**0.32**[D]

A – symbol "×" is an interaction of variables; B – reference category is XAD2 sorbent; C – reference category includes: 37 mm open face cassette, 25 mm closed face cassette (Millipore) and PAS6; D – standard deviation of variance components' estimates generated in procedure whereby a model was evaluated 300 times on random subsets of 50% of the data; NS – variable is not statistically significant and not included in the model or did not improve model fit upon inclusion in the model; NP – not possible to estimate; NA – not applicable; ß – regression coefficient, SE – standard error of regression coefficient; ${}_{BW}S^2_y$ – variance of the distribution of logarithmic means of individual's exposures (between-worker); ${}_{WW}S^2_y$ – variance of the distribution of logarithmic means of exposure from day to day for an individual (within-worker); ${}_{B}R_{0.95}$ – ratio of 97.5th to 2.5th percentile of the between-worker distribution of exposures; ${}_{W}R_{0.95}$ – ratio of 97.5th to 2.5th percentile of the distribution of exposures within a worker.

Table 4.5 presents the estimates of variance components with and without correcting for the significant determinants of exposure (fixed effects). The results presented in Table 4.5 indicate that predictors of exposure identified in our models are predominantly associated with between-worker variance components. It would appear that fixed effects explain a greater proportion of between-worker variance in the benzo(a)pyrene model ({2.00-0.43}/2.00=79%) than they do in the bitumen fume ({2.27-0.99}/2.27=56%) and bitumen vapour models ({2.51-1.16}/2.51=54%).

Table 4.5: Influence of fixed effects and random effects on variance components in models of bitumen fume, bitumen vapour and benzo(a)pyrene exposure among paving workers

Model *	dependent variable					
	$\log_e$(mg/m^3 bitumen fume)		$\log_e$(mg/m^3 bitumen vapour)		$\log_e$(ng/m^3 benzo(a)pyrene)	
	${}_{BW}S^2_y$	${}_{WW}S^2_y$	${}_{BW}S^2_y$	${}_{WW}S^2_y$	${}_{BW}S^2_y$	${}_{WW}S^2_y$
worker and fixed effects	0.99	1.08	1.16	1.26	0.43	1.71
worker	2.27	1.18	2.51	1.30	2.00	1.74
n	1193		510		487	
k	904		346		292	

* – all models include intercept; n – number of exposure measurements; k – number of workers; ${}_{BW}S^2_y$ – estimate of logarithmic between-worker variance; ${}_{WW}S^2_y$ – estimate of logarithmic within-worker variance.

Figure 4.2: Influence of application temperature on bitumen fume (n=855) and bitumen vapour (n=411) exposures in non-mastic applications

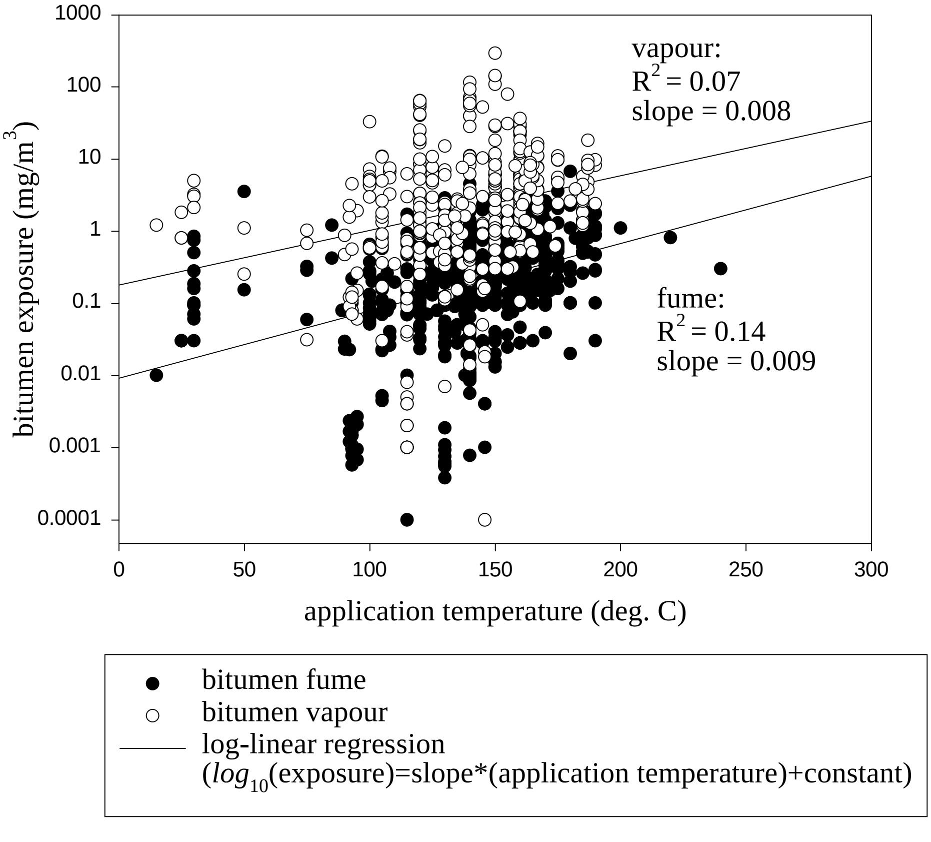
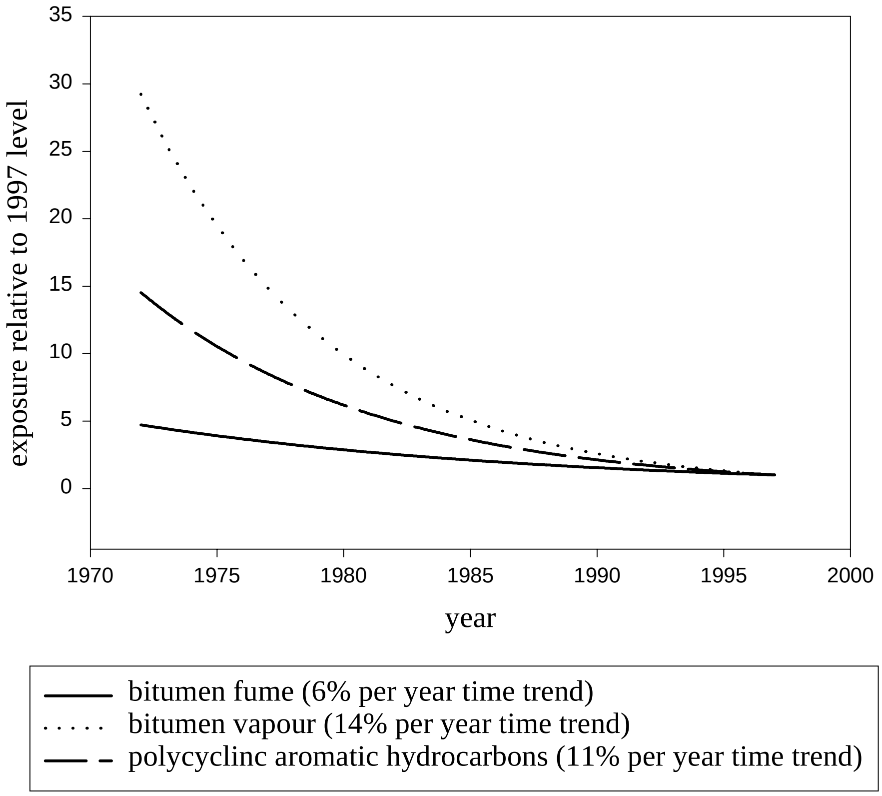


Figure 4.3: Predicted time trends in bitumen fume, bitumen vapour and polycyclic aromatic hydrocarbon exposures, adjusted for production characteristics and sampling methods



Discussion

Comparison with the literature and interpretation of the observed pattern of determinants of exposure

Organic matter content of inhalable dust emitted during paving

Our finding of a high degree of correlation between inhalable dust and its organic matter content implies that little information is gained about bitumen fume exposure by analyzing organic matter content of samples compared to gravimetric analysis. Organic matter content of asphalt dust has been reported to vary considerably, especially under low inhalable dust exposure conditions (3-5). It is evident from Figure 4.1 that the same pattern holds for our data: there is more variability in organic matter content of particulate emissions when their overall level is low. Removing exposure levels that were above 30 mg/m^3 from Figure 4.1had the predictable effect of reducing the range of variables and increasing variability in the studied relationship: R^2 decreased to 0.64. The slope of the relationship also decreased to from 0.93 to 0.74. Thus, our results are in agreement with previously published reports. However, it is quite possible that the apparent change in organic matter content of inhalable dust emitted in road paving is an artifact of increased uncertainty in quantifying relatively low particulate and organic matter levels. Even if there is a 20% decrease in bitumen fume content from high to low dust operations, the effect is likely to be unnoticeable in a statistical model of bitumen fume, since much stronger predictors of exposure are present in road paving (factors of 2 to 5). In fact, applying an alternative relationship for translating inhalable dust into bitumen fume levels, assuming increasing content of organic matter with increasing particulate matter, hardly alters the parameters of the bitumen fume exposure model (data not shown). The coefficient most affected was that for time trend, but it was not significantly different form the one presented in this manuscript (95% confidence, two-tailed t-test). Thus, statistical models appear to be robust with respect to the above assumptions that could have been made about the relationship between inhalable dust and bitumen fume exposure. Nevertheless, since it has been suggested that organic matter content of inhalable dust is dependent on application temperature and asphalt type (3), this issue should be investigated further. The efficiency of different solvents and quantification methods may further confound the issue, but it was not possible to explore it using our data.

Sources of PAHs

The PAHs that comprised the first principal component do not vary across different production conditions in road paving. They represent an overall PAH exposure common to all road paving workers. The identity of the underlying source of these PAHs is unclear. The PAHs in the second principal component and benzo(a)pyrene both appear to represent tar use and PAHs in bitumen fume. These two variables are very good predictors of benzo(a)pyrene exposure levels. We were unable to test whether the second principal component is related to changes in bitumen vapour exposure levels, since no bitumen vapour measurements were collected during the use of tar. However, a comparison of the patterns of regression coefficients in bitumen vapour and benzo(a)pyrene models (see discussion below) indicates that changes in total benzo(a)pyrene exposure may mimic, to some extent, those in bitumen vapour.

Mastic laying

Bitumen fume and vapour exposures arising during mastic laying were 2 to 13 times higher than those observed in association with hot mix paving. This corroborates findings of other researchers, who have indicated that mastic laying results in much higher bitumen fume exposure levels than other paving activities (5-7). In mastic laying elevated bitumen fume and vapour exposures can be expected, since the source of exposure (i.e. the application mixture) is closer to the exposed person's breathing zone owing to the fact that mastic is habitually applied by hand. It has been reported that up to a 2-fold decrease in inhalable dust exposure levels during paving can be explained by an increase in distance between the exposed person's breathing zone and the source of exposure (8). Furthermore, higher temperature of mastic mixes can lead to more fuming. In fact, it was not possible to separate the effects of application temperature from those of mastic laying in the models. Differences in composition and physical properties of bitumen used on mastic paving may also account for this effect. "Worst case" mastic laying corresponded to applying mastic asphalt in indoor environments (e.g. a covered parking lot). The apparent 5- to 6-fold difference between indoor and outdoor exposures observed in our models is of the same order magnitude as those reported by Brandt et al. (1985). It would also appear that the industrial hygienist who conducted the surveys entered into the AWE database were able to consistently identify indoor mastic laying as a "worst case" scenario.

The association of mastic laying with a 4- to 80-fold increase in PAH exposure relative to hot mix paving is rather surprising, since coal tar is not supposed to be used in the formulation of mastic mixes. The explanation for the observed effect may lie with the fact that even though PAH content of mastic emissions may be low, the overall amount of these emissions is so high that it results in PAH exposure comparable to that incurred during the use of coal-tar containing materials. This hypothesis is supported by (a) the high correlation between levels of mastic fume or vapour and benzo(a)pyrene exposures reported earlier and (b) patterns of coefficients in statistical models. However, due to the controversy about cancer risk in mastic laying and the uncertainty about the contribution of the under-layer with coal tar to PAH exposures during mastic laying (9), this issue deserved further attention. If the source of PAHs in mastic laying is the under-layer with coal tar (9), then owing to the fact that coal tar is no longer used in paving, we can assume that the high PAH exposures due to mastic laying are a thing of the past. However, if the mechanism we have suggested is correct, then high PAH exposures (and the associated health risks) due to mastic laying may still be present, especially in indoor environments.

Re-paving or *in-situ* recycling

Re-paving or *in-situ* recycling operations have been associated with elevated bitumen fume and benzo(a)pyrene exposure. This may be due to the fact that coarse particulate is generated during recycling operations in the course of grinding the old asphalt layer. These particles may absorb bitumen fume and vapour generated in heating old asphalt, resulting in elevated bitumen fume rather than vapour exposures. It is not clear as to what defined worst case scenarios in recycling operations. However, there are some indications that the re-paving technique in which old asphalt is heated with a propane burner (hot in-situ recycling) produced these high exposure situations (5). An alternative to hot in-situ recycling is milling and recycling at ambient temperatures. Since bitumen vapour was not monitored during these operations, their effect on bitumen vapour exposure was not possible to estimate. As in the case of mastic laying, it would appear that industrial hygienists conducting the surveys of recycling operations were able to identify a 5-fold increase in exposure as “worst case.” The association between PAH levels and recycling operations may be due to the correlation between fume and PAH concentrations. It is also possible that the same mechanism that leads to elevated fume levels during recycling operations is also responsible for preferential absorption of heavier PAH, such as benzo(a)pyrene, by particles comprising fume. This would lead to elevated PAH content of fume during recycling/re-paving operations.

Surface dressing and oil gravel paving

On the basis of limited data CROW (5) has concluded that surface dressing is associated with elevated fume and PAH exposure relative to hot mix paving. Our results indicate that there is no difference in bitumen fume exposure levels between surface dressing and hot mix paving. It is possible that small differences between these two types of applications do exist, but their magnitude is likely to be small (less than a factor of 2), resulting in negligible contrasts in average fume exposure levels. Our observed association between surface dressing and bitumen vapour can be attributed to differences in modes of applying bitumen to road surfaces. In surface dressing a liquid bitumen solution (cut-back or emulsion) is sprayed onto the road surface, while in other applications (with the exception of oil gravel paving) bitumen is deposited as a part of solid asphalt (a mixture of bitumen and mineral aggregate). It is possible that the spraying of liquid bitumen solution is more conducive to the formation of small droplets and vapour, which are preferentially absorbed by sorbent tubes. It is also likely that bitumen used in surface dressing has a higher proportion of volatile hydrocarbons, originating either from bitumen itself or from the cut-backs which are customarily added to bitumen solutions used in surface dressing. The process of vapour emission during surface dressing is governed by application temperature and vapour pressure of the constituents of the mixture. Given that we cannot expect all surface dressing mixtures to have the same composition, we can expect that application temperature *per se* will not account for the amount of vapour originating in surface dressing. The influence of bitumen composition on the relationship between the amount of bitumen fume emitted and temperature has been reported (10).

Oil gravel resulted in bitumen fume exposures, which were lower than those in the reference category (which includes hot mix paving). This was probably the case because fume formation requires bitumen to be heated (as in surface dressing). However, during oil gravel paving binding material is applied at ambient temperatures, precluding the occurrence of evaporation and condensation processes that lead to fume formation. The weak positive association between oil gravel paving and organic vapour levels is probably a result of the application method, similar to surface dressing, in which vapour and small aerosol droplets are generated during spraying of a liquid. It is also likely that volatile organic materials not present in hot mix asphalt or surface dressing mixtures evaporate during oil gravel paving, resulting in elevated vapour exposure.

The observed pattern of relationships between benzo(a)pyrene exposure and these two application methods suggests that it mirrors patterns of organic matter levels in fume and vapour.

Effects of application temperature

The dependence of bitumen fume, vapour and PAH exposure on application temperature has been reported by other investigators (3,10-14). The rationale for temperature dependence of the asphalt emissions' levels is that the emissions are formed via evaporation of the organic components of asphalt. This evaporation process is governed, at least in part, by the temperature of a given asphalt mix. In our data, application temperatures were most commonly extracted from production records, but in one survey they were measured at the location of a worker. Separate analysis by the method of assessing application temperature did not yield diverging results. We only observed the effect of application temperature, independent of mastic laying, on bitumen vapour. Despite some authors' claims that application temperature is the primary predictor of bitumen fume and vapour exposure levels (3,12,14), in the AWE data the application temperature alone accounts for 7% to 14% of variability in bitumen fume and vapour exposure levels (Figure 4.2). However, the observed slope of the relationship is of the same order of magnitude as reported in the literature.

There are several possible explanations as to why we did not observe a very strong influence of application temperature on exposures in road paving. First, laboratory studies (10,13,14) do not take into account a multitude of factors that may and probably do influence personal exposure in the workplace. Thus, a variable can be expected to have lower predictive power in the 'real world' than it does under controlled laboratory conditions. Second, the model developed by Brandt and De Groot (1994) in a set of laboratory experiments has been validated on a very small number of field observations, and thus its generalization remains uncertain. Third, two reports claiming that application temperature has a strong effect on bitumen fume and vapour exposure (11,12) have not been published in peer-reviewed scientific literature, thus making it difficult to ascertain how the authors arrived at such a conclusion. Incidentally, the data from the last two reports are included in the AWE database and form part of the data set used to build the statistical models presented in this report.

From the point of view of exposure assessment in an epidemiological study, it is quite fortunate that we do not have to rely very heavily on application temperature in making inferences about exposure levels. Our experience has indicated that collecting accurate information about typical application temperatures in the past is difficult, with uncertainty on the order of 10-20°C. Thus, for example, if we had to assign a 2-fold change in exposure level for every 15°C, as suggested by Ekstrom (21), a significant misclassification of exposure would have resulted.

Even though application temperature may not affect the amount of bitumen fume emissions, it may influence their composition (13). Norseth *et al*. (22) found that health effects of bitumen fume exposure were associated with application temperature. This may indicate that the toxic properties of asphalt emission change with change in application temperature. Thus, one of the principal limitations of the AWE database and our predictive models becomes apparent: they do not take into account either bitumen composition or quality and quantity of non-bitumen components of the binder. Questions about bitumen composition are at present difficult to answer (5,13) since bitumen is defined on the basis of its physical properties rather than its chemical composition. Therefore the above mentioned limitation is not an inherent fault of our data, but is merely a reflection of the overall poor current understanding of bitumen chemistry.

Coal tar in paving mixes

The strong relationship between coal tar use and PAH levels observed in our study supports our *a priori* assumption that an assessment of exposure to coal tar can be based on PAH measurements. Our results reveal that in the presence of coal tar, PAH exposures in road paving are elevated by a factor of 5 (i.e. exp(1.68)). However, on the basis of the results of laboratory experiments, PAH content of tar can be assessed to be 100 or even 1000 times higher than that of bitumen (23-26). This apparent difference in the observed effects of coal tar on PAH exposure levels in road paving can be explained by the observation that most benzo(a)pyrene levels were non-detectable, unless coal tar-containing materials were used in paving. Thus, the absolute magnitude of the observed coal tar effect is dependent on the treatment of non-detectable benzo(a)pyrene levels in statistical analysis. On the other hand, some doubts have been raised about how representative laboratory-generated emissions are of those encountered in workplace (27).

Time trends

According to the time trends observed in the AWE data, bitumen fume, bitumen vapour and benzo(a)pyrene exposures have decreased by a factor of 2 to 3 each decade. The possibility that time trend in benzo(a)pyrene levels was due to the manner in which we treated non-detectable values was rejected since there was no time trend in the values we used to replace the non-detectable benzo(a)pyrene exposure measurements. We have no technical data that would explain these patterns. The role of other factors that may affect the time trends, such as those related to social and economic conditions, is difficult to ascertain. The use of time trend for which we have no explanation will lead to biased estimated of exposure only if the time trends themselves are estimated with a bias. There is no reason to believe that our time trend estimates for the asphalt industry are biased. For unbiased exposure assessment for epidemiological purposes it is critical to explain *how* exposure levels have changed, not *why* they have done so.

A recent investigation of world-wide time trends in exposure data (28,29) has indicated that when occupational exposures decrease over time, they generally do so at a rate of 6 to 17% per year (statistically significant downward trends, $p<0.05$). Our results are in agreement with these trends. The limitations of the meta-analysis conducted by Symanski *et al.* (28,29) were their inability (a) to obtain individual measurements, and (b) to adjust time trends for the effects of sampling strategy (notably worst case versus representative) and sampling methods. Our estimates of time trends do not suffer from these limitations, since they are based exclusively on individual measurements (corrected for the effect of area sampling) and are adjusted for sampling strategy, analytical methods and production factors. Thus, our results provide additional evidence of the validity of the time trends obtained by others.

Variability of bitumen and PAH exposures in paving operations

Estimating an arithmetic mean exposure for a group of workers using multiple linear models presented in this report requires one to have an estimate of within-worker (day-to-day) variability of exposure (30). Our estimates of within-worker variance presumably underestimate true day-to-day variability in bitumen and PAH exposures. This arises from sampling strategies employed in collecting repeated exposure measurements, in which exposures were monitored over the duration of one project on several consecutive days. Thus, the collected measurements cannot represent a variety of exposure circumstances (i.e. projects) that paving workers experience in a given year. Nevertheless, the within-worker logarithmic variance for outdoor work, such as road paving, was of similar magnitude (1.40) in other data (31). The reason for this is maybe related to the fact that outdoor work is often not very different from day to day. Consequently, exposure levels can be expected to be determined to a large extent by environmental factors such as wind and rain, which were not accounted for in either data set.

Our results suggest that the predictors of exposure present in our models are related to differences in exposure between workers. These predictors explain at least half of the variability in exposure concentrations between-workers. It has been suggested that process-related variables influence between-worker variance components (31). However, the grouping of workers on the basis of identified predictor variables will not result in uniformly exposed groups, since mean exposures for each worker in these groups can be expected to vary over a 13- to 70-fold range (as assessed by ${}_{B}R_{0.95}$ values).

Methods of measuring bitumen exposure

Area samples of bitumen vapour were 10 times higher than personal ones. This indicates the need for personal sampling in monitoring exposures of road paving workers. A possible explanation for the observed effect is that the stationary samples were placed in areas of high exposure (close to the source, such as the screed of a paving machine) which are avoided by workers. Even though area samples have been generally reported to underestimate personal exposures (32), the bias in area samples is probably highly dependent on their position. Thus, in estimating an individual's exposure level, stationary sampling should be avoided.

Different sorbents have demonstrated varying affinities to bitumen vapour. It is not clear as to why this is the case. Given that the effect of sorbent choice on the measured bitumen vapour level can be substantial (factor of 0.06 in the case of silica gel, as compared to XAD2), this issue should be the subject of further research.

The type of sampling head used to collect bitumen fume appears to have had a significant impact on the observed exposure levels. We have chosen the sampling head employed to collect the majority of samples (37 mm open face Millipore sampler) as a reference category, even though we are aware that its collection efficiency deviates significantly from the toxicologically relevant inhalable dust fraction (33). However, these deviations for small particles, such as those that can be expected to form bitumen fume (<40μm in aerodynamic diameter), are not dramatic (33). Nevertheless, the GGP sampler, a modified version of the GSP sampler whose collection efficiency better adheres to the inhalable convention (33), would probably have formed a more appropriate reference category. Unfortunately, the GGP sampler was used to collect only a limited number of samples, all of them from Germany, making the generalization of the effect of the GGP sampler somewhat questionable. Furthermore, the GGP sampler is expected to outperform the 37 mm open face sampler mostly at low wind speeds (less than 4 m/s), but at high wind speeds both samplers deviate significantly from collecting inhalable dust (33). According to the AWE database, wind speeds during road paving ranged between 0.5 and 33 m/s (n=303, AM = 3.1 m/s, GM = 2.1 m/s, GSD = 2.3). Under such variable wind conditions it is very difficult to predict how the collection efficiencies of samplers would be affected. Unfortunately, wind speed was not recorded during sampling with the GGP, making it impossible to correct the observed "sampler effect" for wind speed. Thus, absolute levels of bitumen fume predicted by our model can underestimate levels of fume available for inhalation by a factor of approximately 3. This has important implication for standard setting and risk assessment, indicating that relative performance of different samplers in outdoor environments should be the subject of further research.

In general, characterization of exposure to bitumen has suffered from a lack of standard methods, which have been demonstrated to collect physiologically and toxicologically relevant fractions of bitumen emissions.

Limitations of the predictive models

The AWE data for paving workers is unbalanced. We attempted to compensate for this by choosing the appropriate statistical model (restricted maximum likelihood algorithm) (34). Nevertheless, we cannot alter the nature of the data. Somewhat different subsets of the AWE data were used to construct predictive models for the three agents raising, the possibility that factors which operated in some subsets may not have been present in others. Consequently, the classical problem of unbalanced data is manifested by the fact that some effects cannot be estimated. Thus, the challenge of obtaining a data set which would allow one to conduct a comprehensive evaluation of the determinants of bitumen (fume and vapour) and PAH exposure remains.

There is noticeable lack of dermal exposure measurements in the AWE database. This reflects the virtual absence of data on dermal exposure in the European asphalt industry, with the exception of one study which measured dermal deposition of PAH during road construction (35). Since dermal route of bitumen exposure can potentially play a role in increasing the risk of adverse health effects among bitumen-exposed individuals, more research is clearly needed to increase our understanding of dermal exposure in the asphalt industry.

Conclusion

Changes in bitumen fume, bitumen vapour and PAH exposures are each associated with somewhat different factors in road paving. In assessing the intensity of exposure among road paving workers, adjustments for time period and the type of work they have performed must be made. Time trend and a small set of production parameters can be used to explain a substantial portion of variability in exposures among paving workers. Our models, despite their limitations, will help to make the assessment of exposures among road paving workers in a multicentric cohort study a data-driven, reproducible process. The models have also revealed a much more complex pattern of determinants of exposure than could have been ascertained, with any degree of certainty, from the review of published reports alone.

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Chapter 5: Are all the members of a paving crew uniformly exposed to bitumen fume, organic vapour and benzo(a)pyrene?

Burstyn I and Kromhout H.: Are all the members of a paving crew uniformly exposed to bitumen fume, organic vapour and benzo(a)pyrene? *Risk Analysis* 20(5):653-663 (2000).

Abstract

Purpose: The goal of this investigation was to assess if and when a crew of paving workers is uniformly exposed to bitumen fume, organic vapour and benzo(a)pyrene.

Methods: Data on paving workers with up to six repeated exposure measurements were extracted from a database of exposure measurements developed within a study of the European asphalt industry (N=591). The uniformity of exposures to bitumen fume, organic vapour and benzo(a)pyrene was evaluated while grouping individuals by job titles, primary tasks, crew membership and use of coal tar (discontinued in Western Europe). The estimated ranges within which 95% of individual mean exposures were expected to fall ($_{BW}R_{0.95}$) were used to assess exposure uniformity. Variance components were estimated by constructing mixed effects models, with grouping variables as fixed effects and worker identity as random effect. The influence of duration of sampling campaign on estimates of exposure variability for a crew was also examined.

Results and Conclusions: There was a substantial variability in exposures between paving crews, as well as persons holding the same "job" or doing the same "task", but each crew was uniformly exposed to bitumen fume and benzo(a)pyrene ($_{BW}R_{0.95}$ 2 and 1, respectively). However, workers within one and the same crew engaged in paving with coal tar-containing binders were not uniformly exposed to benzo(a)pyrene. Also, organic vapour exposures were not uniform among the members of a paving crew ($_{BW}R_{0.95}$ = 15). Sampling campaigns of up to seven months had little impact on the estimates of within- and between-worker variability. These findings should assist investigators studying paving operations in optimizing their sampling, exposure assessment and risk evaluation protocols. They support the notion that only empirically determined predictors of exposure can yield optimal grouping, unlike *a priori* grouping strategies based on general descriptors such as jobs held or tasks performed.

Introduction

Road construction results in a variety of activities that give rise to complex exposure situations (1). Bitumen is the primary binder used in paving, but in the past it has been mixed with coal tar. In Western Europe, coal tar use in road construction has been discontinued. However, milling of old road surfaces may still result in exposure to coal tar-containing materials. Furthermore, road construction workers are potentially exposed to traffic exhaust (from diesel and gasoline engines), silica-containing dust, solvents, and materials that are used to modify properties of bitumen binder (1). Due to the controversy regarding health risks posed by bitumen emissions (2;3), paving operations have come under the scrutiny of epidemiological and industrial hygiene investigations (4-6). An understanding of the magnitude and sources of variability in bitumen (or asphalt, as it is known in North America) exposures is essential to this research. Our earlier results indicated that uniformly exposed groups of paving workers could not be identified on the basis of time period, type of paving and application temperature (7). We observed a historical decrease in bitumen fume, organic vapour and benzo(a)pyrene exposure levels. Elevated organic vapour exposures at higher asphalt temperatures, an increase in benzo(a)pyrene exposure because of the use of coal tar, and differences in exposure profiles among mastic paving, *in-situ* re-paving, surface dressing and oil gravel paving operations were described. It has also been reported by various investigators, that exposure levels to bitumen fume and polycyclic aromatic hydrocarbons (PAH) vary to such an extent that it is justifiable to subdivide a paving crew into separate exposure groups (e.g. for a crews engaged in hot mix paving: paver drivers, rakermen, roller drivers) (8;9). Jongeneelen et al. (10) reported that there can be substantial variability in average exposures among members of a road paving crew during surface dressing with coal tar-containing binder. Experience from other industries suggests that most occupational groups assembled on the basis of job title and location are not uniformly exposed (11). However, until now a formal evaluation of uniformity of exposure among members of a paving crew has never been conducted. Knowing whether or not there are uniformly exposed groups in the paving industry provides a basis for the design of (a) efficient exposure monitoring strategies and (b) effective exposure assessment and assignment for epidemiological studies and risk evaluation. Thus, the aim of this paper is to identify, if at all possible, groups of paving workers that have similar exposure profiles for bitumen fume, organic vapour and benzo(a)pyrene.

Methods and Materials

The between-worker variance component (${}_{BW}R_{0.95}$) is used to estimate the range within which 95% of individual mean exposures fall (12)(13). It is the basis of defining uniformity of exposure for a group, i.e. how broad is the distribution of mean exposures within a given group of individuals. Two different criteria have been proposed for identifying uniformly exposed groups (13). If ${}_{BW}R_{0.95}$ is less than 2, the group is uniformly exposed according to Rappaport (13). However, so long as individual mean exposure lies within the range of 0.5 to 2 times the group mean, a group is considered to be uniformly exposed according to the Health and Safety Executive of the U.K. (this implies a ${}_{BW}R_{0.95} < 4$) (12). Both criteria are best applied as a result of estimating within- and between-worker variance components. In order to do this, a data set of repeated exposure measurements among individuals is required. Repeated exposure measurements among paving workers were obtained from the AWE database constructed for the IARC study of cancer risk among European asphalt workers (14). Crews were identified on the basis of date of measurement, location of work-project and identification codes of individual workers. We identified the job title and primary task of each crew member during exposure monitoring.

Three measures of full-shift time weighted average exposure were considered in this study: (a) bitumen fume, defined as the organic matter content of particulate emissions in paving, (b) organic vapour, defined as the organic matter content of gas phase emissions in paving and (c) the sum of benzo(a)pyrene in fume and vapour. Bitumen fume was typically collected by 37 mm or 25 mm Millipore samplers onto a particulate filter from which it was extracted using a variety of organic solvents. Organic vapour was collected by either XAD2 or silica sorbent tubes. Organic matter in fume and vapour phases was quantified using gas chromatography coupled with mass spectroscopy. Identification of benzo(a)pyrene was carried out via either mass spectroscopy or liquid chromatography. Analytical methods for a number of surveys included in the analysis were not sufficiently described to adjust for the effects of these methods on observed exposure levels. However, the same methods were employed within each survey, implying that within-crew variance components were unaffected by sampling and analytical methods.

Distributions of the exposure variables were examined in order to ascertain if their skew justified logarithmic transformation prior to statistical modeling. Workers were grouped according to job title, primary task and which crew they belonged to. Variance components were estimated using multiple linear mixed models. In these models, grouping variables were treated as fixed effects and worker identity was introduced as a random effect. The models have the following general form:

$$Y_{ij|\beta 1 \ldots \beta n} = \mu + \beta_1 + \ldots + \beta_n + \chi_i + \varepsilon_{ij}$$

$Y_{ij|\beta 1 \ldots \beta n}$ = natural logarithm of the exposure concentration measured on the j^{th} day of the i^{th} worker in n groups defined by the variables $\beta_1 \ldots \beta_n$;

μ = true underlying mean of log-transformed exposure averaged over all groups;

$\beta_1 \ldots \beta_n$ = fixed effects of n grouping variables (tasks, job titles, tar use or crews) ;

χ_i = random effect of the i^{th} worker;

ε_{ij} = random within-worker variation.

The restricted maximum likelihood (REML) algorithm was used to estimate variance components because of the unbalanced nature of the data. The algorithm assumes that χ_i and ε_{ij} are normally distributed with zero means and variances ${}_{BW}\sigma_y^2$ and ${}_{WW}\sigma_y^2$, respectively, which are mutually independent (compound symmetry covariance structure). These variances are estimated as between-worker (${}_{BW}S_y^2$) and within-worker (${}_{WW}S_y^2$) variance components. The between-worker variance component was used to estimate the range within which 95% of individual mean exposures fall: ${}_{BW}R_{0.95}$=exp(3.92×(logarithmic between-worker standard deviation))(13).

Conceptually, ${}_{BW}R_{0.95}$ can be better understood when defined as an estimate of the ratio of 97.5th and 2.5th percentiles of between-worker distribution of exposure concentrations (in original units) for a given group or a grouping scheme. Thus,

$${}_{BW}R_{0.95} = \exp((\bar{Y} + Z_{0.975} \times {}_{BW}S_y) - (\bar{Y} - Z_{0.975} \times {}_{BW}S_y)) =$$

$\exp(2 \times Z_{0.975} \times {}_{BW}S_y) =$

$\exp(3.92 \times {}_{BW}S_y)$,

where $\overline{Y}$ = logarithmic mean of exposure for a given group, ${}_{BW}S_y$ is a group or pooled estimate of logarithmic standard deviation of between-worker exposure distribution, and $Z_{0.975}$ is 97.5th percentile of standard normal distribution ($Z \sim N(0,1)$). Analogous definition applies to ${}_{WW}R_{0.95}$ – estimated range within which 95% of day-to-day estimates of exposure for an individual fall.

Average expected contrast in exposure estimates (**ε**) was also estimated for each grouping as a ratio of the between-group variance estimate and the sum of the between- and within-group variance estimates: $\boldsymbol{\varepsilon} = {}_{BG}S_y^2/({}_{BG}S_y^2 + {}_{WG}S_y^2)$ (15). Between-group variance was estimated as the difference between ${}_{BW}S_y^2$ for model with random effect worker only and ${}_{BW}S_y^2$ for the model with both fixed grouping and random worker effects. The sum of the between- and within-group variances for a model with a grouping variable (fixed effect) was estimated as ${}_{BW}S_y^2$ for model with random effect worker only. This is only correct approximation if we assume that grouping variable had no impact on ${}_{WW}S_y^2$, which held for our data (workers changed neither jobs titles nor tasks nor tar use status between measurements in our data set).

Within- and between-worker variance components for each exposure measure were also computed separately for each crew. The distributions of these variance components were examined using histograms and normal probability plots, and the appropriate descriptive statistics were computed. To assess the impact of sampling campaign duration on the variance components, variance components estimated for each crew were plotted against the duration of sampling campaign. The duration of sampling campaign was defined as a difference (in days) between the first and the last calendar date on which a crew was monitored.

MS Access 2.0 (Microsoft Corp.) was employed in data management tasks. Graphs were prepared in SigmaPlot 4.01 (SPSS Inc.). All statistical analyses were executed in SAS 6.12 (SAS Institute) utilizing either **proc mixed** or **proc glm**.

Results

Upon examination of the AWE data, 31 crews of paving workers with at least two workers that had a minimum of two repeated exposure measurements were identified (Table 5.1). These 591 measurements were collected between 1978 and 1996, primarily in asphalt paving operations in Scandinavia (Norway and Sweden). In most surveys all members of a crew that spend most of their time working on-site were monitored. Truck drivers who delivered asphalt from the asphalt plants were typically excluded from monitoring by the original investigators. Most crews were monitored for 2 to 3 consecutive days. However, some crews were monitored during various projects over periods spanning up to 5 months. The number of repeated exposure measurements varied from 2 to 6 (median: 4). The median number of samples per crew was 11 (range: 6 to 81). The median number of workers per crew was 4 (range: 2 to 10). Not all measurements resulted in the quantification of all three agents of interest. Bitumen fume was determined in 61% of samples (362/591), organic vapour was determined in 38% of samples (222/591), and benzo(a)pyrene was determined in 31% of samples (181/591).

Table 5.1: Description of crews

Country	Year	Start Date	Stop Date	Job Title(s)	Number of Samples	Number of Workers
Norway	1992	12-May	13-May	asphalt paving	6	3
		25-May	27-May	asphalt paving	9	7
		11-Jun	15-Sep	asphalt paving	17	6
		3-Jun	16-Dec	Asphalt paving and surface dressing	30	6
		6-Jul	8-Jul	asphalt paving	9	3
		25-Aug	27-Aug	asphalt paving	11	5
	1991	6-Aug	7-Aug	asphalt paving	8	4
		19-Aug	20-Aug	asphalt paving	8	4
		20-Aug	23-Aug	asphalt paving	15	4
		12-Aug	15-Aug	surface dressing	16	4
		28-Aug	29-Aug	asphalt paving, recycling	8	4
		26-Aug	29-Aug	surface dressing	8	2
		1-Sep	9-Sep	asphalt paving, emulsion spraying	16	4
		13-Sep	24-Sep	asphalt paving	20	4
		11-Oct	17-Oct	asphalt paving	16	4
		20-Nov	26-Nov	asphalt paving	8	2
	1987	1-Jun	29-Oct	asphalt paving	50	9
		16-Jun	3-Jul	asphalt paving	55	9
		22-Jun	25-Sep	asphalt paving	75	10
		22-Jun	4-Sep	asphalt paving	81	10
		27-Jul	30-Jul	mastic laying	18	8
		17-Aug	20-Aug	Recycling	16	4
	1978	June		asphalt paving	14	8
France	1996	20-Aug	23-Aug	asphalt paving	26	6
	1980	19-Aug	20-Aug	Surface dressing	6	2
		25-Aug	26-Sep	Surface dressing	8	3
		3-Sep	4-Sep	Surface dressing	8	2
		3-Jul	4-Jul	Surface dressing	6	2
		24-Jul	25-Jul	Surface dressing	6	3
Netherlands	1993	24-May	25-May	Recycling	6	3
Sweden	1985	5-Jun	7-Jun	asphalt paving	11	3

A description of the observed exposure levels is presented in Table 5.2. It is apparent that there was substantial variability in all exposure measures (geometric standard deviations of at least 5). According to histograms and normal probability plots (data not shown), all three exposure measures followed skewed exposure distributions that were reasonably well approximated by log-normal distributions. Thus, the natural logarithms of exposure measures were used in subsequent analysis.

Estimates of variance components (Table 5.3) indicate that the members of a crew of paving workers had similar exposures to bitumen fume and benzo(a)pyrene. As expected, the within-worker (day-to-day) variability in exposure was unaffected by grouping schemes. It was substantial in magnitude and varied widely from agent to agent (${}_{WW}R_{0.95}$ 30 to 450). Organic vapour exposure showed by far the greatest tendency to vary between individuals employed within a paving crew. However, between-worker variability of organic vapour exposure was 10 times lower within a crew than within a job title or task across crews (as measured by change in ${}_{BW}R_{0.95}$).

In general, contrast in mean individual exposure was highest when crew was used to group workers (Table 5.3 and 5.4), confirming that for this population uniformly exposed groups (crews) are the optimal units for epidemiological studies.

Table 5.2: Exposure levels among paving workers from AWE database for whom repeated exposure measurements were collected

Exposure	n	AM	SD	GM	GSD	Range
Bitumen fume (mg/m^3)	362	0.54	1.7	0.15	6.9	<LOD – 21.5
Organic vapour (mg/m^3)	222	7.3	17	1.5	6.1	<LOD – 140
Benzo(a)pyrene (ng/m^3)						
All samples	181	118	458	9	8	<LOD – 4910
No tar	155	45	126	6	6	<LOD – 934
With coal tar	26	551	1088	156	5	6 – 4910

n = sample size, AM = arithmetic mean, SD = standard deviation, GM = geometric mean, GSD = geometric standard deviation (unitless), LOD = method limit of detection.

Overall between-worker differences in average exposure levels were large for all three exposures (factor 230-1500). Grouping across crews by job title or tasks alone reduced these differences only to a very limited extent (factor 100-1100). In grouping by job titles, segregating mastic work (regression coefficient (β) = 3.2, p = 0.02) and re-paving (β = 2.5, p = 0.07) was responsible for a small reduction in overall between-worker variability in bitumen fume exposure. Adjusting for organic vapour exposure among emulsion paving workers (β = -3.9, p <0.07) was responsible for a limited reduction in observed overall between-worker differences in organic vapour exposure. It was not possible to assess the effect of mastic work on variability in organic vapour exposures, since organic vapour was not monitored during mastic paving. Controlling for lower exposure to benzo(a)pyrene during hot mix asphalt paving (β = -2.5, p = 0.004), as compared to surface dressing and re-paving, was responsible for a reduction in the overall between-worker variability estimate.

The following tasks affected the overall between-worker variability in bitumen fume exposure: paver operator (β = 0.7, p = 0.07), heating old asphalt (β = -4.9, p = 0.01), and grader operator (β = 3.9, p = 0.01). The tasks influencing the overall between-worker variability in organic vapour exposure were performed during surface dressing: spraying operator (β = 1.2, p = 0.09), helper on aggregate spreader (β = 2.2, p = 0.02), and chipping sprayer (β = 3.3, p = 0.04). Grader operator (β = 3.2, p = 0.02) was the only task that affected the overall between-worker differences in benzo(a)pyrene exposure.

As shown in Table 5.4, between-worker variability in benzo(a)pyrene exposure across crews depended greatly on the use of coal tar. Crews in our data either worked only with coal tar-containing binders or only with tar-free binders. The overall between-worker differences in benzo(a)pyrene exposure increased by a factor of about 50 due to coal tar use (as judged by change in ${}_{BW}R_{0.95}$). In fact, the four crews that used coal tar-containing materials were not uniformly exposed to benzo(a)pyrene. Crews that did not use coal tar were uniformly exposed to benzo(a)pyrene. Conversely, day-to-day differences in benzo(a)pyrene exposure were much smaller when coal tar was used in paving materials, than day-to-day variability in benzo(a)pyrene exposure during tar-free paving.

We further explored the effect of binders' benzo(a)pyrene content on exposure levels by extracting from the AWE database 34 observations for which the benzo(a)pyrene content of binder used in surface dressing operations was known.[1] These samples were a subset of those analyzed in Table 5.4. Each crew in the subset used only one type of binder as described below. Twenty samples were collected from crews that used coal tar and the rest from those that did not. In these data three types of binder were used: bitumen fluxed with petroleum oil

[1] This subset of data originated from an unpublished 1980 survey by National Institute of Scientific Research (INRS), France.

(6 samples, one crew), bitumen modified by "vapo cracking residue" (8 samples, one crew), and bitumen mixed with coal tar of various quality (20 samples, 3 crews). Petroleum oil contained <1 mg/kg benzo(a)pyrene and "vapo cracking residue" contained 440 mg/kg benzo(a)pyrene. On average, the benzo(a)pyrene content of the coal tar used in binder varied from 1670 to 7900 mg/kg. The amount of coal tar added to the asphalt binder was substantial: up to 50% in so-called "tar bitumen". Benzo(a)pyrene in binder can come from either bitumen itself or additives (petroleum oil, "vapo cracking residue" and coal tar in this case). We observed a very strong correlation between the benzo(a)pyrene content of the binder used in surface dressing and that of the additives (r=0.99, p<0.0001, n=34), supporting the notion that bitumen is not the primary source of benzo(a)pyrene in the binder. Personal benzo(a)pyrene exposures increased as the benzo(a)pyrene content of a binder becomes greater (Figure 5.1). Measurements collected during application of mixtures low in benzo(a)pyrene content had the lowest variability (bitumen fluxed with petroleum oil and free of coal tar, benzo(a)pyrene content of binder: <1 mg/kg).

Table 5.3: Assessment of uniformity of exposure in various groupings of paving workers

Model	**Models' parameter estimates**								
Exposure	*Bitumen fume (mg/m³)*			*Organic vapour (mg/m³)*			*Benzo(a)pyrene (ng/m³)*		
	Logarithmic variance estimate	$R_{0.95}$	ε^E	Logarithmic variance estimate	$R_{0.95}$	ε^E	Logarithmic variance estimate	$R_{0.95}$	ε^E
Worker only [A]			N/A			N/A			N/A
BW	3.48	1499		2.07	281		1.95	238	
WW	0.76	30		1.29	86		2.43	451	
Job title [B]			0.10			0.17			0.28
BW	3.13	1028		1.72	171		1.40	103	
WW	0.77	31		1.32	90		2.15	314	
Task [C]			0.08			0.17			0.26
BW	3.21	1122		1.71	168		1.45	112	
WW	0.74	29		1.34	93		2.46	468	
Tar use [D]			N/A			N/A			0.71
BW	N/A			N/A			0.56	19	
WW	N/A			N/A			2.39	428	
Crew			0.99			0.77			0.99
BW	0.02	2†		0.47	15		0.01	1†	
WW	0.75	30		1.32	90		2.43	451	
Number of measurements	362			222			181		
Number of workers	116			65			60		
Number of job titles	6			4			4		
Number of tasks	17			13			15		
Number of crews	24			16			17		

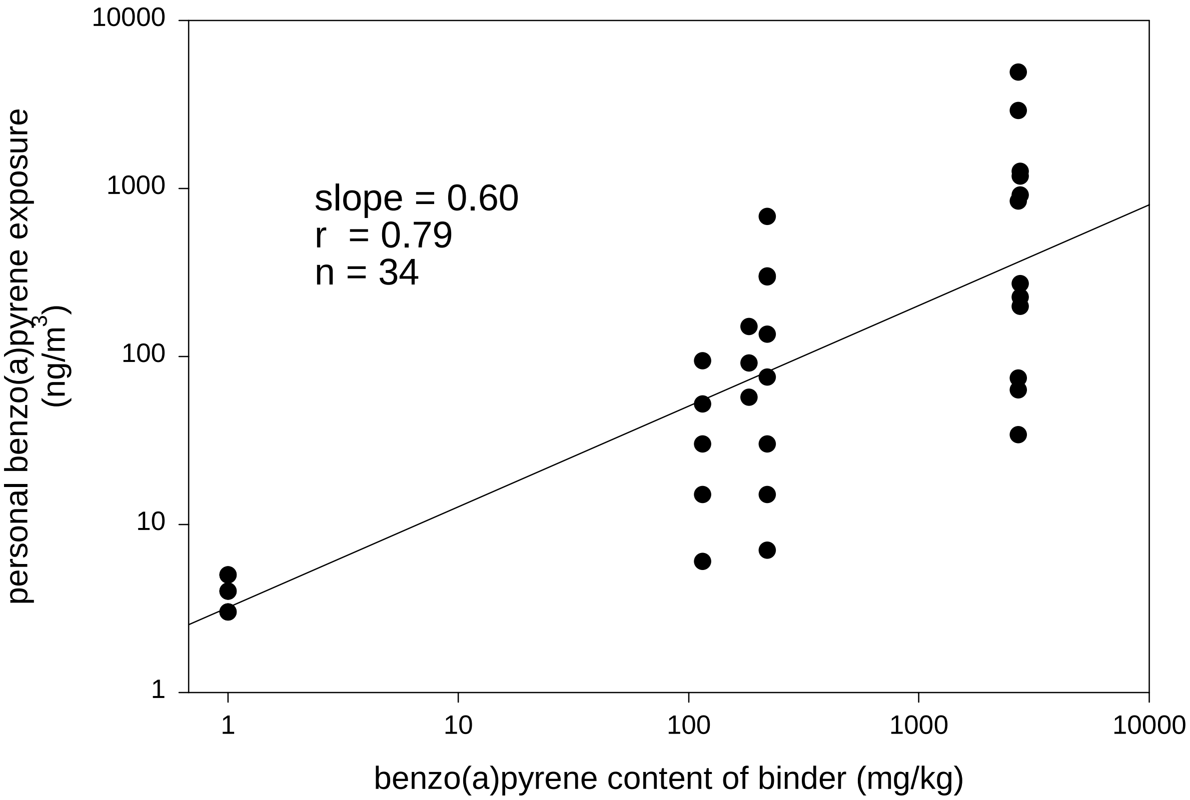
BW = between worker, WW = within worker, $R_{0.95}$ = estimated ratio of 97.5th to 2.5th percentile of exposure distribution, N/A = not applicable; † – ${}_{BW}R_{0.95}<2$, therefore group is uniformly exposed, according to definition of Rappaport (13). A – worker effect was random in all models; B – job titles (6): asphalt paving, surface dressing, mastic worker, emulsion paving, recycling (re-paving), other workers in paving operations (see text for detailed description of how these affect variance components' estimates); C – tasks (17): chipping sprayer, driver, driver of aggregate spreader, foreman/supervisor, heating old asphalt, helper on aggregate spreader, paving machine operator, rakerman, roller driver, screedman, shoveler, spraying operator, milling machinist, grader operator, remixer, laborer, unknown (see text for detailed description of how these affect variance components' estimates); D – regression model (all coefficients had p = 0.0001): (ng/m^3 benzo(a)pyrene) = exp ($3.3 \times$ (if coal tar used then 1, else 0)+1.7); 26 samples from applications of coal tar; E – contrast in exposure between groups: estimated (between group variance/sum of between- and within-group variances).

Table 5.4: Comparison of variance components estimates for benzo(a)pyrene exposure in paving performed with and without the use of coal tar.

Model	Coal Tar Use					
	No			Yes		
	Logarithmic variance estimate	$R_{0.95}$	ε	Logarithmic variance estimate	$R_{0.95}$	ε
Worker only *			N/A			N/A
BW	0.34	10		2.45	462	
WW	2.65	591		0.27	8	
Crew **			0.97			0.20
BW	<0.01	1		1.97	245	
WW	2.55	523		0.27	8	
Number of measurements	155			26		
Number of workers	50			10		
Number of crews	13			4		

BW = between worker, WW = within worker, $R_{0.95}$ = estimated ratio of 97.5th to 2.5th percentile of exposure distribution, **ε =** contrast in exposure between groups: estimated (between group variance/sum of between- and within-group variances); * – random worker effect and an intercept; ** – fixed crew effect, random worker effect and an intercept.

Figure 5.1: Correlation between benzo(a)pyrene content of binder and personal benzo(a)pyrene exposure levels in surface dressing (some binders were modified with coal tar, see text for details).



The distribution of estimated within- and between-worker variance components for each crew separately appeared to be left-skewed and deviated substantially from the expected normality. There was no relationship between within- and between-worker variance components. Table 5.5 indicates that the majority of crews were uniformly exposed to bitumen fume and benzo(a)pyrene and half of crews were uniformly exposed to organic vapour. Crews with heterogeneous individual average exposures to bitumen fume and vapour were engaged in asphalt paving, recycling operations and spraying emulsion. Differences in benzo(a)pyrene exposure between workers within a crew appeared to be the greatest when coal tar-containing material was used in surface dressing.

Table 5.5: Logarithmic between-worker variance components' estimates (S^2_{BW}) for each crew.

Exposure	Number of crews	Median	($_{BW}R_{0.95}$)	90^{th} % ile	Job titles of crews in upper 10^{th} % ile	Number (%) of crews uniformly exposed †
Bitumen fume	24	<0.001	(1.0)	0.11	Asphalt paving and recycling	22 (92)
Organic vapour	16	0.05	(2.4)	0.70	Asphalt paving and emulsion spraying, work in tunnels	9 (56)
Benzo(a)pyrene	17	<0.001	(1.0)	1.25	Surface dressing with coal tar-containing material	12 (71)

† – a group can be considered uniformly exposed if S^2_{BW} is at least less than 0.125, i.e. $_{BW}R_{0.95} < 4$, following Health and Safety Executive of the U.K. (12).

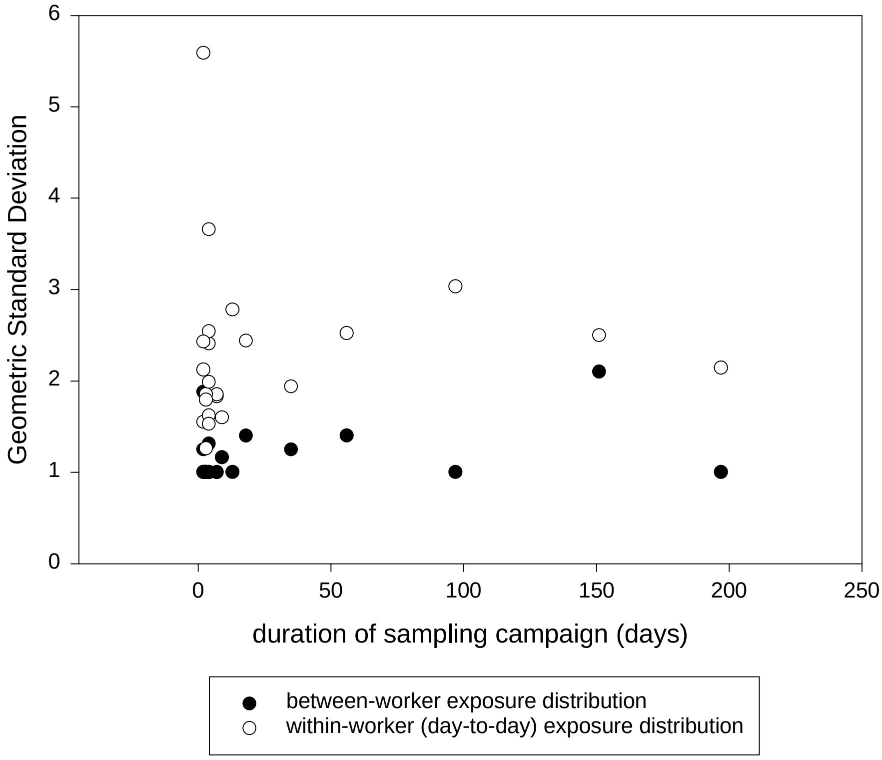
Results exploring the influence of the total duration of the monitoring period on estimates of exposure variability are presented in Figures 5.2 to 5.4. They produce little evidence that estimates of either within- or between-worker variability estimates depend on the duration of a sampling campaign.

Discussion and Recommendations

Caution is advised in extrapolating our findings to paving outside of Scandinavian countries and Northern Europe. Paving technology and materials may be sufficiently different in other parts of the world to produce different variance components than those observed in our data. However, our results should apply to most situations in Western Europe because our earlier analyses indicated absence of systematic differences in exposure patterns among seven European countries (7).

Uniformity of exposures to bitumen fume and benzo(a)pyrene of a crew of paving workers can be an artifact of the data being collected primarily during single projects. This may be the case if between-worker variance estimates change if monitoring is conducted over a number of projects that employ different machines and are associated with diverse production conditions. The net effect in such a scenario can be towards an increase in between-worker variance and therefore an increase in non-uniform exposures. Estimates of within-worker variability can also be increased by changes in either weather conditions or the particulars of the tasks that a person performed, both of which are more likely to be observed in longer surveys. If there are such trends, our data is insufficient to detect them.

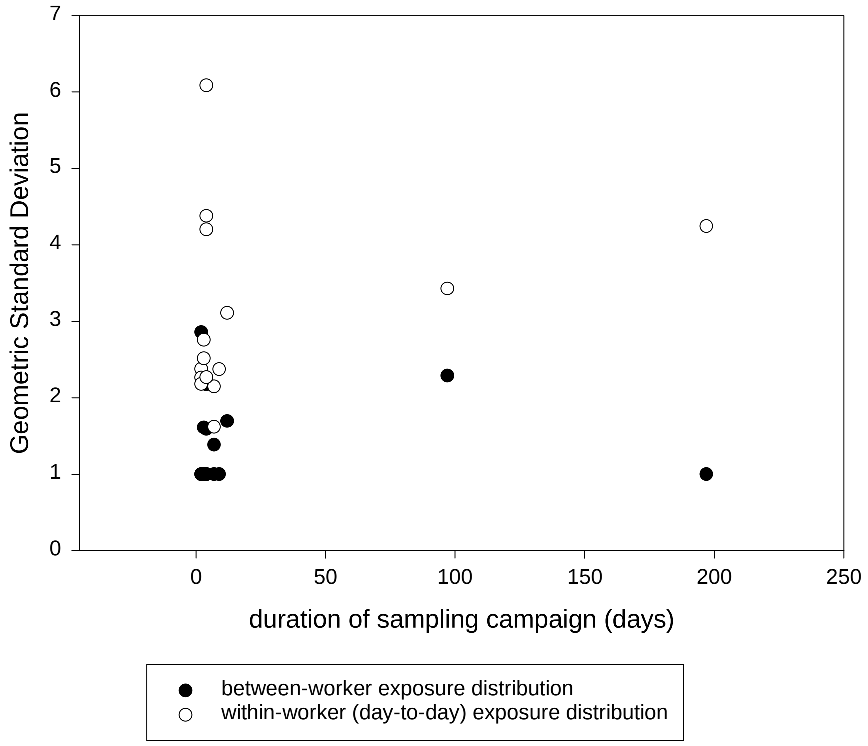
Figure 5.2: Bitumen fume exposures: Relationship between duration of sampling campaign per crew and exposure variance components.



Grouping road-paving workers into crews did not generally produce groups uniformly exposed to organic vapour (44% had a ${}_{BW}R_{0.95} \geq 4$). It appeared that exposures to more volatile compounds showed greater variability between members of a paving crew. However, this comparison might be confounded by differences between sets of crews used to estimate variance components for each agent. We are prepared to speculate that localized high concentrations of gaseous bitumen emissions are only available for inhalation for some paving crew members before dissipating into the environment. The spatial distribution of these volatile compounds is also more likely to be susceptible to the influence of wind than that of heavier particulate emissions. This is in part confirmed by observation that tasks increasing between-worker organic vapour variability were performed during operations, in which workers are spread further apart from each other (surface dressing). The same tasks had no effect on the estimates of bitumen fume exposure variability. Nevertheless, differences between crews were a much greater source of variability in organic vapour exposure than differences between jobs and tasks across crews.

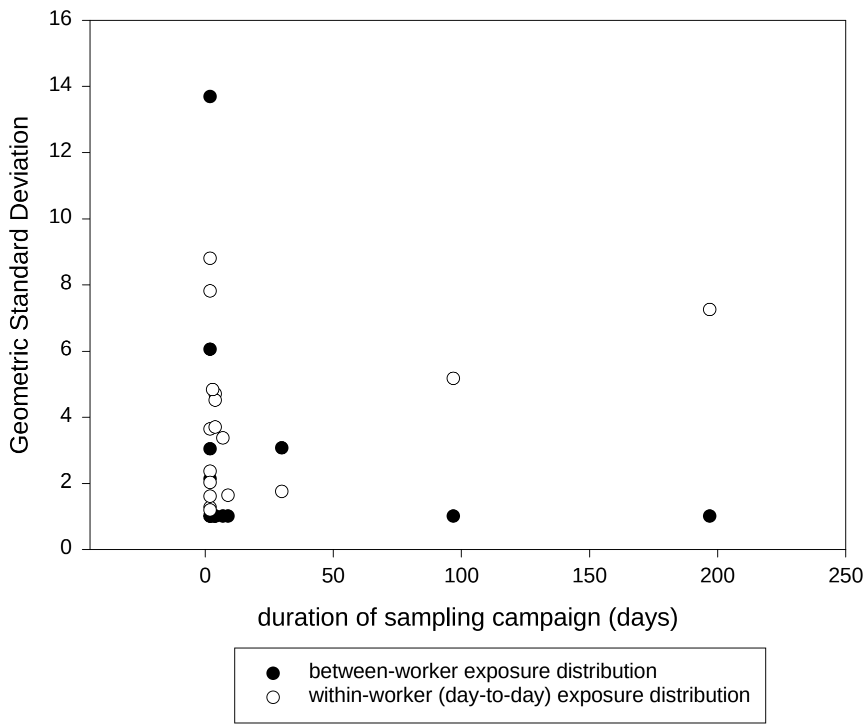
It is important to note that a group of individuals uniformly exposed to one set of agents may not be uniformly exposed to other agents. In fact, only exposure through inhalation was considered due to the limitations of the data. The optimal grouping for dermal exposures in paving may very well be different from that for inhaled agents. This further emphasizes the need to rely on measurement data rather than subjective judgement in attempting to assemble uniformly exposed groups in studies of workplace hazards. Furthermore, uniformity of exposure to an agent may depend on production characteristics, as illustrated by the effect of coal tar use on uniformity of a crew's exposure to benzo(a)pyrene.

Figure 5.3: Organic vapour exposures: Relationship between duration of sampling campaign per crew and exposure variance components.



The observed effect of coal tar on uniformity of benzo(a)pyrene exposures deserves closer scrutiny. It has been observed earlier that coal tar is the primary predictor of benzo(a)pyrene exposure in paving (7). When coal tar is not used in paving, all members of a paving crew can be expected to be exposed to benzo(a)pyrene contained in bitumen. Since bitumen fume exposures are uniform for a paving crews and benzo(a)pyrene tends to be more prevalent in bitumen fume, rather then vapour emission, benzo(a)pyrene exposures can be expected to be uniform for a crew engaged in tar-free paving. On the other hand, when coal tar is used in paving, it is the coal tar content of the asphalt mix or surface dressing material, and not the level of bitumen emissions that should have the principal impact on benzo(a)pyrene exposure levels. As our data demonstrates, the coal-tar content of binders used in paving as well as the benzo(a)pyrene content of these coal tars varies across projects, and consequently between crews, to a much greater extent than the benzo(a)pyrene content of pure bitumen. Thus, large differences in benzo(a)pyrene exposures between workers of different crews/projects can be expected, when paving is performed using binders that contain coal tar or other benzo(a)pyrene-rich additives. It is harder to account for differences in benzo(a)pyrene exposure within a crew using coal tar over a short period of time. Our data (4 crews only) was insufficient to explore the relationship between benzo(a)pyrene exposure and the different tasks performed by members of a crew paving with coal tar-containing materials.

Figure 5.4: Benzo(a)pyrene exposures: Relationship between duration of sampling campaign per crew and exposure variance components.



It is of theoretical interest that within- and between-worker variance components were statistically independent. This satisfies one of the assumptions inherent in the application of our statistical models. Furthermore, in the case of bitumen fume and benzo(a)pyrene, the between-worker variance components derived from modeling the entire data set were almost identical to the measures of central tendency of the variance components computed for each crew (i.e. medians). In the case of organic vapour, the between-worker variance component derived from modeling the entire data set was greater than that estimated from examining variance components from each crew. Furthermore, the median of between-worker variance of organic vapour exposure indicates that crews tended to be uniformly exposed to organic vapour ($S^2_{BW} = 0.05$), whereas analysis of the entire data set led to the opposite conclusion ($S^2_{BW} = 0.47$). The second estimate however is a weighted average across crews, heavily influenced by a few crews with large differences in individual average exposures. On the other hand, the estimated variance components of the individual crews can be expected to be imprecise because of a small number of repeated measurements. Given that the 90^{th} percentile of the distribution of between-worker variance for organic vapour is 0.70, the difference between the two estimates will not be statistically significant. Notwithstanding this complication, it appears that the choice of statistical tools did not affect general assessment of uniformity of exposures of paving personnel. Nevertheless, it should be noted that our results indicate that crews of paving workers were *on average* uniformly exposed to bitumen fume and benzo(a)pyrene. The situation may be different for individual crews (as we have illustrated with the case of the effect of tar use on uniformity of benzo(a)pyrene exposure), emphasizing the need to re-evaluate uniformity of exposure in each particular situation. It has been recently demonstrated that for some construction trades between-worker exposure variance components cannot be pooled across different jobs (16). This emphases that both methods[2] for assessing uniformity of exposures for a broad sector of industry have their merits.

Another theoretical concern over our analysis relates to the assumptions of log-normality of exposure for all subgroups in our analyses. Small size of these groups precluded any meaningful distribution testing. Deviation from log-normality would bias our variance component's estimates. However, experience in occupational exposure monitoring so far provides ample assurance that most exposure distributions are skewed and approximately log-normal (13). A related issue to distribution testing is expected low precision of variance estimates for some subgroups with few observations. This would lead to uncertainty about variance component's estimates, especially when estimated for each crew separately. Pooled variance estimates (from mixed-effects models) are likely to be more stable. Pooling within-worker variance may also seem problematic because day-to-day variability may not be homogeneous for members of the same crew. However, it is exceedingly difficult to obtain precise estimates of exposure variability for an individual since it requires multiple repeated full-shift measurements (certainly more that 2 to 4!). Consequently, it has become a common justified practice to pool this variance component by collecting limited number of measurements for an individual (17).

An individual-based exposure assessment strategy can be efficient if between-worker variance in exposure exceeds within-worker variance (18;19). In the case of paving workers, we have shown that in paving there is no consistent pattern in the ratios of variance components across agents. Furthermore, it is doubtful whether individual-based exposure assessment is feasible in large studies, such as those required to assess cancer risk among paving workers. An alternative is to employ a group-based exposure assessment strategy, in which average exposure for a group is assigned to every member of that group. As with individual-based exposure strategies, grouping reduces misclassification of exposures if differences between groups are greater than differences within groups (20).

From our analyses it has become apparent that crew is a very efficient grouping factor. However, without knowledge of the actual factors affecting exposure, grouping by crew will not be very informative. It has been demonstrated that optimal grouping strategies in exposure assessment for epidemiological studies can only be derived on the basis of factors that affect exposure (e.g. production characteristics)(19). We have reported earlier that differences in production characteristics have an important impact on between-worker exposure variability and have no effect on within-worker exposure variability during paving (7). However, grouping by these production factors alone did not result in uniformly exposed groups. We have also demonstrated in this paper that a grouping strategy based on job titles and tasks was not effective, but grouping workers into crews produced a dramatic improvement in uniformity of exposures. Which characteristics of a crew produced such stark between-crew differences? At least in part this must be due to differences in climatic and production conditions under which each crew operated and which we were not able to adjust for directly (e.g. temperature, humidity, wind speed, equipment, asphalt composition, amount of binder used and production rate). It is encouraging that if we were able to control for all of these factors, we would have been able to construct uniformly exposed groups

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[2] The first method : modeling entire data set in which variance estimates are pooled across crews; the second method: estimating variance components for each crew independently.

without resorting to the "crew" variable. However, it is also possible that each crew has its own distinct mode of performing task. These differences may result in a "crew effect" which is independent of production characteristics.

Conclusion

Our results indicate that in monitoring bitumen fume and benzo(a)pyrene (in tar-free applications) exposures among a crew of paving workers can be viewed as uniform. In other words, average exposure of a random sample of workers monitored from a crew during a single paving project is likely to be typical for all members of that crew. In monitoring volatile compounds during paving, and benzo(a)pyrene during handling of coal tar-containing materials, each worker in a paving crew must be considered individually.

Likewise, all members of a paving crew can be expected to incur the same risk from bitumen fume and benzo(a)pyrene exposure (in tar-free applications) during a paving project. However, risk due to exposure to the volatile components of asphalt emissions and benzo(a)pyrene during paving with coal tar-containing mixes is likely to vary from one member of a paving crew to the next.

These findings should assist investigators studying paving operations in optimizing their sampling, exposure assessment and risk evaluation protocols. Thus, in epidemiological investigations of paving, no precision is gained by characterizing exposures of an individual at task level when average exposure is assessed for their crew. Conversely, grouping individuals with the same tasks across crews can be expected to result in severe exposure misclassification. This implies that "job" and "task" are poor surrogates for production characteristics, which are much more influential determinants of exposure. Therefore, our findings support the notion that *a priori* grouping based on general descriptors like jobs held or tasks performed cannot be expected to yield the optimal grouping. Instead, grouping strategies should be based on empirically determined predictors of exposure.

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Chapter 6: Validity of empirical models of exposure in asphalt paving.

Burstyn I, Boffetta P, Burr GA, Cenni A, Knecht U, Sciarra G, Kromhout H: Validity of empirical models of exposure in asphalt paving. *Occupational and Environmental Medicine* (submitted, 2000).

Abstract

Objectives: We investigated validity of empirical models of exposure developed for a historical cohort study of asphalt paving in Western Europe.

Methods: Internal validity was assessed in a cross-validation procedure. External validity was evaluated using data not used to develop the original models. For bitumen fume and benzo(a)pyrene, correlation between observed and predicted exposures was examined. Bias and precision were estimated with respect to data not used to build the original models.

Results: All models were internally valid but imprecise. Predicted bitumen fume exposures tended to be lower (average factor of 3) 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 a similar to expected effect of re-paving and a larger than expected effect of tar use. Overall, benzo(a)pyrene models underestimated exposures by 51%.

Conclusions: Possible bias due to underestimation of the impact of coal tar on benzo(a)pyrene exposure levels must be explored in sensitivity analysis of the exposure-response relationship. Validation of the models, albeit limited, increased our confidence in their applicability to exposure assessment in the historical cohort study of cancer risk among asphalt workers.

Introduction

Increasingly in occupational and environmental epidemiology the quality of studies and their subsequent usefulness for risk assessors and regulators depends on the validity of their exposure assessment. This trend is in part due to the recognition of the fact that most of the remaining unidentified health risks due to occupational and environmental factors are likely to be low (relative risks of the order of 2-3) and can be easily missed because of misclassification of exposure (1). These weak associations, however, can have a profound public health impact if their causative agents are highly prevalent (1). Two examples illustrate the crucial role that exposure assessment plays in modern occupational epidemiology. Between 1976 and 1993, twenty studies of cancer risk among asphalt workers (mostly road pavers) have been conducted, many of which suggested that this occupation entailed an elevated lung cancer risk. (2). However, these studies suffered from failure to differentiate between coal tar and bitumen (or asphalt, as it is known in the USA) exposures. As a result, this substantial 17 year research effort has been proven to be of limited use in the evaluation of carcinogenicity of the main agent that asphalt workers are currently exposed to -- bitumen (3)(4), hampering any preventive measures. Another example is that of exposure to electromagnetic fields and occupational cancer. A study's ability to detect an association between electromagnetic fields and elevated cancer risks to a large extent depends on assumptions made in exposure modelling, emphasising the importance of validating exposure models (5)(6,7). Consequently, analyses of sensitivity of risk estimates to assumptions made in exposure assessment are becoming an integral part of analysis of epidemiological studies (5)(6-11). This manuscript addresses validation of exposure models for asphalt paving workers, the most numerous bitumen-exposed group in an international historical cohort study of bitumen.

The International Agency for Research on Cancer (IARC) is co-ordinating a multicentric investigation of cancer among asphalt workers. The study is an industry-based historical cohort assembled in seven European countries (Denmark, Finland, France, Germany, The Netherlands, Norway, Sweden) and Israel. Coal tar use has been progressively discontinued in Western Europe, resulting in the possibility to disentangle any effects of its exposure from that of bitumen. The overall aim of the exposure assessment for the study is to develop an exposure matrix which can be used to assess the exposures to the agents of interest (either quantitatively or semi-quantitatively) in a country-, company-, job- and time period-specific manner. With this goal in mind, we developed statistical models of bitumen fume, organic vapour and benzo(a)pyrene (as a representative of 4-6 ring polycyclic aromatic hydrocarbons) exposure during paving operations (12). These models were based on exposure data gathered from previously collected industrial hygiene measurements in the participating countries (13). We assessed the robustness (internal validity) of the models using a cross-validation procedure. Since then, additional exposure data from road paving operations were obtained, allowing us to validate the empirical models against these newly acquired measurements.

Methods

The mixed effects models evaluated in this paper have been described in detail elsewhere (12) and are summarised in Table 6.1. These models were aimed at identifying the factors predicting changes in exposure levels of road paving workers to exposures to bitumen fume, organic vapour and benzo(a)pyrene. They revealed a declining (6 to 14 percent per year) trend in exposures to bitumen fume, organic vapour and benzo(a)pyrene with time.

Furthermore, differences in exposure levels were observed between different methods of paving. Coal tar use was demonstrated to be the most important predictor of benzo(a)pyrene exposure, but the magnitude of this effect was somewhat less than that expected on the basis of laboratory studies. The differences in sampling and analytical methods were accounted for. There were no differences between comparable paving operations among countries.

The general model used to study the fixed and random effects is described by the following expression:

$$Y_{ij}|_{\beta_1 \ldots \beta_n} = \mu + \beta_1 + \ldots . . + \beta_n + \chi_i + \varepsilon_{ij}$$

$Y_{ij}|_{\beta_1 \ldots \beta_n}$ = natural logarithm of the exposure concentration measured on the j^{th} day of the i^{th} worker in presence of the $\beta_1 \ldots \beta_n$ determinants of exposure;

μ = true underlying mean of log-transformed exposure averaged over all determinants of exposure;

$\beta_1 \ldots \beta_n$ = fixed effects of the determinants of exposure;

χ_i = random effect of the i^{th} worker;

ε_{ij} = random within-worker variation.

The Restricted Maximum Likelihood algorithm estimated variance components derived from the mixed effect models. The algorithm assumes that χ_i and ε_{ij} are normally distributed with zero means and variances ${}_{BW}\sigma^2$ (between-worker logarithmic exposure variance) and ${}_{WW}\sigma^2$ (within-worker logarithmic exposure variance), respectively, which are mutually independent.

The precision and internal validity of each model in Table 6.1 was assessed by evaluating its parameters on random subsets of 50 percent of the data, similar to what was done in other evaluations of exposure models (14). Splitting the data in half aims to maximise the power of data-splitting (15). At each evaluation, predictions of the models were compared to the remaining 50 percent of the data by estimating bias and precision of the models using a procedure similar to that proposed by Hornung (16). Bias was defined as the mean difference between predicted and measured values on logarithmic scale; precision was defined as the standard deviation of bias. In cross-validation, both bias and precision were estimated on a logarithmic scale, since they appeared to follow log-normal distribution in histograms (i.e. natural logarithms of predicted and observed values were compared). We ran 300 evaluations for each model.

In addition, the models were validated against external data obtained from the United States (17-22), Germany (measurements were only partially described in this publication) (23) and Italy (unpublished). These data were made available to us after the original statistical models were constructed. The key features of these newly acquired data are summarised in Table 6.2. Three US benzene-soluble matter measurements from 1982 were excluded from the current analysis because they were collected during an experimental application of sulphur-containing asphalt. All bitumen fume and Italian benzo(a)pyrene measurements were collected using personal samplers. However, due to the limited number of benzo(a)pyrene measurements we also used stationary samples collected in Germany (23). We computed Pearson correlation of the predicted and observed values. We also compared 95 percent confidence intervals of the geometric means of survey-specific predicted and measured exposure levels. Bias and precision of the models were re-estimated in a manner similar to that used for the internal validation. These were calculated on a logarithmic scale, because bias followed a left-skewed distribution that approximated normal distribution after logarithmic transformation. Effect of German sampling method on benzo(a)pyrene exposure could not be estimated using data that the original model was based on. Therefore, we recalculated predicted values for the German study, taking into account that (a) benzo(a)pyrene is present mostly in fume phase in asphalt work and that (b) GGP sampler used in Germany tends to collect 3.3 (= exp(1.20)) times more dust than sampler used in the original benzo(a)pyrene exposure models (Table 6.1).

Analyses were carried out in SAS version 6.12 (SAS Institute, Cary, NC), Microsoft Excel 7.0 (Microsoft Corporation, Seattle, WA) and SigmaPlot 4.01 (SPSS Inc., Chicago, IL). Data management and acquisition were facilitated by the use of Microsoft Access 2.0 (Microsoft Corporation, Seattle, WA).

Results

Precision and internal validity

Cross-validation revealed that most point estimates of the parameters of the three models were similar to those estimated by modelling the entire data set (Table 6.1). The exceptions to this pattern were the estimates of the models' intercepts. This suggested that even though the estimates of relative differences between identified determinants were stable, one could expect a greater uncertainty in the absolute value of predictions generated by the models. The estimates of the effect of oil gravel paving in the organic vapour model varied substantially, suggesting different direction of the effect in some subsets of the data compared to the model based on complete data set. The estimate of the effect of surface dressing on benzo(a)pyrene exposure behaved in a similar manner.

According to the results of cross-validation presented in Table 6.3, all models showed negligible negative average relative bias (-1 to -3 percent). However, bias ranged from -37 to 45 percent, implying individual predictions can be biased. Precision tended to be a factor of 1.1 to 1.4 greater than the within-worker standard deviation in all three models. However, the estimated ranges of the two statistics overlapped, except in the case of the bitumen fume model. This indicates that the imprecision in all three models is comparable to that which we predicted would arise from day-to-day fluctuations in exposure levels.

External validity of bitumen fume and benzo(a)pyrene models

The correlation between observed and predicted bitumen fume exposures for the US data was weak, but statistically significant (Pearson correlation coefficient (r) = 0.28, p = 0.004; N = 98). For the data obtained from Germany and Italy, the relationship between observed and predicted benzo(a)pyrene exposure levels was much stronger (r = 0.45, p = 0.0001; N = 339). Even though observed and predicted values for both bitumen fume and benzo(a)pyrene are significantly correlated, a linear regression model does not fit the data well (data not shown). The relationship between geometric means of measured and predicted values of bitumen fume and benzo(a)pyrene exposure are illustrated in Figures 1 and 2. In Figure 6.1, measured mean values correspond to the results of each Health Hazard Evaluation conducted by US NIOSH. The Figure indicates that the bitumen fume model tends to underestimate exposure

Table 6.1: Statistical models* of bitumen fume (mg/m^3), organic vapour (mg/m^3) and benzo(a)pyrene (ng/m^3), partially adapted from (12), and their internal validity (stability of parameter estimates)

Determinant of exposure #	**Bitumen fume** β_o##	β_c***	R†††	**Organic vapour** β_o	β_c	R	**Benzo(a)pyrene** β_o	β_c	R
Mastic laying	0.88	0.90	0.30 - 1.31	0.78	0.86	-0.20 - 2.60	1.27	1.28	0.68 - 1.72
Mastic laying × worst case (indoors) **	1.71	1.72	0.86 - 2.66	1.70	1.66	0 - 3.42	3.07	2.97	0 - 5.29
Recycling	0.89	0.87	0.24 - 1.65	NS			1.51	1.50	0.73 - 2.31
Recycling × worst case **	1.67	1.66	0.71 - 2.48	NP‡‡			NS		
Surface dressing	NS			1.88	1.92	1.11 - 2.46	0.38	0.38	-0.16 - 1.05
Oil gravel	-1.51	-1.58	-2.91 - (-0.55)	0.48	0.59	-0.38 - 1.77	-0.65	-0.68	-1.03 - (-0.28)
Tar use	NS			NS			1.68	1.69	0.57 - 2.43
Years before 1997	0.062	0.057	0.042 - 0.074	0.135	0.142	0.086 - 0.207	0.107	0.109	0.054 - 0.160
Application temperature in non-mastic paving(°C)	NS††			0.009	0.009	0.003 - 0.017	NS		
Area sample	NS			2.26	2.34	1.37 - 3.42	NS		
Sorbent type †									
Silica	NA¶¶			-2.74	-2.54	-3.28 - (-1.62)	NS		
Charcoal	NA			-0.95	-1.03	-1.51 - (-0.39)	NS		
Sampling head ‡									
37 mm closed face	-1.32	-1.37	-1.72 - (-1.04)	NA			NS		
GGP	1.20	1.15	0.94 - 1.44	NA			NP		
Intercept ¶	-2.09	-0.78	-0.97 - (-0.60)	-1.19	0.37	0.08 - 0.65	0.91	1.24	0.92 - 1.52
$_{BW}S^2{}_y$ ‡‡‡	0.99	0.94	0.45 - 1.52	1.16	1.11	0.17 - 1.90	0.43	0.42	0 - 1.38
$_{WW}S^2{}_y$ ¶¶¶	1.08	1.18	0.54 - 1.68	1.26	1.31	0.63 - 2.22	1.71	1.72	0.61 - 2.54
% variance explained by fixed effects		41			36			43	
Number of observations		1193			510			487	

* Sample calculation: geometric mean of benzo(a)pyrene exposure for 1980 during surface dressing with coal tar = exp(0.91+(97-80)×0.107+0.38+1.68) = 120 ng/m^3; † Reference category is XAD2 sorbent; ‡ Reference category includes: 37 mm open face cassette, 25 mm closed face cassette (Millipore) and PAS6;

¶ Corresponds to hot mix paving in 1997; # All variables were categorical 1/0 unless otherwise specified; ** Symbol "×" denotes a multiplicative interaction of variables; †† Variable is not statistically significant and therefore is not included in the model or did not improve model fit upon inclusion in the model; ‡‡ Not possible to estimate; ¶¶ Not applicable; ## Regression coefficient obtained through modelling entire data set (12); *** Average regression coefficient estimated through cross-validation procedure (see text for description); ††† Range in model parameter estimated through cross-validation procedure (see text for description); ‡‡‡ Estimated variance of the distribution of logarithmic means of individual's exposures (between-worker); ¶¶¶ Estimated variance of the distribution of logarithmic means of exposure from day to day for an individual (within-worker).

Table 6.2: Description of data used in evaluation of external validity.

Agent	Country	Time period	Tar use	Work performed	N ¶	K #	Minimum	Maximum
Bitumen fume * (mg/m^3)	USA	1994 – 1997	No	Hot mix paving	98	64	0.01	1.26
Benzo(a)pyrene (ng/m^3)	Germany †	1985 – 1986	"Carbo-Bitumen," contains 25-30% coal tar	*In-situ* recycling	42	N/A**	500	22000
				Hot mix paving	249	N/A	10	17800
	Italy ‡	1995 – 1999	No	Hot mix paving	48	28	0.6	6.5

* Measured as benzene-soluble particulate, closed-face 37-mm sampler, NIOSH methods; † Measured by a combination of GGP particulate sampler with glass-fiber filter, followed by XAD2 sorbent tube, all measurements were obtained from one-hour stationary samples placed the anticipated position of a worker; ‡ Measured by a combination of 37 mm closed-face Millipore particulate sampler with Teflon filter, followed by XAD2 sorbent tube; ¶ Number of observations; # Number of workers; ** Number of workers is not applicable because samples were stationar

Table 6.3: Assessment of bias * and precision † of the models of exposure to bitumen fume, organic vapour and benzo(a)pyrene in a cross-validation procedure ‡ (internal validity).

Model	Parameter	Mean	Minimum	Maximum	${}_{WW}S_y$ ¶	
					Original estimate	Estimated range
Bitumen fume	Bias	-0.03	-0.28	0.19	–	–
	Precision	1.48	1.37	1.60	1.03	0.73-1.30
	Relative bias (%)	-3	-24	21	–	–
Organic vapour	Bias	-0.01	-0.34	0.34	–	–
	Precision	1.57	1.39	1.77	1.12	0.79-1.49
	Relative bias (%)	-1	-29	41	–	–
Benzo(a)pyrene	Bias	-0.01	-0.47	0.37	–	–
	Precision	1.47	1.29	1.65	1.31	0.78-1.59
	Relative bias (%)	-1	-37	45	–	–

* Bias = mean difference between predicted and measured values (i.e. natural logarithms of exposure); relative bias = (exp(bias)-1)×100%, equivalent to: {(predicted-measured)/measured}×100%; † Precision = standard deviation of bias; ‡ Conducted by repeating the following procedure 300 times: (1) estimate models parameters on random 50% of data, (2) generate predictions for the remaining 50% of the data and (3) calculate bias and precision using each set of observed and predicted values; ¶ Within-worker logarithmic standard deviation $({}_{WW}S^2_y)^{0.5}$, calculated from Table 6.1.

levels even though for five out of six surveys these differences can be expected to be due to chance (95 percent confidence intervals of observed and estimated values overlap). In Figure 6.2, measured mean values correspond to different exposure scenarios, as indicted by the Figure's legend. It would appear that there is a reasonable degree of agreement between observed and predicted means for recent measurements in tar-free environments. However, benzo(a)pyrene exposure model tended to underestimate exposure levels for the circumstances in which tar was used in Germany. The observed effect of *in-situ* recycling on benzo(a)pyrene exposure was similar to that expected on the basis of previously developed statistical model.

Bias and precision of estimated exposures to bitumen fume and benzo(a)pyrene relative to external measurement data are illustrated in Table 6.4. Bitumen fume and benzo(a)pyrene models showed negative bias, -70 and -82 percent respectively. Their precision was similar to that observed in cross-validation. Correction for sampling method used in Germany further decreased estimate of relative bias to -51 percent.

Table 6.4: Assessment of bias, * precision † and relative bias ‡ of the models of bitumen fume and benzo(a)pyrene with respect to external data (external validity).

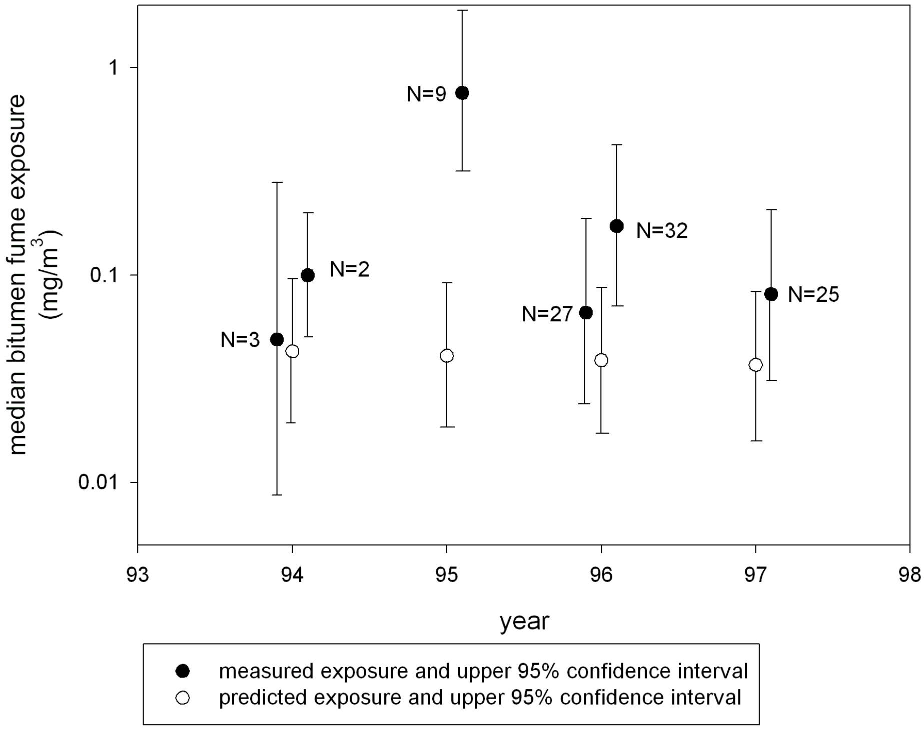
Model	Parameter	Estimate
Bitumen fume (n=98)	Bias	-1.23
	Precision	1.35
	Relative bias (%)	-70
Benzo(a)pyrene (n=339)	Bias	-0.71¶ (-1.74)#
	Precision	1.72 ¶ (1.82) #
	Relative bias (%)	-51 ¶ (-82) #

* Mean of $\log_e$(predicted) - $\log_e$(measured); † Logarithmic standard deviation of bias; ‡ (exp(bias)-1)×100%; equivalent to: {(predicted-measured)/measured}×100%; ¶ Estimated obtained after correcting for GGP sampler use in Germany; # Estimated obtained before correcting for GGP sampler use in Germany.

Discussion

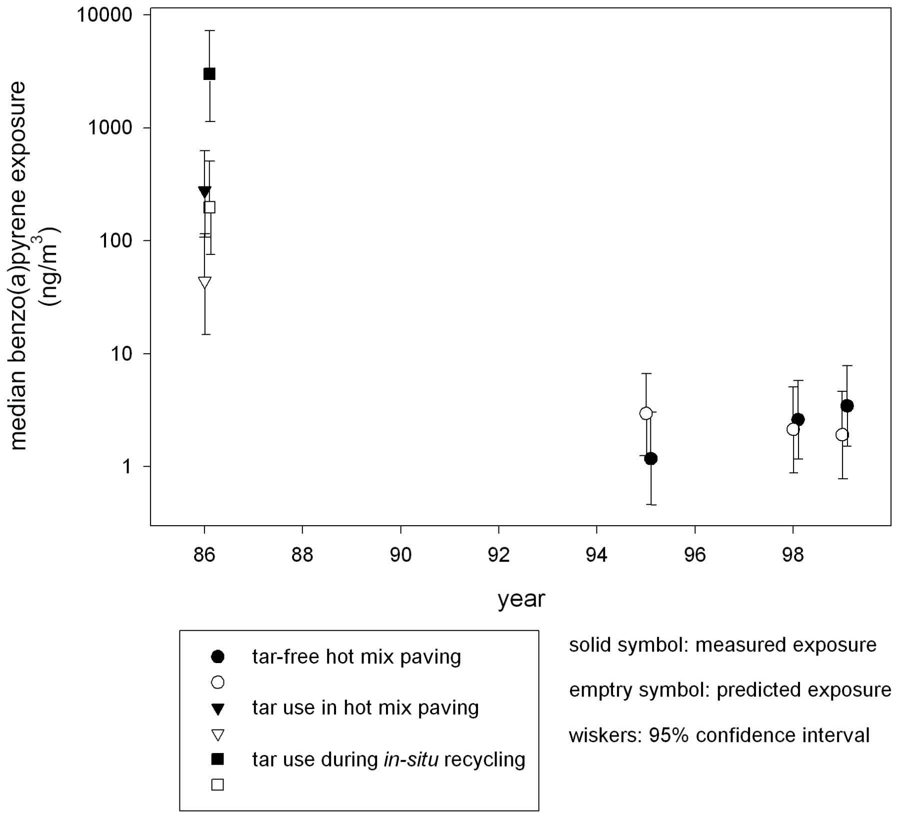
An investigation of the models' robustness revealed that most parameters of models for bitumen fume, organic vapour and benzo(a)pyrene we developed earlier had little average bias. This gives us some assurance that the models adequately described the data. Therefore, if the data is representative of exposures experienced by asphalt workers, then the application of these models in an epidemiological study will result in valid estimates of exposure intensity. However, the models had relatively poor precision, probably resulting mostly from large day-to-day variances. This is adequate because our goal was to model between-worker differences in exposure. The original models did explain a substantial 54 to 79 percent of the estimated between-worker variance, implying that the between-worker variance is reflected by the variables used in the calculation of exposure intensity estimates for the exposure matrix to be employed in epidemiological analyses (12).

Figure 6.1: Measured versus predicted median bitumen fume exposures for each one of six NIOSH Health Hazard Evaluation used in external validation; all measurements are from hot mix paving in the USA.



Overall comparison of the individual predictions of bitumen fume and benzo(a)pyrene exposure models to external data revealed a significant, but weak correlation, but the regression of observed on predicted values had very poor fit. This arose from the fact that measured data had a much wider range, implying that absolute values predicted by our models for each individual observation may be inaccurate. Furthermore, discrepancies in ranges suggest that our models may underestimate any contrasts that exist between different groups of subjects, leading to reduction in power to detect quantitative exposure-response relationships. Precision of the bitumen fume and benzo(a)pyrene models, when evaluated against external data, was of the same order of magnitude as those observed in cross-validation. Bias estimates derived from internal cross-validation were lower than those seen in the external comparisons, which indicated that our models can underestimate bitumen fume and benzo(a)pyrene concentrations by a factor of two to three. Underestimating exposures, especially those occurring further in the past and lying at the upper edge of exposure distribution, as suggested by Figure 6.2, would lead to overestimate of dose-response relationships based on quantitative indices of exposure (e.g. cumulative exposure).

Figure 6.2: Measured versus predicted median benzo(a)pyrene exposures; measurements from Italy and Germany. *



* All samples collected during tar use were stationary one hour measurements at the expected location of a worker, obtained in Germany. Predictions for German data were not corrected for GGP sampler use in this figure. All samples from tar-free paving were collected in Italy

Data used to construct the original exposure models was based primarily on measurements collected in Scandinavia. USA and Italy are not participating in the cohort study, therefore they did not contribute any data to the original models. However, some German bitumen fume exposure data was used in constructing the original bitumen fume exposure model. These discrepancies in data source may have contributed to differences between estimates of bias in internal and external validations.

It is possible that negative bias with respect to bitumen fume measurements from the USA is due to either chance or systematic differences between road paving practices in Western Europe and the USA. Unfortunately, comparable data on bitumen fume exposure was not available in Western Europe, and we had to resort to US data for assessment of external validity. The two-to-four times greater pace of paving in the USA compared to Western Europe and differences in the types of asphalt mixes used (Max von Deviver, personal communications) may well explain observed higher exposures in the USA. If that is the case, apparent bias in our bitumen fume models probably does not impeded applicability of our models to the European situation.

In an external validation of benzo(a)pyrene model, differences in sampling methods, such as use of short-term stationary samples and differences in method of extraction of organic matter may also contribute to the observed discrepancies between predicted and observed values (12,24). An alternative reason for this discrepancy may arise from the fact that the coal tar content of asphalt binder, an important predictor of benzo(a)pyrene exposure (25), was not taken into account in the original models. Even if a model that takes this factor into account could be constructed, the coal tar content of asphalt binder would be impossible to estimate with any precision in an industry-wide cohort study. Thus, our models may underestimate benzo(a)pyrene exposure under circumstances similar to those monitored in the German data (25-30 percent coal tar in asphalt binder). Nonetheless, the estimate of the effect of coal tar use derived from the validation data set is within a range that can be expected on the basis of the results of laboratory studies (12).

In IARC study of asphalt industry we resorted to empirical modelling of exposures for paving workers. Model-based exposure assessment might have numerous advantages over exposure assessment based solely on the experts' opinions. One of these advantages is that the use of statistical models of exposure in epidemiological studies allows data-driven sensitivity analysis of exposure-response relationships (5,6,11,26). We also have previously shown that interpretable empirical models can be derived despite limitations of the data (12,25). In this paper we have further demonstrated that these models can be expected to produce reasonably accurate predictions, i.e. have inaccuracy on the order of day-to-day variability in exposure. Such examination of patterns of exposure within road paving industry would not have been possible on the basis of previously published reports, which would have formed the basis of subjective expert evaluations as a method for exposure assessment (24). Therefore, when measurement data are available, their use for exposure assessment should be considered as the primary basis of assessing exposure intensity. Subjective evaluation of exposures should be used only as the last resort (e.g. few or no measurements; well-known errors in analytical procedures used to obtain available measurements). This is especially relevant for large multicentric international studies in which calibration of different assessors may prove to be very difficult. If expert evaluation of exposures is the only available option in exposure assessment, the penalty is paid in the form of uncertainty about where the weaknesses of the exposure assessment protocol lie. Subjective evaluations, just like any other exposure assessment procedure must be validated (8). The most direct method of validating any exposure model is through workplace measurements (27,28), but other validation methods are also available (8,16,29,30).

We have demonstrated that previously developed models of bitumen fume, organic vapour and benzo(a)pyrene are internally valid and robust. However, they can underestimate exposures under certain circumstances, especially those further in the past. Model estimates can be expected to be imprecise, making them most suitable for group-based exposure predictions in which all members of a group are assigned the same average exposure, instead of individual-based exposure predictions. Limited validation against external measurement data revealed that the patterns described by the original bitumen fume and benzo(a)pyrene models were also present in the validation data sets. This provided an additional guarantee that the originally derived models provided useful estimates of bitumen fume and benzo(a)pyrene exposure. Despite these encouraging findings, we should note that the evaluation of external validity was possible only to a limited extent, since validation data sets lacked the diversity of exposure scenarios needed for a more comprehensive evaluation. Overall, results indicated that further improvements couldn't presently be made to the three original models. However, the consequences of assigning a higher multiplier to the effect of coal tar on benzo(a)pyrene will be explored in sensitivity analysis. Validation of the models increased our confidence in their applicability to exposure assessment in the historical cohort study of cancer risk among asphalt workers.

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Chapter 7: Estimating exposures in asphalt industry for an international epidemiological cohort study of cancer risk.

Burstyn I, Boffetta P, Kauppinen T, Heikkilä P, Svane O, Partanen T, Stücker I, Frentzel-Beyme R, Ahrens W, Merzenich H, Heederik D, Hooiveld M, Langård S, Randem B, Järvholm B, Bergdahl I, Shaham J, Ribak J, Kromhout H: Estimating exposures in asphalt industry for an international epidemiological cohort study of cancer risk. (submitted).

Abstract

Objective: To describe the development of an exposure matrix for known and suspected carcinogens for a multi-centric international cohort study of asphalt workers.

Methods: Production characteristics in the companies enrolled in the study were ascertained via a questionnaire and consultations with industry representatives and industrial hygienists. Exposures to bitumen fume, organic vapour, polycyclic aromatic hydrocarbons (PAH), diesel fume, silica and asbestos were assessed semi-quantitatively using company questionnaires and expert opinions on relative exposure intensities. Quantitative exposure estimates for road paving workers were derived by applying regression models (based on monitoring data) to exposure scenarios identified by company questionnaires. Frequency of coal tar use was derived directly from the questionnaires. All estimates were standardized to an 8-hour work-shift. The resulting exposure matrix was time period-, company- and job class-specific.

Results: Most of 203 firms from eight countries enrolled in the study were engaged in asphalt paving (51%) and mixing (94%). Coal tar use was most common in Denmark and the Netherlands, but its frequency declined dramatically since between 1960 and early 1970's; the practice is now obsolete in the studied countries. The highest bitumen fume, organic vapour and PAH exposures were assessed among roofers and waterproofers. Exposure matrix assessed non-monotonic historical decrease in exposures to all agents except for silica and diesel exhaust. The modeled bitumen fume and coal tar exposures were moderately correlated (r=0.34), with the highest correlation for pre-1960 time period (r=0.47). There was a very strong correlation among bitumen fume, organic vapour and PAH exposures (r=0.78 to 0.98).

Conclusion: We cannot distinguish among health risks associated with bitumen fume, organic vapour and PAH exposures. Adjustment of risk estimates for coal tar exposure should be possible. Our approach produced a data-driven exposure matrix that can be challenged in future studies and easily re-estimated.

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 asphalt industry were excluded from the study. Throughout this manuscript we will use the European convention of referring to 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 (1)(2-9). 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 7.1 explicitly defines agents that were assessed. The objective of this report is to describe the development of an exposure intensity matrix for the IARC multi-centric international cohort study of cancer risk among European asphalt workers.

Table 7.1: 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 vapour	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.

Methods

Exposure measurements and supplementary data

In order 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 (10) 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 comprised 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 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=2007). 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 1960's, but the majority of samples were collected in the late 70's 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 (11) are summarized below. Bitumen fume and organic vapour levels did not 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 vapour and benzo(a)pyrene steadily declined over the last 20 years at a rate of 6 to 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 vapour 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 vapour 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 7.2.

Information about workplaces

We gathered information about companies enrolled in the study through a company questionnaire 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 company questionnaires is presented in Table 7.3. 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 company questionnaires were checked for errors, omissions and inconsistencies. Company questionnaire information was also compared with information about production characteristics derived from the exposure measurement reports (AWE data). Lastly, information gathered by company questionnaires and any additional information 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.

Table 7.2: Predictive models ($\log_e$(Exposure) = $\sum_{all\ j}$ ($ß_j$×Determinant of exposure j) + intercept) of bitumen fume, organic vapour and benzo(a)pyrene exposures, adjusted for sampling strategy and analytical methods (adapted from chapter 4).

Determinant of exposure	Estimates of models' parameters					
	Bitumen fume (mg/m^3)		Organic vapour (mg/m^3)		Benzo(a)pyrene (ng/m^3)	
	ß [E]	**M [F]**	ß [E]	**M [F]**	ß [E]	**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[A]	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 vapour 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, $M = e^{ß+\text{interaction term}}$ (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: e.g. bitumen fume exposure during mastic laying in 1997 is 2.4×0.12 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.

Building study-specific exposure matrix

The Road Construction Workers' Exposure Matrix (ROCEM) was developed on the basis of company questionnaires, analysis of the AWE database and expert judgements. 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 company questionnaire 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) company questionnaire 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 vapour and benzo(a)pyrene (proxy of 4-6 ring PAH). Regression models described in Table 7.2 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 experiences N exposure *scenarios* (S_{1j}, S_{2j}, ... S_{ij} ... S_{Nj}) in a given time interval *j* according to the following formula:

$M_j = \Sigma \{X_{ij} \times f(S_{ij})\}$ for all S_{ij}'s that fall into time interval *j*, {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 company questionnaires. However, company questionnaires 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. Worst case scenario in mastic laying corresponded to indoor work. 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 7.2, according to the following formula (12):

$X_{ij} = \exp(m_{ij} + ½ \, {}_{WW}\hat{S}^2)$, {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 7.2).

Time intervals *j* were defined by company questionnaire 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 vapour 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).

Table 7.3: Type of information gathered by company questionnaires 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, 1960-64, 1965-69, 1970-74, 1975-79, 1980-84, 1985-89, 1990-96.

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 continuos 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, lime stone
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

Semi-quantitative estimates of exposure intensity for bitumen fume, organic vapour 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 vapour 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 vapour exposures during mastic laying outdoors and corresponding exposures during other paving;

3. indoor mastic laying was associated with a four fold increase in PAH exposure compared to outdoor mastic laying;

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 1000 times higher than that of bitumen (13-16). Our estimate of 5-fold difference was made on the basis of multiple regression models 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. The PAH that derived from diesel exhaust are 'counted' as part of diesel exhaust exposure (see below).

6. Time trend in bitumen fume, organic vapour 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 7.2. We also assumed that there was no time trend before 1970. Only in Finland a separate time trend for bitumen fume in waterproofing/roofing was estimated: exposure intensity was assumed to be three before 1985, two for 85-89 time period and 0.5 for 90-96 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 a job classes

Semi-quantitative exposure estimates also reflected differences between job classes. Semi-quantitative exposure estimates described so 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 7.4). 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 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 vapour and PAH exposure between road paving and asphalt mixing.

Table 7.4: Comparison of exposure levels in paving and asphalt mixing in seven surveys that monitored exposures in both job classes (extracted from AWE database).

Job class	Bitumen fume (mg/m^3)		Organic vapour (mg/m^3)		Benzo(a)pyrene (ng/m^3)	
	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

The AWE database did not contain sufficient information to compare bitumen fume and organic vapour 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 vapour 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 company questionnaires. 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. Furthermore, it was assumed that silica exposures in building construction were on-average half (intensity=0.5) of those arising in ground construction (intensity=1). 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 company questionnaires). 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 company questionnaires.

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 paragraphs 'exposure' refers to semi-quantitative exposure estimates. The approach we adopt below is analogous to the one employed by Macalusoi et al. in assessing exposures for jobs which were "poorly specified" in a cohort study of synthetic rubber workers (17). 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 7.5. We also assumed that office administration and management personnel were not exposed to either agent of interest (exposure intensity of *zero* for all agents).

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-hour work-shifts. These 'duration adjusted' indices were be calculated for each company and time period according to the following formulas:

$$_{D}M_j = M_j \times (W_j/8) \qquad \{3\}$$

$$_{D}SQ_j = SQ_j \times (W_j/8) \qquad \{4\}$$

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 company questionnaires. For job classes not covered by company questionnaires, 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 company questionnaires.

Missing values

Missing values in the exposure matrix arose due to missing company questionnaire 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 company questionnaire 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 company questionnaires). 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 vapour 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 vapour and benzo(a)pyrene exposure among pavers) only 2.6% of person-pears used replacement values.

Table 7.5: Country-specific definitions of exposures in selected job classes.

	Job Class (definition and assumptions about exposure profile)				
Country	**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
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).

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 covered the entire countries for operations. One company questionnaire was obtained from each, even though it was recognized that there may have been important differences in work practices between different sub-division of the firm. 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 company questionnaires 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 company questionnaires, Finland – six, the Netherlands – six, Germany – 123 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 1960’s to mid-1970’s in the cohort. The steepest average decline in coal tar use was observed in Denmark (from almost universal use to complete discontinuing of the practice). In the Dutch firms enrolled in the study, 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 1990’s. Germany and Sweden reported that at its peak in 1960’s 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 1960's, 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

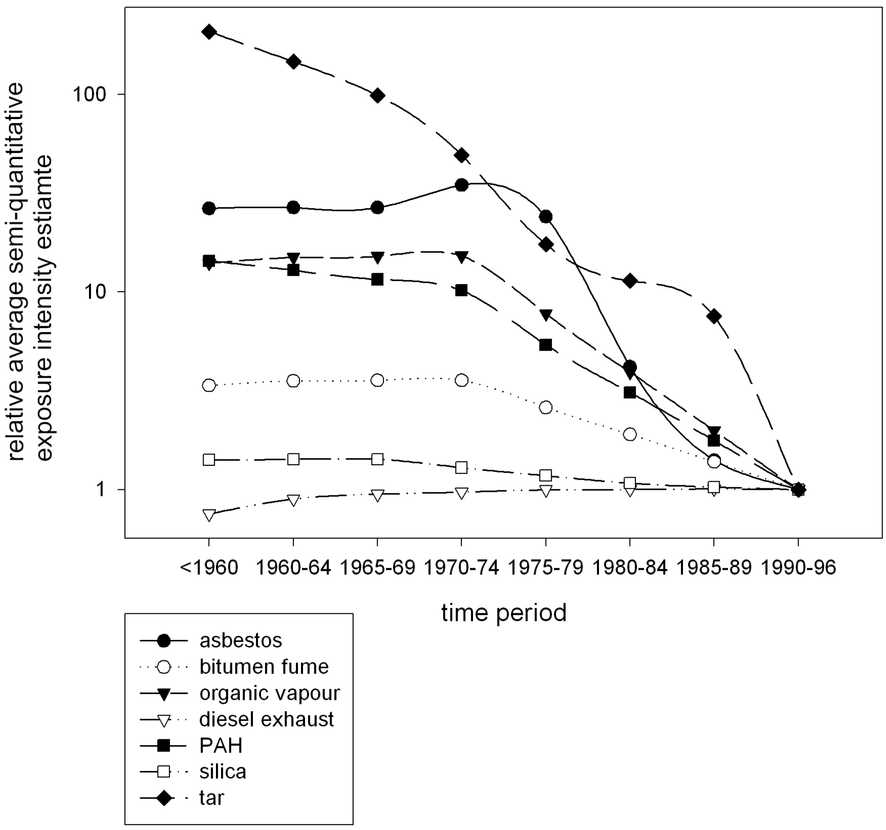
In order to illustrate time trends in all agents of interest, irrespective of actual scale for each agent, average exposure estimates have been expressed relative to average estimates for each agent in 1990-96 time period and plotted versus time periods (Figure 7.1). It is clear that the exposure matrix 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 1990-96. However, exposures to silica and diesel exhaust remained virtually unchanged. Slight increase in diesel exhaust exposures in the 1960's can be attributed to substitution, in paving operations, of petrol-powered machines with diesel-powered ones. Quantitative exposure estimates for bitumen fume, organic vapour and benzo(a)pyrene among pavers are summarized in Table 7.6. Modeled time trends in these exposures are illustrated in Figures 7.2 to 7.4. 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 vapour and PAH exposures, exceeding those occurring in paving by a factor of 1.5 to 3. Estimated exposures in paving and asphalt mixing were similar for most agents, except that (a) asphalt 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.

Table 7.6: 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
	1960-64	61	1.33	0.66	50	0.21	3.42
	1965-69	70	1.30	0.61	47	0.21	3.42
	1970-74	77	1.46	1.04	71	0.21	6.99
	1975-79	86	1.04	0.66	63	0.15	5.12
	1980-84	87	0.80	0.49	61	0.50	3.96
	1985-89	91	0.59	0.38	64	0.34	2.90
	1990-96	93	0.44	0.28	64	0.06	2.24
Organic vapour (mg/m^3)	All	573	59	86	146	1	827
	<1960	42	107	131	122	18	827
	1960-64	58	112	119	106	19	827
	1965-69	66	106	101	95	19	827
	1970-74	71	105	97	92	17	827
	1975-79	81	54	50	93	9	421
	1980-84	82	27	25	93	4	214
	1985-89	86	13	13	100	2	109
	1990-96	87	6	4	67	1	31
Benzo(a)pyrene (ng/m^3)	All	573	146	262	179	5	3079
	<1960	42	322	298	93	47	1387
	1960-64	58	274	295	108	41	1193
	1965-69	66	229	261	114	41	1144
	1970-74	71	246	434	176	41	3079
	1975-79	81	124	239	193	24	1803
	1980-84	82	71	138	194	29	1120
	1985-89	86	39	75	192	15	651
	1990-96	87	24	46	192	5	403

A – number of cells in ROCEM with company questionnaire inputs; B – arithmetic mean; C – standard deviation; D – coefficient of variation in %; E – minimum value; F – maximum value.

Figure 7.1: Time trends in semi-quantitative exposure scores.



The procedure employed in constructing the exposure matrix resulted in only weak-to-moderate correlation between tar use and all other agents except for silica (Table 7.7). 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 vapour) to 0.93 (bitumen fume and benzo(a)pyrene). Strong rank correlation among semi-quantitative estimates of PAH, bitumen fume and organic vapour was not due to extreme values (examined graphically, results not shown).

Discussion

Estimated quantitative exposure intensities

Quantitative estimates of exposure intensity among pavers (Table 7.6) 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 1970-74 to 1990-96. This in part reflected positive association between exposure levels and their variability inherent in log-normal statistic model used to assess exposure intensities. However, it may be a sign of convergence and standardization of work practices since changes in variability must also derive from the distribution of production conditions reported in company questionnaires. An alternative explanation is that recall of working conditions more remote in time was subject to a greater error. However, if this latter effect was present, it did not operate strongly in pre 1960-1969 time period due to absence of time trend in exposure variability. In pre-1960-1969 time period variability of exposure estimates was on the same order or smaller than in 1970-74, 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 1960's. In relative terms, variability over time was estimated to have been less pronounced for bitumen fume and organic vapour. Relative variability in benzo(a)pyrene exposure estimates increased in time, probably due to different times of cessation 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.

Table 7.7: Pair-wise rank (Spearman) correlation between semi-quantitative exposure scores to different agents in the exposure matrix (correlation coefficient, (number of pairs)); all p=0.0001, unless otherwise noted.

Agents	Bitumen fume	Organic vapour	Diesel exhaust	PAH	Silica	Tar
Asbestos	0.14 (3986)	0.13 (3987)	0.07 (5035)	0.17 (3975)	0.04 [A] (4952)	0.30 (4390)
Bitumen fume		0.98 (4089)	0.44 (4063)	0.96 (4069)	0.05 [B] (3972)	0.34 (3900)
Organic vapour			0.38 (4064)	0.97 (4069)	0.04 [C] (3973)	0.37 (3900)
Diesel exhaust				0.35 (4054)	0.16 (5031)	0.20 (4469)
PAH					0.03 [D] (3971)	0.46 (3902)
Silica						-0.06 [E] (4386)

A – p=0.01; B – p=0.001; C – p=0.005; D – p=0.07; E – p=0.0002.

Historical exposure patterns in quantitative exposures estimates for pavers

Figures 7.2-7.4 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 company questionnaires. 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 1970-74 to pre-1960 levels and only after that started to decline again. The pattern for organic vapour in Norway is different in that exposures steadily increased until the middle of 1970's. The pattern for organic vapour is probably due to discontinuation of oil gravel paving in favor of surface dressing, with the latter producing higher organic vapour 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 vapour 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 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 company questionnaires 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 vapour 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. Even if we consider that correlation between bitumen fume exposure and tar use have been stronger in the past, the weak nature of that correlation makes it unlikely that analyses with lagged bitumen fume exposure estimates will be substantially confounded by tar use. 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 meaningful analysis.

Validity of exposure matrix

The validity of the present exposure matrix 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 (10). The validity of models based on that data and used in quantitative exposure intensity estimation has already been assessed as satisfactory (18). Bitumen fume, organic vapour and benzo(a)pyrene exposure models were internally valid but imprecise. Predicted bitumen fume exposures tended to be lower (average factor of 3) 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 a similar to expected effect of re-paving and a larger than expected effect of tar use. Overall, benzo(a)pyrene models underestimated exposures by 51%.

Figure 7.2: Assessed time trend in average bitumen fume exposure (pavers only).

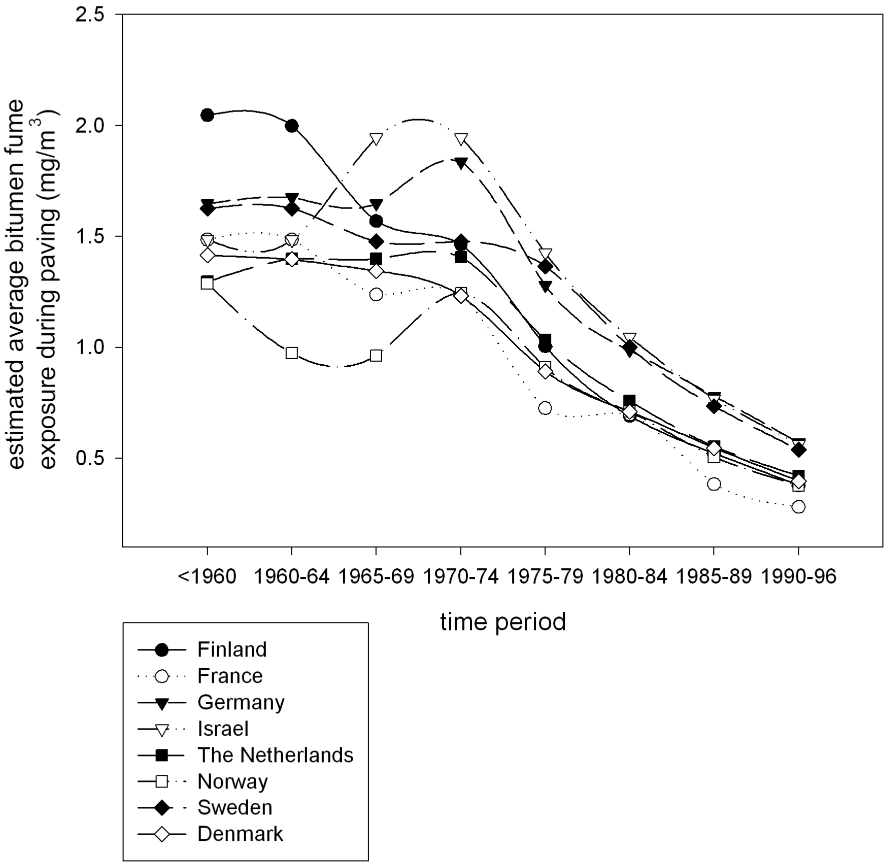


Figure 7.3: Assessed time trend in average organic vapour exposure (pavers only).

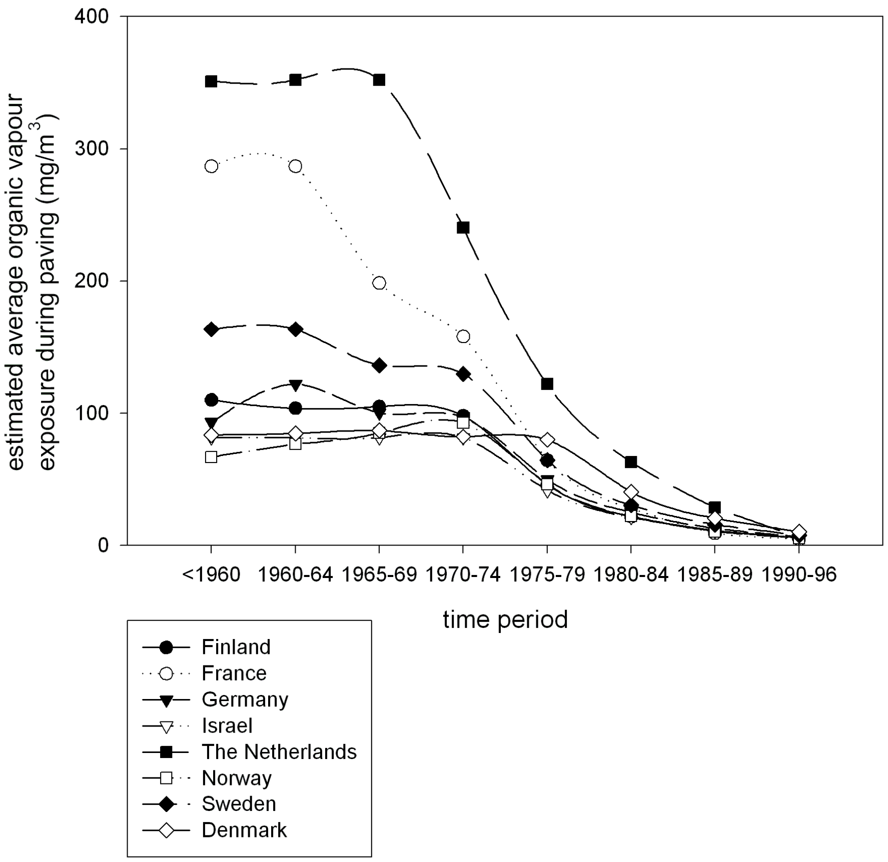
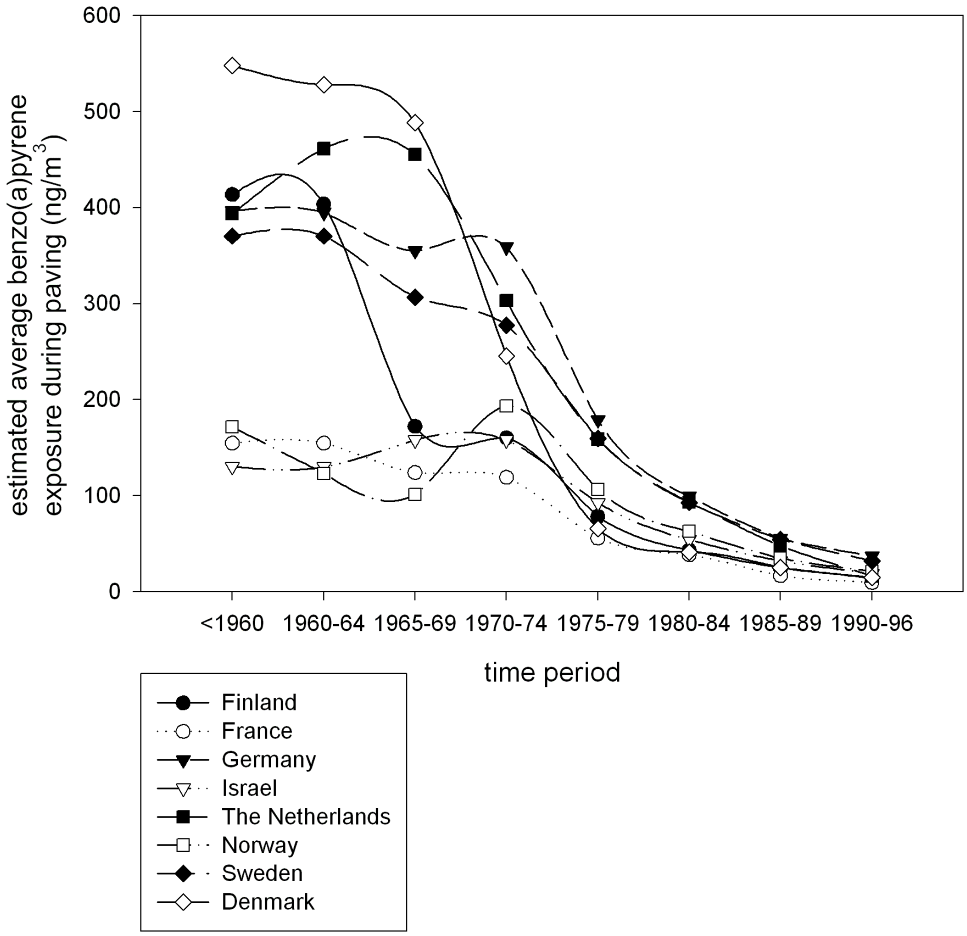


Figure 7.4: Assessed time trend in average benzo(a)pyrene exposure (pavers only).



In semi-quantitative exposure estimation, the AWE data was relied upon as much as possible, ensuring that they were defensible and reproducible. However, spare exposure monitoring data forced us also to make assessments based exclusively on professional judgement 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.

Company questionnaires 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 company questionnaires. Consequently, it was not possible to standardize responses to company questionnaires 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 (though impractical in a cohort design due to 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, exposure matrix presented in this manuscript may be further improved if case-control study nested in the cohort of asphalt workers were to be carried out. The deterministic nature of exposure matrix 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 multi-centric 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 exposure matrix could not have been developed with any degree of certainty by relying exclusively on "expert evaluation" methodology. In applying the exposure matrix to epidemiological analyses, we cannot distinguish among health risks associated with bitumen fume, organic vapour and PAH exposures. Adjustment of risk estimates for coal tar exposure should be possible. Our approach also produced an exposure matrix that can be challenged in future studies and easily re-estimated, if necessary.

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Chapter 8: Evaluation of performance of different exposure assessment approaches and indices in analysis of an association between bitumen fume exposure and lung cancer mortality.

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Abstract

Objective: To evaluate performance of different exposure assessment approaches in cohort study of cancer risk among European asphalt workers.

Methods: Exposure to bitumen fume among pavers and lung cancer risk was the focus of this methodological investigation. Members of the cohort selected for analysis were males employed in asphalt paving only, for at least one paving season. An inception/entry sub-cohort was also identified among these persons. Three exposure indices were considered: duration of exposure (years), average exposure (mg/m^3) and cumulative exposure (mg/m^3*years). Two latency models were considered for an association between lung cancer and bitumen fume: with and without a 15-year lag. Standardized mortality ratios (SMRs) and 95% confidence intervals (CI) were computed. We examined rank correlations among bitumen fume exposure indices. Relative risk associated with bitumen fume exposure was estimated via Poisson regression. All models were adjusted for coal tar exposure (ever/never), age, calendar period and country. Competing exposure-response models were compared using a log-likelihood ratio test (measure of model fit).

Results: We selected 12,367 male workers employed only in asphalt paving for at least one paving season for analysis. In the cohort, there were 134 deaths due to lung cancer versus 106.91 expected (SMR=1.25; 95%CI: 1.05-1.48). Only exposure ranks based on strata of duration and cumulative exposure indices were correlated. There was no association between lung cancer risk and either duration or cumulative exposure. However, there was the suggestion of an increase in lung cancer risk accompanying rise in average exposure. Only models with average bitumen fume exposure (with or without lag) markedly improved model fit. Average bitumen fume exposure indices with and without 15-year lag improved model fit to the same extent.

Conclusions: We found a positive association between average bitumen fume exposure and lung cancer mortality risk. This association could be the result of confounding by other carcinogenic exposures and lifestyles. No clear latency model emerged from analysis. Constructing quantitative exposure indices appeared to have been justified because (a) the healthy worker effect confounded any associations between duration of exposure and lung cancer mortality risk and (b) we identified statistically significant associations between bitumen fume exposure and lung cancer risk that require further investigation.

Introduction

This study of cancer risk in the European asphalt industry was prompted by an ongoing controversy over the carcinogenicity of emissions derived from bitumen, a binder used in asphalt (1-8).[1] The controversy was prompted by results of previous studies of the health effects of emissions derived from bitumen (the current binder used in the asphalt mix in Western Europe) that suggested that asphalt workers were at elevated risk for lung cancer (1-9). The International Agency for Research on Cancer (IARC) coordinated the study. One of the components of the study was the assessment of occupational exposures to known and suspected lung carcinogens in the asphalt industry. There is a belief among some epidemiologists and exposure assessors that quantitative exposure assessment of exposure intensity, when possible, is preferable to semi-quantitative and qualitative methods of assessing exposure (10-12). This is driven, at least in part, by the need to conduct quantitative risk assessment on the basis of human exposure data. Nonetheless, quantitative exposure assessment has rarely been performed for large historical occupational cohorts, primarily due to lack of sufficient exposure monitoring data. For a multicentric epidemiological study of lung cancer among persons exposed to bitumen, we constructed a large database of exposure measurements (13) that was used to build statistical models of exposure intensity to bitumen fume (14), the main exposure agent of interest. The elaborated model was shown to be reasonably valid (15) and was applied to construct a study-specific exposure matrix with quantitative bitumen fume exposure estimates for workers in asphalt paving (16). Another approach to assessing exposure among asphalt paving workers would be to assume that they were all exposed to the same concentration of bitumen fume. This would lead to differences in cumulative bitumen fume exposure among asphalt pavers, depending only on exposure duration. In this report we set out to compare the performance of these two exposure assessment approaches, under different latency assumptions, in exposure-response modeling of bitumen fume and lung cancer for asphalt paving workers.

Methods

Cohort

IARC coordinated assembly of a retrospective cohort of asphalt workers from European companies in the asphalt industry (road paving, asphalt mixing and roofing) in eight countries (Denmark, Finland, France, Germany, the Netherlands, Norway, Sweden and Israel). Asphalt workers in the context of this study were defined as individuals involved in handling asphalt, from its manufacture at an asphalt plant to its application in road paving. In addition, a small number of roofers and waterproofers were enrolled in the study in some countries. There were also employees in the target companies that had been employed in ground and building construction. Employees of oil refineries who might be considered asphalt workers were excluded.

The current analysis focused on those members of the cohort who were employed only in asphalt paving, in order to enable quantitative exposure assessment and reduce the possibility of confounding due to exposures to carcinogens from outside the asphalt industry. Female subjects were excluded from analysis because they represented a small proportion of the cohort. Furthermore, the Swedish cohort was also excluded from the current analysis because duration of exposure could not be accurately estimated for the majority of its members. This

[1] Throughout this manuscript we will use the European convention of referring to the binder used in asphalt mixes as 'bitumen'. In the USA, the binder is referred to as 'asphalt'.

was a consequence of the fact that the job histories in Sweden consisted only of the job held at the time of entry into the cohort. Lastly, a minimal duration of employment of one paving season was applied for inclusion in the cohort. All subjects selected for analyses were exposed to bitumen fume because bitumen was always used in the binder during asphalt paving.

The procedures for identification of suitable companies varied in the participating countries, as did the number and average size of the companies included in the study. A basic requirement was the availability of a complete retrospective employee roster during the enrollment period. Personal identifiers and employment histories of workers were abstracted from company records.

Employment histories were coded according to a classification of jobs, which was constructed for the study (chapter 7). These job classes formed the basis for the linkage between employment histories of individual workers and estimates of exposure derived from the Road Construction Workers' Exposure Matrix (ROCEM, see chapter 7).

Exposure assessment

Details of exposure assessment were presented in chapter 3 (construction of exposure measurement database), chapter 4 (statistical modeling of bitumen fume exposure among pavers), chapter 6 (validation of the bitumen fume exposure models) and chapter 7 (assembling the study-specific exposure matrix ROCEM). This process will only be briefly reviewed here. In chapter 3 we described how individual exposure measurements from European asphalt companies, in countries enrolled in the cohort, were assembled into a single database. The exposure data comprised industrial hygiene measurements of exposure levels for a variety of agents among asphalt workers, and supplementary information. The supplementary information allowed linkage of exposure measurements with information on production conditions in firms recruited for the study, collected via company questionnaires. Most of the available exposure data was collected in the participating countries as of February 1999 (N of measurements 2007). The major contributors (70% of samples) were the four Nordic countries, with 35% of samples collected in Norway. The earliest samples originated from the late 1960's, and the majority were collected in the late 1970's and between 1985 and 1997. The data set was judged to be sufficiently large and balanced to permit statistical modeling of the intensity of exposure to bitumen fume in paving operations.

In chapter 4, we presented how exposure measurement data was used to construct a predictive model of bitumen fume exposure. The model identified a declining time trend in exposure concentrations between 1970 and 1997. Mastic laying, re-paving, surface dressing, and oil gravel paving were significant determinants of bitumen fume exposure. It was concluded that for road paving workers, bitumen fume exposure intensity could be assessed on the basis of time period and production characteristics. In chapter 6 we described how bitumen fume exposure model was validated by comparing predicted values with those measured in the USA. The data used in this external validation was not used to construct the models described in chapter 4. Predicted bitumen fume exposures tended to be lower (average factor of 3) than concentrations found during paving in the USA. This apparent bias might be attributed to known differences between Western European and USA paving practices. In addition, the internal validity of the bitumen fume exposure model was evaluated by a modified cross-validation procedure. The bitumen fume exposure model appeared to be internally valid but imprecise. Overall, the validity of bitumen fume exposure models was assessed as satisfactory, given the available exposure data.

In chapter 7, we described the linkage of the statistical models of exposure to the company questionnaires to produce a study-specific exposure matrix, ROCEM. Production characteristics in the companies enrolled in the study were ascertained via a questionnaire and consultations with industry representatives and industrial hygienists. Quantitative exposure estimates for road paving workers were derived by applying regression models (based on monitoring data, chapter 4) to exposure scenarios identified by company questionnaires. Information on coal tar use was derived directly from the questionnaires. All estimates were standardized to an 8-hour work-shift. The resulting exposure matrix was time period-, company- and job class-specific. The exposure matrix showed a non-monotonic historical decrease in bitumen fume exposure, with exposure temporarily rising in the 1970's due to substitution of oil gravel paving (cold application) with hot mix asphalt paving. According to the exposure matrix, road pavers were not exposed to asbestos and there was no variability in their exposures to respirable silica and asbestos. Estimates of bitumen fume, organic vapour and PAH were strongly correlated, indicating that their health effects could not be assessed independently. On the other hand, there was little correlation between coal tar use and bitumen exposure concentrations, indicating that it might be possible in the cohort to adjust for potential confounding by coal tar exposure.

Exposure indices

In the analyses with ROCEM-based estimates of exposure, we derived for each worker the following indices of bitumen fume exposure: (a) duration of exposure, (b) cumulative exposure (product of exposure duration and intensity, integrated over work-history) and (c) average exposure over the work history (ratio of cumulative exposure and duration of exposure). In estimating duration of exposure we had to correct for the seasonal nature of work in the asphalt industry, given that the working season in any given year varied between companies and countries. This was achieved by weighting duration of exposure for each full calendar year employed in paving by the ratio of working season duration (in months) to 12 months (full calendar year). Each incomplete calendar year of employment was not weighted by season duration because it was assumed that in such cases job histories reflected actual duration of work. Working season duration estimates were derived from company questionnaires, and were specific to each company and job class combination. In order to model the latency associated with lung cancer, additional indices were created of duration of exposure, average exposure and cumulative exposure, after ignoring the last 15 years before death or end of follow-up (15 year lag).

For each quantitative exposure index, unexposed subjects formed a separate category, and exposed subjects were divided into quartiles, each including approximately one fourth of lung cancer deaths (International Classification of Diseases (ICD) 9th revision: code 162). Subjects with unknown exposure were excluded from analysis. The same cut-points for the definition of quartiles were kept in analyses of subsets of the cohort (e.g., inception cohort) in order to permit a direct comparison across subsets.

To assess the influence of truncated job histories and follow-up times, analyses were also repeated on the "inception cohort", comprising only subjects who entered employment in the participating firms after or at the start of follow-up.

Follow-up and statistical analysis

A follow-up for mortality was conducted in all participating countries. The earliest follow-up started in 1953, and the latest ended in 2000. The overall loss to follow-up was 0.6% and varied little between countries.

Standardized mortality ratios (SMRs) were computed for persons employed only as pavers, allowing comparison of risk to the general population. Age-, calendar period- and sex-specific national mortality reference rates were computed using the mortality data bank of the World Health Organization. The expected numbers of deaths were derived by multiplying the accumulated person-years by the national reference rates across sex, age, and calendar-year strata, and SMRs were calculated as ratios of observed and expected numbers of deaths. An in-house IARC computer program was used to estimate the individual contribution to each stratum and to calculate SMRs and 95% confidence intervals (95%CI) based on the Poisson distribution of observed numbers of deaths. SMRs were not calculated if the number of expected deaths was zero.

Rank correlation between different indices of bitumen exposure was examined using Spearman correlation coefficients.

Relative risks (RR) and associated 95% confidence intervals were estimated using Poisson regression (17). All Poisson regression models included age (0-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80+ years), calendar period of exit from cohort (≤1974, 1975-1979, 1980-1984, 1985-1989, 1990 and later), country and coal tar use (yes/no). The coal tar exposure variable was included in the models in order to test for potential confounding of an effect of bitumen fume exposure (if any) by coal tar exposure.

An improvement in model fit, upon addition of bitumen fume exposure index, was evaluated using a profile log-likelihood ratio test (18). Degrees of freedom for the log likelihood ratio (LL) test were equal to the number of levels of a categorical variable added to the model, minus one. The log-likelihood ratio test was computed as

$$-2\times(\text{change in LL due to bitumen fume exposure variable}).$$

The log-likelihood ratio follows an approximately chi-squared distribution that can be used to evaluate the statistical significance of the test. A one-sided chi-squared p-value was used, because we expected model fit to either improve or remain unchanged.

Poisson regression analyses were carried out in STATA 6.0. Person-year allocation was carried out in SAS 6.12 (using an in-house computer program developed at IARC).

Results

We selected 12,367 male workers employed only in asphalt paving for one or more paving seasons for analysis. Among these persons, 8,472 belonged to the inception cohort. In the entire cohort selected for analysis, a total of 1,625 persons were reported to have died at the end of the follow-up versus 1,656.56 expected, yielding an SMR of 0.98 (95%CI: 0.93-1.03). The SMR for all malignant neoplasms (ICD-9, codes 140-208) was close to the expected value (SMR=0.99; 408 observed; 95%CI: 0.90-1.09). There were 134 deaths due to lung cancer versus 106.91 expected. This constituted a statistically significant increase in lung cancer risk compared to the general population (SMR=1.25; 95%CI: 1.05-1.48).

Duration and cumulative exposure indices were highly correlated (r=0.82). However, cumulative and average exposure indices were not correlated (r=0.09). Likewise, duration and average exposure indices were not correlated (r=-0.19). Lagged exposure variables showed a similar pattern: r=0.92 between lagged cumulative and duration exposure indices, r=0.52 between average and duration exposure indices, and r=0.61 between average and cumulative exposure indices. All p-values for Spearman rank correlation coefficients were less then 0.00001.

Table 8.1 presents relative risk estimates quantified through Poisson regression models. There appears to be no association between duration of bitumen fume exposure and lung cancer mortality, with some suggestion of a decrease in risk for persons with longer duration of exposure. Cumulative bitumen fume exposure was also not associated with lung cancer risk. These patterns persisted for the inception cohort and upon lagging duration and cumulative exposure variables. An increase in average bitumen fume exposure was associated with a statistically significant rise in risk of lung cancer mortality. Lagged average bitumen fume exposure followed an unusual pattern. Person exposed 15 years prior to diagnosis (unexposed group in lagged analysis) were at a higher risk of lung cancer mortality than persons in the lowest quartile of lagged average bitumen fume exposure. However, as the level of lagged average bitumen fume exposure increased, so did the risk of lung cancer mortality. The highest quartiles of average lagged bitumen fume exposure were associated with a statistically significant higher risk of lung cancer mortality than the "unexposed" category.

Only average exposure indices (lagged or not) improved model fit (Table 8.2). Both lagged and non-lagged average bitumen fume exposure variables produce the same improvement in the fit of a model that included only age, calendar period, country and coal tar use. This implies that both lagged and un-lagged average bitumen fume exposure variables fit data equally well.

Table 8.1: Various estimates of bitumen fume exposure among persons employed only in asphalt paving and risk of lung cancer mortality; all models adjusted for age, calendar period, country, and coal tar exposure (Sweden excluded, one season of employment inclusion criteria applied).

Lag	Exposure metric (units)	Exposure group	All persons				Inception cohort only			
			N [A]	py [B]	RR [C]	95%CI [D]	N [A]	py [B]	RR [C]	95%CI [D]
15 years	Duration (years)	0	53	124543	1.00	--	25	33502	1.00	--
		0.003-<1.45	21	22112	0.75	0.43-1.31	15	6294	0.61	0.26-1.44
		1.45-<3.90	24	17512	0.86	0.50-1.47	12	6996	0.41	0.17-1.01
		3.90-<8.05	17	13838	0.67	0.36-1.23	10	6681	0.33	0.13-0.85
		8.05-30.30	19	10552	0.83	0.43-1.61	15	7089	0.39	0.14-1.12
	Average (mg/m^3)	0	53	124543	1.00	--	25	33502	1.00	--
		0.71-<1.21	22	37044	0.39	0.22-0.69	6	7879	0.16	0.05-0.47
		1.21-<1.32	20	8707	0.89	0.49-1.62	15	5493	0.35	0.14-0.88
		1.32-<1.47	20	6954	1.16	0.64-2.11	16	5113	0.43	0.17-1.10
		1.47-6.46	19	11309	1.92	1.00-3.68	15	8575	1.68	0.66-4.26
	Cumulative (mg/m^3-years)	0	53	124543	1.00	--	25	33502	1.00	--
		0.004-<1.61	20	21840	0.76	0.43-1.33	13	5244	0.64	0.26-1.54
		1.61-<3.71	19	13935	0.86	0.49-1.55	10	5285	0.46	0.18-1.16
		3.71-<9.57	20	16567	0.63	0.35-1.12	12	8202	0.31	0.12-0.77
		9.57-47.04	22	11672	0.96	0.51-1.78	17	8329	0.41	0.15-1.12
0 years	Duration (years)	0.41-<1.75	34	59439	1.00	--	16	10875	1.00	--
		1.75-< 4.59	38	54838	0.93	0.58-1.48	19	16757	0.87	0.45-1.70
		4.59-<9.87	35	41072	0.87	0.54-1.41	22	15286	0.87	0.45-1.70
		9.87-41.53	27	33051	0.59	0.88-1.06	20	17644	0.46	0.21-1.00
	Average (mg/m^3)	0.31-<1.03	32	121790	1.00	--	12	26290	1.00	--
		1.03-<1.23	36	26441	2.73	1.65-4.53	17	6904	2.86	1.25-6.55
		1.23-<1.37	33	18704	2.42	1.35-4.34	25	12912	1.91	0.79-4.59
		1.37-5.38	33	21465	3.38	1.95-5.86	23	14457	2.45	1.05-5.71
	Cumulative (mg/m^3-years)	0.33-<2.16	33	81084	1.00	--	14	14089	1.00	--
		2.16-<4.61	32	38858	1.28	0.78-2.08	15	12366	1.19	0.57-2.49
		4.61-<9.66	33	35821	1.06	0.65-1.73	21	14550	1.03	0.52-2.05
		9.66-71.96	36	32637	1.02	0.87-1.04	27	19558	0.79	0.38-1.63

A = number of lung cancer deaths; B = person-years; C = relative risk estimates; D = 95 percent confidence interval for RR.

Table 8.2: Comparison of fit (via log likelihood ratio test [A]) of the bitumen fume - lung cancer mortality models in a cohort of persons who were only employed in asphalt paving.

Model		Population					
		All persons			Inception cohort only		
Lag	Exposure metric	ν [B]	-2LLR [C]	p [D]	ν [B]	-2LLR [C]	p [D]
15 years	Duration	4	2.084	0.72	4	6.610	0.16
	Average	4	22.557	0.0002	4	19.895	0.0005
	Cumulative	4	3.297	0.51	4	7.509	0.11
0 years	Duration	3	4.161	0.24	3	5.036	0.17
	Average	3	23.585	0.00003	3	7.345	0.06
	Cumulative	3	1.156	0.76	3	1.421	0.70

A = comparison of model that included age, calendar period, country, and coal tar exposure (type A) *versus* model that included age, calendar period, country, coal tar exposure and bitumen fume exposure variable (type B); B = degrees of freedom for log likelihood (LL) ratio test; C = $-2\times(LL_{\text{type A}} - LL_{\text{type B}})$; D = p-value for the log-likelihood ratio test: p(chi-squared(-2LLR)), one-sided because we expected model fit to either improve or remain unchanged.

Discussion

Comparison to general population

Patterns of SMRs suggested that persons exposed to bitumen fume during paving, as a group, were at increased risk of lung cancer compared to the general population. However, this increase in lung cancer risk cannot be attributed to any specific agent on the basis of SMR analyses alone.

Duration, average and cumulative exposure indices

A downward trend, though not statistically significant, in risk of lung cancer mortality was observed with increased duration of employment as a paver and hence bitumen fume exposure. This is symptomatic of the "healthy worker effect" whereby healthier individuals remain employed longer. However, such an effect has been reported to be weaker for cancer than for any other cause of death (19). The healthy worker effect, governing the relationship between duration of exposure and lung cancer mortality, is likely to confound association between lung cancer mortality and cumulative exposure. This is probably at least in part due to the fact that average exposure intensity spanned a narrower range of values (factor of 17=5.38/0.31) than duration of exposure (factor of 101=41.53/0.41). Consequently, cumulative exposure was determined more by duration of exposure than by its intensity.

Models with an average exposure index better explained lung cancer mortality risk. They suggested a positive association between the risk of lung cancer mortality and average bitumen fume exposure. The other two indices were not associated positively with the risk of lung cancer mortality. Such patterns for chronic diseases, including cancer, have been observed in other occupational cohorts, but the cause of such patterns is poorly understood (20,21). If the mechanism of bitumen carcinogenesis involves either a threshold or non-linearity at lower doses in exposure-response curves (as has been suggested for other carcinogens (22)), then we may expect average bitumen exposure to be more closely associated with cancer risk than exposure duration. However, too little is known about the possible mechanism of bitumen carcinogenesis to develop with argument further. The difficulty in interpreting a model that shows an association between risk of lung cancer mortality and average exposure is that it implies, unrealistically, that exposure for any length of time (within the range of the data) at the same exposure level confers the same relative risk. Better methods for controlling for the healthy worker effect may lead us to the ability to model a more biologically plausible relationship between lung cancer risk and cumulative exposure. Information on reasons for retirement from asphalt work may be helpful in this regard, since it may help us to identify the population of workers who left the industry because of health problems. Data on differences in lifestyle factors between long-term and short-term workers may be helpful in this regard. Furthermore, it has been suggested that adjustment for person-years in active employment may correct for confounding by the healthy worker survivor effect in studies of cumulative exposure (23).

Latency model

As indicated by model fit tests, neither latency model considered in this investigation appeared to outperform the other. In order to develop a better latency model, we may need to perform time-windows analysis, to explore the possibility that exposures in different time windows may confound one another (24). In such analyses, the contribution of lagged exposure (say, by 15 years) to change in risk of health outcome can be adjusted for an exposure that occurred 15 years prior to the outcome. The validity of the use of the strength of exposure-response association *per se* in an selecting optimal time-window model has recently been called into question (25,26) amid suggestions that in latency analysis an incorrectly specified model may lead to differential bias in exposure estimates (26). Thus, given the declining time trend in exposure intensity (chapter 7), for average exposure, if lag was too long, biologically effective exposure would be overestimated, and if lag was too short, biologically effective exposure would be underestimated. The opposite should hold for duration of exposure (and duration-driven cumulative exposure): if lag was too long, biologically effective exposure would be underestimated; if lag was too short, biologically effective exposure would be overestimated. Differential underestimation of exposure can be expected to produce overestimation of an exposure-response relationship. Conversely, differential overestimation of exposure can be expected to produce underestimation of an exposure-response relationship. In practice, as in our data, it might be very difficult to distinguish between a well-specified latency model and bias due to differential exposure misclassification produced by lagging. Model fit, measured by the log-likelihood ratio test, has been suggested to overcome these complications in differentiating between competing latency models (25), but more research is needed to develop practical guidelines for resolving these difficulties (26).

Exposure misclassification: job histories and exposure matrix

Truncated job histories may be another source of exposure misclassification in the study. If follow-up started after the date of first employment, we would underestimate a person's exposure. Such differential misclassification of exposure would tend to produce negative bias in exposure-response relationships. However, when we attempted to control for this factor by restricting analyses to the inception (entry) cohort we did not observe a stronger exposure-response relationship.

Non-differential misclassification of exposure could have arisen from imprecision in the exposure matrix. Errors in the exposure matrix may have originated either from the statistical model of exposure intensity or from the company questionnaires. Statistical models were demonstrated to be imprecise, but valid (chapter 6). This made them suitable for grouped model-based exposure assessment, such as we utilized, where non-differential misclassification of exposure is reduced on group level (chapter 6 and 7). This grouping of exposure estimates occurred on three sequential levels. On the first level, exposure measurements were pooled to estimate exposures for a number of exposure scenarios by using mixed effects models (chapter 4). On the second level, exposures for an average/typical person described by a company questionnaire were estimated. This second level of grouping was achieved in construction of the exposure matrix (chapter 7). On the third and final level, individual exposure estimates obtained from application of the exposure matrix to job histories were grouped to form exposure groups for epidemiological analyses. These sequential levels of aggregating data can be expected to improve validity of risk parameter estimation at the expense of loss in precision if they result in Berkson-type error (27-29).

However, we cannot predict the direction and magnitude of errors due to the company questionnaires (the backbone of this exposure assessment), because validity of company questionnaire data was not evaluated systematically. One of the key factors in creating duration-driven exposure indices for the epidemiological analyses was adjustment of exposure duration for the length of the paving season. Length of paving season was assessed as a single value for all pavers in a given firm. This did not allow for the working season to vary from year to year and in response to changes in paving technology and weather. Thus, it is likely that our data did not adequately reflect the seasonal nature of work, introducing errors into duration-driven exposure indices used in exposure-response modeling.

As in many studies, we cannot predict with certainty either the direction or the magnitude of bias in exposure estimates and the resultant exposure-response associations. It would appear that the most immediate reduction in bias from exposure assessment procedure could be achieved by improving our knowledge of the job histories of study subjects. This can be most efficiently achieved in a nested case-control study design, in which we can focus our efforts on reconstructing exposure histories for individuals most informative for relative risk estimation.

Confounding

The main potential confounder that we did not take into account in the cohort phase of the study was cigarette smoking. As an established risk factor for lung cancer, if cigarette smoking was not equally frequent in all exposure groups (and time periods), it could produce a distortion in the observed relationship between bitumen fume and lung cancer mortality risk. This is particularly true for the observed positive association between average exposure and risk of lung cancer mortality because (a) the highest average exposures could only have been experienced due to employment before 1970 (chapter 7) and (b) smoking prevalence has declined among asphalt workers over time (30). Inclusion of age and calendar period at exit may have partially adjusted for such "birth cohort" effects in the study. Information on the cigarette smoking habits of cohort members was not readily available, but can, potentially, be obtained in a nested case-control study from the next-of-kin or medical records.

Other sources of confounding in the study may be due to incomplete occupational histories for cohort members. This would occur if (a) they were exposed to carcinogens while employed outside of the asphalt industry or asphalt companies not recruited for the cohort and (b) there was a correlation between exposures to carcinogens from outside of the asphalt industry and bitumen fume. As a result, in current analysis we may be attributing to bitumen fume risk incurred due to exposure to another carcinogen or carcinogens.

It is also possible that in our analyses we did not completely adjust for coal tar exposure, owing to the fact that coal tar exposure was assessed in a fairly crude manner, without taking into account the amount of coal tar added to the asphalt mix. We have demonstrated in chapter 5 that the tar content of asphalt may vary considerably, producing a wide range of PAH exposures. To explore this issue further we need to model the health risks of bitumen exposure on a tar-free sub-cohort. However, a coal tar-free sub-cohort may have too little power for comprehensive exposure-response modeling (60 lung cancer deaths and 134,063 person-years).

Bitumen fume effects observed in our analyses can also be attributed to organic vapour or PAH, since exposures to these three agents were strongly correlated (chapter 7). Thus, our results implicate exposure to asphalt emissions as a whole, and not bitumen in particular, as a risk factor for lung cancer.

Conclusion

We found a positive association between average quantitative bitumen fume exposure and lung cancer mortality risk, lending support to the hypothesis of the carcinogenicity of bitumen fume in absence of coal tar exposure. This association must be interpreted through further analyses and/or a case-control study nested within the cohort, since it may be the result of confounding by other carcinogenic exposures and lifestyles. Duration of exposure and cumulative exposure were not associated with lung cancer mortality risk, weakening the evidence for carcinogenicity of bitumen fume. No clear latency model emerged from the analysis. Constructing quantitative exposure indices appeared to have been justified because (a) the healthy worker effect confounded any associations between duration of exposure and lung cancer mortality risk and (b) we identified statistically significant associations between bitumen fume exposure and lung cancer risk that require further investigation. Valid assessment of average exposure gains particular significance for analyses in which duration of exposure is confounded by the healthy worker effect and/or those analyses for which exposure intensity range is narrow (as is expected to be the case in future studies because occupational exposures continue to decline (31)). This may be especially true for studies with low expected relative risks that are likely to dominate occupational and environmental epidemiology in developed countries in the future (32).

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Chapter 9: General discussion.

I shall be telling this with a sigh
Somewhere ages and ages hence:
Two roads diverged in a wood, and I --
I took the one less traveled by,
And that has made all the difference.

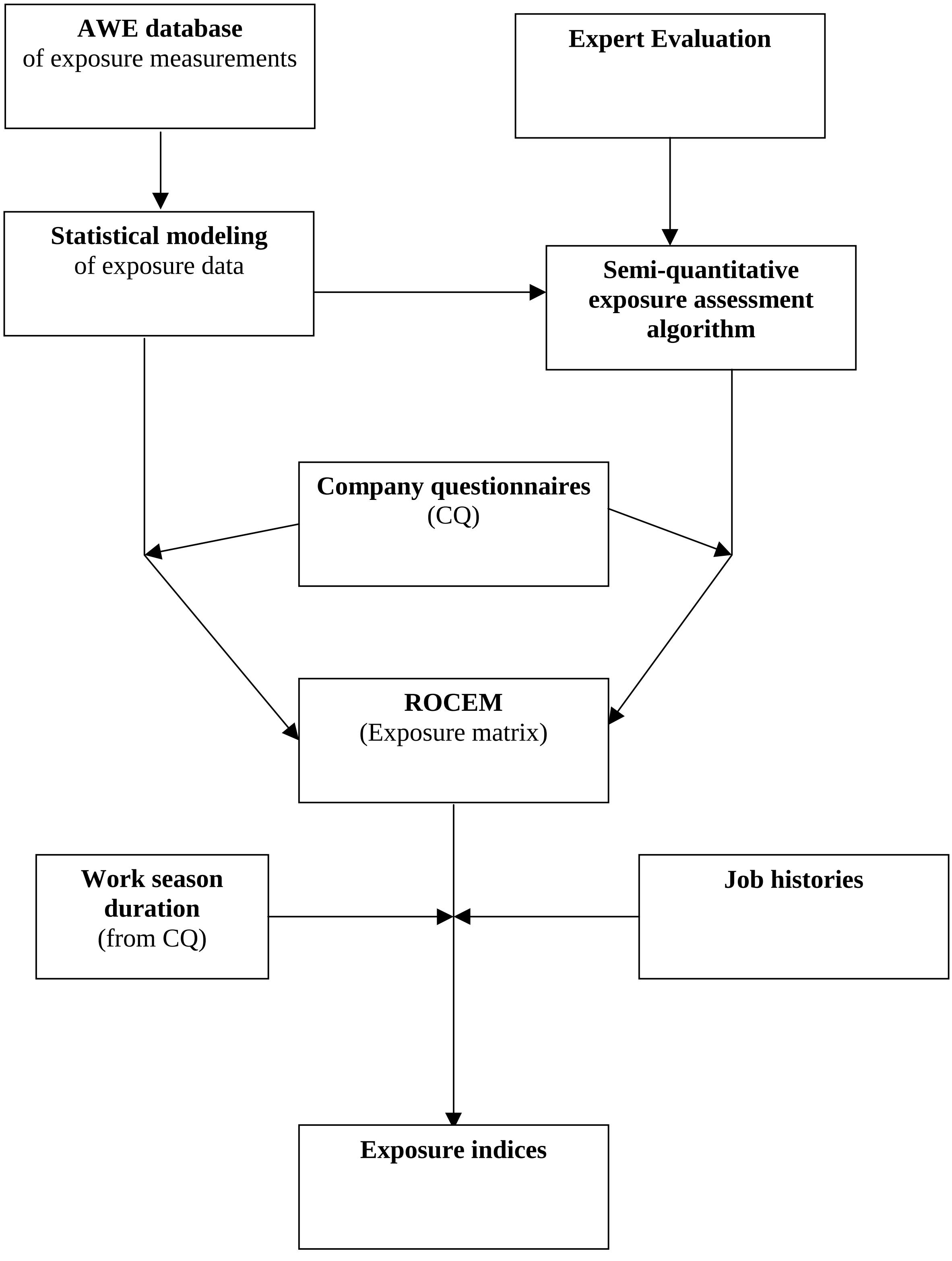
Robert Frost, "The road not taken", 1920

This investigation was launched to assess exposures as part of an epidemiological study of cancer risk due to bitumen exposure. In order to do so, we first reviewed the scientific literature on exposure levels and determinants of exposure in the asphalt industry. Since a literature review *per se* was deemed to be insufficient to assess exposures, we collected individual exposure measurements from the European asphalt industry into a common database. This database provided sufficiently comprehensive data to construct statistical models for exposure to bitumen fume, organic vapour and benzo(a)pyrene among pavers, the most numerous asphalt-exposed group in the industry. The database also supported estimates of time trends, effects of indoor work, and differences between key job classes that were used to derive semi-quantitative exposure estimates. When exposure measurements were not available, we resorted to evaluations by a panel of occupational hygienists to devise an algorithm for semi-quantitative exposure estimation. Statistical models and models based on expert evaluations were subsequently combined with information from company questionnaires to construct a study-specific exposure matrix. Major steps of exposure assessment are summarized in Figure 9.1. Performance of different exposure assessment approaches was evaluated in modeling a possible association between bitumen fume exposure and lung cancer mortality. In this concluding chapter, we will place this thesis into a broader context of methodological developments in exposure assessment. We will also devote more effort than in preceding chapters to presenting advantages and limitations of our methods. Lastly, we will try to draw lessons from our experience for other multicentric occupational cohort studies.

Role of literature review in exposure assessment

A review of published exposure reports may be helpful in reconstructing exposure (1), though some have found it to be of limited use (2). There has never been a formal evaluation of the usefulness of literature review in modeling exposures for international multicentric cohort studies, however literature review is a logical starting point for exposure reconstruction. Examination of published reports on exposure patterns in the road construction (asphalt) industry revealed that they were of limited usefulness in assessing exposure for the epidemiological study (chapter 2). This primarily arose from the diversity of methods employed in different surveys and formats in which investigators reported their results. In an attempt to overcome this, we assembled a database of individual exposure measurements in the asphalt industry (chapter 3). It was hoped that the newly acquired data would lead to better insights into patterns of exposure in the asphalt industry that may be helpful in reconstructing historical exposures.

Figure 9.1: Flow chart of main processes in exposure assessment for cohort study of cancer risk among European asphalt workers.



The literature review also helped us to define which agent we should endeavor to assess in the epidemiological study. Clearly, for a study of cancer risk we had to focus on exposures to known and suspected carcinogens. Furthermore, our strongest *a priori* hypothesis was of bitumen carcinogenicity to the lungs and respiratory tract, based on a literature review (3) and the evaluation of bitumen carcinogenicity by the International Agency for Research on Cancer (IARC) (4,5) . Therefore, first and foremost, we had to assess bitumen exposure in the study. Known and possible carcinogens, coal tar, polycyclic aromatic compounds (PAHs), asbestos, respirable silica and diesel exhausts were potential confounders (chapter 2). In this list, the definition of both bitumen and PAH exposures posed the greatest challenge. The chemical composition of bitumen itself and its emissions in the workplace are poorly understood. In absence of a chemical-specific marker for bitumen exposure, we hypothesized that total organic matter was an adequate measure of bitumen emissions. The semi-volatile nature of bitumen forced us to consider both bitumen fume (particles and droplets) and vapour as separate agents. Assessment of PAH exposure focused on 4-6 ring PAH, such as benzo(a)pyrene, that have traditionally been associated with carcinogenic activity (6). Other agents in asphalt work may also play a role in conferring cancer risk (e.g. sulfur-substituted compounds form recycled rubber, amines in emulsions, and vapours of diesel oil occasionally used as a slip agent), but absence of information on levels and determinants of their concentrations precluded their assessment. Dermal exposure was also not assessed due to scarcity of information on the subject.

Exposure databases

There is mounting evidence that it is possible to collect large numbers of occupational exposure measurements into a common database from many different countries (chapter 3)(7-11). The data in these databases comprise individual exposure measurements plus supplementary information that place these measurements into their correct context. One of the key elements in supplementary information is the identity of the monitored individual, which enables the identification of repeated exposure measurements within a person. Repeated measurements of full-shift time-weighted average exposure have been demonstrated to be of pivotal importance in using exposure measurement data in assessing exposures in an epidemiological study, because exposure concentrations were demonstrated to vary in time and from person to person (7,12,13). Thus, a single measurement of exposure cannot be considered representative of a person's and his/her co-workers' exposure. The data assembled into these databases was neither originally collected for the explicit purpose of storage in a central database, nor was it ever intended to be used for exposure assessment or determinants of exposure analyses. However, these databases have either been shown to produce (chapter 3)(7),(8,14) or have the potential (9) to produce important advances in our understanding of the temporal and spatial variability of occupational exposures. Most importantly, these databases play a crucial role in elucidating the magnitude of variability (7,8,15) and time trends (14,16,17) in exposure concentrations. They also make available to exposure assessors unpublished data, to which they otherwise would not have had access (9). For example, our database primarily contained data that was never before presented in the peer-reviewed scientific literature (chapter 3).

Given the importance of assembling exposure information into common databases, recognized by the American Conference of Governmental and Industrial Hygienists that organized a symposium on application of occupational exposure databases (18), it is imperative that this process is both facilitated and standardized. Contents of such databases have been a subject of extensive discussions (19). However, the practical steps to establishing databases of occupational exposure measurements have received little attention. In order to facilitate and standardize retrieval of complex exposure information (exposure measurement accompanied by supplementary information) we have developed a database management system (DBMS) that proved functional when used by researchers across Western Europe (chapter 3). We were first to describe vital elements of such a DBMS in occupational hygiene literature (see below and in chapter 3), though Ritchie and Cherrie (20) have independently reached the same conclusions. The key to a successful DBMS for creating international exposure databases is a balance between flexibility of database structure and rigor of logical checks of data quality. We produced a DBMS that aspired to achieve this balance. One of the greatest challenges in striking this balance was to anticipate what type of data might become available for entry into the database. Perhaps standardization of how exposure measurements were documented across jurisdictions may have helped alleviate this complication. However, such standardization should be undertaken with caution, avoiding the danger of stifling the creativity of the occupational hygienist, which is so vital to high-quality occupational hygiene surveys. Nonetheless, we have demonstrated that these complications can be overcome through close collaboration between data providers and managers of the DBMS, producing a valuable occupational hygiene resource (i.e. exposure database) in a timely manner with a relatively small investment of resources. Increasingly, it is becoming standard methodology to assemble occupational exposures into a common database prior to assessing exposures in international studies in occupational epidemiology (chapter 3) (9,11). We hope that this trend will persist, giving researchers the opportunity to lend exposure assessment greater credibility as a scientific endeavor.

Statistical exposure models: asphalt paving

Empirical exposure modeling

We were able to utilize exposure monitoring data to derive predictive models of exposure among asphalt pavers to three major agents of interest: bitumen fume, organic vapour and benzo(a)pyrene (proxy for carcinogenic PAH) (chapter 4). Statistical models are becoming a routine trick of the exposure assessor trade (21,22). They provide a good approach to summarizing exposure patterns, and utilize an explicitly defined statistical framework for predicting or retrospectively assessing exposures (in absence of a clear theoretical model for deterministic modeling). Methods of identifying determinants of exposure have undergone considerable development (23). They have been recently enhanced by easy access to the mixed effects modeling methodology through the introduction of SAS **proc mixed** (SAS Institute, Cary, NC, USA) (24-26). We have attempted to take advantage of these methodological developments, and were the first to apply mixed effects models in assessing exposure for a study in occupational epidemiology (chapters 3, 5 and 7).

One of the difficulties with applying regression models to assessing exposure, as it has been highlighted in recent reviews of exposure assessment methods (21,22), is the need to extrapolate exposure concentrations to situations for which no measurements are available. For this to affect our methodology, data used to construct the models would have to be non-representative of work practices in the epidemiological study. We have no evidence that this was the case in our study. However, such a possibility cannot be entirely excluded. Differences in sampling strategy, selection of persons and work-sites for monitoring, as well as variability in analytical methods may have affected validity of our model-based inferences. We have attempted to correct for the above factors in building the models, but the ultimate test of how successful we were came from model validation (see below and in chapter 6). We also observed that (a) the dynamic nature of paving complicates selection of "worst case" exposure situations, and (b) the small size of paving crews usually allows for measuring exposures of all crew members. These factors diminish the likelihood that sampling strategy was a significant source of bias. Another approach to investigating how representative our data was would be to compare the frequency of different exposure scenarios in the exposure measurement database to their occurrences in the industry. However, the required information on national patterns of production was not available. Correction for all of these possible sources of bias in the data and resultant models has rarely, if ever, been as thorough and scientifically rigorous as in the work of Seixas et al (27). This was made possible by the exceptional quality of supplementary information on methods and sampling strategy that were recorded alongside measurements of exposure concentrations. It is worth noting that such supplementary information was not collected for the express purpose of supporting exposure assessment in an epidemiological study, but rather to assess compliance. Nonetheless, even compliance monitoring data, viewed with the greatest suspicion by exposure assessors and epidemiologists, was reported to result in only 10-15% bias in exposure assessment (28).

The determinants of exposure that we used in exposure reconstruction were not necessarily the ones with the best ability to explain variability in exposure levels, but those that could have been ascertained retrospectively. Thus, area paved (29) and coal tar content of asphalt mix (chapters 5, 6), important predictors of exposure levels to bitumen fume and PAH, respectively, could not be ascertained retrospectively from firms enrolled in the cohort. However, what was not achieved in the cohort phase of the study might be possible in a nested case-control study design. This may be so, because in a nested case-control design, exposure assessment can be expected to focus on fewer subjects, allowing us to collect more detailed information on production circumstances.

One proposed solution to filling gaps in the knowledge that can be derived from exposure monitoring data has been to resort to expert evaluations, abandoning statistical modeling altogether. In extrapolation through statistical models, assumptions are explicitly stated and thus can be challenged in subsequent studies. On the contrary, expert evaluations can rarely be subjected to the same scrutiny because they contain hidden assumptions made by the assessors. Nonetheless, when no monitoring data is available, expert judgement or deterministic models remain the only options for the exposure assessor. However, obtaining information needed to apply deterministic models can be problematic in retrospective studies. In occupational epidemiology, the utility of stochastic models in reconstructing exposures in absence of monitoring data so far has not been evaluated in practice. As we gain more insight into the variability of exposure, stochastic modeling may become an option for exposure assessors.

We used statistical models to systematically reduce the number of possible determinants of exposure. We were forced to adopt this approach because exposure measurement data did not cover all circumstances of interest (firms, time periods, technologies). The ideal scenario, of having personal exposure measurements for all cohort members throughout their employment history will never be realized in studies of occupational epidemiology, although several studies approached this goal (30-32). It should be noted, however, that in one of these studies, a study of US coal miners, such an extensive exposure monitoring effort may not have been needed if patterns of exposure variability were first examined in a pilot study (32). We consider the approach of reducing determinants of exposure to the statistically and mechanistically important ones to be preferable because it has been demonstrated that such model-based exposure estimates provide less biased exposure estimates in situations common to occupational health studies (33,34). This is a consequence of exposures varying systematically both from day to day and from person to person. The number of measurements that is required for obtaining an unbiased estimate of long-term exposure for a person is, most of the time, too large to be feasible in most occupational exposure surveys. This is a consequence of the fact that in general, day to day variability in exposure exceeds between-worker variability in exposure (7). Therefore, an approach has been adopted in which a person's exposure is estimated from the measurements of other individuals, monitored in situations a given subject experienced but was not necessarily monitored.

Uniform exposure groups

Would we have been able to improve exposure assessment via an alternative approach, using more specific job titles or even tasks to form groups with similar exposures? Examination of these alternative groupings did not show improvements in contrasts between exposure groups (chapters 4, 5). This confirmed the appropriateness of the group-based exposure assessment that we employed for exposure reconstruction for the cohort (chapters 4 and 7). The discovery that crews of pavers were uniformly exposed to bitumen fume indicated that close examination of production conditions within each participating firm can lead to the substantial improvements in exposure contrast needed to achieve an efficient exposure assessment strategy. Identification of this elusive "crew factor" may be possible through future exposure surveys. Historical assessment of this "crew factor" may be possible in the nested case-control phase of the epidemiological study, if production records (e.g. bitumen source, bitumen hardness, area paved, etc.) come under closer scrutiny.

Model validation

In a key step of developing the exposure assessment protocol, we carried out both internal and external validation of the exposure models developed for asphalt paving workers (chapter 6). The possibility of differential misclassification was observed, but evidence for it being a serious problem depended on how common the use of asphalt with high coal tar content was in the cohort (chapter 6). Specifically designed exposure surveys or experiments can be conducted to further evaluate validity of the statistical models. Such studies would provide the most severe test of our statistical models.

Implications for epidemiological analyses

Confounding

A factor distorts (confounds) an association between a health outcome and an exposure of interest in an epidemiological study if (a) it is correlated with the exposure of interest and (b) is itself a risk factor for the health outcome, but is not an intermediate step in the causal pathway from exposure to disease (35). Confounding may lead to mistaken identification of a risk factor merely due to its correlation with an "unmeasured" or "unknown" causal agent. Previous studies have already established that asphalt workers were at elevated risk of lung cancer compared to the general population (3). Coal tar (a human carcinogen according to

IARC) has been used in asphalt paving in the past in Western Europe alongside with bitumen (chapter 2). Therefore, coal tar exposure is one of the main potential confounders of any association between bitumen fume exposure and cancer risk (3). Consequently, the major objective of the study was to disentangle the effects of bitumen from those of coal tar in an attempt to clarify whether observed excess risk was due to bitumen fume or other known carcinogens. Examination of the contents of the exposure matrix indicated that we were be able to reach this objective (chapter 7). We have demonstrated that bitumen fume exposure concentration and frequency of coal use were only weakly correlated (chapter 7). This implies that coal tar exposure is not likely to confound estimates of risks associated with bitumen fume exposure. This is a result of the discontinuation of coal tar use in most paving operations in Western Europe, resulting in a substantial portion of asphalt workers in the cohort being exposed to bitumen, but not coal tar. Exposures to respirable silica, asbestos and diesel exhaust were not correlated with estimated bitumen fume exposure (chapter 7), implying that exposures to these carcinogens (chapter 2) are not likely to confound cancer risks due to bitumen fume.

Other potential confounders considered in the study were 4-6 ring carcinogenic PAH (such as benzo(a)pyrene) and organic vapour (both of bitumen and non-bitumen origin). We have observed that estimates of exposure to PAH, bitumen fume and organic vapour were highly correlated, implying that were unable to attribute health effects to bitumen *per se* (chapter 7). We were also unable to differentiate between cancer risk due to 4-6 ring PAH from bitumen and non-PAH bitumen components. Likewise, we could not differentiate between cancer risk from organic vapour (of bitumen and non-bitumen origin) and bitumen fume.

The contribution of a dermal route to bitumen dose has not been assessed in this study due to (a) the lack of appropriate historical monitoring data (chapter 3) and (b) the absence of information on the contribution of dermal absorption of bitumen condensate to total bitumen dose in asphalt industry. However, dermal exposure has been shown to be important in studies of other occupational carcinogens (36-38). Thus, dermal exposure to bitumen may act as a confounder of the association with assessed inhalation exposure, if different ranking of bitumen exposure (and dose) can be obtained on the basis of dermal and inhalation exposures. This is clearly an area that requires further research, especially since there is some evidence of dermal exposure to organic matter in the asphalt industry (chapter 2)(29).

Other potential confounders not considered in the epidemiological study are (a) lifestyle factors (e.g. cigarette smoking (39), (b) environmental carcinogen exposures (e.g. radon (40)), (c) occupational carcinogen exposures outside of a subject's employment in asphalt industry and (d) occupational carcinogen exposures in asphalt firms not included in the cohort. For example, if cigarette smoking, as an established risk factor for lung cancer (39), was not equally frequent in all exposure groups, it could produce a distortion of any exposure-response relationship in the cohort. Information on the cigarette smoking habits of cohort members was not readily available, but can potentially be obtained in a nested case-control study from the next-of-kin or medical records. We also do not have data on other confounders, but it may be possible to assess these in a nested case-control study.

Bias due to errors in estimates of exposure intensity

The estimates of exposure intensity for different scenarios can be biased. This would arise if statistical models of exposure were biased. We have demonstrated that the statistical models of exposure to bitumen fume, organic vapour and PAH among pavers were mostly free of bias (chapter 6). Models developed for assessment in job classes other than paving (inter- and intra-job class multipliers) were based in part on exposure data, but were mostly derived from a set of assumptions agreed upon by occupational hygienists conducting the study (chapter 7). These multipliers are the weakest link in the semi-quantitative estimates of exposure intensity. Bias in exposure intensity estimates for exposures that occurred prior to the 1970's are also subject to greater uncertainty because of lack of exposure data from that time. Lack of exposure measurements for the pre-1970 time period also forced us to assume no time trends in exposure intensity before the 1970's, but this can not be verified empirically.

Bias due to errors in estimates of exposure frequency from company questionnaires

The second source of bias can arise from errors and inaccuracies in the company questionnaires. Company questionnaires may contain errors both due to the responder's lack of qualifications to answer certain questions or questions being misunderstood. To minimize this problem, all company questionnaires were reviewed for logical inconsistencies and re-evaluated during a meeting of experts from each country. Extensive consultations were also conducted with national collaborators to clarify the meaning of questions. The design of the company questionnaire was based on a questionnaire used in the Finnish component of the study, after extensive consultations with asphalt industry representatives. Nonetheless, two major problems with the company questionnaires became apparent in the course of the study.

First, questions about frequency of use of material such as coal tar or frequency of a specific task (e.g. surface dressing) were ambiguous. Were the questions about proportion of the work force or proportions of time spend by a typical individual? For example, if 10 persons out of a 100 employed in paving worked full-time with coal tar, frequency of coal tar use would be 0.1 (situation A). On the other hand, if all 100 pavers spent on average 1 day out of 10 working with coal tar, they also would have been assessed as having had coal tar use with frequency of 0.1 (situation B). Clearly, in situation A only 10% of persons ever used coal tar, while in situation B 100% of persons used coal tar. We had no other choice but to interpret such questions as if they referred to frequency of person-time devoted to task or contact with material. Consequently, the two situations should have been assigned the same exposure. For a disease without "no observable effect level" in exposure-response analysis, at group level in both situations we should expect the same risk. However, for disease with a "no observable effect level", the two situations may well be associated with different group-level risks, producing exposure misclassification if both situations are treated equally in exposure response analysis. This type of question, therefore, was unnecessarily ambiguous. It would have been better to split the questions about frequency of material use or task performed into two: (a) about proportion of persons affected and (b) proportion of time the affected persons worked with the material or in the task.

The second problem with company questionnaires was that they were designed before the rest of the exposure assessment protocol was fully developed. Consequently, the original company questionnaires collected from the majority of firms were missing a number of key questions required for exposure estimation, and on the other hand contained a lot of questions that were never used in exposure assessment. This became apparent only after the analysis of exposure measurement data (chapter 4). We attempted to remedy this during a second round of company questionnaire evaluation by experts from each country. This could have produced errors because we could no longer guarantee that persons most familiar with the firms supplied the answers.

Thirdly, company questionnaires split the history of production conditions into pre-set five-year blocks. The exceptions to this rule were in that the exact years of discontinuation of coal tar and asbestos use were solicited for each job class. This approach was adopted under the assumption that production conditions were constant within each time block. It would have been preferable to obtain a more accurate description of how production conditions changed in the past (on a yearly basis), but it was not considered feasible in the cohort design. Again, this source of error might be eliminated in a nested case-control study by focusing on the job histories of individuals most informative for risk estimation.

We also had to consider a trade-off between precision and bias in answers supplied in company questionnaires. This discussion arose from the fact that some countries (Sweden and France) supplied only one questionnaire that was supposed to represent working conditions across these countries. In France only one firm was recruited (albeit consisting of many sub-divisions spread all over the country), while in Sweden one company questionnaire was compiled to represent all Swedish firms because they were judged to be all similar. In contrast, questionnaires from individual firms and for large companies, from their subdivisions, were obtained from the rest of the cohort. The primary rationale for the Swedish and French approach was that one representative questionnaire provided unbiased information for that country, resulting in unbiased exposure estimates on a group (country) level. However, such estimates can be expected to be very imprecise, since we observed large within-country variability in answers obtained from other countries. At the same time, answers to a questionnaire obtained from particular firms and sub-divisions of firms may have been more biased when a respondent was not very familiar with the history of production conditions in a particular firm or sub-division. We have no evidence that obtaining numerous questionnaires from within each country leads to more biased exposure estimates. However, loss of precision can substantially undermine our ability to elucidate exposure-response associations. In fact, it has been recently argued that small bias is a fair price to pay for increased precision in statistical estimates (41,42). Therefore, we recommend that in the future studies the collection of one questionnaire to characterize production conditions in an entire country should be abandoned.

Bias due to exposure assignment: Linking the exposure matrix to job histories

An additional source of error is likely to appear in linking the exposure matrix to the job histories. Study subjects may have been allocated to incorrect job classes, and duration of their work in each job class may have been recorded with error. This error in duration of work can be especially troublesome due to the seasonal nature of asphalt and road construction work with working season varying from year to year and in response to changes in paving technology and weather. It is not clear that our data will adequately record this seasonal nature of the work of cohort members. However, we attempted to address this problem in estimation of the duration of exposure (employment) by weighting each complete calendar year of employment by the duration of working season and leaving each incomplete calendar year in employment un-weighted. However, the accuracy of this approach was judged to be limited. An alternative method of obtaining exact start and end dates of work for each year of employment may be used in a case-control study to improve accuracy of exposure assignment.

Grouping exposure estimates

Exposure assessment can be defined as "the process of estimating exposure levels through measurement, modeling, and other procedures." (43) Exposure assignment, on the other hand, is the result of applying the results of exposure assessment to computing exposure indices for epidemiological analysis (43). We have discussed numerous sources of errors in exposure estimation and assignment procedures. Errors in quantitative exposure intensity estimates may lead to biased exposure estimates for individual subjects in the cohort (chapter 6). In order to alleviate this problem, we employed group-level exposure assessment in exposure-response modeling. The likelihood of error in the quantitative exposure intensity estimate at group level should be substantially smaller (chapter 6). The same is likely to apply to semi-quantitative exposure estimates as well, though we did not evaluate their validity. Grouping of exposure estimates occurred at three sequential levels. At the first level, exposure measurements were pooled to estimate exposures for a number of exposure scenarios by using mixed effects models (chapter 4). At the second level, exposures for an average person described by a company questionnaire were estimated (chapter 7). This second level of grouping was achieved in construction of the exposure matrix. The first two levels of grouping were analogous to exposure assessment conducted in a study of pig farmers (33,44). If group-level estimates were unbiased, we would expect that when applied in exposure-response modeling they would produce unbiased exposure-response slopes with inflated errors (34,45). However, if group-level means were biased, exposure-response relationships would be attenuated (45). Such attenuation due to grouping may also occur under certain relative magnitudes of variance components, but such conditions are likely to be uncommon in occupational epidemiology (34).

On the third and final level, individual exposure estimates obtained from application of the exposure matrix to job histories (e.g. by calculating cumulative and average exposures) were grouped to form exposure categories for epidemiological analyses (chapter 8). Grouping was based on allocating the same number of lung cancer cases to each non-zero exposed exposure category. The zero-exposed category was always kept separate as a reference group. This served to satisfy the requirements of the statistical technique used to model exposure-response relationships (Poisson regression) (46,47). Exposure assignment carried out at this level and subsequent grouping does not reduce attenuation in an exposure-response relationship (43), because it does not produce a Berkson-type error structure that aggregates exposure estimates around an *a priori* identified unbiased mean value (45) [1]. Instead, on the third level groups were formed from values that may well have belonged to different underlying distributions, thereby producing biased group means that carry the same error structure (and exposure misclassification) as individually assigned exposure estimates. However, in presence of clear multi-modality, such as exposed and unexposed groups, appropriate grouping of assigned exposure estimates reduces non-differential exposure misclassification. Thus, opportunities to reduce attenuation of exposure-response association by producing Berkson-type error structure appear to lie in exposure *assessment*, not in the subsequent exposure *assignment* and exposure-response modeling.

Bias in exposure assessment: concluding remarks

Though we have no evidence that any of the sources of bias described above would produce differential errors, that possibility cannot be excluded. This is especially true for errors in

[1] pre-defined means in the theorem proven by Dr. J. Berkson

answers to company questionnaires, because a respondent can be expected to either consistently over- or under-estimate the frequency of key tasks that lead to "high" or "low" exposures. In collecting company questionnaires, we had no mechanism to ensure that the respondent was familiar with the firms' operations for the entire period of interest (in most cases, its entire existence). Therefore, for each company, the directionality of such bias might be different for different time periods assessed, depending on the impressions of a respondent of whether things were 'better" or "worse" in the past. As described above, study subjects were pooled across time periods, companies and countries to form exposure groups for epidemiological analyses. This implies that estimates with different directions of bias are likely to be aggregated into the same group. Consequently, this directionality of bias might result in diluted exposure-response relations. However, we cannot predict what bias, if any, may be present in the exposure-response analyses.

As in many studies, we cannot predict with certainty either the direction or magnitude of bias in exposure estimates and the resultant exposure-response associations. However, we have done our best to identify sources of possible biases. It would appear that the most immediate reduction in bias from exposure assessment procedure could be achieved by improving our knowledge of the job histories of study subjects and histories of production in various companies.

Selection of exposure indices in exposure-response modeling

In chapter 8 we compared the performance of different assigned indices of exposure in exposure-response modeling of lung cancer mortality risk and bitumen fume exposure. A downward trend, though not statistically significant, in the risk of lung cancer mortality was observed with increased duration of employment as a paver. This is symptomatic of the "healthy worker effect" whereby healthier individuals remain employed longer. However, such an effect has been reported to be weaker for cancer than for any other cause of death (35). The healthy worker effect, governing the relationship between duration of exposure and lung cancer mortality, is likely to confound association between lung cancer mortality and cumulative exposure. This is probably at least in part due to the fact that average exposure intensity spanned a narrower range of values than duration of exposure. Consequently, cumulative exposure was more determined by duration of exposure than by its intensity.

Models with average exposure index better explained lung cancer mortality risk than models with cumulative and duration indices (chapter 8). They suggested a positive association between the risk of lung cancer mortality and average bitumen fume exposure. Such patterns for chronic diseases have been observed in other occupational cohorts (and for other carcinogens), but the cause of such patterns is poorly understood (48,49). Difficulty with interpreting a model that shows an association between risk of lung cancer mortality and average exposure is that it implies, unrealistically, that exposure for any length of time (within the range of the data) at the same exposure level confers the same relative risk. Both better methods for controlling for healthy worker effect and better understanding of mechanism of possible bitumen carcinogenesis may lead us to the ability to model a more biologically plausible relationship between lung cancer risk and cumulative exposure (50,51).

Selection of latency model

Analyses performed in chapter 8 allowed us to examine the influence of latency assumptions on exposure response modeling in the study. Exposure indices both without lag and with 15-

year lag were considered. As indicated by model fit tests, neither latency model considered in this investigation appeared to outperform the other. In order to develop a better latency model, we may need to perform time-windows analysis, to explore the possibility that exposures in different time windows may confound one another (52). In such analyses, the contribution of lagged exposure (say, by 15 years) to change in risk of health outcome can be adjusted for an exposure that occurred 15 years prior to the outcome. The validity of the use of the strength of exposure-response association *per se* in selecting an optimal time-window model has recently been called into question (53,54) amid suggestions that in latency analysis an incorrectly specified model may lead to differential bias in exposure estimates (54). Thus, given the declining time trend in exposure intensity (chapter 7), for average exposure, if the lag was too long, biologically effective exposure would be overestimated, and if the lag was too short, biologically effective exposure would be underestimated. The opposite should hold for duration of exposure (and duration-driven cumulative exposure): if the lag was too long, biologically effective exposure would be underestimated; if the lag was too short, biologically effective exposure would be overestimated. Differential underestimation of exposure can be expected to produce overestimation of an exposure-response relationship. Conversely, differential overestimation of exposure can be expected to produce underestimation of an exposure-response relationship. In practice, as in our data, it might be very difficult to distinguish between a well-specified latency model and bias due to differential exposure misclassification produced by lagging. Model fit, measured by the log-likelihood ratio test, has been suggested to overcome these complications in differentiating between competing latency models (53), but more research is needed to develop practical guidelines for resolving these difficulties (54).

Challenges of conducting an international multicentric cohort study of small-to-medium size enterprises

The present study is unique in that it attempted to reconstruct exposures in small to medium-sized companies dispersed over a large geographic area. This would present a formidable challenge even in the absence of the international dimension of the study, and might be the reason why so many large-scale epidemiological studies are often conducted in large firms. One of the challenges we faced was limited documentation of past production conditions in small firms (55). Small firms also tend to lack their own staff occupational hygienists and exposure measurements. In addition, firms enrolled in the study often changed ownership or were acquired by other firms, disputing the continuity of record keeping of exposure-related information. This factor also probably contributed to erosion in the continuity of knowledge of past production conditions by engineers and managers, the persons responsible for completing the company questionnaires. Another complication is that small firms may have limited resources and manpower to devote to liaison with researchers. Despite fruitful and extensive collaboration with the asphalt industry at national levels, this may not have been sufficient to acquire accurate information of consistent quality from each company. Not only were the studied firms predominantly small in size, they also performed mostly outdoor work in locations spread over vast geographical areas. This implied both great diversity of working conditions and inability to apply the rigid division into exposure zones traditional for factory-based exposure assessments (56). These factors produced greater challenges than those encountered in exposure assessment for studies conducted by IARC in more traditional industries consisting of large firms (57-61).

Future of exposure assessment in multicentric international studies in occupational epidemiology

Occupational epidemiology has been successful in identifying causes of cancer that originate from workplace exposure (62). However, some subgroups, such as small businesses, have not been extensively studied by occupational cancer epidemiologists (62). It is also likely that outsourcing and automation will continuously reduce the size of the workforce in firms that have been traditionally seen as "large" enterprises. Likewise, the need for quantitative risk assessment and identification of specific causative agents have highlighted the importance of exposure assessment based on personal exposure measurement data. Valid and precise estimation of exposures is also likely to play a central part in identifying new carcinogens in the future because "strong" risk factors have already been identified, leaving occupational and environmental epidemiologists with the challenge of discovering and characterizing "weak" associations (63). Therefore, it has been claimed that the future of occupational epidemiology lies, at least in part, in studies of small firms and in refining exposure methods, both in terms of assessing validity of exposure estimates and in understanding the sources and magnitude of variability in exposures (62). Furthermore, case-control designs are making a comeback in occupational epidemiology as the design of choice for studies of workforces employed in small companies (62).

Skepticism about the possibility of achieving high quality quantitative exposure assessment in international multicentric studies of occupational hazards is reflected by exposure assessment methodology applied in other occupational cohort studies conducted by the International Agency for Research on Cancer. In an ongoing study of pulp and paper industries, exposure reconstruction was carried out using expert evaluations supported by descriptions of production processes and exposure measurement data (Dr. T. Kauppinen, personal communications). In that study, exposure data was not used to construct statistical exposure models. Experimentally derived multipliers have been used in an international study of cancer risks of inhaling man-made mineral fibers in the European insulation wool industry in order to extrapolated from current to past exposure levels (57). However, the same study primarily relied on expert judgement and detailed interviews with plant management to reconstruct historical exposures (58), although the process was structured and thoroughly documented (59). In a study of cancer risk among European welders, "quantitative estimates were derived from consultation of literature sources and of some company data", relying primarily on the judgement of experts to reconstruct exposures (60). In a retrospective exposure assessment for an IARC cohort exposed to phenoxy herbicides, chlorophenols and dioxins, investigators relied on a combination of expert judgement, literature review and application of deterministic source-receptor models to reconstruct exposures (61). None of the four studies described above attempted to develop statistical models to reconstruct exposures, although all of them retrieved or could have retrieved large and comprehensive sets of exposure measurements. Our work indicates that it is possible to accomplish data-driven quantitative and semi-quantitative exposure assessment, with minimal reliance on expert evaluation of factors that affect exposure, in an international multicentric epidemiological study.

We accepted the challenge of Stewart and colleagues (21) that "… historical exposure assessment requires an opportunistic approach, taking advantage of what information is available and developing creative and innovative approaches to exploit that information". We have also followed the recommendation to be explicit about the quality and quantity of information used in exposure assessment (21). Our work also rests heavily on the shoulders of another review of methodological developments in the field of retrospective exposure assessment carried out by Seixas and Checkoway (22). In meeting these challenges and attempting to fulfill these recommendations lies the future of exposure assessment in multicentric international epidemiological studies. The future of exposure assessment in these epidemiological studies is in the transfer of experience and methodological lessons learned in smaller national or firm-based studies. Conversely, if quantitative exposure assessment is possible, as we have demonstrated, in the "worst case" scenario of a multicentric international epidemiological study, than surely it is well within the realm of possibility of smaller studies. Therefore, our experience should give hope to exposure assessors struggling to produce quantitative exposure estimates in studies of all scopes and sizes. However, unearthing and accessing sufficient data for quantitative exposure assessment often requires international collaboration, implying that we might be able to attain a better quality of exposure assessment in large international studies than in smaller national- or firm-based ones. This is contrary to the dominant thinking in the field. This emphasizes that it is worth collecting detailed information about workplaces in international multicentric epidemiological studies because it is possible to obtain high quality estimates of exposure intensity, which can be translated into accurate exposure estimates for cohort members if enough is known about their job history. However, it may be worthwhile to invest into reconstructing detailed occupational histories only in nested case-control study designs. Thus, aspirations and opportunities for high-quality exposure assessment should not depend on study size. The quality of exposure assessment, first and foremost, depends on effective application of new and existing quantitative exposure assessment methods. The sophistication of these methods is approaching a point where exposure assessment can cease to be the Achilles' heel of even the most challenging of occupational cohorts.

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Summary

There is a long-standing controversy about the health effects of fumes and vapors generated during paving and waterproofing with bitumen-based materials. There is some evidence that such fumes may have be causally related to both acute and chronic health effects. The International Agency for Research on Cancer (IARC) evaluated the carcinogenicity of bitumens in 1985 and 1987. It classified steam-refined and air-refined bitumens as possible human carcinogens (IARC Group 2B). However, evidence for the carcinogenicity of undiluted bitumens was inadequate (IARC Group 3). The main uncertainty in evaluation arose from the inability to exclude the possibility of exposure of pavers and roofers to both coal tar (a recognized carcinogen) and bitumen. With coal tar use voluntarily discontinued by the asphalt industry in Western Europe, industry, regulators, scientists and government agencies received an opportunity to learn whether it is likely that bitumen exposure *per se* is carcinogenic. As a result, a historical multicentric cohort of asphalt workers was assembled by IARC in eight countries (Denmark, Finland, France, Germany, the Netherlands, Norway, Sweden and Israel). Assessment of historical exposures to known and suspected carcinogens (bitumen, organic vapour, coal tar, respirable silica, diesel exhaust, and asbestos) in the cohort became the main objective of this dissertation.

As the first step in reconstructing exposures among European asphalt workers, I reviewed published reports on exposures in the industry (chapter 2). The majority of firms enrolled in the cohort were expected to be involved in road construction, therefore this subset of asphalt workers became the focus of the literature review. Workers in the road construction industry include asphalt plant workers, ground construction workers and road paving workers. These individuals can be exposed to a wide range of potentially hazardous substances. A summary of levels of exposure to different substances measured during road construction was presented. Modern road paving workers are typically exposed to 0.1 to 2 mg/m^3 of bitumen fume, which includes 10 to 200 ng/m^3 of benzo(a)pyrene. Sampling strategies and analytical methods employed in each reviewed survey were briefly described in the chapter. The published reports provide some insight into the identity of factors that influence exposure to bitumen among road construction workers: type of work performed, meteorological conditions, and temperature of paved asphalt. However, there was a lack of (a) comprehensive and well-designed studies that evaluate determinants of exposure to bitumen in road construction, and (b) standard methods for bitumen sampling and analysis. Information on determinants of other exposures in road construction was either absent or limited. I concluded that data available through published reports have limited value in assessing historical exposure levels in road construction industry.

Because published literature did not contain sufficient data for historical exposure assessment, I set out to collect individual exposure measurements from both published and unpublished studies of the European asphalt industry (chapter 3). Thus, I endeavored to construct a database of exposure measurements, which would be used to retrospectively assess the intensity of various exposures in an epidemiological study of cancer risk among asphalt workers. The database was developed as a stand-alone Microsoft Access 2.0 application, which could work in each of the national centers. Exposure data included in the database comprised measurements of exposure levels, plus supplementary information on production characteristics which was analogous to that used to describe companies enrolled in the study. The database was successfully implemented in eight countries, demonstrating flexibility and data security features adequate to the task. The database allowed retrieval and consistent coding of 38 data sets, of which 34 have never been described in peer-reviewed scientific literature. I was able to

collect most of the intended data. As of February 1999 the database consisted of 2007 sets of measurements from persons or locations. The measurements appeared to be free from any obvious bias. The methodology embodied in the creation of the database can be usefully employed to develop exposure assessment tools in epidemiological studies.

Once the database of industrial hygiene measurements in the asphalt industry was constructed, I used it to created models of bitumen fume, organic vapour and polycyclic aromatic hydrocarbons (PAH) exposure intensity among paving workers, the most numerous bitumen-exposed group in the cohort (chapter 4). Individual exposure measurements from pavers (N=1581) were available from all countries enrolled in the study. Correlation patterns between exposure measures were examined and factors affecting exposure were identified using statistical modeling (mixed-effects models). Inhalable dust appeared to be a good proxy of bitumen fume exposure. Bitumen fume and organic vapour levels were not correlated. Benzo(a)pyrene level appeared to be a good indicator of PAH exposure. All exposures steadily declined over 20 years prior to 1997. Mastic laying, re-paving, surface dressing, oil gravel paving and asphalt temperature were significant determinants of bitumen fume exposure. Coal tar use dictated PAH exposure levels. I concluded that for paving workers, exposure intensity could be reconstructed quantitatively on the basis of time period and production characteristics.

Having constructed predictive models of exposure among pavers (chapter 4), I explored whether alternative exposure intensity assessment schemes may have produced more optimal exposure grouping for epidemiological analyses (chapter 5). In order to achieve this objective I investigated whether a crew of paving workers is uniformly exposed to bitumen fume, organic vapour and benzo(a)pyrene. Uniformly exposed groups form the ideal unit for exposure assessment and risk evaluation, because all persons within a uniformly exposed group have the same exposure and can be easily contrasted with members of other uniformly exposed groups. Data on paving workers with up to six repeated exposure measurements were extracted from the database of exposure measurements (chapter 2, N=591). The uniformity of exposures to bitumen fume, organic vapour and benzo(a)pyrene was evaluated while grouping individuals by job titles, primary tasks, crew membership and use of coal tar. The estimated ranges within which 95% of individual mean exposures were expected to fall ($_{BW}R_{0.95}$) were used to assess exposure uniformity. Variance components were estimated by constructing mixed effects models, with grouping variables as fixed effects and worker identity as a random effect. The influence of duration of sampling campaign on estimates of exposure variability for a crew was also examined. I found that there was substantial variability in exposures between paving crews, as well as persons holding the same "job" or doing the same "task", but each crew was uniformly exposed to bitumen fume and benzo(a)pyrene ($_{BW}R_{0.95}$ 2 and 1, respectively). However, workers within one and the same crew engaged in paving with coal tar-containing binders were not uniformly exposed to benzo(a)pyrene. Also, organic vapour exposures were not uniform among the members of a paving crew ($_{BW}R_{0.95} = 15$). Sampling campaigns of up to seven months had little impact on the estimates of within- and between-worker variability. These findings support the notion that only empirically determined predictors of exposure can yield optimal grouping, unlike *a priori* grouping strategies based on general descriptors such as jobs held or tasks performed. Finally, it was observed that on the basis of the available data, I could not produce more uniform exposure groups by employing different exposure models than those described in chapter 4.

Model validation is one of the key steps in developing any statistical model. Therefore, chapter 6 was devoted to investigation of validity of empirical models of exposure developed in chapter 4. Internal validity was assessed in a cross-validation procedure. External validity was evaluated using data not used to develop the original models. For bitumen fume and benzo(a)pyrene, the correlation between observed and predicted exposures was examined. I observed that all models were internally valid but imprecise. Predicted bitumen fume exposures tended to be lower (average factor of 3) 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 the external validity of the benzo(a)pyrene exposure model revealed a similar to expected effect of re-paving and a larger than expected effect of tar use. Overall, benzo(a)pyrene models underestimated exposures by 51%. I concluded that possible bias due to underestimation of the impact of coal tar on benzo(a)pyrene exposure levels must be explored in sensitivity analysis of the exposure-response relationship. Validation of the models, albeit limited, increased our confidence in their applicability to exposure assessment in the historical cohort study of cancer risk among asphalt workers.

After statistical models of exposure were developed (chapters 3-6), I applied them to the creation of an exposure matrix for known and suspected carcinogens for a multi-centric international cohort study of asphalt workers (chapter 7). Procedures were also developed for semi-quantitative estimation of exposure for (a) cohort members not employed in paving and (b) agents for which few or no exposure measurements were available (chapter 7). Production characteristics in the companies enrolled in the study were ascertained via a questionnaire and consultations with industry representatives and industrial hygienists. Exposures to bitumen fume, organic vapour, PAH, diesel fume, silica and asbestos were assessed semi-quantitatively using company questionnaires and expert opinions on relative exposure intensities. Quantitative exposure estimates for road paving workers were derived by applying regression models (chapters 2, 3) to exposure scenarios identified by company questionnaires. Frequency of coal tar use was derived directly from the questionnaires. All estimates were standardized to an 8-hour work-shift. The resulting exposure matrix was time period-, company- and job class-specific. Most of 203 firms from eight countries enrolled in the study were engaged in asphalt paving (51%) and mixing (94%). Coal tar use was most common in Denmark and the Netherlands, but its frequency has declined dramatically since between 1960 and early 1970's; the practice is now obsolete in the studied countries. The highest bitumen fume, organic vapour and PAH exposures were assessed among roofers and waterproofers. The exposure matrix assessed a non-monotonic historical decrease in exposures to all agents except for silica and diesel exhaust. The modeled bitumen fume and coal tar exposures were moderately correlated, with the highest correlation for the pre-1960 time period. There was a very strong correlation among bitumen fume, organic vapour and PAH exposures. Upon examination of the elaborated exposure matrix, it was concluded that it will not be possible to distinguish among the health risks associated with bitumen fume, organic vapour and PAH exposures. Furthermore, I observed that adjustment of risk estimates for coal tar exposure should be possible. The quality of company questionnaire information was the weakest point of constructing the exposure matrix. My approach produced a data-driven exposure matrix that can be challenged in future studies and easily re-estimated.

Having constructed a study-specific exposure matrix (chapter 7), I evaluated the performance of different exposure assessment and assignment approaches based on the outcome of the analysis of the hypothesized relationship between bitumen fume exposure and lung cancer mortality (chapter 8). Three exposure indices were considered: duration of exposure (years), average exposure (mg/m^3) and cumulative exposure (mg/m^3*years). In estimating exposure duration I had to make corrections for the seasonal nature of asphalt work, which was not reflected in job histories of cohort members. This was achieved by using a crude estimate of the duration of the paving season supplied by each firm in the company questionnaire. Two latency models were considered for the association between lung cancer and bitumen fume: with and without 15-year lag. I examined rank correlation among bitumen fume exposure indices. Relative risk associated with bitumen fume exposure was estimated via Poisson regression. All models were adjusted for coal tar exposure (ever/never), age, calendar period and country. Exposure-response models were compared using a log-likelihood ratio test (measure of model fit). I selected 12,367 male workers employed only in asphalt paving for at least one paving season for analysis. In this sub-cohort, there were 134 deaths due to lung cancer. Only exposure ranks based on strata of duration and cumulative exposure indices were correlated. There was no association between lung cancer risk and either duration or cumulative exposure. However, there was a suggestion of an increase in lung cancer risk accompanying rise in average exposure. Only models with average bitumen fume exposure (with or without lag) markedly improved model fit. Average bitumen fume exposure indices with and without 15-year lag improved model fit to the same extent. In conclusion, I found a positive association between average bitumen fume exposure and lung cancer mortality risk. This association can be a result of confounding by other carcinogenic exposures and lifestyles. No clear latency model emerged from analysis. Constructing quantitative exposure indices appeared to have been justified because (a) the healthy worker effect confounded any associations between duration of exposure and lung cancer mortality risk and (b) I identified statistically significant associations between bitumen fume exposure and lung cancer risk that require further investigation. Many of the unresolved issues in the cohort analysis may be remedied in a nested case-control study.

Samenvatting

Over de gezondheidseffecten van blootstelling aan dampen en gassen, die vrijkomen bij asfalteren, dakbedekken en waterdichtmaken met bitumen bestaat geen eenduidig beeld. Er zijn aanwijzingen dat dergelijke dampen en gassen causaal gerelateerd zijn aan zowel acute als chronische gezondheidseffecten. Het International Agency for Research on Cancer (IARC) evalueerde de carcinogeniteit van bitumen in 1985 en 1987. Het classificeerde stoom-geraffineerde en lucht-geraffineerde bitumen als mogelijk humaan carcinogeen (IARC Groep 2B). Echter de bewijslast voor de carcinoginiteit van niet-bewerkte bitumen was ontoereikend (IARC Groep 3). De voornaamste onzekerheid kwam voort uit het feit dat de mogelijkheid van gelijktijdige blootstelling aan koolteer (een bewezen carcinogene verbinding) bij asfalteerders, dakbedekkers en waterdichtmakers niet uit te sluiten was. Nadat de asfaltverwerkende industrie in West-Europa vrijwillig was gestopt met het gebruik van koolteer ontstond een situatie waarin de industrie, regelgevers, wetenschappers en regeringsinstanties de kans kregen om te onderzoeken of de blootstelling aan bitumendampen op zich carcinogeen is. Dit heeft geresulteerd in een historisch cohortonderzoek onder asfaltwerkers in acht landen (Denemarken, Duitsland, Finland, Frankrijk, Nederland, Noorwegen, Zweden en Israël) onder leiding van het IARC. Het karakteriseren van de historische blootstelling aan erkend en verdacht carcinogenen (bitumendampen, organische gassen, koolteer, respirabel silica, dieseluitlaatgassen en asbest) van alle werknemers in het cohort was het belangrijkste doel van het onderzoek beschreven in dit proefschrift.

Als eerste stap in de reconstructie van de historische blootstelling van deze Europese asfaltwerkers zijn gepubliceerde wetenschappelijke rapporten over blootstellingen in deze industrie onderzocht (hoofdstuk 2). Van de meerderheid van de bedrijven die meededen aan het onderzoek werd verwacht dat ze hun activiteiten in de wegenbouw ontplooiden. Het literatuuronderzoek heeft zich dan ook voornamelijk beperkt tot deze subgroep van asfaltwerkers. Tot deze groep behoren werknemers van asfaltcentrales, asfalteerders en grondwerkers. Deze individuen blijken te zijn blootgesteld aan een wijd scala van mogelijk gevaarlijke stoffen. Op basis van het literatuuronderzoek is inzicht gekregen in de gemiddelde blootstellingconcentraties tijdens het aanleggen van wegen. Een moderne wegenbouwer heeft een typische blootstelling aan bitumendampen van 0,1 tot 2 mg/m^3, met daarin 10-200 ng/m^3 benzo(a)pyreen. Meetstrategieën en analytische methoden die gebruikt zijn in de verschillende onderzoeken zijn kort beschreven. De gepubliceerde rapporten gaven tot op zekere hoogte inzicht in een aantal factoren die van invloed zijn op de blootstelling aan bitumen van wegenbouwers, zoals soort uitgevoerd werk, meteorologische omstandigheden en temperatuur van het asfalt. Echter er bleek gebrek te zijn aan (a) omvangrijke en goed opgezette studies naar determinanten van blootstelling aan bitumendampen in de wegenbouw en (b) standaard methoden voor het monsteren en analyseren van bitumendampen. Informatie over determinanten voor blootstellingen aan andere stoffen ontbrak nagenoeg compleet. Geconcludeerd is dat de beschikbare gegevens in gepubliceerde rapporten slechts beperkte waarde hadden voor de reconstructie van de historische blootstelling van de werknemers in het internationale cohortonderzoek.

Omdat de gepubliceerde studies niet genoeg informatie bevatten voor het karakteriseren van de historische blootstelling, zijn vervolgens de gegevens van individuele metingen verzameld van zowel gepubliceerde als niet-gepubliceerde studies in de Europese asfaltverwerkende industrie (hoofdstuk 3). Hiertoe is een databestand ontwikkeld, dat uiteindelijk gebruikt is voor het schatten van de intensiteit van de historische blootstelling in de epidemiologische studie naar kankerrisico bij asfaltwerkers. Het databestand is ontwikkeld als een vrijstaande Microsoft

Access 2.0 applicatie, die in elk van de participerende centra moest werken. Blootstellinggegevens die in het databestand zijn ingevoerd bestonden uit concentraties en additionele gegevens over productiekarakteristieken, deze karakteristieken waren vergelijkbaar met gegevens die zijn gebruikt om de bedrijven in de epidemiologische studie te beschrijven. Het databestand is op een succesvolle manier geïmplementeerd in acht landen, waarmee duidelijk is geworden dat deze methode van dataverzameling in hoge mate flexibel en accuraat was. Het databestand maakte het mogelijk 38 datasets te ontsluiten en op een consistente manier te coderen. Van deze 38 datasets waren de resultaten van 34 nog nooit eerder in de openbare "peer-reviewed" wetenschappelijke literatuur beschreven. Het grootste deel van de benodigde informatie kon op deze manier worden verzameld. In februari 1999 bestond het databestand uit 2007 individuele metingen van personen of locaties (een meting leverde vaak concentraties van meerdere chemische verbindingen op). De metingen bleken vrij te zijn van duidelijke vertekeningen. Geconcludeerd is dat de gebruikte methodologie voor het creëren van het databestand succesvol kan worden toegepast bij het karakteriseren van historische blootstellingen in epidemiologisch onderzoek.

Nadat het databestand met meetgegevens uit de asfaltverwerkende industrie was samengesteld, zijn statistische modellen ontwikkeld voor de intensiteit van de blootstelling aan bitumendampen, organische gassen en polycyclische aromatische koolwaterstoffen (PAK) voor asfalteerders, de grootste groep aan bitumen blootgestelde werknemers in het cohortonderzoek (hoofdstuk 4). Persoonlijke blootstellingmetingen van asfalteerders (N=1581) waren aanwezig van alle landen in de studie. Correlatiepatronen tussen verschillende blootstellingen zijn onderzocht en factoren die de blootstelling beïnvloeden zijn geïdentificeerd met behulp van statistische modellen (zgn. "mixed effects" modellen). Blootstelling aan inhaleerbaar stof bleek een goede maat te zijn voor de blootstelling aan bitumendampen. De blootstellingen aan bitumendampen en organische gassen bleken niet gecorreleerd te zijn. Alle blootstellingen bleken consequent gedaald te zijn gedurende de 20 jaren voorafgaand aan 1997. Het leggen van mastiekasfalt, herasfalteren, slijtlaag aanbrengen, koud asfalteren ("oil gravel paving") en verwerkingstemperatuur van het asfalt bleken statistisch significante determinanten te zijn voor blootstelling aan bitumendampen. Gebruik van koolteer bleek de voornaamste determinant voor de blootstelling aan PAK te zijn. Geconcludeerd is dat voor asfalteerders de intensiteit van de blootstelling kwantitatief gereconstrueerd kon worden op basis van tijdsperiode en informatie over eerdergenoemde productiekarakteristieken.

Nadat voorspellende statistische modellen voor de blootstelling van asfalteerders zijn ontwikkeld (hoofdstuk 4), is nagegaan of alternatieve classificaties van de intensiteit van de blootstelling meer optimale groeperingen voor de epidemiologische analyses zouden hebben opgeleverd (hoofdstuk 5). Om dit te bewerkstelligen is nagegaan of een asfaltploeg uniform blootgesteld is aan bitumendampen, organische gassen en benzo(a)pyreen. Uniform blootgestelde groepen werknemers zijn ideaal voor blootstellingkarakterisering en risicoanalyse, omdat alle individuen in een dergelijke groep dezelfde blootstelling hebben en daardoor op een eenvoudige manier vergeleken kunnen worden met individuen van andere uniform blootgestelde groepen. Uit het databestand (hoofdstuk 2) zijn gegevens van in de tijd herhaalde metingen bij asfaltploegen geselecteerd (hoofdstuk 2, N=591). Het aantal herhaalde metingen per persoon bedroeg maximaal zes. De uniformiteit van de blootstellingen aan bitumendampen, organische gassen en benzo(a)pyreen is vervolgens geëvalueerd voor individuen gegroepeerd op basis van hun functie, voornaamste taken, ploeg en gebruik van koolteer. Het geschatte bereik waarbinnen 95% van de individuele gemiddelde blootstellingen vallen, diende als maat voor uniformiteit van de blootstelling. Variantiecomponenten zijn geschat door middel van zogenaamde "mixed-effects" modellen, waarbij groepering als "fixed" effect en de identiteit van de asfalteerder als “random” effect werden beschouwd. De invloed van duur van de meetperiode op de schattingen van de variabiliteit van de blootstelling is ook bekeken. Er bleek een substantiële hoeveelheid variabiliteit te zijn tussen asfaltploegen, tussen personen die dezelfde functie hadden of dezelfde taken uitvoerden. Elke asfaltploeg bleek echter uniform blootgesteld aan bitumendampen en benzo(a)pyreen ($_{BW}R_{0.95}$ 2 en 1, respectievelijk). Werknemers van een asfaltploeg die werkten met koolteerhoudende producten daarentegen bleken niet uniform blootgesteld aan benzo(a)pyreen te zijn geweest. Ook de blootstelling aan organische gassen was niet uniform voor een asfaltploeg ($_{BW}R_{0.95}$ =15). Langere meetperioden met een duur tot zeven maanden hadden nauwelijks invloed op de schattingen van de binnen- en tussenpersoonvariatie in blootstelling. Deze bevindingen bevestigen de notie dat slechts empirisch vastgestelde determinanten van de blootstelling en niet standaardclassificaties gebaseerd op functie en taakinhoud van de blootstelling tot een optimale groepering zullen leiden. Tenslotte is vastgesteld dat op basis van de beschikbare gegevens het niet is meer uniforme blootstellinggroepen te formeren, dan die beschreven in hoofdstuk 4.

Validatie van een model is één van de cruciale stappen bij het ontwikkelen van een statistisch model. Daarom is hoofstuk 6 toegewijd aan het vaststellen van de validiteit van de empirische modellen voor de blootstelling zoals ontwikkeld in hoofdstuk 4. Interne validiteit is vastgesteld aan de hand van een zogenaamde kruis-validatie methode. De externe validiteit is geëvalueerd met behulp van extra blootstellinggegevens, die niet zijn gebruikt bij het ontwikkelen van de originele empirische modellen. Voor de blootstelling aan bitumendampen en benzo(a)pyreen is de correlatie tussen geobserveerde en voorspelde blootstellingconcentraties onderzocht. Alle empirische modellen bleken een goede interne validiteit te hebben, maar bleken wel onnauwkeurig te zijn. Voorspelde concentraties bitumendampen waren lager (gemiddeld een factor 3) dan concentraties vastgesteld tijdens asfalteren in de VS. Deze vertekening zou het gevolg kunnen zijn van verschillen tussen Europese en Amerikaanse methoden van asfalteren. Evaluatie van de externe validiteit van het empirische model voor benzo(a)pyreen liet goede overeenkomsten zien bij het hergebruiken van asfalt, maar gaf te lage schattingen bij het gebruik van koolteer. Over het algemeen werd de blootstelling aan benzo(a)pyreen door de modellen 51% te laag geschat. Geconcludeerd is dat de vertekening, die mogelijk een gevolg zou kunnen zijn van deze onderschatting, verkend moet worden door het uitvoeren van sensitiviteitsanalyses van de blootstelling-respons relatie. Ondanks de beperkingen, heeft het valideren van de statistische modellen het vertrouwen vergroot in het toepassen van dit soort modellen voor het karakteriseren van historische blootstellingen in het cohortonderzoek naar kankerrisico bij asfaltwerkers.

Nadat de statistische modellen voor de blootstelling waren ontwikkeld (hoofdstuk 3-6) zijn ze toegepast bij het creëren van een blootstellingmatrix voor bewezen en mogelijke carcinogenen voor het internationale cohortonderzoek (hoofdstuk 7). Ook zijn procedures ontwikkeld voor semi-kwantitatieve schattingen van de blootstelling van (a) cohortleden werkzaam in asfalteren en (b) voor agentia waarvan geen of nauwelijks meetgegevens voorhanden waren (hoofdstuk 7). Karakteristieken van productiemethoden in de deelnemende bedrijven zijn geïnventariseerd met behulp van vragenlijsten en consultaties met vertegenwoordigers van de industrie en arbeidshygiënisten. De blootstellingen aan bitumendampen, organische gassen, polycyclische aromatische koolwaterstoffen, dieseluitlaatgassen, kwarts en asbest zijn semi-kwantitatief vastgesteld op basis van de bedrijfsvragenlijsten en het oordeel van experts over de relatieve hoogte van de intensiteit van de blootstelling. Kwantitatieve schattingen van de blootstelling van asfalteerders zijn gemaakt door het toepassen van de ontwikkelde statistische regressiemodellen (hoofdstuk 2 en 3) op scenario’s geïnventariseerd met de bedrijfsvragenlijsten. De frequentie van koolteergebruik is direct afgeleid van de vragenlijst. Alle berekeningen zijn gestandaardiseerd naar een achturige werkdag. De blootstellingmatrix was specifiek voor tijdsperiode, bedrijf en functiegroep. Het merendeel van de 203 bedrijven uit de acht landen hielden zich bezig met asfalteren (51%) en asfaltmengen (94%). Koolteergebruik kwam het meest voor in Denemarken en Nederland, maar de frequentie is dramatisch gedaald tussen 1960 en begin zeventiger jaren; koolteer wordt tegenwoordig niet meer gebruikt in de deelnemende landen. De hoogste blootstellingen aan bitumendampen, organische gassen en PAK zijn geschat voor dakbedekkers en waterdichtmakers. De blootstellingmatrix liet een niet-monotone historische daling in blootstelling zien voor alle agentia behalve kwarts en dieseluitlaatgassen. De geschatte blootstelling aan bitumendampen en de geschatte blootstelling aan koolteer waren matig gecorreleerd. De hoogste correlatie is gevonden voor de periode voor 1960. De correlaties tussen blootstelling aan bitumendampen, organische gassen en PAK waren zeer sterk. Op basis van de blootstellingmatrix is geconcludeerd dat het onmogelijk is onderscheid te maken tussen de mogelijke gezondheidseffecten ten gevolge van blootstelling aan bitumendampen, organische gassen en PAK. Echter, het corrigeren van risicoschattingen voor blootstelling aan koolteer is mogelijk. De kwaliteit van de bedrijfsvragenlijsten is beschouwd als de zwakste schakel bij het construeren van de blootstellingmatrix. De gekozen benadering leverde een op meetgegevens gebaseerde blootstellingmatrix op. Deze matrix kan in toekomstige studies aangevochten worden en kan zonodig eenvoudig gereconstrueerd worden.

Nadat de blootstellingmatrix was geconstrueerd (hoofdstuk 7), is de werking van verschillende manieren van blootstellingkarakterisering en – toekenning bekeken door middel van het bestuderen van de uitkomsten van de veronderstelde relatie tussen blootstelling aan bitumendampen en sterfte aan longkanker (hoofdstuk8). Blootstelling-respons relaties op basis van drie blootstellingsmaten zijn vergeleken: duur van de blootstelling (jaren), gemiddelde blootstelling (mg/m^3) en cumulatieve blootstelling (mg/m^3.jaren). Tijdens het schatten van de blootstellingduur zijn correcties gemaakt voor seizoensgerelateerde arbeid in deze sector, omdat dit niet tot uiting kwam in het geregistreerde beroepsverleden van de werknemers in het cohort. Deze correcties zijn gemaakt door middel van een ruwe schatting van de duur van het asfaltseizoen zoals dat is aangegeven door de deelnemende bedrijven in de bedrijfsvragenlijsten. Twee modellen (met en zonder 15-jaar latentietijd) zijn gebruikt om het verband tussen longkanker en bitumendampen te bestuderen. Allereerst zijn de rangcorrelaties tussen de drie blootstellingmaten bekeken. Het relatieve risico voor blootstelling aan bitumendampen is vervolgens geschat met behulp van Poisson regressie analyse. Alle modellen zijn gecorrigeerd voor blootstelling aan koolteer (ooit/nooit), leeftijd, kalenderperiode en land. Blootstelling-respons modellen zijn vergeleken door middel van zgn. “log-likelihood” ratio test (maat voor de fit van het model). Alleen 12.367 mannelijk asfalteerders, die minimaal één seizoen gewerkt hadden als asfalteerder, zijn voor deze analyses geselecteerd. In dit deelcohort bleken 134 werknemers overleden te zijn aan longkanker. Slechts de duur van de blootstelling en de cumulatieve blootstellingmaat bleken gecorreleerd te zijn. Verder is geen verband aangetoond tussen risico op longkanker en duur van de blootstelling nog met cumulatieve blootstelling aan bitumendampen. Daarentegen is wel een verband aangetoond tussen een verhoogd risico op longkanker en gemiddelde blootstelling aan bitumendampen. Slechts de modellen met gemiddelde blootstelling en de twee latentietijden lieten een duidelijk betere fit zien. Een positief verband tussen gemiddelde blootstelling aan bitumendampen en sterfte aan longkanker is aangetoond. Echter, het kan niet uitgesloten worden dat dit verband een resultaat is van andere niet onderkende maar wel gecorreleerde carcinogene blootstellingen dan wel levensstijlfactoren. Uit de epidemiologische analyse kwam geen duidelijk latentiemodel naar voren. De investering om te komen tot kwantitatieve blootstellingmaten lijkt gerechtvaardigd te zijn omdat (a) door het sterke “gezonde werknemers” effect, elk verband tussen duur van de blootstelling en longkankerrisico versluierd werd en (b) statistisch significante associaties zijn gevonden tussen gemiddelde blootstelling aan bitumendampen en longkanker, die nader onderzocht moeten worden. Veel van de onduidelijkheden, die overgebleven zijn na uitvoering van het cohortonderzoek kunnen mogelijk worden ontrafeld in een patiënt-controle onderzoek binnen het onderzochte internationale cohort asfaltwerkers.

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About the author

Igor Burstyn was born in Kiev, the Union of Soviet Socialist Republics, on April 22, 1971. He completed secondary education in the Secondary School No. 115 in Kiev in 1988, but graduated from the Lord Beaverbrook Secondary High School in Calgary, Canada, in 1989. In the same year he was awarded the Alexander Rutherford Scholarship. Igor Burstyn started post-secondary education at Cariboo College in Kamloops, Canada, and continued it at the University of British Columbia, Vancouver, Canada. He graduated from the University of British Columbia with the degree of a Bachelor of Science (Microbiology Major) in 1993, having remained on the Dean's Honour List for the duration of the entire program. As an undergraduate student, he was awarded the Alexander Durdle Scholarship (1991) and two National Sciences and Engineering Research Council Undergraduate Studentships (1992 and 1993). After a year spent considering his career and education options, in 1994 Igor Burstyn entered the Master of Science program in Occupational Hygiene at the University of British Columbia. This was made possible, at least in part, by funding from the National Sciences and Engineering Research Council Post-Graduate Fellowship (1994-1996). He designed and successfully carried out an investigation into the determinants of exposure to inhalable dust and allergens in bakeries, defending a thesis on the subject in 1996. The same year he was a awarded Master of Science degree. In 1997, Igor Burstyn joined the Occupational and Environmental Health Group of Wageningen University (since May 2000 located at Utrecht University), the Netherlands, in order to pursue the degree of Doctor of Philosophy. His training was conducted through active involvement in an international multicentric cohort study of the European asphalt industry. Igor Burstyn spent a year at the International Agency for Research on Cancer (IARC), Lyon, France, as part of the tenure of an IARC Special Training Award (1997 - 2000). In 2000, he took an active part in a series of European Union workshops on new and emerging occupational health issues. In January 2001, Igor Burstyn was appointed at Utrecht University as a Junior Researcher. This position allowed him to be involved in an international collaboration on developing a framework of exposure database for the European Chemical Industry Council, and to participate in a study of historical trends in exposure among Dutch commercial painters. He also continues to be actively engaged in analysis and interpretation of the cohort study and the design of a nested case-control study, both of European asphalt workers.

Appendix

Reclaimed materials and recycling in the asphalt Industry: Implications for occupational health

Burstyn I and Kromhout H: Reclaimed Materials and Recycling in the Asphalt Industry: Implications for Occupational Health. National Institute for Working Life Workshop: Does recycling lead to new problems in the working environment? March 20 – 22, 2000, Brussels, Belgium (abstract of the oral presentation).

Introduction

Typically, asphalt is a mixture of inorganic filler (sand, gravel, limestone) and bitumen as an organic, petroleum-derived binder. In an increasing number of countries, old asphalt or demolition waste is being used to produce new asphalt. According to the European Asphalt Pavement Association,[1] over 90% of the total road network has an asphalt surface, and the product is 100% recyclable. There are more than 10,000 companies involved in the production and/or laying of asphalt in Europe. Little is known about how the use of recycled materials in asphalt and the reclaiming of the asphalt surface itself may affect occupational exposures and the health of asphalt workers. However, data from US studies of crumb-rubber modified asphalt and information obtained during the IARC study of cancer risk among European asphalt workers can shed some light on the issue.

Reclaimed materials in asphalt

Reclaimed materials, such as old road surfaces, demolition waste, and rubber tires, have been and still are being used in making asphalt. In 1991, US Congress introduced the requirement of minimum crumb rubber (CR) content of asphalt used in federally funded paving. This was prompted by the health, fire and solid waste problems posed by discarded tires. However, concern over health effects of CR-modified asphalt halted implementation of the legislation. It was observed that paving with CR-modified asphalt was associated with elevated exposures to sulfur-substituted hydrocarbons found in vulcanized rubber (e.g. benzothiazole 3.3 to 233 $\mu g/m^3$) and with an increase in acute health symptoms among pavers.[2] According to company questionnaires obtained from seven European countries and Israel, rubber-modified asphalt may have been used to some extent by about 10-14% of companies since 1970’s. Furthermore, since exposures in the rubber industry have been recognized to lead to elevated cancer risk, potential transfer of some of these carcinogenic exposures to the asphalt industry is a cause for concern.

Recycling of asphalt

Recycling of asphalt road surfaces started in Western Europe in the 1980’s. Typically, specialized crews or firms within the asphalt industry do this work. The old layer of asphalt is stripped and mixed with new asphalt, either at an asphalt plant or at the paving site (*in situ* re-paving), and re-applied to the road surface. In hot re-paving, the old asphalt is heated with propane burners prior to removal from the road.

[1] http://www.eapa.org/
[2] A Miller, et al..: Acute health effects of conventional and crumb rubber modified asphalt among road pavers. AIHCE, 1999, abstract 67 (http://www.aiha.org/abs99/9genih2.html)

In an analysis of exposure data collected in Europe, these re-paving operations, with respect to hot mix paving, were found to be associated with a 13-fold (worst case, probably hot re-paving) to 2-fold increase in bitumen fume exposures, and an 11- to 5-fold increase in benzo(a)pyrene exposures. The carcinogenicity of benzo(a)pyrene has been established, whereas that of bitumen is controversial. Full-shift time-weighted average bitumen fume exposures during re-paving were on the order of 0.50 to 2 mg/m^3. During re-paving of coal tar-containing road materials in 1985-86, the median 2-hour-average of benzo(a)pyrene exposure of 3008 ng/m^3 (n=42,GSD=3.1) was observed. In the studies conducted in the Netherlands between 1988 and 1993, recycling of tar containing asphalt was associated with geometric mean full-shift benzo(a)pyrene exposures on the order of 120 ng/m^3 (n=36, GSD=3.3). In a tar-free environment, re-paving was associated with benzo(a)pyrene exposure that were less than 20 ng/m^3 (n=14). Therefore it is not surprising that in the Netherlands, the last and the most recent country in Western Europe to discontinue coal tar use in asphalt, coal-tar-containing asphalt is treated as hazardous waste and is recycled differently than tar-free asphalt.[3] Full-shift respirable quartz exposures during milling of asphalt in the Netherlands, in 1999, were reported to exceed 0.075 mg/m^3 exposure limit with some milling machines (n=32, range 0.010 to 1.038 mg/m^3). These exposures can be controlled.

Statistical models constructed on the basis of European exposure data from paving indicate that overall inhalable exposure levels to bitumen fume and benzo(a)pyrene declined between 1970 and 1997. Since the overall proportion of person-hours devoted to re-paving in the asphalt industry is small (5-15%), we can demonstrate that this is likely to have little impact on the overall time trend, unless frequency of re-paving operations increases dramatically.

Conclusions

There are indications that recycling activities may increase exposure of asphalt workers. The impact on the health of workers of the use of reclaimed materials in asphalt and that of re-cycling asphalt should be carefully studied, especially as the frequency of these operations increases in the future. It is to be hoped that we can retain the benefits of recycling asphalt and using reclaimed materials in paving without endangering the health of individuals who perform such work.

[3] CROW (1997) Hergebruik van asfalt met teer (Re-use of coal-tar containing asphalt. Publication 109, ISBN 90-6628-234-7.