Occupational exposure to carcinogens in the European Union

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Abstract

***Objectives*—To construct a computer assisted information system for the estimation of the numbers of workers exposed to established and suspected human carcinogens in the member states of the European Union (EU).**

***Methods*—A database called CAREX (carcinogen exposure) was designed to provide selected exposure data and documented estimates of the number of workers exposed to carcinogens by country, carcinogen, and industry. CAREX includes data on agents evaluated by the International Agency for Research on Cancer (IARC) (all agents in groups 1 and 2A as of February 1995, and selected agents in group 2B) and on ionising radiation, displayed across the 55 industrial classes. The 1990–3 occupational exposure was estimated in two phases. Firstly, estimates were generated by the CAREX system on the basis of national labour force data and exposure prevalence estimates from two reference countries (Finland and the United States) which had the most comprehensive data available on exposures to these agents. For selected countries, these estimates were then refined by national experts in view of the perceived exposure patterns in their own countries compared with those of the reference countries.**

***Results*—About 32 million workers (23% of those employed) in the EU were exposed to agents covered by CAREX. At least 22 million workers were exposed to IARC group 1 carcinogens. The exposed workers had altogether 42 million exposures (1.3 mean exposures for each exposed worker). The most common exposures were solar radiation (9.1 million workers exposed at least 75% of working time), environmental tobacco smoke (7.5 million workers exposed at least 75% of working time), crystalline silica (3.2 million exposed), diesel exhaust (3.0 million), radon (2.7 million), and wood dust (2.6 million).**

***Conclusion*—These preliminary estimates indicate that in the early 1990s, a substantial proportion of workers in the EU were exposed to carcinogens.**

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Effective prevention of occupational cancer requires knowledge on occurrence of exposure but information on the numbers of workers exposed is seldom available. As a part of a European project on the estimation of the burden of occupational cancer in Europe,[1] an international group of experts was established to provide documented estimates of the number of workers in the European Union (EU) exposed to carcinogens by country, agent, and industry. A first version of an exposure information system called CAREX (carcinogen exposure) was constructed by the Finnish Institute of Occupational Health (FIOH) to support the estimation process. CAREX was further developed by a group of experts, which included additional experts on national exposure from different countries in the EU as part of the CAREX network.

Material and methods

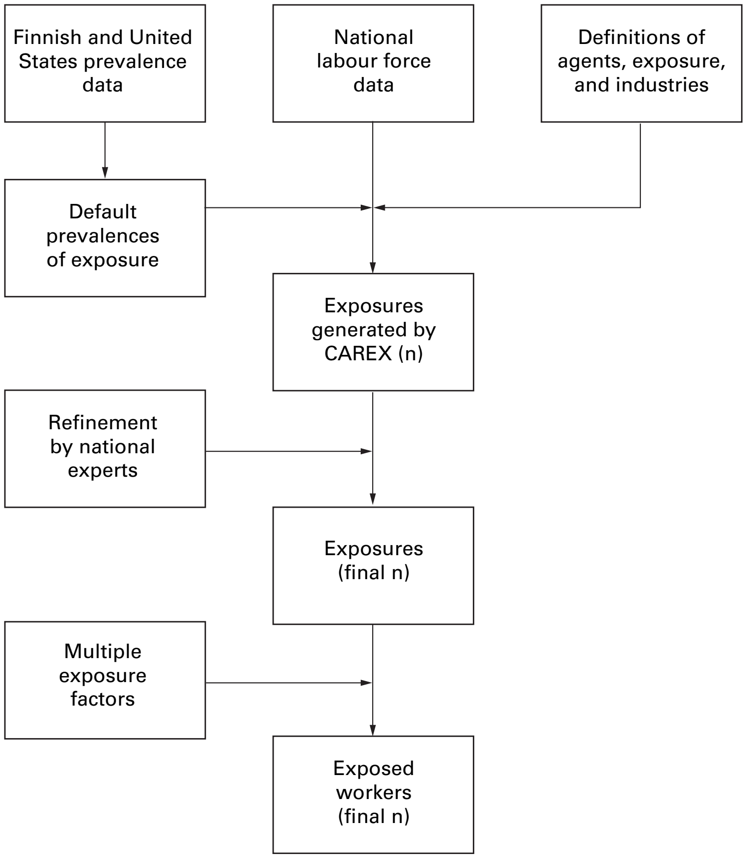
OVERVIEW OF THE METHOD

The assessment procedure is outlined in the figure. The main phases of the assessment were the following: (*a*) definition of agents and occupational exposure; (*b*) definition of industries and collection of labour force data; (*c*) collection of exposure measurement data and descriptive exposure data; (*d*) generation of default estimates of exposures by the CAREX system on the basis of United States and Finnish exposure data and estimates; (*e*) earmarking of exposures of low level; (*f*) estimation of multiple exposures to convert the number of exposures to the number of exposed workers; and (*g*) generation of final estimates of exposures by national experts in selected countries. To support the estimation and to document the basis for estimates, a CAREX exposure information system was designed and constructed. It is an MS Access database which can be run on personal computers.

AGENTS COVERED AND DEFINITION OF OCCUPATIONAL EXPOSURE

CAREX covers all agents, groups of agents, and mixtures which the International Agency for Research on Cancer (IARC) had classified to group 1 (carcinogenic to humans) and group 2A (probably carcinogenic to humans) as of February 1995. Selected agents from group 2B (possibly carcinogenic to humans) were also included. In addition, ionising radiation was included, although not yet evaluated by IARC.

Many of the group 1 and 2A agents are polycyclic aromatic hydrocarbons (PAHs) or their mixtures, and they were merged under that



CAREX estimation procedure. See table 1 for details on use of Finnish and United States prevalence data to generate default prevalences. Estimates were refined by national experts in Denmark, France, Italy, and The Netherlands. Also, CAREX includes exposure measurement data and selected data on exposure by occupation and sex.

title. The PAHs include coal tar pitches, coal tars, untreated and mildly treated mineral oils, shale oils, soots and creosotes, as well as benzo(a)pyrene and other single PAH compounds. The reason for this regrouping was that PAHs almost always occur in occupational settings as complex mixtures and evaluation of exposures to a single PAH is not usually possible. However, tobacco smoke (passive exposure at work) and diesel exhaust, although recognised also as complex mixtures containing PAHs, were assessed separately. Ultraviolet radiation A, B, and C were merged under the title artificial ultraviolet radiation, which was assessed separately from solar radiation. Exposure to hepatitis viruses B and C were not assessed due to difficulties in defining the concept of exposure.

The definition of occupational exposure to an agent in CAREX provided the relevant routes of exposure (inhalatory, dermal, or both of them) and the non-occupational background level, which was used as the minimum criterion of occupational exposure. If a CAREX agent was a group of substances, the definition listed the most common substances included. The definition noted in some cases inclusions or exclusions of borderline exposures—for example, occasional paint removal was not considered to entail exposure—and national deviations from the general definition—for example, agent X in country Y was considered to entail exposure also when it occurred as an impurity in polymeric materials.

Most agents and groups of agents in CAREX (n=85 items, including PAHs as one item) were assessed according to a detailed industry specific procedure which provides 55 industry specific estimates for the number of exposed workers per country and agent. The assessment of nine agents, including artificial ultraviolet radiation, erionite, and *Helicobacter pylori*, followed a country specific procedure which provides only one estimate per country and agent. Carcinogenic exposure circumstances evaluated by IARC (n=15 items) were only briefly described in CAREX. No assessment was appropriate or feasible for some of the carcinogenic agents (n=8 items, betel quid, some viruses, salted fish, etc) for which exposure is not primarily occupational. They were included in the database but the number of occupationally exposed workers was assumed to be zero.

CHARACTERISATION OF INDUSTRY AND LABOUR FORCE

The numbers of exposures and exposed workers in CAREX were estimated mainly for industrial classes (CAREX industries) at the three digit level of United Nations (UN) international standard industrial classification (ISIC) revision 2 (1968). For some non-manufacturing sectors, one or two digit levels were used as the assessment level. The number of industrial classes in CAREX was 55 .

The number of employed people used in the calculation was the mean number of employed people in 1990–3, because more recent uniform labour force statistics were not available. As far as possible, we tried to include all people employed in each industry by covering salaried workers, self employed workers, working family members, and part time workers. The main source of labour force data was the Organisation for Economic Co-operation and Development (OECD) which has uniformly collected labour force statistics according to the ISIC revision 2 classification since the late 1960s. Available national statistics were also used and whenever needed, national experts corrected and completed the data.

EXPOSURE MEASUREMENTS AND DESCRIPTIONS IN CAREX

A valid estimation of the level of exposure in CAREX would have required that the levels—for example, high and low—were accurately defined, and that enough knowledge on exposure circumstances from different countries was available. An initial study indicated that a systematic estimation of exposures by level in each of the 15 EU countries was unfeasible during the present project. However, CAREX contains agent and industry specific measurement data to enable users of the database to arrive at their own estimations and conclusions on exposure levels. CAREX also includes some data on carcinogenic exposures by occupation and sex at the national level.

Table 1 Rational to derive default (first) estimates of exposure from the United States and Finnish exposure prevalences

	Finnish prevalence		
	Valid	*Invalid*	*Zero*
United States prevalence:			
Valid	AVE	USA	AVE
Invalid	FIN	AVE	ZERO
Missing	FIN	OWN	ZERO
Zero	AVE	ZERO	ZERO

AVE=average prevalence of exposure in Finland and the United States was used; USA=prevalence in the United States was used; FIN=prevalence in Finland was used; OWN=own national estimate was proposed; ZERO=no exposure was assumed to occur.

DEFAULT ESTIMATES

Our preference was to use original national estimates on carcinogenic exposures, but their poor availability forced us to adopt an approach in which most estimates were derived indirectly on the basis of information from the two reference countries with reasonably comprehensive data (Finland and the United States).

After conversion of the Finnish and United States industrial classifications to ISIC revision 2 of UN 1968 format, the estimated number of workers exposed to the IARC agents under study were listed by industry. These absolute figures were converted to exposure frequencies (prevalences) by dividing them by the employed labour force of the industry concerned. These prevalences were used to calculate three alternative estimates (AVE, USA, FIN) for exposures in other countries (table 1). The estimate considered to be the most valid by professional judgement was set as the default value. When the estimate was not unanimously considered to be zero, usually the average (AVE) value was used. If the average prevalence was not used, the reason was documented in CAREX. In rare cases in which both United States and Finnish estimates were considered invalid, AVE was used because the United States prevalence was regarded as too high and the Finnish one as too low.

ESTIMATES OF LOW LEVEL

If the level of exposure was considered to be close to the background level (in ambient or indoor air), the estimate was marked as such. However, the background exposure may vary and is often difficult to specify. Many low exposures in Finnish data involved handling of small amounts of carcinogens in laboratories, pharmacies, or hospitals. Low exposures were tagged by professional judgement in Finland. The United States National Occupational Exposure Survey (NOES) did not classify exposures by level and therefore low exposures could not be systematically identified. The Finnish estimates which were judged as low were used as one basis to mark NOES estimates. However, no NOES data were considered as invalid on this basis, which resulted in tagging of some exposures in laboratories as low level in the United States when similar exposures were not considered to entail exposure exceeding the background level in Finland. Similarly, exposure to many impurities in polymeric materials and metal alloys were considered as low exposure in the United States and as being negligible in Finland. Another criterion to assign a low exposure flag to NOES data was an obvious discrepancy with the Finnish data without an evident reason. For example, if there were over 10 000 exposed workers in a CAREX industry in NOES and none in Finland, it was assumed that the United States exposures were of low level. Also, some very small estimates of the number of workers potentially exposed were considered to reflect low exposure in the NOES data.

ESTIMATES OF MULTIPLE EXPOSURE

The concept exposure in CAREX does not refer to the number of exposure events—for example, five times a year—but to the occurrence of agent specific exposures of a worker. For example, if one worker is exposed to two agents, the number of exposed workers is one, but the number of exposures is two. The distinction between exposure and exposed worker is necessary in the calculation of total numbers of exposed workers in a CAREX industry, or in a country. If all exposures within an industry are totalled, the same workers may be counted several times (in cases of multiple exposure) and an overestimate results. Therefore we developed industry specific factors (multipliers), which converted the number of exposures to number of exposed workers. These multiple exposure factors were derived in CAREX for the Finnish data only, and are based on the assessment of additivity of exposed subgroups by one member of the team (TK). The United States NOES data did not allow for the derivation of multiple exposure factors by CAREX industry coding (ISIC revision 2). The Finnish multipliers were used in the present analysis also for other EU countries.

ESTIMATION PROCEDURES BY COUNTRY

Default estimates generated by the CAREX system were used to describe exposure in Austria, Belgium, Germany, Great Britain, Greece, Ireland, Luxembourg, Portugal, Spain, and Sweden. There is a Swedish national report on exposure to carcinogens[2] but because the definitions and estimation procedures were different from the CAREX system, these Swedish estimates were not incorporated in CAREX.

The estimates of the reference countries were based on direct national data. The Finnish estimates were generated and documented in CAREX as accurately as possible at subindustrial level. The main sources of Finnish data were the reports of a comprehensive estimation survey (SUTKEA project) carried out by industrial hygienists of the Finnish Institute of Occupational Health (FIOH) in the late 1980s and early 1990s.[3] Another basic source of information was the Finnish national register of workers exposed to carcinogens (ASA register) kept by FIOH since 1979.[4] If neither SUTKEA nor ASA provided estimates, other available sources, such as the FINJEM exposure information system of the FIOH, were

Table 2 Numbers of employed workers, exposures, and exposed workers (in thousands) in the European Union by industry in 1990–3

ISIC-2 code	Industry	Employed workers (n)	Exposures (n)	Exposed workers (n)
11	Agriculture and hunting	7900	3000	3000
12	Forestry and logging	410	560	350
13	Fishing	230	150	150
21	Coal mining	370	1	1
22	Crude petroleum and natural gas production	130	43	43
23	Metal ore mining	62	150	29
29	Other mining	270	450	190
311–2	Food manufacturing	2700	330	310
313	Beverage industries	410	59	59
314	Tobacco manufacture	88	4	4
321	Manufacture of textiles	1300	240	220
322	Manufacture of wearing apparel	1500	350	340
323	Manufacture of leather and products of leather	180	41	40
324	Manufacture of footwear	460	89	88
331	Manufacture of wood and wood and cork products	770	620	500
332	Manufacture of furniture and fixtures	790	810	600
341	Manufacture of paper and paper products	730	170	140
342	Printing, publishing, and allied industries	1700	450	440
351	Manufacture of industrial chemicals	1000	460	350
352	Manufacture of other chemical products	950	380	340
353	Petroleum refineries	130	85	74
354	Manufacture of petroleum and coal products	26	18	18
355	Manufacture of rubber products	380	140	140
356	Manufacture of plastic products	840	380	330
361	Manufacture of pottery, china, and earthware	260	250	170
362	Manufacture of glass and glass products	300	200	130
369	Manufacture of other non-metallic mineral products	640	530	430
371	Iron and steel basic industries	850	560	380
372	Non-ferrous metal basic industries	360	230	160
381	Manufacture of fabricated metal products	2800	1300	810
382	Manufacture of machinery except electrical	3800	1200	830
383	Manufacture of electrical machinery	3000	470	440
384	Manufacture of transport equipment	3000	1500	970
385	Manufacture of instruments, etc	540	200	190
39	Other manufacturing industries	400	120	110
41	Electricity, gas, and steam	1200	480	430
42	Water works and supply	220	84	84
5	Construction	11000	9000	6100
6	Wholesale and retail trade and restaurants	24000	4200	3500
711	Land transport	4200	1900	1700
712	Water transport	350	250	180
713	Air transport	450	330	290
719	Services allied to transport	1400	630	580
72	Communication	2600	610	590
8	Financing, insurance, real estate, business services	13000	1100	1100
91	Public administration and defence	11000	1600	1600
92	Sanitary and similar services	1400	430	360
931	Education services	9000	370	330
932	Research and scientific institutes	490	140	100
933	Medical, dental, other health services	8200	810	730
934	Welfare institutions	4000	220	210
935–9	Business, professional, and other organisations	1500	230	230
94	Recreational and cultural services	2100	280	270
95	Personal and household services	32000	3800	1600
96	International organisations	160	1	1
	Total	139000	42000	32000

used.[5] The basic criterion for assigning exposure in Finland was that the annual exposure dose at work exceeded the non-occupational dose.

The United States was the other reference country in the CAREX system. The United States data in CAREX came from the NOES conducted by the United States National Institute for Occupational Safety and Health (NIOSH). The NOES was a nationwide observational survey conducted in a sample of 4490 establishments from 1981–3.[6–9] The target population was defined as employees working in establishments or job sites in the United States employing eight or more workers in a defined list of standard industrial classifications. Generally, these classifications emphasised coverage of construction, manufacturing, transportation, private and business service, and hospital industries. The NOES had little or no sampling activity in agriculture, mining, wholesale or retail trades, finance and real estate, or government operations. The NOES considered recordable potential exposure. A potential exposure had to meet two criteria to be recorded: (*a*) a chemical, physical, or biological agent, or a tradename product had to be found close enough to an employee that one or more physical phases of that agent or product were likely to enter or contact the body of the employee; and (*b*) the duration of the potential exposure had to meet the minimum duration guidelines (at least 30 minutes a week on an annual average, or at least once a week for 90% of the weeks of the working year).

Denmark, France, Italy, and the Netherlands produced estimates which are adjusted for the labour force structure and account for exposure patterns in the country. The Danish estimates were based on several nationwide surveys.[10–14] If no appropriate estimates were available from the Danish surveys, the default estimates of the CAREX system were used, unless they were considered invalid for Denmark on the basis of subjective judgement.

Table 3 Numbers of exposures by agent (in thousands) in the European Union in 1990–3

Agent	*Exposures (n)*	*IARC group**
Acrylamide	31	2A
Acrylonitrile	32	2A†
Adriamycin	18	2A
Aflatoxins	2	1
4-Aminobiphenyl	0	1
Arsenic and arsenic compounds	150	1
Asbestos	1200	1
Azacitidine	1	2A
Azathioprine	2	1
Benzene	1400	1
Benzidine	7	1
Benzidine based dyes	14	2A
Beryllium and beryllium compounds	67	1
Bischloroethyl nitrosourea (BCNU)	10	2A
Bis(chloromethyl)ether (BCME)	2	1
1,3-Butadiene	32	2A
1,4-Butanediol dimethanesulphonate (Myleran)	3	1
Cadmium and cadmium compounds	210	1
Captafol	8	2A
Carbon tetrachloride	75	2B
Ceramic fibres	62	2B
Chlorambucil	10	1
Chloramphenicol	12	2A
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)	2	2A
Chlorozotocin	<1	2A
Chromium VI compounds	800	1
Cyclosporin	10	1
Cisplatin	25	2A
Cobalt and its compounds	240	2B
Cyclophosphamide	45	1
Diesel engine exhaust	3000	2A
Diethylstilbestrol	<1	1
Diethyl sulphate	2	2A
Dimethylcarbamoyl chloride	0	2A
Dimethyl sulphate	10	2A
Epichlorohydrin	48	2A
Estrogens, non-steroidal	5	1
Estrogens, steroidal	5	1
Ethylene dibromide	1200	2A
Ethylene oxide	47	1
N-Ethyl-N-nitrosourea	0	2A
Formaldehyde	990	2A
Glasswool	930	2B
Hepatitis B virus (HBV)	Not estimated	1
Hepatitis C virus (HCV)	Not estimated	1
Ionising radiation	150	—
Lead and inorganic lead compounds	1500	2B
Melphalan	10	1
Methyl-CCNU	<1	1
N-Methyl-N-nitrosourea	0	2A
4,4'-Methylene bis(2-chloroaniline) (MOCA)	3	2A
Methylene chloride	280	2B
MNNG	1	2A
Mustard gas (sulphur mustard)	1	1
2-Naphthylamine	2	1
Nickel compounds	560	1
Nitrogen mustard	3	2A
N-Nitrosodiethylamine	13	2A
N-Nitrosodimethylamine	14	2A
Oral contraceptives, combined	5	1
Oral contraceptives, sequential	5	1
p-Chloro-o-toluidine and its strong acid salts	1	2A
Pentachlorophenol	49	2B
Phenacetin	3	2A
Polychlorinated biphenyls (PCB)	15	2A
Polycyclic aromatic hydrocarbons (PAH)	980	1–3
Procarbazide hydrochloride	<1	2A
Radon and its decay products	2700	1
Silica, crystalline	3200	2A‡
Solar radiation (at least 75% of working time)	9100	1
Styrene	400	2B
Styrene-7,8-oxide	86	2A
Sulphuric acid mist	710	1
Talc containing asbestiform fibres	28	1
Tetrachloroethylene	820	2A
Thiotepa	3	1
Tobacco smoke, environmental (at least 75% of working time)	7500	1
Treosulfan	0	1
Trichloroethylene	280	2A
1,2,3-Trichloropropane	1	2A
Tris(2,3-dibromopropyl)phosphate	<1	2A
Vinyl bromide	0	2A
Vinyl chloride	40	1
Vinyl fluoride	0	2A
Wood dust	2600	1
Total	42000	

*IARC groups: 1=carcinogenic to humans; 2A=probably carcinogenic to humans; 2B=possibly carcinogenic to humans; 3=unclassifiable as to carcinogenicity to humans.
†Re-evaluation 1999 (group 2B). ‡Re-evaluation of occupational exposure 1997 (group 1).

The French estimates were based on the observational SUMER survey[15] conducted in 1994, and the COLCHIC database of occupational exposure measurements maintained by the National Institute of Research on Safety (INRS). If no data were available from the SUMER study, the estimates were based on knowledge of different INRS experts, or on default estimates of CAREX. All temporary workers independently of the employing sector in France were coded to ISIC "wholesale and retail trade and restaurants and hotels" resulting in occurrence of unexpected exposures in that class.

The Italian estimates were generated by CAREX system and modified by a national expert who based his judgements either on his own experience or on the evaluations received from a group of Italian industrial hygienists. These industrial hygienists had developed an industrial activity or exposure matrix within the framework of an occupational hazards surveillance programme in 1996–7 in the Piedmont region.

The Dutch estimates were generated by the CAREX system and modified by a national expert who used several inputs. These included the WAUNC database of the Wageningen University, containing approximately 20 000 chemical exposure measurements as a data source. Input from colleagues was used to some extent. Also, unpublished data from the Ministry of Social Affairs and Employment on the occurrence of exposure to carcinogens by industry and process was taken into account.

Results

There were about 32 million workers (23% of the total employed) in the 15 countries of the EU exposed to the agents covered by CAREX in 1990–3 (table 2). These workers had altogether 42 million exposures (1.3 exposures for each exposed worker on average). Exposure to carcinogenic agents or factors was widespread in many industrial classes included in CAREX. Industries where exposures were most prevalent include forestry (solar radiation), fishing (solar radiation), other mining (silica, diesel exhaust), wood and furniture industries (wood dust, formaldehyde), manufacture of mineral products (silica), construction (silica, solar radiation, diesel exhaust), and air transport (environmental tobacco smoke, ionising radiation).

The total numbers of exposed workers by agent are presented in table 3. The most common exposures in the EU countries were solar radiation (9.1 million workers exposed at least 75% of working time), environmental tobacco smoke (7.5 million workers exposed at least 75% of working time), crystalline silica (3.2 million exposed), diesel exhaust (3.0 million), radon (2.7 million), wood dust (2.6 million), lead and inorganic lead compounds (1.5 million), and benzene (1.4 million). For seven agents (4-aminobiphenyl, dimethylcarbamoyl chloride, N-ethyl-N-nitrosourea, N-methyl-N-nitrosourea, treosulfan, vinylbromide, and vinylfluoride) no occupational exposure was identified as having occured in the EU.

Table 4 The most common carcinogen exposures (in thousands) by country in 1990–3

Agent	*A*	*B*	*D*	*DK*	*E*	*F*	*FIN*	*GB*	*GR*	*I*	*IRL*	*L*	*NL*	*P*	*S*
Solar radiation	240	200	2400	180	1100	1500	180	1300	460	560	110	14	290	370	240
Tobacco smoke, environmental	180	190	2000	100	670	1200	110	1300	170	770	58	11	350	210	210
Silica, crystalline	100	74	1000	59	400	110	83	590	87	280	29	7	170	83	86
Diesel exhaust	79	67	720	71	270	410	39	470	79	550	21	4	110	73	81
Radon	72	86	820	0	280	520	49	560	66	38	24	4	0	92	99
Wood dust	82	55	680	51	400	180	65	430	51	320	18	4	95	86	84
Lead and its compounds	37	30	460	23	100	140	13	250	24	290	9	3	49	33	35
Benzene	49	21	470	49	90	70	14	300	35	190	11	2	43	43	34
Asbestos	15	10	160	9	57	140	7	95	15	680	6	1	14	16	12
Ethylene dibromide	46	17	440	27	81	10	12	280	33	170	10	2	19	40	31
Formaldehyde	17	16	130	90	71	310	11	94	10	180	3	0.6	16	36	11
PAH	19	17	210	13	55	120	6	110	13	350	4	2	26	21	18
Glasswool	23	19	250	14	92	130	12	140	17	150	6	2	34	19	20
Tetrachloroethylene	19	12	210	11	47	140	3	120	14	180	5	1	21	21	16
Chromium (VI) compounds	18	19	260	25	57	70	10	130	10	130	5	1	29	21	21
Sulphuric acid mist	7	10	100	4	20	380	2	42	3	120	2	1	10	5	8
Nickel compounds	12	15	200	11	43	50	8	85	6	79	3	1	19	12	17
Styrene	6	10	110	36	28	50	3	54	4	66	2	0.5	12	7	9
Methylene chloride	2	3	29	23	7	60	1	15	1	130	1	0.2	3	3	2
Trichloroethylene	2	2	33	7	6	110	1	16	1	90	1	0.1	3	2	2
Total, exposures	1100	910	11100	880	4000	6000	650	6600	1100	5600	330	63	1400	1200	1100
Total, exposed workers	790	730	8300	680	3100	4900	510	5000	910	4200	260	48	1100	970	820
Exposed/employed (%)	25	21	24	24	25	23	24	22	27	24	24	25	17	24	20

A=Austria; B=Belgium; D=Germany; DK=Denmark; E=Spain; F=France; FIN=Finland; GB=Great Britain; GR=Greece; I=Italy; IRL=Ireland; L=Luxembourg; NL=The Netherlands; P=Portugal; S=Sweden.

Exposure to hepatitis viruses B and C may occur in the treatment of blood but the numbers of exposed workers could not be estimated.

An estimated 22–24 million workers were exposed to group 1 IARC carcinogens. The most common exposures among group 1 agents were to solar radiation, environmental tobacco smoke, crystalline silica, radon, and wood dust.

These figures are conditional to the minimum criteria of exposure. If low level exposures (close to the non-occupational background) are excluded, the numbers of exposed workers would be 15%–20% lower. On the other hand, the figures for solar radiation and environmental tobacco smoke would have been still higher if short term exposure had been included. The estimate for the number of workers exposed to radon was high. The source of radon exposure is the ground which in certain regions emits radioactive radon gas exposing mainly employees working regularly in ground floors of buildings. The high number of workers considered still to be exposed to benzene was predominantly due to car repair where dermal contact with gasoline containing benzene may occur.

The numbers of exposed workers by country (table 4) ranged from about 50 000 in Luxembourg to over 8 million in Germany. The proportion of exposed workers from the employed labour force varied between 17% in the Netherlands and 27% in Greece. Solar radiation was a very prevalent exposure in countries such as Greece, Portugal, Spain, and Ireland, where agriculture and fishing are the main industries. Passive smoking at work was estimated to be the most common exposure in Great Britain, the Netherlands, and Italy. Relatively high prevalence of exposure to silica and radon were typical of Finland. Formaldehyde was reported to be a common air contaminant in Denmark and France. Asbestos, diesel exhaust, and PAHs were prevalent exposures in Italy. However, these comparisons between countries should be considered with caution because the country specific exposure patterns were not taken into account in all countries, and there were probably also differences between countries in the inclusion of low and potential exposures.

Discussion

The strengths of the CAREX system are its systematic nature, wide coverage, and ease of use. CAREX tries to apply basically the same definitions and procedures to each country, which tends to improve the comparability and consistency of results across countries. It covers all industries in an international classification of industries and is able to provide both national and industry specific estimates. Major known and suspected carcinogens found in the occupational environment, as evaluated by IARC, are included. CAREX is easy to use in personal computers and can be used to produce a large selection of reports. It can be applied to new (non-EU) countries to generate preliminary estimates of numbers of exposed workers, provided that reasonably accurate statistics on the national labour force are available.

The validity of the CAREX estimates was extensively discussed in the planning team before the construction of CAREX, and several measures to improve validity were adopted. Firstly, all estimates were standardised by the labour force structure of individual countries. Secondly, uniform definitions of agents and of occupational exposure, with inclusions and exclusions, were used to improve consistency. Thirdly, preliminary estimates were in some countries checked and modified by national experts familiar with the exposure situation in their own country. Fourthly, exposures in the reference countries were documented and estimated as specifically (at the subindustrial level) as possible to provide a sufficient knowledge base for the estimations in other countries. Fifthly, industrial hygiene data and descriptive information of exposures were included in the database to support estimation efforts. Sixthly, estimates suspected to represent low levels of occupational exposure were marked to allow their inclusion or exclusion since low exposures may have a strong effect on the estimated numbers of exposed. Seventhly, preliminary estimates for non-reference countries were selected by professional judgement to be the most valid out of alternative estimates AVE, FIN, United States, OWN, or ZERO. Despite of these precautions and the aids included in the CAREX system, there are still many validity issues of concern—such as differences of country specific use patterns for carcinogens, differences of national survey protocols, time frame, national industrial coding systems (conversion difficulties), and assessment of multiple exposures. These points are discussed separately below.

Omission of country specific exposure patterns may bias results seriously. One illustrative example is exposure to radon from the ground which is higher in Finland than in most EU countries possibly resulting in overestimation in other countries if not adequately checked by national experts. Similar potential for bias concerns crystalline silica, because Finnish stone and construction materials often contain granite and thereby silica. Solar radiation has the opposite potential for bias. Direct use of Finnish prevalence figures (prevalence of regular outdoor workers) is likely to result in underestimation for countries in southern Europe where many part time outdoor workers will be occupationally exposed to higher doses than regular outdoor workers in Finland due to more intense solar radiation. The industrial substructure of many countries may also differ considerably from the United States and Finland depending on the type of products or processes used. This may be true particularly for the chemical industries.

Different legislation may lead to large variations in exposure patterns between countries, as is the case of asbestos or passive smoking at work. Sometimes the use pattern is strongly influenced by national price policy. For example, exposure to ethylene dibromide (scavenger agent in leaded gasoline) decreased drastically in Finland in 1990–3 when unleaded gasoline was substituted for more expensive leaded gasoline.

Because the average prevalence of the United States and Finland was preferred in the CAREX procedure, the preliminary estimates inherently assume that the exposure pattern of the country is typically between that of a large country—such as the United States—and that of a smaller country—such as Finland. This assumption may be fairly valid for large European countries (such as the United Kingdom, France, Germany, Italy, and Spain) where a wide range of processes and exposures occur. However, the CAREX procedure probably provides incorrect non-zero estimates for rare exposures which do not occur in small countries with less varying economic structure—such as Luxembourg.

The adjustment of default estimates to correspond with the national situation turned out to be problematic. The national adjustment resulted in an increase of the total number of workers exposed to CAREX agents in Denmark (+15%) and France (+4%), but a decrease in Italy (-7%) and the Netherlands (-17%). The impact of the adjustment was also agent specific, extending from nil to substantial—for example, radon. Although national experts were able to adjust figures to correspond better to exposure patterns of their countries, it is likely that the adjustments were sensitive to the definition of exposure—for example, inclusion or exclusion of potential and low exposures—in survey data and other exposure information used by the experts.

The concept of exposure in the reference countries differed. The Finnish protocol required in most cases that non-occupational exposure, measured as annual dose, had to be exceeded, whereas the United States protocol considered potential exposure. The Finnish approach sets the minimum exposure generally at a higher level than the United States approach, and results therefore in lower proportions of exposed workers. The CAREX system compromises between these two concepts by usually applying the average of the United States and Finnish prevalences to calculate preliminary estimates for other countries. This means that the concept of exposure in CAREX is somewhere between potential exposure (as in the United States) and exposure exceeding non-occupational background (as in Finland). CAREX therefore includes some exposures which may be lower than the background. If exposures marked as low (close to the non-occupational background) are excluded, the total number of exposures drops by 3% in Finland and by 31% in the United States. For other countries, whose estimates are mainly based on average exposure prevalences occurring in Finland and the United States, the share of low exposures would be on this basis 15%–20%.

The United States data were based on an observational field survey and the Finnish data on professional judgement. Both methods have their advantages and disadvantages. The NOES survey was sensitive in identifying exposures whereas the Finnish procedure often neglected small exposed groups and atypical exposures. However, sometimes the opposite was the case. For example, the NOES sample did not include any nickel refineries and was therefore unable to identify nickel exposure in ISIC 372 (manufacture of other metals). The Finnish professional judgement identified nickel refineries and provided a more reliable estimate in this case.

The reference data from the United States came from a field survey performed in 1981–3. Exposure patterns have probably changed after that in the United States and elsewhere. For example, the production or use of some agents—for example, asbestos—has been restricted since then. Although CAREX did not use clearly outdated United States figures as default values, all of them could probably not be identified. Therefore some of the resulting CAREX estimates may follow too closely the

United States exposure situation in the early 1980s when occupational exposure to some carcinogens probably happened more often than in 1990–3. The Finnish estimates were for the assessment period 1990–3.

Conversions between different industrial coding systems were used in the processing of labour force statistics and United States (NOES) exposure data. The main part of labour force statistics came from OECD directly in the UN ISIC revision 2 coding system. However, the OECD data were not coded originally according to UN ISIC but according to national classifications which are then converted to UN ISIC. In the conversions, different definitions of the employed populations and estimations of missing values caused some inaccuracy and incomparability to the labour force statistics used in CAREX. The United States labour force figures and exposure data were converted from United States standard industrial classification (SIC) (1987 version) through UN ISIC revision 3 to UN ISIC revision 2. The conversion was carried out at the maximal level of specificity to minimise conversion errors. Despite conversion problems, the order of magnitude of the labour force figures in the reference countries is probably correct and not a main source of error.

The CAREX system applied Finnish values to other EU countries in estimating the degree of multiple exposure. This sometimes resulted in estimates of exposed workers which exceeded even the total labour force of industrial classification. In those cases, the Finnish multiplier clearly underestimated multiple exposure in that country and was inappropriate. National modifications of multiple exposure multipliers are therefore necessary, especially if the exposure pattern is likely to differ significantly from the Finnish one.

The numbers of workers exposed to known or suspected carcinogens generated by the CAREX system and the network of national experts are the first estimates published for the EU and some of the member countries. In that respect this new approach turned out to be feasible and successful. The results suggest that the number of workers exposed to carcinogenic substances and factors in 1990–3 amounted to about 32 million workers, or about 23% of the total number of workers employed in the EU. Of these at least 22 million were exposed to agents classified as definite human carcinogens by the IARC. Substantial parts of all exposures originated from natural sources (ultraviolet radiation from the sun, radon from the ground) or from activities not related to work as such (environmental tobacco smoke at work). The contribution of these environmental factors was almost half out of 42 million exposures. The level of exposure for many exposed groups was low, and consequently also the risk of cancer for such groups is likely to be low. If worker groups identified as being exposed to low levels close to the levels originating from ambient and indoor air were to be excluded, the numbers of exposed workers would drop by 15%–20%.

Empirical validity testing of CAREX would require well defined and comprehensive field surveys and measurements because validity may vary by agent, industry, and country. Such surveys are laborious and expensive to carry out. We think that the CAREX procedure, especially when supplemented by the assessments of national experts, has produced relatively valid estimates. However, the continuation of this work is recommended for several reasons. Firstly, some of the estimates reported are already outdated. Exposure in many countries has been recently restricted for some agents including asbestos and passive smoking at work. Also leaded gasoline (including ethylene dibromide) has been replaced in some countries largely by unleaded gasoline (including MTBE). Secondly, national exposure patterns were not taken into account in all countries. For example, new data on national radon concentrations would help to improve estimates on occupational radon exposure. Thirdly, the estimates of the reference countries could be critically reviewed against industrial hygiene measurement data which may lead to exclusions of some exposures in CAREX. By contrast, some exposures may have to be added to CAREX. For example, exposure to silica in potato farming (machine sorting of potatoes grown in sandy ground) was not considered to entail exposure elsewhere than in The Netherlands. Industrial hygiene data could be surveyed to find out if exposures like this should be recognised also in other countries. The assessment team could learn from each other's data, which would probably increase awareness of unidentified exposures and risks at a national level. The continuation of work would increase the validity of national estimates and would thereby facilitate quantitative risk assessment, priority setting, and effective prevention of occupational cancer at the European and national levels.

A substantial part of the CAREX data are freely available on the internet through the Finnish Institute of Occupational Health (http://www.occuphealth.fi/list/data/CAREX), or through the IARC (http://www.iarc.fr). The Spanish version of CAREX is under preparation at Institut Municipal d'Investigació Mèdica in Barcelona (http://www.imim.es).

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Vancouver style

All manuscripts submitted to *Occup Environ Med* should conform to the uniform requirements for manuscripts submitted to biomedical journals (known as the Vancouver style.)

Occup Environ Med, together with many other international biomedical journals, has agreed to accept articles prepared in accordance with the Vancouver style. The style (described in full in the *JAMA*[1]) is intended to standardise requirements for authors, and is the same as in this issue.

References should be numbered consecutively in the order in which they are first mentioned in the text by Arabic numerals on the line in square brackets on each occasion the reference is cited (Manson[1] confirmed other reports[2][3][4][5]). In future references to papers submitted to *Occup Environ Med* should include: the names of all authors if there are three or less or, if there are more, the first three followed by *et al*; the title of journal articles or book chapters; the titles of journals abbreviated according to the style of *Index Medicus*; and the first and final page numbers of the article or chapter. Titles not in *Index Medicus* should be given in full.

Examples of common forms of references are:

1 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomed journals. *JAMA* 1993;**269**:2282-6.
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