Environmental Burden of Disease Series, No. 6

Occupational carcinogens

Assessing the environmental burden of disease at national and local levels

Tim Driscoll
Kyle Steenland
Annette Prüss-Üstün
Deborah Imel Nelson
James Leigh

Series Editors
Annette Prüss-Üstün, Diarmid Campbell-Lendrum, Carlos Corvalán, Alistair Woodward

World Health Organization
Protection of the Human Environment
Geneva 2004

WHO Library Cataloguing-in-Publication Data

Occupational carcinogens: assessing the environmental burden of disease at national and local levels / Tim Driscoll ... [et al.].

(Environmental burden of disease series / series editors: Annette Prüss-Üstün ... [et al.] ; no. 6)

1.Carcinogens, Environmental - adverse effects 2.Occupational exposure 3.Lung neoplasms - chemically induced 4.Leukemia - chemically induced 5.Mesothelioma - chemically induced 6.Cost of illness 7.Epidemiologic studies 8.Risk assessment - methods 9.Manuals I.Driscoll, Tim. II.Prüss-Üstün, Annette. III.Series.

ISBN 92 4 159147 1 (LC/NLM classification: QZ 202)
ISSN 1728-1652

Suggested Citation

Tim Driscoll, et al. *Occupational carcinogens: assessing the environmental burden of disease at national and local levels*. Geneva, World Health Organization, 2004. (Environmental Burden of Disease Series, No. 6).

Printed by the WHO Document Production Services, Geneva, Switzerland.

Table of Contents

List of Tables

List of Figures

Preface

The disease burden of a population, and how that burden is distributed across different subpopulations (e.g. infants, women), are important pieces of information for defining strategies to improve population health. For policy-makers, disease burden estimates provide an indication of the health gains that could be achieved by targeted action against specific risk factors. The measures also allow policy-makers to prioritize actions and direct them to the population groups at highest risk. To help provide a reliable source of information for policy-makers, WHO recently analysed 26 risk factors worldwide, including occupational carcinogens, in the *World Health Report* (WHO, 2002).

The Environmental Burden of Disease (EBD) series continues this effort to generate reliable information, by presenting methods for assessing the burden of disease from occupational exposure to carcinogens at national and local levels. The methods in the series use the general framework for global assessments described in the *World Health Report* (WHO, 2002). The introductory volume in the series outlines the general method (Prüss-Üstün et al., 2003), while subsequent guides address specific environmental risk factors. The guides on specific risk factors are organized similarly, first outlining the evidence linking the risk factor to health, and then describing a method for estimating the health impact of that risk factor on the population. All the guides take a practical, step-by-step approach and use numerical examples. The methods described in the guides can be adapted both to local and national levels, and can be tailored to suit data availability. The EBD series of guides aim to provide rational information that can help to design protective measures for reducing workplace risks.

Affiliations and acknowledgements

This document was prepared by Tim Driscoll, Kyle Steenland, Annette Prüss-Üstün, Deborah Imel Nelson and James Leigh, and edited by Annette Prüss-Üstün, Diarmid Campbell-Lendrum, Alistair Woodward and Carlos Corvalán.

Tim Driscoll is from the School of Public Health, University of Sydney and ELMATOM Pty Ltd. Kyle Steenland is at the Rollins School of Public Health. Deborah Imel Nelson is at the School of Civil Engineering and Environmental Science, University of Oklahoma. James Leigh is at the School of Public Health, University of Sydney. Annette Prüss-Üstün, Diarmid Campbell-Lendrum and Carlos Corvalán are at the World Health Organization, Geneva. Alistair Woodward is from the Wellington School of Medicine, New Zealand.

The authors would like to thank Marisol Concha-Barrientos and Marilyn Fingerhut, who contributed to the carcinogens component of the Global Burden of Disease project, and the many reviewers whose comments helped to improve this guide.

We also thank the United States of America Environmental Protection Agency for supporting the development of the EBD approaches. This report has not been subjected to agency review and therefore does not necessarily reflect the views of the agency. Finally, we are grateful to Kevin Farrell and Eileen Brown who put this document into its final format.

Abbreviations

AF	Attributable fraction (equivalent to the IF, or impact fraction).
CAREX	International information system on occupational exposure to carcinogens.
CRA	Comparative risk assessment.
DALY	Disability-adjusted life year.
EBD	Environmental burden of disease.
IF	Impact fraction.
ILO	International Labour Organization
PEL	Permissible exposure level.
RR	Relative risk.
SMR	Standard mortality ratio.
USA	United States of America.

Glossary of terms

Economically Active Population: All people in the population who are working or seeking work. This parameter includes people in paid employment, the self-employed, those who produce goods and services for their own household consumption, and those unemployed who are seeking work.

Standardized Mortality Ratio (SMR): The ratio of the number of events observed in a study population to the number that would be expected if the study population had the same specific rates as the standard population, multiplied by 100.

IARC groups:

Group 1	Carcinogenic to humans
Group 2A	Probably carcinogenic to humans
Group 2B	Possibly carcinogenic to humans
Group 3	Not classifiable as to its carcinogenicity to humans
Group 4	Probably not carcinogenic to humans

Summary

This guide provides practical advice for assessing the current burden of disease from past and current occupational exposures to carcinogens. The outcomes of such exposures include lung cancer, leukaemia and malignant mesothelioma. The disease burden is measured in terms of the number and proportion of deaths from these conditions, as well as in terms of total disability (using disability-adjusted life years, or DALYs).

Exposure at national level is estimated using workforce data for the country, as well as exposure data for carcinogens in different industries (based on European data). The relative risk for cancer for each carcinogen is estimated from international literature. This information is combined to estimate the impact in each country of occupational exposures to carcinogens. This figure is termed the population attributable fraction (AF), and AF estimates are presented as fractions of the deaths and disability that are caused by occupational exposures to carcinogens. The number of deaths attributable to the occupational exposures to carcinogens can then be estimated by multiplying the AF by the number of deaths in the country. The extent of disability can also be estimated by multiplying the AF by disease-specific estimates of DALYs.

1. Introduction

1.1 Overview

This guide provides practical advice for assessing the current burden of disease that results from past and current occupational exposures to carcinogens. The disease outcomes considered are lung cancer, leukaemia and malignant mesothelioma, and the disease burden is described both in terms of deaths and DALYs.

1.2 Identification of the risk factors

The International Agency for Research on Cancer (IARC, 2002) has classified 150 chemical or biological agents as known or probable human carcinogens, and exposures to many of these carcinogens (e.g. asbestos, cadmium and benzene) occur in occupational settings. Occupational exposure is defined as any contact between the human body and a potentially harmful agent or environment in the workplace. Specific exposures are related to the type of work that people do (i.e. occupation), where they do it (e.g. the industrial sector – also called the economic sector) and the measures that are taken to limit exposures. The probability that a worker will develop cancer is influenced by the total dose of carcinogen received, the potency of the carcinogen, the presence of other exposures (notably tobacco smoking), and individual susceptibility. Excess exposure to carcinogens can lead to changes at the cellular level, resulting in the uncontrolled growth of abnormal cells that invade and destroy normal tissues in the lung, blood system, etc.

The exposures included in this guide were selected on the basis of the strength of the evidence for causality, the magnitude of the risk arising from the exposure, and the likely availability of data. For an agent to be classified as carcinogenic, there must be sufficient evidence from studies on humans. Sufficient evidence implies that a causal relationship has been established between human cancer and exposure to the agent, mixture, or exposure circumstance, and that chance, bias and confounding can be ruled out with reasonable confidence. IARC has classified 87 agents, mixtures, or exposure circumstances as Group 1 Carcinogenic to Humans, including various chemical compounds, pharmaceuticals, and bacterial and viral infections. An additional 63 agents, mixtures, or exposure circumstances have been classified as Group 2A Probably Carcinogenic to Humans (IARC, 2001). With the exceptions described below, the analysis in this document includes IARC Group 1 and 2A carcinogens associated with cancers of the lung, leukaemia, and malignant mesothelioma (Table 1).

Table 1 Selected occupational carcinogens and health outcomes

Occupational carcinogen	Outcome
Arsenic, asbestos, beryllium, cadmium, chromium, diesel exhaust, nickel, silica	Cancer of the trachea, bronchus, or lung
Benzene, ethylene oxide, and ionizing radiation	Leukaemia
Asbestos	Malignant mesothelioma

The most important lung carcinogens in occupational settings are asbestos, radon, arsenic, chromium, silica, beryllium, nickel, cadmium and diesel exhaust. The most important agents for leukaemia are benzene, ionizing radiation and ethylene oxide. Asbestos is a causal agent of asbestosis, lung cancer and malignant mesothelioma, and silica causes silicosis in addition to lung cancer (the role of asbestos in asbestosis and silica in silicosis is also considered in a forthcoming guide in the EBD series, on occupational airborne particulates). Several important carcinogens (e.g. radon) are not evaluated in this guide, either because there are no evaluative criteria from the IARC, or because exposure data are limited or nonexistent.

1.3 The burden of disease from occupational exposures

Methods have been developed that allow disease burdens to be estimated for particular occupational exposures, or that examine the overall contribution of occupational exposures to the occurrence of cancer. In Canada, Kraut (1994) estimated the extent of occupational disease morbidity and mortality by comparing data from the national workers' compensation boards with data from the United States of America (USA) and Canada (adjusted to the Canadian workforce), and applying a proportionate model of overall disease incidence obtained through literature review. They estimated that each year there were between 77 900 and 112 000 new cases of occupational disease, and between 2381 to 6010 deaths attributable to occupational disease. Another study reviewed data from national surveys and applied an AF proportion method, and estimated that 6–10% of cancers in the USA were related to occupation (Leigh et al., 1997).

The relative risks of exposure for nine lung carcinogens (arsenic, asbestos, beryllium, cadmium, chromium, diesel fumes, nickel, silica and radon) were estimated for the USA, using inverse variance and a random effects model, and major cohort studies of the specific agents (Steenland et al., 1996). Agents to which relatively few workers were exposed (bis(chloromethyl)ether, coke oven and coal gasification fumes, and soot) were not analysed, nor was smoking considered, except for using relative risk estimates adjusted for smoking. The combined relative risk values for all lung carcinogens (except radon) ranged from 1.31 to 3.69, from which it was estimated that past exposures to occupational carcinogens (except radon) accounted for lung cancer in 9000–10 000 men and 900–1900 women in the USA annually. These figures represent approximately 9% of the lung cancer deaths in males and 2% in females, or 0.5% of all deaths annually in the USA.

To estimate the number of occupational deaths from lung cancer and other outcomes, the AFs from several studies were applied to the deaths occurring in 1997 in the USA (Steenland et al., 2003). The population attributable risk for lung cancer ranged from 6.1% to 17.3% for men, and was 2% for women. For bladder cancer, the corresponding range was 7–19% for men, and was 11% for women. Occupational exposures accounted for 85–90% of malignant mesothelioma cases in men, and 23–90% of those in women. The combined population attributable risk for leukaemia was calculated to be 0.8–2.8%.

Markowitz et al. (1998) estimated the total number of deaths in New York State attributable to occupational exposures, using data from the New York State Workers' Compensation Board, the USA Occupational Safety and Health Administration, disease registries maintained by the New York State Department of Health, and physicians' reports. For each disease, the percentage of deaths that could be attributed to occupation was multiplied by the disease-specific mortality totals. It was estimated that 10% of all deaths from cancer, 100% of deaths from all pneumoconioses, and 1–3 % of deaths from all chronic respiratory, cardiovascular, neurological, and renal diseases were due to occupational exposures.

To estimate the proportion of deaths in Australia that were attributable to occupational exposure to hazardous substances, Morrell et al. (1998) used published figures for major disease categories in countries similar to Australia. The proportion of mortality for each disease category that was attributable to occupational exposures to hazardous substances was applied to the number of deaths in Australia from 1989 to 1992. The data were supplemented by limited direct information on acute exposures to hazardous substances, and national information on malignant mesothelioma. The results suggested that approximately 1% of all deaths in Australia are due to occupational cancers.

Nurminen & Karjalainen (2001) estimated the proportion of fatalities related to occupational factors in Finland. The average number of exposed workers in Finland was estimated from census data stratified by gender, age, occupation and industry, and from the FINJEM national job-exposure matrix. Relative risks were obtained from review of epidemiological studies, focusing on risk estimates that were most valid for the Finnish exposure circumstances. The authors used AF methodology to determine the proportion of deaths in the population attributable to occupational factors, and reported that 30% of these deaths in 1996 were caused by cancer. Occupational lung cancer accounted for 0.9% of all deaths, and leukaemia, malignant mesothelioma and other cancers together accounted for another 0.2% of all deaths. The authors attributed 24% of bronchus and lung cancers (29% for men and 5.3% for women) to occupational exposures to combined risk factors. The AFs for urinary cancer were 10.3% overall, and 14.2% for men and 0.7% for women. Occupational risk factors also accounted for 10.9% (18.5% for males, 2.5% for females) of leukaemia deaths, the majority (17.8% for males and 2.3% for females) from electrical occupations. In contrast, only 0.7% (males) and 0.2% (females) of leukaemia deaths were attributable to occupational exposure to benzene. For malignant mesothelioma cases, an average of 71.3% (90% for males, 25% for females) was attributed to occupation.

These review studies assessed risk measures for the main sites of the body affected by occupational cancers, including the lung (which, for the purposes of the current approach, includes the trachea, bronchus and lung), the haematopoietic system (represented by leukaemia for this approach), and the mesothelium.

2. Summary of the methods

The methods described in the following approach follow those used in the occupational carcinogen section of the WHO Global Burden of Disease project (Concha-Barrientos et al., 2004). The first step is to identify known occupational carcinogens. The second step is to identify the proportion of the country population with exposure to the chemical or physical agent, and divide this proportion into high-exposure and low-exposure groups. Third, given exposure to the carcinogen, the relative risk for cancer is determined from the literature. Fourth, to determine the global impact of carcinogens, information on the fraction of the population exposed is combined with data on the risks. The impact of a carcinogen is described in terms of the fraction of deaths and disability caused by the carcinogen, and is termed the population AF, or IF.

For malignant mesothelioma, several different approaches are suggested. The AFs are multiplied by the number of deaths from lung cancer and leukaemia to obtain an estimate of the annual number of deaths caused by occupational exposures. For mesothelioma, the annual number of deaths is not always available in each country or subregion. In such cases, an alternative approach is to estimate the number of mesothelioma deaths due to asbestos exposure from the fraction of lung cancer deaths due to asbestos exposure.

AFs are also multiplied by estimated disease-specific DALYs, which are weighted estimates of the number of years lived with the disability. The weighting refers to the severity of the disability. To calculate DALYs requires an estimate of the age at which a disease occurs, an estimate of the duration of the disease, and often an estimate of the life expectancy of the person who is ill. The calculation also requires a severity weighting for the disability, which is based on expert judgement. The weighting is 1.0 in the case of premature death due to the disease, and the DALYs in effect become an estimate of the years of life lost due to premature death. DALYs can be calculated for all diseases regardless of cause, provided that certain parameters are known (e.g. the severity weighting, duration of illness and age of onset). A table of DALYs, by disease, is shown for different subregions in Table 5, and more information is available from WHO (www.who.int/evidence/bod)[1].

[1] Select consecutively "Global burden of disease estimates", "GBD 2001 estimates", "Estimates by subregion", and then "DALY".

3. Choice of health outcomes

Work-related malignant conditions can arise from a variety of exposures, but we consider only the three main documented occupational cancers: lung cancer, leukaemia and malignant mesothelioma. Although other cancers are known to have occupational causes, there are not enough data on exposure and risk, and the number of cases are too few, for the data to be included in this guide. These other cancers (and their causative agents) include:

- bladder cancer (aromatic amines, benzidine dyes and methylene-bis-ortho-chloroaniline);
- liver cancer (vinyl chloride);
- nasal cavity and middle ear cancer (hardwood dust, chromium VI compounds, nickel compounds);
- bone and articular cartilage cancer (ionizing radiation);
- skin cancer (arsenic, by-products of distillation, ionizing radiation);
- lung cancer (from passive smoke in the workplace).

Although studies have shown that some exposures increase a person's risk of developing certain malignancies, it is rarely possible to conclusively link cancer in an individual to a particular exposure. Therefore, it is not possible to estimate the burden of cancer attributable to occupational exposures simply by counting the number of attributable cases of one or more types of cancer. Instead, population studies must be used.

In the comparative risk assessment (CRA) study of Concha-Barrientos et al. (2004), the criteria used to assess causal connections between exposures and outcomes of interest were a consistent relationship between the risk factor and the outcome across different studies and settings; and the strength of the evidence of the relationship. Data sources were evaluated to assess the strength of the evidence linking specific cancers with exposure to chemical or physical agents.

The sources of data used here to identify occupational carcinogens for lung cancer and leukaemia, as well as literature on the relationship between mesothelioma and asbestos, are given in Table 2. Mesothelioma is caused only by asbestos, and is unlike lung cancer and leukaemia, which can be caused by a variety of agents, only some of which are occupational. On the other hand, not all mesothelioma is caused by occupational exposure to asbestos; some asbestos exposure is non-occupational.

Table 2 Sources used to assess the strength of evidence for causality for selected occupational carcinogens

Selected risk factor	Health outcome	Examples of key sources of evidence for causality
Occupational carcinogens	Lung cancer and leukaemia	International Agency for Research on Cancer (IARC), various dates. Agents and groups of agents, mixtures, and exposure circumstances evaluated by IARC as Group 1 (carcinogenic to humans), or Group 2A (probably carcinogenic to humans).
Lung carcinogens	Cancer of the trachea, bronchus or lung	Steenland et al. (1996); Nurminen & Karjalainen (2001); K. Steenland et al. (2003).
Leukaemogens	Leukaemia	BEIR V (1990); IARC (1997); Lynge, Anttila & Hemminki (1997).
Asbestos	Malignant mesothelioma	IARC (1977); IPCS (1998); Hodgson & Darnton (2000), Yano et al. (2001).

4. Relative risk estimates from the literature

For this analysis, relative risks were determined for lung cancer and leukaemia, and were assumed to apply equally to the risk of developing the malignant condition (incident cases) and to the risk of dying from the condition (fatal cases). Two levels of exposure are chosen: high exposure is above the relevant USA Permissible Exposure Level (PEL), and low exposure below it. We do this because available exposure and risk measures are often reported in terms of the PEL; and because the Occupational Safety and Health Administration of the USA has not changed the PELs for many carcinogens since they were adopted in 1971. This allows a stable benchmark for comparisons, which is appropriate for cancers with long latency periods (Concha-Barrientos et al., 2004). The relative risks, and estimates of the proportion of the population occupationally exposed to lung carcinogens and leukaemogens, were then used to calculate AFs.

A different approach was taken for malignant mesothelioma. To calculate AFs we did not first estimate relative risks for exposed workers versus a non-exposed population, because populations not exposed to asbestos do not have mesothelioma, which is caused only by asbestos. However, while mesothelioma is uniquely caused by asbestos, not all asbestos exposure is occupational. Thus, we used an estimate that 90% of male mesothelioma and 25% of female mesothelioma is caused by occupational asbestos exposure (Nurminen & Karjalainen, 2001; Steenland et al., 2003). We then multiplied these percentages (which are AFs) by the number of mesothelioma deaths in a subregion or country. For cases in which the number of mesothelioma deaths are not available, we outline a different approach that estimates occupationally-caused mesothelioma deaths as a proportion of the lung cancer deaths caused by asbestos.

Of the reviews described above, only three provided summary measures of relative risk, or information that can be used to determine such measures, for one or more of the main agents and outcomes of interest (Steenland et al., 1996; Nurminen & Karjalainen, 2001; K. Steenland et al., 2003). The study of Nurminen & Karjalainen (2001) focuses on Finland and preferentially uses studies based in Scandinavia, or thought to be most relevant to Finland. Most of the relative risk estimates relate to lung cancer, but AFs are presented for leukaemia and malignant mesothelioma. Although the Steenland et al. (1996) study focuses on the USA, it includes more data of suitable quality. The Steenland et al. (2003) study provides information on the relative risks for mortality similar to that in the Steenland et al. (1996) study. All studies provide similar summary measures of relative risk for lung cancers, but the Steenland et al. (1996) results are used preferentially because they are generally based on a broader range of studies. However, Steenland et al. (1996) provide information only on lung cancer.

The literature used to estimate the relative risks for exposures to specific carcinogens is presented in Annex 1. The carcinogens and associated relative risks for lung cancer and leukaemia are summarized in Table 3.

Table 3 Estimated relative risks for lung carcinogens and leukaemogens included in this study

Risk factor	Relative risk[a]	95% CI[b]
Lung carcinogens[c]		
Arsenic	3.69	3.06–4.46
Asbestos	2.00	1.90–2.11
Beryllium	1.49	
Cadmium	1.49	0.96–2.22
Chromium	2.78	2.47–3.52
Diesel exhaust	1.31	1.13–1.44
Nickel	1.56	1.41–1.73
Silica	1.33	1.21–1.45
Leukaemogens[d]		
Benzene (low exposure)	2.0	1.8–2.2
Benzene (high exposure)	4.0	3.6–4.4
Ionizing radiation (low exposure)	1.22	1.07–1.70
Ionizing radiation (high exposure)	1.57	1.18–2.88
Ethylene oxide (low exposure)	1.1	
Ethylene oxide (high exposure)	3.5	

[a] The relative risks for lung carcinogens are based on Steenland et al. (1996, 2003); Nurminen & Karjalainen (2001). The relative risks for the leukaemogens are based on BEIR V (1990); IARC (1997); Lynge, Anttila & Hemminki (1997); Steenland et al (2003).

[b] 95% confidence interval.

[c] The health outcomes of the lung carcinogens are cancers of the trachea, bronchus or lung.

[d] The health outcome of the leukaemogens is leukaemia.

5. Estimation of exposure

To estimate the proportion of workers exposed to carcinogens for lung cancer and leukaemia, we use the exposed proportions of workers in the industrial sectors or occupations who were exposed to the carcinogens (from CAREX, a European survey described below in Section 5.2). This was the approach recently used in a global estimate of the disease burden (Ezzati et al., 2002; WHO, 2002; Concha-Barrientos et al., 2004). However, should exposure data be available for the national or local level, they should be used instead of the CAREX data. For the CRA project (Concha-Barrientos et al., 2004), routine employment data were used to determine the proportion of people in each industrial sector. The exposed populations were then divided into high and low exposure groups. This information was then combined with the CAREX data to estimate the proportion of workers exposed at high or low levels to the carcinogens.

The method for estimating the proportion of people exposed to occupational carcinogens, as well as the exposure levels, requires the following information:

i. the proportion of the workforce employed in each sector;

ii. the proportion of workers exposed to individual carcinogens;

iii. the likely turnover of workers;

iv. the estimated level of exposure;

v. the proportion of the population who are in the workforce.

Ideally, the above information should come from data assessed in the country or study area, particularly the first three requirements, but since this is not always possible values based on the global analysis can be used (Concha-Barrientos et al., 2004).

5.1 The proportion of the workforce employed in each sector

The approach used in this guide requires information on the employment distribution of workers among the different industrial sectors of a country. This information is required for the same sectors that are used in the CAREX survey, which are agriculture, mining, manufacturing, electricity, construction, trade, transportation, finance and communications. The proportion of workers in each sector should be available from employment surveys or other employment information collected by the government. If the information on the employment sectors is not in the same groupings as used in the CAREX survey, available groupings should be allocated to the CAREX groups as best as possible.

5.2 The proportion of workers exposed to individual carcinogens

If country-level data are not available, the proportion of workers in each employment sector who are exposed to carcinogens can be estimated from the CAREX survey (FIOH, 1998). This survey of 139 carcinogens presents data on the proportion of workers in the European Union exposed to higher-than-background levels of the

carcinogens (IARC Class 1, 2A, and selected 2B agents) between 1990–1993. The survey provides information on the proportion of workers exposed to each carcinogen, *not* the level of exposure. If CAREX data are to be used for a national assessment, an assumption is that for each carcinogen the proportion of exposed workers in a CAREX employment sector is similar to that of the country under study. It also has to be assumed that the exposure probabilities are the same for male, female, younger and older workers, because the CAREX study does not provide that level of resolution. The analysis in this guide incorporates information from CAREX on eight lung carcinogens and three leukaemogens (Table 4).

Table 4 Proportion of the workforce exposed to carcinogens, by industry sector[a]

Carcinogen	Agri-culture	Mining	Manufac-turing	Electrical	Construc-tion	Trade	Transpor-tation	Finance	Services
Lung carcinogens									
Silica	0.004	0.230	0.023	0.014	0.189	0.000	0.00476	0.000	0.001
Cadmium	0.000	0.000	0.005	0.003	0.003	0.000	0.00065	0.000	0.000
Nickel	0.000	0.020	0.017	0.004	0.000	0.000	0.00003	0.000	0.000
Arsenic	0.001	0.001	0.004	0.001	0.001	0.000	0.00000	0.000	0.000
Chromium	0.000	0.003	0.021	0.004	0.002	0.000	0.00370	0.000	0.002
Diesel fumes	0.006	0.220	0.011	0.034	0.058	0.005	0.13438	0.000	0.009
Beryllium	0.000	0.001	0.002	0.001	0.000	0.000	0.00011	0.000	0.000
Asbestos	0.012	0.102	0.006	0.017	0.052	0.003	0.00684	0.000	0.003
Leukaemogens									
Benzene	0.001	0.002	0.003	0.001	0.001	0.01	0.00500	0	0.02
Ionizing radiation	0	0.011	0	0.034	0	0	0.00400	0	0.0
Ethylene oxide	0.00012	0.00137	0.0006	0.00006	0.00027	0	0.00002	0	0.00057

[a] Source: CAREX survey (FIOH, 1998).

5.3 Occupational turnover

In contrast to occupational injury, in which the worker is only at risk during exposure to potentially unsafe conditions, cancers have long latency periods. Once the disease process has begun, the worker continues to be at risk, even after exposure ceases. This means that people who were exposed in the past must be considered as currently exposed, even if they are currently working in jobs with no exposure, or are retired. Occupational turnover refers to the annual replacement of workers in jobs, and accounts for exposed workers who leave their jobs. Occupational turnover increases the number of people exposed to an occupational risk, so at any given time the total number of people who have *ever* been exposed will be greater than the number *currently* exposed. Occupational turnover therefore has to be considered when estimating the number of exposed people. If the turnover cannot be estimated at national or local level, a turnover factor of four can be used. This factor was estimated on the basis of published data on labour turnover rates, on published cohort data, and on modelling of cohorts with varying mean lengths of exposure (Nelson et

al., 2002; Concha-Barrientos et al., 2004). The turnover adjustment factor is multiplied by the estimated number of workers currently exposed, to estimate the number of workers ever-exposed.

5.4 The level of exposure

If available, country-level measurements should be used to partition workers into high and low levels of exposure. For the purposes of this analysis, high levels of exposure are defined as being above the relevant USA PEL, and low levels as being below the PEL. If national or local data are not available, a mean partitioning factor can be used that is based on cohorts reported in the literature (Concha-Barrientos et al., 2004). According to this review, exposed populations in industrialized subregions (countries in subregion A; Annex 2) can be partitioned into 0.10 with high exposure and 0.90 with low exposure. For industrializing subregions (countries in subregions B, C, D, E), the exposed populations can be partitioned 50:50 into the high and low exposure categories.

5.5 The proportion of the population in the workforce

The proportion of the total population in the workforce (i.e. the Economically Active Population – see Glossary) is required for the assessment in this guide. This information should be available from employment surveys or other employment information collected by the national or local government (e.g. the ministry of labour, or its equivalent).

6. Estimated average relative risks for lung cancer and leukaemia

6.1 Lung cancer

The relative risks we propose are based on the approach taken in the CRA analysis (Concha-Barrientos et. al., 2004). Using the data of Steenland et al. (1996), a mean relative risk of 1.6 is estimated for workers exposed to eight lung carcinogens (not including radon). The mean relative risk is calculated from an average of the relative risks for each lung carcinogen, weighted by the proportion of workers exposed to each carcinogen. To estimate an uncertainty range for the mean relative risk, weighted lower and upper 95% confidence intervals are calculated for the relative risks of each substance (except beryllium, for which there were no estimated confidence intervals). This yields a 95% confidence interval of 1.4–1.8.

Relative risks can also be estimated separately by subregion. Again, the subregional relative risks can be weighted for each carcinogen, using the proportions of workers in each subregion who have been exposed to each carcinogen. However, the resulting average relative risks are not meaningfully different (all are close to 1.6) and imply a level of accuracy that is not justified by the data. Therefore, 1.6 is used for all subregions.

To produce relative risk estimates for low and high exposures, the mean relative risks are partitioned into values that correspond to low and high levels of exposure. Data for the USA are used because these are the most reliable and comprehensive. Based on these data, lung carcinogen exposures for 90% of workers in the USA are at or below one fifth of the carcinogen PEL values, and 10% are above the PEL values. This information is combined with an estimate of 9% for the USA population AF for occupation-derived lung cancer (Steenland et al., 1996), to calculate a mean relative risk of 1.6 (95% CI: 1.4–1.8). This relative risk is partitioned into a relative risk of 1.3 (95% CI: 1.2–1.4) for low-level exposures to lung carcinogens, and 1.9 (95% CI 1.7–2.1) for high-level exposures.

6.2 Leukaemia

As for the lung carcinogens, the relative risks for each leukaemogen are combined into summary relative risks, one for the low-exposure group and one for the high-exposure group. Again, this can be done separately for each subregion, using the exposure prevalence of the workforce in each subregion to weight the exposure-specific risks. As with the lung carcinogens, however, the resulting average relative risks are not meaningfully different from each other and we advise they not be used. Confidence intervals are calculated by weighting the estimated confidence intervals of the relative risks for benzene and ionizing radiation, taken from the literature (there is none for ethylene oxide). In contrast to the lung cancer carcinogens, low and high exposure relative risks are available for each leukaemogen from the literature (benzene: Lynge et al., 1997; ionizing radiation: BEIR V, 1990; IARC, 2000; ethylene oxide: Steenland et al., 2003) and these are directly incorporated into low and high exposure summary measures, after weighting. The resulting estimates of relative risks

for the low exposure and high exposure groups are 1.9 (95% CI: 1.7–2.1) and 3.6 (95% CI: 3.2–4.2), respectively.

7. Estimating the disease burden

To obtain estimates of the AF for lung cancer and leukaemia that arise from occupational exposure to carcinogens, we combine exposure information with relative risk information. This approach follows that used in the WHO Global Burden of Disease project (Ezzati et al., 2002; WHO, 2002) for occupational carcinogens (Concha-Barrientos et al., 2004). Although the estimates from the CRA project are based on WHO subregions (Concha-Barrientos et al., 2004), we use a method that allows countries with appropriate employment data to use the information to produce their own estimates.

The following information is required to estimate the burden of disease from occupational lung cancer and leukaemia:

i. the proportion of the population exposed and the level of exposure (see Section 5);
ii. the relative risk of developing the outcome of interest (lung cancer or leukaemia) in exposed individuals (see Section 6);
iii. the total number of deaths and/or DALYs due to lung cancer (or leukaemia) in the country (or subregion). For the use of health statistics see Prüss-Üstün et al. (2003).

For requirement "ii", we propose using synthesized relative risks, based on estimates in the global analysis. Several options are available for requirement "iii". Although national health statistics are preferable, some information is also available from WHO.

The method for determining the disease burden from malignant mesothelioma is simpler, and requires only knowledge of the number of deaths due to malignant mesothelioma in the country. This method is described in Section 7.3.

7.1 Estimating the attributable fraction

The AF (or IF) is calculated using the following equation (Prüss-Üstün et al., 2003):

$$IF = \frac{\Sigma\, P_i\, RR_i - 1}{\Sigma\, P_i\, RR_i} \qquad \textit{(Equation 1)}$$

where:

P_i = Proportion of the population at exposure category "i" (including the unexposed proportion). For the current example, $AF = P_{background} \times RR_{background} + P_{low\ exposure} \times RR_{low\ exposure} + P_{high\ exposure} \times RR_{high\ exposure}$);

RR_i = Relative risk at exposure category "i", compared to the reference level.

7.2 Estimating the number of deaths and DALYs

The number of deaths attributable to occupational lung cancer (or leukaemia) can be estimated by multiplying the total number of lung cancer (or leukaemia) deaths in the country or study area (obtained from routine deaths data) by the AF for that country (estimated using Equation 1). This can be done separately for males and females, since they have different employment characteristics and attributable risks. The sum of these two provides an estimate of the total number of deaths due to occupational lung cancer (or leukaemia).

The method used to estimate the number of DALYs attributable to occupational carcinogens can depend on the type of data available in the country. If the country has performed a national burden of disease study (e.g. Prüss-Üstün et al., 2003), or has directly estimated the number of DALYs caused by lung cancer or leukaemia, the attributable number of DALYs is estimated as for deaths (multiply the AF by the number of DALYs for the disease). This calculation should be performed separately for males and females, and for different age groups, if the data are available.

If there are no country-level data on the number of DALYs attributable to leukaemia and lung cancer, the following data can be used:

- WHO prior estimates for the country, available upon request from WHO (see Prüss-Üstün et al., 2003 for further details).

- WHO subregional estimates of the number of attributable DALYs could be multiplied by the ratio of the country population to the subregional population. This country-level estimate of the number of DALYs that are attributable to leukaemia or lung cancer is only preliminary, however, as it assumes that the disease rates are similar in all countries of the subregion. Subregional DALY estimates are available from the site www.who.int/evidence (select: "Burden of disease", "GBD estimates", "GBD 2000 Version 2 estimates", "Estimates by subregion"). The *World Health Report* also contains a summary of these tables, but the data are not distributed into gender and age groups. As examples, the number of DALYs estimated for lung cancer and leukaemia in the global analysis are given in Table 5.

Further information on alternative health statistics can be found in Prüss-Üstün et al. (2003).

Table 5 DALYs due to occupational lung cancer and leukaemia, by sex, for all WHO subregions

Subregion	Lung cancer		Leukaemia	
	Male	Female	Male	Female
AFR D	6 081	1 190	2 430	922
AFR E	9 140	2 332	4 293	1 941
AMR A	52 573	12 741	3 846	3 175
AMR B	34 163	3 994	3 962	3 711
AMR D	1 810	231	1 530	885
EMR B	10 105	704	1 719	793
EMR D	14 211	1 574	3 387	842
EUR A	89 037	9 468	5 945	3 724
EUR B	60 231	5 178	3 135	1 619
EUR C	126 599	13 771	2 268	2 080
SEAR B	31 690	2 763	2 908	1 972
SEAR D	109 089	10 679	9 911	1 489
WPR A	22 977	3 292	1 393	816
WPR B	257 373	75 847	19 377	10 909

7.3 Malignant mesothelioma

As described earlier, malignant mesothelioma is essentially caused only by exposure to asbestos, and most of that asbestos exposure, particularly in men, occurs in occupational settings. Lacking more specific data, we have assumed that the proportion of cases of malignant mesothelioma that are due to occupational exposure to asbestos is the same across countries. The AF taken from the literature is 90% for males and 25% for females (Nurminen & Karjalainen, 2001; Steenland et al., 2003). The number of malignant mesothelioma deaths related to work can be estimated by multiplying the total number of malignant mesothelioma deaths in the country (obtained from routine deaths data) by the AFs for males and females, and summing the results.

In many countries the number of mesothelioma deaths is unknown and a different approach must be taken to estimate the AF. One alternative is to use the ratio of mesothelioma deaths to lung cancer deaths in asbestos-exposed populations, taken from epidemiological studies of exposed cohorts. This has been estimated to be approximately 0.5 (Ulvestad et al., 2002; Luo et al., 2003), but note that this will vary between cohorts and countries. Therefore, the number of lung cancer deaths due to asbestos (calculated using the above method) can be multiplied by 0.5 to give an estimate of the number of mesothelioma deaths due to occupational asbestos exposure. Both this method and the first method (that takes the AF from the literature) can be used, but the first method is simpler, and is likely to be more

accurate if the country has death statistics that include detailed information as to cause of death.

It is more complicated to estimate the number of DALYs due to malignant mesothelioma that arises from occupational exposure, and this will not be discussed here. Instead, indicative values for the number of deaths and DALYs estimated in the global analysis are given in Table 6.

Table 6 DALYs and deaths due to malignant mesothelioma, by sex, for all WHO subregions[a]

Subregion	Males		Females	
	DALYs	Deaths	DALYs	Deaths
AFR D	2 317	175	1 441	107
AFR E	2 679	199	2 049	144
AMR A	1 151	101	447	40
AMR B	4 364	341	1 309	97
AMR D	594	47	116	9
EMR B	1 360	102	203	14
EMR D	3 213	238	1 518	99
EUR A	1 714	157	625	60
EUR B	3 026	250	1 812	147
EUR C	5 181	434	3 581	340
SEAR B	3 593	278	1 972	145
SEAR D	15 464	1 165	10 106	641
WPR A	790	72	334	31
WPR B	25 844	1 979	15 973	1 189

[a] Data taken from the global analysis of the disease burden, which used estimated risks applied to estimated exposures at the WHO subregional level (Ezzati et al., 2002; WHO, 2002).

A worked example is shown in Section 9 using data for WHO subregion AFR D, but the same approach could be used with data from individual countries.

8. Sources of uncertainty

8.1 Relative risk

When the relative risk values used in this analysis are based on disease incidence studies, the incidence rate ratio is assumed to be comparable to the corresponding mortality risk ratio. This is probably true for lung cancer and malignant mesothelioma, since most people who develop lung cancer or malignant mesothelioma will die directly, or fairly directly, of the disease. In contrast, people with leukaemia generally have a higher five-year survival rate. This means that the number (and rate) of deaths from leukaemia is not likely to be the same as the number (and rate) of incident cases. Nevertheless, the relative rate is still likely to be the same in many situations, although there are insufficient data to confirm or refute this assumption for the outcomes of interest in this study.

In this project (and the CRA project), summary relative risks related to occupational exposures are calculated from published studies of the cancers of interest. Usually, there are several good-quality studies available for each exposure, since we include only confirmed or probable carcinogens in the exposures of interest. When more than one study is available, we use the best-quality studies to determine the relative risk. Although estimates of relative risk sometimes vary widely between studies, this is not surprising given the variation in the level of exposure, in the period of follow-up, in the level and control of confounders, and in the opportunity for selection and measurement bias between the studies. The summary relative risks are an attempt to identify the best estimate of the "average" relative risks for the exposure levels of interest.

The relative risks are not related to any absolute measure of cumulative exposure, because the necessary exposure–risk data are not available. As mentioned, the studies we use are based on cohorts that were exposed for different periods of time, followed up for different periods of time, and that varied in the length of time between the cessation of exposure and follow-up. The cohorts are probably not typical of the entire exposed workforce, as cohort studies tend to be based on workforces that are fairly stable, but no more-typical cohorts have been studied.

Also not known is the average duration of exposure of all the relevant populations on which the relative risks are based, as some of the summary measures are based on meta-analyses that covered countries with a wide range of exposure durations. The average duration of exposure in the populations to which the relative risks are applied is also not known. It is important to recognize that the relative risks are *not* based on duration, but are simply calculated for exposed versus non-exposed populations, without consideration of duration. Although more quantitative data would be desirable, they are not available for the risk estimates, and are unlikely to be available at the level of detail required for the populations to which the risk estimates would be applied.

8.2 Sex

For the current analysis, the same mean relative risk values for low and high exposures are applied to both males and females. There are few studies of occupational cancer in females, but such studies that have been conducted suggest that men and women are at comparable risk of occupational cancer for most workplace exposures (Stellman, 1994; Jahn et al., 1999). However, others have highlighted the potential for gender-related differences in exposures (Setlow, Lawson & Woods, 1998). Job assignments, for example, may be based on gender, which could lead to differential exposures and thus differential risks between men and women. However, in this study we have not attempted to account for gender-based variation in exposure because of lack of data.

8.3 Age

The method presented here does not account for age-related differences in exposure or risk. This is because relative risk data are rarely available for separate age groups, and only occasionally available by years employed. Older people can be expected to have a higher level of absolute risk of disease, because their cumulative exposure would usually be higher and the risk of disease usually increases with cumulative exposure. The advantage of using relative risks is that the same AF (which is based on relative risk) will give less mortality in younger ages than in older ages when more people die because of accumulated exposures to cancer agents. This approach, of reporting a single relative risk for different ages, has been used elsewhere (Peto et al., 1992).

The biological effect of a given exposure is likely to be similar in young and middle-aged adults. The effect in older people is not as easy to predict, since age-dependent changes in body processes might change the body's susceptibility to the effects of the exposure. However, for the exposures considered in this report, it is unlikely that there would be major changes to the relative risk with age, provided exposure–disease latencies are taken into account.

8.4 Smoking

Smoking is the main potential confounder of lung cancer, and potentiates the effect of some exposures (notably to asbestos). Smoking does not appear to contribute significantly to the risk of leukaemia and malignant mesothelioma. For this analysis, whenever possible we use studies that control lung cancer risk estimates for the effects of smoking. However, we do not account for subregion-specific smoking rates or levels when developing the final risk estimates, since there are no data. This should not matter significantly, because the relative risk estimates account for the effect of smoking.

8.5 Nutrition

No attempt has been made to account for the effects of nutrition on the exposure–risk estimates. Although populations with poor nutrition may have an increased risk of

developing disease compared to populations with good nutrition, there are not enough data to adjust the risk estimates for poor nutrition. To the extent that poor nutrition does increase risk at a given exposure level, the risks will be underestimated for countries and subregions which have relatively poor nutrition.

8.6 Latency

All of the conditions considered in this analysis have a long latency period between exposure and the development of recognizable disease. Most of the risks estimated by studies therefore include effects from both past and current exposures, which can introduce uncertainty because past and current exposures may not have the same associated risks. The data presented here describe the current burden from workplace exposures, both past and present. If the risks associated with exposures have decreased over the past 10–30 years, our population AFs will overestimate the attributable burden from current exposures.

8.7 Omitted exposures

Some potential carcinogens are excluded from this study, either because workplace exposure levels to the carcinogen are very low, or because there is limited evidence that the carcinogen causes the conditions of interest, or because there are no data for the carcinogen in CAREX. The carcinogens include acrylonitrile, bis(chloromethyl)ether, radon, soot, tetrachloroethylene, trichloroethylene, xenylamine, 4-nitrobiphenyl, and polycyclic aromatic hydrocarbons. The total burden of malignant conditions arising from workplace exposure is likely to be underestimated by excluding these agents, but the underestimation is unlikely to be significant.

8.8 Omitted conditions

We also exclude some malignancies that can, or probably can, result from workplace exposures, because there is no information about relevant exposures or risks. Examples include renal cell carcinoma, angiosarcoma of the liver and brain tumours. Bladder cancers caused by aromatic amines and dyes, including 2-naphthylamine, benzidine-based dyes, and methylene-bis-ortho-chloroaniline, are not included in this study because global exposure data are not available. As a result of the omissions, the total burden of malignant conditions arising from workplace exposure will be underestimated, although the underestimation is unlikely to be significant.

8.9 Occupational turnover

To determine the proportion of people exposed, it is necessary to use a correction factor for occupational turnover. This factor allows for the movement of people in and out of various jobs and for the continuation of risk once exposure ceases. The rates and ages at which the movements occur are usually not known with any degree of certainty, since we depend on information available in the country. This may

introduce uncertainty into the disease burden estimates (Concha-Barrientos et al., 2004).

8.10 Mesothelioma estimates

Although we assume the AFs are constant across countries, it is likely that the actual proportions of mesothelioma cases attributable to occupational exposure (and the corresponding AFs) vary. The variation depends on the relative exposure to asbestos in occupational and non-occupational settings, and on the occupational tasks in which males and females participate in the country. There is no information for estimating the variation between countries, but it is not likely to be large. The ratio of mesothelioma deaths to lung cancer deaths can also be expected to vary between countries. It will be affected by smoking prevalence, since combined smoking and asbestos exposures increase the risk of developing lung cancer in a multiplicative fashion. Again, however, there is no information on how the ratio varies between countries, but the variation is not likely to be large.

9. Worked example: occupational cancer in Africa D

The following worked example for Africa D (AFR D)[1], one of the subregions in the global analysis, gives step-by-step guidance on how to estimate the disease burden for occupational lung cancer in males. The analysis would provide more meaningful estimates for national policy-makers if country-level data were used, rather than data for an entire subregion such as AFR D. Countries are therefore encouraged to choose their population, or a subset of it, for estimating health impacts. The corresponding disease burden for females, as well as the total disease burden of occupational lung cancer, can be calculated using the same method. Consequently, only the results are given, without showing the detailed calculations. Information on leukaemia and malignant mesothelioma is also provided, but in less detail.

In the following worked example, calculations and results are highlighted in grey.

9.1 Occupational lung cancer

9.1.1 Proportion of the workforce in industry sectors

The proportion of male workers in each industry sector for AFR D can be obtained from the International Labour Organization (ILO), and the data are reproduced in Table 7. For individual countries, the information should be available from relevant government departments and the ILO.

Table 7 Proportion of the male workforce employed in industry sectors, AFR D[a]

Sector	Proportion of male workforce
Agriculture	0.550
Mining	0.011
Manufacturing	0.093
Electrical	0.009
Construction	0.036
Trade	0.058
Transportation	0.039
Finance	0.029
Services	0.164
Total	1.000

[a] (Source: ILO, 2000)

[1] See Annex 2 for a list of countries in AFR D.

9.1.2 Exposure in industry sectors

Eight carcinogens are included in the exposure assessment for lung cancer, with separate estimates for each carcinogen by industry sector. For each industry sector, the proportions of male workers exposed to the individual lung carcinogens are from CAREX (Table 8). The proportions are assumed to be the same for all countries of subregion AFR D, and for both sexes.

Table 8 Proportion of male workers exposed to lung carcinogens, by industry sector[a]

Carcinogen	Agriculture	Mining	Manufac-turing	Electrical	Construc-tion	Trade	Transpor-tation	Finance	Services
Silica	0.004	0.230	0.023	0.014	0.189	0.000	0.00476	0.000	0.001
Cadmium	0.000	0.000	0.005	0.003	0.003	0.000	0.00065	0.000	0.000
Nickel	0.000	0.020	0.017	0.004	0.000	0.000	0.00003	0.000	0.000
Arsenic	0.001	0.001	0.004	0.001	0.001	0.000	0.00000	0.000	0.000
Chromium	0.000	0.003	0.021	0.004	0.002	0.000	0.00370	0.000	0.002
Diesel fumes	0.006	0.220	0.011	0.034	0.058	0.005	0.13438	0.000	0.009
Beryllium	0.000	0.001	0.002	0.001	0.000	0.000	0.00011	0.000	0.000
Asbestos	0.012	0.102	0.006	0.017	0.052	0.003	0.00684	0.000	0.003

[a] Source: CAREX (FIOH, 1998).

9.1.3 Proportion of the male workforce exposed to lung carcinogens

To estimate the proportion of the male workforce in an industry sector that has been exposed to a given lung carcinogen, the proportion of the male workforce in the industry sector (Table 7) is multiplied by the proportion of workers in the sector who are exposed to the carcinogen (Table 8). This calculation is performed for each industry sector–carcinogen pair in Table 8. The proportions for each carcinogen are summed across all eight sectors, to provide an estimate of the proportion of the total male workforce exposed to that carcinogen. The workforce proportions for each carcinogen are then summed, to provide an estimate of the proportion of the total male workforce exposed to lung carcinogens (Table 9).

Table 9 Proportion of the male workforce exposed to lung carcinogens, AFR D

Carcinogen	Agriculture	Mining	Manufac-turing	Electrical	Construc-tion	Trade	Transpor-tation	Finance	Services	Totals
Silica	0.002	0.003	0.002	0.000	0.007	0.000	0.000	0.000	0.000	0.014
Cadmium	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
Nickel	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.002
Arsenic	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
Chromium	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.003
Diesel fumes	0.004	0.002	0.001	0.000	0.002	0.000	0.005	0.000	0.002	0.016
Beryllium	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Asbestos	0.007	0.001	0.001	0.000	0.002	0.000	0.000	0.000	0.000	0.011
										0.048

Therefore, the proportion of the current, total male workforce exposed to lung carcinogens = 0.048.

9.1.4 Workforce turnover

In the absence of local data, the workforce turnover factor is estimated to be four (see Section 5.3). This means that the proportion of people ever exposed is four times the proportion who are currently exposed. This turnover factor is assumed to be the same for each of the countries in the AFR D subregion, and for males and females.

proportion of the male workforce ever exposed =

proportion of male workforce currently exposed × turnover factor

= 0.048 × 4

= **0.192**

Therefore, the proportion of the male workforce ever exposed to lung carcinogens = 0.192.

9.1.5 Partitioning high and low exposure

On the basis of available international data, workers are partitioned into those exposed at high level and those exposed at low level (see Section 5.4). For countries in A subregions, the partitioning factors for the proportion of workers having high and low exposure are 0.1 and 0.9, respectively. In contrast, the corresponding partitioning factors for countries in subregions B–E are 0.5 and 0.5, respectively.

Both high and low partitioning factors for AFR D = 0.5.

To estimate the proportions of the male workforce ever exposed at high and at low levels, the proportion of the male workforce ever exposed is multiplied by the high and low partitioning factors, respectively.

proportion of the male workforce ever exposed at high level =

proportion of the male workforce ever exposed × partitioning factor for high exposure

= 0.192 × 0.5

= 0.096

Similarly:

proportion of the male workforce ever exposed at low level =

proportion of the male workforce ever exposed × partitioning factor for low exposure

= 0.192 × 0.5

= **0.096**

Thus:

The proportion of the male workforce ever exposed to lung carcinogens at high level = 0.096.

The proportion of the male workforce ever exposed to lung carcinogens at low level = 0.096.

9.1.6 Proportion of the population who are in the workforce

The Economically Active Population[1] for males in AFR D is obtained from ILO sources. For individual countries, the information should be available from relevant government departments and the ILO.

Economically Active Population for males in AFR D = **0.85**

9.1.7 Proportion of the male population exposed to lung carcinogens

The proportion of the total male population (15 years of age and older) ever exposed to carcinogens is estimated by multiplying the proportion of ever exposed males in the workforce by the proportion of males in the workforce (i.e. the Economically Active Population for males). Overall exposure is determined by summing the proportions of male workers ever exposed at either high or low levels.

proportion of the male population ever exposed =

proportion of male workforce ever exposed × proportion of males in the workforce

= 0.192 × 0.85

= **0.164**

Therefore, the proportion of the total male population over 15 years of age ever exposed to lung carcinogens = 0.164.

9.1.8 Proportion of males exposed to high and low levels of carcinogen

The proportion of the total male population above 15 years of age is determined separately for the high and low exposure levels, using the proportion of all male workers ever exposed to carcinogen at high levels and at low levels.

proportion of the male population ever exposed at high level =

proportion of the male workforce ever exposed at high level × proportion of the male population in the workforce

= 0.096 × 0.85

= **0.082**

Similarly:

proportion of the male population ever exposed at low level =

proportion of the male workforce ever exposed at low level × proportion of the male population in the workforce

= 0.096 × 0.85

= **0.082**

Therefore, the proportion of the male population ever exposed to lung carcinogens at high level = 0.082.

The proportion of the male population ever exposed to lung carcinogens at low level = 0.082.

The proportion of the male population who have never been exposed is estimated by subtracting the proportion exposed (at high and low levels) from 1.0.

proportion of the male population never exposed to lung carcinogens =

total male population – proportion of males exposed at high and low levels

= 1.0 – (0.082 + 0.082)

= **0.836**

Therefore, the proportion of the male population who have never been exposed to lung carcinogens is 0.836.

9.1.9 Relative risk of dying of lung cancer

The relative risk of dying of lung cancer following exposure to occupational carcinogens is obtained from Section 6.1. Relative risks can be adjusted for differences in the employment distribution of different subregions, but in practice the variation is too small to be taken into account. The same risks are used for males and females.

[1] See Glossary of terms for definition.

Table 10 Relative risk for lung cancer, AFR D

Subregion	Level	RRa	Low 95%CI[b]	High 95% CI[b]
AFR D	Background	1.0	1.0	1.0
	Low	1.3	1.2	1.4
	High	1.9	1.7	2.1

[a] RR = relative risk.
[b] Low and high 95% CI refer to lower and upper 95% confidence intervals, respectively.

9.1.10 Estimating the attributable fraction

The AF for occupation lung cancer for males is based on the standard formula (Equation 1, Section 7.1), using the proportion of the total male population 15 years or older ever exposed and the relevant relative risks (Table 10). The step-by-step calculations can easily be programmed into a spreadsheet, with an example output shown in the following box.

Proportion of the male workforce currently exposed = 0.048

Turnover factor = 4

Partitioning factors (high, low) = 0.5, 0.5

Male employment participation proportion = 0.85

Proportion of male workers ever exposed = 0.048 × 4 = 0.192
Proportion of male workers ever exposed (low level) = 0.192 × 0.5 = 0.096
Proportion of male workers ever exposed (high level) = 0.192 × 0.5 = 0.096
Proportion of the male population ever exposed (low level) = 0.096 × 0.85 = 0.082
Proportion of the male population ever exposed (high level) = 0.096 × 0.85 = 0.082
Proportion of the male population never exposed = 1.0 – (0.082 + 0.082) = 0.836

$$AF = IF = \frac{\Sigma P_i RR_i - 1}{\Sigma P_i RR_i} \qquad (Equation\ 1)$$

Males	Workers currently exposed	Workers ever exposed	Workers ever exposed by level	Population ever exposed by level	RR mean	Pi × RRi
	0.048	0.192				
Unexposed			0.0	0.836	1.00	0.836
Low			0.096	0.082	1.3	0.106
High			0.096	0.082	1.9	0.155
∑Pi × RRi						1.098
IF						**0.089**

Therefore, for males in AFR D, the AF (IF) for lung cancer arising from occupational exposures to lung carcinogens is 0.089, or 8.9%.

Using the same approach, but incorporating the lower and upper 95% confidence limits for each of the relative risks estimates, the 95% confidence interval for the AF is estimated to be 0.069–0.109, or 6.9–10.9%.

Using the same approach for females produces the following results:

Females	Workers currently exposed	Workers ever exposed	Workers ever exposed by level	Population ever exposed by level	RR mean	Pi × RRi
	0.031	0.125				
Background			0.0	0.934	1.00	0.934
Low			0.062	0.033	1.3	0.043
High			0.062	0.033	1.9	0.063
∑Pi × RRi						1.040
IF						**0.038**

Therefore, the AF (IF) for lung cancer arising from occupational exposures to lung carcinogens for females in AFR D is 0.038, or 3.8% (the 95% confidence interval is 2.9–4.7%).

9.1.11 Estimating deaths due to occupational lung cancer

National statistics should be used to estimate the number of occupational lung cancer deaths at national level. For the example of AFR D, the total number of deaths in the year 2001 from lung (and trachea and bronchus) cancer was about 9200 in the population 15 years and older – 6600 males and 2600 females (www.who.int/evidence/bod)[1], or Annex Table 2 of the World Health Report (WHO, 2002)). This distribution of lung cancer deaths between males and females is similar to the global distribution reported in the World Health Report, which found that males comprised 73% of lung cancer deaths (WHO, 2002). The number of these male deaths that are attributable to occupational exposures to carcinogens is estimated by multiplying the total number of lung cancer deaths in males (6600) by the AF for occupation-related lung cancer in males (8.9%, Section 9.1.10).

male deaths from lung cancer due to occupational exposures =

total deaths from lung cancer in males 15 years or older × AF for lung cancer in males from occupational exposures

= 6600 × 0.089

= **590**

[1] Select: "Global burden of disease estimates", "GBD 2001 estimates", "Estimates by subregion", and "Mortality".

Therefore, in 2001, it is estimated there were approximately 590 male deaths in the AFR D subregion due to lung cancer caused by occupational exposures to carcinogens.

Using the same approach for females, we estimate there were **99** (2600 × 0.038) deaths due to occupational exposures to carcinogens.

Therefore, in 2001, there were approximately **690** deaths in the AFR D subregion due to lung cancer caused by occupational exposures.

9.1.12 Estimating DALYs due to occupational lung cancer

The total number of DALYs for lung cancer in AFR D was 98 000 in the year 2001 (www.who.int/evidence/bod)[1]. The numbers of DALYs lost were 67 000 for males and 31 000 for females. The proportion of these due to occupational exposures is estimated by multiplying the total DALYs lost by the AF for lung cancer from occupational exposures (see Section 9.1.10, *Estimating the attributable fraction*).

DALYs for lung cancer in males in AFR D due to occupational exposures =

total DALYs from lung cancer in males 15 years or older × AF for lung cancer from occupational exposures

= 67 000 × 0.089

= **5960**

Therefore, in AFR D in 2001, it is estimated there were 5989 DALYs lost to lung cancer caused by occupational exposures in males.

Using the same approach, the corresponding figure for females is 31 000 × 0.038 = **1180**.

Therefore, in 2001, approximately **7140** DALYs were lost in the AFR D subregion to lung cancer caused by occupational exposures.

9.2 Occupational leukaemia

The steps outlined in this section closely follow the example for lung cancer outlined in Section 9.1

9.2.1 Proportion of the workforce in each industry sector

The industry distribution of the workforce used in the lung cancer calculations (Table 7) also applies to the calculations for leukaemia. The relevant proportions used in the leukaemia calculations are reproduced in Table 11.

[1] Select: "Global burden of disease estimates", "GBD 2001 estimates", "Estimates by subregion", and "DALY".

Table 11 Proportion of the male workforce employed in each industry, AFR D[a]

Industry	Proportion of male workforce
Agriculture	0.550
Mining	0.011
Manufacturing	0.093
Electrical	0.009
Construction	0.036
Trade	0.058
Transportation	0.039
Finance	0.029
Services	0.164

[a] (Source: ILO, 2000)

9.2.2 Exposure in industry sectors

The exposure to leukaemogens is obtained from local data or, in this example, from the CAREX study (Table 4). The relevant data from Table 4 are reproduced in Table 12.

Table 12 Proportion of the workforce exposed to leukaemogens, by industry sector[a]

Carcinogen	Agri-culture	Mining	Manufac-turing	Electrical	Construc-tion	Trade	Transpor-tation	Finance	Services
Benzene	0.001	0.002	0.003	0.001	0.001	0.01	0.00500	0	0.02
Ionizing radiation	0	0.011	0	0.034	0	0	0.00400	0	0
Ethylene oxide	0.00012	0.00137	0.0006	0.00006	0.00027	0	0.00002	0	0.00057

[a] Source: CAREX survey (FIOH, 1998).

9.2.3 Proportion of the workforce exposed to leukaemogens

The proportion of the male workforce in AFR D exposed to leukaemogens is obtained by multiplying the proportion of males employed in each industry (Table 11) by the estimated exposed proportion of males within each industry sector (Table 12). The results are shown in Table 13.

Table 13 Proportion of the male workforce exposed to leukaemogens, AFR D[a]

Carcinogen	Agri-culture	Mining	Manufac-turing	Electrical	Construc-tion	Trade	Transpor-tation	Finance	Services	Total
Benzene	0.0006	0.0000	0.0003	0.0000	0.0000	0.0006	0.0002	0.0000	0.0033	0.0050
Ionizing radiation	0.0000	0.0001	0.0000	0.0003	0.0000	0.0000	0.0002	0.0000	0.0000	0.0006
Ethylene oxide	0.0001	0.0000	0.0001	0.0000	0.0000	0.0000	0.0000	0.0000	0.0001	0.0002
Total										0.0058

[a] Source: CAREX survey (FIOH, 1998).

Therefore, in AFR D the proportion of the current male workforce exposed to leukaemogens = **0.0058**.

9.2.4 Workforce turnover

In the absence of local information, a turnover factor of 4 is used to calculate the proportion of the male workforce ever exposed to leukaemogens.

proportion of the male workforce ever exposed to leukaemogens =

proportion of male workforce currently exposed × turnover factor

= 0.0058 × 4

= **0.023**

Therefore, the proportion of the male workforce ever exposed to leukaemogens = 0.023.

9.2.5 Partitioning high and low exposure

The proportions of the male workforce ever exposed at high and low levels of leukaemogens are calculated using the same high and low partitioning factors as used for lung cancer.

proportion of the male workforce ever exposed at high level =

proportion of the male workforce ever exposed × partitioning factor for high exposure

= 0.023 × 0.5

= **0.012**

proportion of the male workforce ever exposed at low level =

proportion of the male workforce ever exposed × partitioning factor for low exposure

= 0.023 × 0.5

= **0.012**

Therefore, the proportion of the male workforce ever exposed to leukaemogens at high level = 0.012.

The proportion of the male workforce ever exposed to leukaemogens at low level = 0.012.

9.2.6 Proportion of the male population in the workforce

Economically Active Population for males in AFR D = **0.85**.

(This is the same as in Section 9.1.6.)

9.2.7 Proportion of the male population exposed to leukaemogens

proportion of the male population 15 years or older ever exposed to leukaemogens

=

proportion of the male workforce ever exposed to leukaemogens × proportion of the male workforce 15 years or older

= 0.023 × 0.85

= **0.020**

Therefore, the proportion of the total male population 15 years of age or older ever exposed to leukaemogens = 0.020.

This calculation for leukaemogens is equivalent to that for lung cancer (Section 9.1.7).

9.2.8 Estimating the proportion of males exposed at high and low levels of leukaemogen

proportion of males in the workforce ever exposed at high level of leukaemogen =

proportion of the workforce ever exposed at high level of leukaemogen × proportion of males in the workforce

= 0.012 × 0.85

= **0.0099**

Similarly, for the low level of leukaemogen:

proportion of males in the workforce ever exposed at low level of leukaemogen =

proportion of the workforce ever exposed at low level of leukaemogen × proportion of males in the workforce

= 0.012 × 0.85

= **0.0099**

This calculation for leukaemogens is equivalent to that for lung cancer (Section 9.1.8).

Therefore, the proportion of the male population ever exposed to leukaemogens at high level = 0.0099.

The proportion of the male population ever exposed to leukaemogens at low level = 0.0099.

Also:

proportion of the male population who have never been exposed to leukaemogen =

total male population –proportions of males who have ever been exposed to leukaemogen at high level and at low level

= 1.0 – (0.0099 + 0.0099)

= **0.980**

Thus, the proportion of the male population who have never been exposed to leukaemogens is 0.980.

9.2.9 Relative risk of developing leukaemia

The relative risks of dying of leukaemia in AFR D (Section 6.2) are reproduced in Table 14 for high and low levels of exposure to leukaemogen. The same risks are used for males and females.

Table 14 Leukaemia relative risk, AFR D

Subregion	Exposure level	RR	Low 95% CI[a]	High 95% CI[a]
AFR D	Background	1.0	1.0	1.0
	Low	1.9	1.7	2.1
	High	3.6	3.2	4.2

[a] Low and high 95% CI refer to lower and upper 95% confidence intervals, respectively.

9.2.10 Estimating the attributable fraction

A summary of the steps outlined above and the calculation of the AF are presented below.

Currently exposed proportion of the male workforce = 0.0058

Turnover factor = 4

Partitioning factor, low = 0.5

Partitioning factor, high = 0.5

Male employment participation proportion = 0.85

Proportion of male workers ever exposed = 0.0058 × 4 = 0.23
Proportion of male workers ever exposed (low level) = 0.023 × 0.5 = 0.012
Proportion of male workers ever exposed (high level) = 0.023 × 0.5 = 0.012
Proportion of the male population ever exposed (low level) = 0.012 × 0.85 = 0.0099
Proportion of the male population ever exposed (high level) = 0.012 × 0.85 = 0.0099
Proportion of the male population never exposed = 1.0 – (0.0099 + 0.0099) = 0.980

$$AF = IF = \frac{\Sigma P_i RR_i - 1}{\Sigma P_i RR_i} \qquad \textit{(Equation 1)}$$

Males	Workers currently exposed	Workers ever exposed	Workers ever exposed, by level	Population ever exposed, by level	Mean RR	$P_i \times RR_i$
	0.006	0.023				
Background			0	0.980	1	0.9803
Low			0.012	0.0099	1.9	0.0187
High			0.012	0.0099	3.6	0.0355
∑Pi × RRi						1.0345
IF						**0.033**

In AFR D, therefore, the AF (IF) for leukaemia in males from occupational exposures to leukaemogens is 0.033, or 3.3%.

Using the same approach, but incorporating the lower and upper 95% confidence limits for each of the relative risk estimates, the 95% confidence interval is estimated to be 0.028–0.041, or 2.8–4.1%.

Using the same approach for females produces the following results:

Females	Workers currently exposed	Workers ever exposed	Workers ever exposed, by level	Population ever exposed, by level	Mean RR	Pi × RRi
	0.0052	0.021				
Background			0.0	0.9890	1.0	0.9890
Low			0.0104	0.0055	1.9	0.0104
High			0.0104	0.0055	3.7	0.0198
∑Pi × RRi						1.0192
IF						**0.019**

In AFR D, therefore, the AF (IF) for leukaemia in females from occupational exposures to leukaemogens is 0.019, or 1.9% (the 95% confidence interval is 1.6–2.3%).

9.2.11 Estimating deaths due to occupational leukaemia

In 2001, the total number of deaths from leukaemia in AFR D was 7500 for the age group 15 years and older, with 4400 deaths in males and 3900 in females (www.who.int/evidence/bod)[1]. The number of these deaths attributable to occupational exposure to leukaemogens can be estimated as follows:

male deaths from leukaemia due to occupational exposures =

total males deaths from leukaemia × AF for males with leukaemia from occupational exposures

= 4400 × 0.033

= **145**

In 2001, therefore, occupational exposures caused approximately **145** male deaths from leukaemia in the AFR D subregion.

Using the same approach, the number of female deaths from occupational exposures to leukaemogens is estimated to be **66** (3500 × 0.019).

In the year 2001, therefore, occupational exposures to leukaemogens caused approximately **210** deaths from leukaemia in the AFR D subregion.

9.2.12 Estimating DALYs lost to occupational leukaemia

In 2001, 145 000 total DALYs were lost to leukaemia in AFR D for people 15 years of age or older, with 71 000 DALYs lost for males and 48 000 for females (www.who.int/evidence/bod)[2]. The number of these DALYs lost due to occupational exposures can be calculated as follows:

DALYs lost from leukaemia in males due to occupational exposures =

total DALYs lost from leukaemia in males × AF for leukaemia from occupational exposures

= 71 000 × 0.033

= **2340**

Therefore, in the year 2001 in the AFR D subregion, it is estimated that occupational exposures were responsible for the loss of **2340** DALYs to leukaemia in males.

Using the same approach, the corresponding number of DALYs lost to leukaemia in females is estimated to be **910** (48 000 × 0.019).

---

1 Select: "Global burden of disease estimates", "GBD 2001 estimates", "Estimates by subregion", and then "Mortality".

2 Select: "Global burden of disease estimates", "GBD 2001 estimates", "Estimates by subregion", and then "DALY".

Therefore, in 2001 in the AFR D subregion, it is estimated that **3250** DALYs were lost to leukaemia caused by occupational exposures.

9.3 Malignant mesothelioma

9.3.1 Number of deaths due to malignant mesothelioma

Estimates of the number of deaths due to malignant mesothelioma start with the AF taken from the literature (0.90 for males and 0.25 for females). These proportions are applied to national level statistics on the number of deaths from malignant mesothelioma (when available). Information on the number of deaths from malignant mesothelioma is not readily available for AFR D, so a calculation with numbers is not presented here.

An alternative approach is to estimate the number of deaths from lung cancer due to occupational exposure to asbestos, and apply a ratio of 0.5 mesothelioma deaths for every lung cancer death in asbestos-exposed persons (determined from the literature). The number of lung cancer deaths due to asbestos is determined as described in Section 9.1, using the asbestos-exposed proportion of the population (Table 9), and an asbestos-specific relative risk of 2.0 (Table 3). For simplicity, only one exposure level is used. This produces the following results for males:

Proportion of the male workforce currently exposed = 0.011

Turnover factor = 4

Partitioning factor (high) = not used

Partitioning factor (low) = not used

Male employment participation proportion = 0.85

Proportion of male workers ever exposed = $0.011 \times 4 = 0.044$

Proportion of the male population ever exposed = $0.044 \times 0.85 = 0.039$

Proportion of the male population never exposed = $1.0 – (0.039) = 0.961$

$$AF = IF = \frac{\Sigma P_i RR_i - 1}{\Sigma P_i RR_i} \qquad \textit{(Equation 1)}$$

Males	Workers currently exposed	Workers ever exposed	Population exposure, by level	Mean RR	Pi × RRi
	0.011	0.046			
Unexposed			0.961	1.0	0.961
Exposed			0.039	2.0	0.078
∑Pi × RRi					1.039
AF					**0.038**

Therefore, for males in AFR D the AF (IF) for lung cancer from occupational exposure to asbestos is 0.038, or 3.8%.

In 2001, the total number of male deaths from lung (and trachea and bronchus) cancer for AFR D was 6600 for the population 15 years and older, and the number of female deaths was 2600 (see Section 9.1.11). The proportion of these male deaths due to occupational asbestos exposure is estimated by multiplying the total male deaths by the AF for males estimated above (3.8%).

male deaths from lung cancer due to occupational asbestos exposure =

total lung cancer deaths in males 15 years or older × AF for males for lung cancer from occupational asbestos exposure

= 6600 × 0.038

= **251**

This number is multiplied by 0.5 (because the ratio of mesothelioma deaths to lung cancer deaths in asbestos-exposed persons is estimated to be 0.5:1 – see Section 7.3).

male deaths from mesothelioma due to occupational asbestos exposure =

male deaths from lung cancer due to occupational asbestos exposure × proportion of mesothelioma to lung cancer deaths in asbestos-exposed persons

= 248 × 0.5

= **124**

Therefore, in 2001 in the AFR D subregion, it is estimated there were **124** male deaths due to mesothelioma caused by occupational exposure to asbestos.

The corresponding number of lung cancer deaths in women is estimated to be **62**, and the estimated number of deaths due to mesothelioma caused by occupational exposure to asbestos is **31**.

Therefore, in 2001 in the AFR D subregion, it is estimated there were **155** deaths due to mesothelioma caused by occupational exposure to asbestos.

The calculation for DALYs is not straightforward and is not presented here.

10. Policy actions to reduce the burden

Assessments of the burden of disease can be important guides for policy-makers. They allow the effects of different risk factors to be compared, and can therefore help in prioritizing health issues. The methods described above can also be used to give a detailed breakdown of the effects of specific workplace carcinogens, rather than just the total burden of all major carcinogens. This may allow efforts to reduce risk to be targeted more appropriately.

Various options are available to reduce the burden of occupationally-related lung cancer, leukaemia and malignant mesothelioma. The primary approach is to stop or minimize exposure to the causative substances. Ideally, this involves eliminating the requirement for the substance in work tasks, either by modifying the work task, or substituting the exposure with a less hazardous substance. In extreme cases, substances can be banned or restricted by government statute.

However, such elimination or substitution may be practically difficult, and engineering solutions are often required. These include isolating the process from the worker, enclosing the process, decreasing dust levels through wet work methods, and using ventilation to minimize the level of worker exposure (e.g. decreasing the concentration of the substance in the breathing zone; shielding the worker from hazardous radiation).

These approaches should be used first, but if they do not result in suitable levels of exposure, then personal protective equipment, such as respirators and protective clothing, may be required. Such equipment should not be used as the sole means of exposure control, because the equipment is often hard to use for extended periods, and can be difficult to maintain. Therefore, even if the equipment is used exactly as intended during all periods of potential exposure, this may not decrease exposures to desired levels.

Other administrative approaches that can be used to minimize the effects of exposure include regular exposure monitoring, either environmental or personal, and restricting the number of workers who conduct tasks involving hazardous exposures, as well as the length of time that these workers are potentially exposed.

11. References

BEIR V (1990). Health effects of exposure to low levels of ionizing radiation: BEIR V. Washington, DC, National Academy Press.

Bhatia R, Lopipero P, Smith A (1998). Diesel exhaust exposure and lung cancer. *Epidemiology,* 9:84–91.

Burdorf A, Swuste PH, Looman CW (1998). Estimating the future developments in mesothelioma mortality due to historical asbestos use and its consequences for public health. In: Peters BA, Peters BJ, eds. *Sourcebook on asbestos diseases.* Charlottesville Lexis, 18:145–167.

Checkoway H (2000). Epidemiological evidence on the carcinogenicity of silica: factors in scientific judgment. *Annals of Occupational Hygiene*, 44:483–487.

Concha-Barrientos M, Imel ND, Driscoll T, Steenland K, Punnett L, Fingerhut M, Prüss-Üstün A, Corvalán C, Leigh J, Tak SW (2004). Selected occupational risk factors. In: Ezzati M, Lopez AD, Murray CJL, eds. *Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors*. Geneva, World Health Organization.

Enterline P, Marsh G, Esmen N, Henderson V, Callahan C, Paik M (1987). Some effects of cigarette smoking, arsenic, and SO_2 on mortality among US copper smelter workers. *Journal of Occupational Medicine*, 29:831–838.

Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJL, and the Comparative Risk Assessment Group (2002). Selected major risk factors and global and regional burden of disease. *Lancet*, 360(9343):1347–1360.

FIOH (1998). *CAREX database*. Helsinki, Finnish Institute of Occupational Health. (http://www.ttl.fi/NR/rdonlyres/4444380F-B1FB-4D01-A974-0B6A9E663CFA/0/1_description_and_summary_of_results.pdf).

FIOH (1999). *CAREX database*. Helsinki, Finnish Institute of Occupational Health (http://www.ttl.fi/Internet/English/FIOH+in+action/Departments/Department+of+Epidemiology+and+Biostatistics/carex_eng.htm).

Hayes R, Yin S, Dosemeci M, Li G, Wacholder S, Travis L, Li C, Rothman N, Hoover R, Linet M (1997). Benzene and the dose-related incidence of hematologic neoplasms in China. *Journal of the National Cancer Institute,* 89:1065–1071.

Hnizdo E, Sluis-Cremer G (1991). Silica exposure, silicosis, and lung cancer: a mortality study of South African gold miners. *British Journal of Industrial Medicine*, 48:53–60.

Hodgson J, Darnton A (2000). The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure. *Annals of Occupational Hygiene*, 44:565–601.

IARC (1977). *Asbestos*. Lyon, France, IARC (Monograph 14).

IARC (1980). *Some metals and metallic compounds*. Lyon, France, IARC (Monograph 23).

IARC (1987a). *Overall evaluations of carcinogenicity: an updating of IARC Monographs 1–42(Suppl. 7). Lyon, France, IARC.*

IARC (1987b). *Silica and some silicates*. Lyon, France, IARC (Monograph 42).

IARC (1989). Diesel and gasoline engine exhausts and some nitroarenes. Lyon, France, IARC (Monograph 46).

IARC (1990a). *Chromium, nickel and welding*. Lyon, France, IARC (Monograph 49).

IARC (1990b). *Cancer*. Geneva, IARC Scientific Publication.

IARC (1993). Beryllium, cadmium, mercury, and exposures in the glass manufacturing industry. Lyon, France, IARC (Monograph 58).

IARC (1997). Silica, some silicates, coal dust and para-aramid fibrils. Lyon, France, IARC (Monograph 68).

IARC (2000). *Ionizing radiation, part 1: X- and gamma (γ)-radiation, and neutrons. Lyon, France, IARC (Monograph 75).*

IARC (2001). *Overall evaluation of carcinogenicity to humans*. Lyon, France, IARC (http://193.51.164.11/monoeval/crthall.html, accessed October 2001).

IARC (2002). *IARC monographs programme on the evaluation of carcinogenic risks to humans*. Lyon, France, IARC (http://193.51.164.11, accessed 2002).

ICNCM (1990). Report of the International Committee on Nickel Carcinogenesis in Man. *Scandinavian Journal of Work Environmental Health*, 16:1–84.

ICRP (1991). *Recommendations of the International Commission on Radiological Protection.* Oxford, International Commission on Radiological Protection, ICRP Publication 60(21):1–3.

ILO (1995). Economically active population, by industry and by occupation. *Year Book of Labour Statistics*, 54th issue. Geneva, International Labour Organization.

ILO (2000). *ILO yearbook of labour statistics, 59th issue*. Geneva, International Labor Organization.

ILO (2001). *Laborsta, the labour statistics database*. Geneva, International Labour Organization (http://laborsta.ilo.org/ accessed 2003).

ILO (2002). *Economically active population 1950–2010*, 4th ed., rev. 2. Geneva, International Labour Organization.

IPCS (1998). *Chrysotile asbestos*. Geneva, International Programme on Chemical Safety (Environmental health criteria, No. 203).

Jahn I, Ahrens W, Bruske-Hohlfeld I, Kreuzer M, Mohner M, Pohlabeln H, Wichmann H, Jockel K (1999). Occupational risk factors for lung cancer in women: results of a case–control study in Germany. *American Journal of Industrial Medicine*, 36:90–100.

Jarup L, Nordberg G (1998). Cancer. Scandinavian Journal of Work and Environmental Health, 24:34–36.

Kauppinen T, Toikkanen J, Pedersen D, Young R, Ahrens W, Boffetta P, Hansen J, Kromhout H, Maqueda Blasco J, Mirabelli D, de la Orden-Rivera V, Pannett B, Plato N, Savela A, Vincent R, Kogevinas M (2000). Occupational exposure to carcinogens in the European Union. *Occupational and Environmental Medicine*, 57:10–18.

Kraut A (1994). Estimates of the extent of morbidity and mortality due to occupational diseases in Canada. *American Journal of Industrial Medicine*, 25:267–278.

Lee P (2001). Relation between exposure to asbestos and smoking jointly and the risk of lung cancer. *Occupational and Environmental Medicine*, 58(3):145–153.

Leigh J, Hendrie L, Berry D (2001). *2001 Australian mesothelioma register report*. Canberra, NOHSC.

Leigh J, Davidson P, Hendrie L, Berry D (2001). Malignant mesothelioma in Australia 1945 to 2000. *American Journal of Industrial Medicine*, 41:188–201.

Leigh J, Markowitz S, Fahs M, Shin C, Landrigan P (1997). Occupational injury and illness in the United States. Estimates of costs, morbidity, and mortality. *Archives of Internal Medicine*, 28;157(14):1557–1568.

Lipsett M, Campleman S (1999). Occupational exposure to diesel exhaust and lung cancer: a meta-analysis. *American Journal of Public Health*, 89:1009–1017.

Luo S, Liu X, Mu S, Tsai SP, Wen CP (2003). Asbestos related diseases from environmental exposure to crocidolite in Da-yao, China. I. Review of exposure and epidemiological data. *Occupational and Environmental Medicine*, 60(1):35–41.

Lynge E, Anttila A ,Hemminki K (1997). Organic solvents and cancer. *Cancer Causes and Control*, 8:406–419.

Markowitz SB, Fisher E, Fahs MC, Shapiro J, Landrigan PJ (1998). Occupational disease in New York State: a comprehensive examination. *American Journal of Industrial Medicine*, 16:417–435.

Morrell S, Kerr C, Driscoll T, Taylor R, Salkeld G, Corbett S (1998). Best estimate of the magnitude of mortality due to occupational exposure to hazardous substances. *Occupational and Environmental Medicine*, 55:634–641.

Nagano T (2002). Mesothelioma in Japan. In: Robinson BWS, Chahinian AP, eds. *Mesothelioma*. London, Martin Dunitz, pp 351–358.

Nelson DI, Driscoll T, Prüss-Üstün A, Fingerhut M, Concha M, Corvalan C, Leigh J (2002). Exposure assessment for the global burden of occupational injuries. In: *American Industrial Hygiene Conference and Exposition, 2 June 2002, San Diego, USA*. (Available at http://www.aiha.org/aihce02/handouts.htm).

Nurminen M, Karjalainen A (2001). Epidemiologic estimate of the proportion of fatalities related to occupational factors in Finland. *Scandinavian Journal Work Environmental Health*, 27:161–213.

Peto J, Hodgson JT, Matthews FE, Jones JR (1995). Continuing increase in mesothelioma mortality in Britain. *Lancet*, 345:535–539.

Peto R, Lopez AD, Boreham J, Thud M, Heath C Jr (1992). Mortality from tobacco in developed countries: indirect estimation from national vital statistics. *Lancet*, 339:1268–1278.

Peto J, Decarli A, La Vecchia C, Levi F, Negri E (1999). The European mesothelioma epidemic. *British Journal of Cancer*, 79:666–672.

Prüss-Üstün A, Mathers C, Corvalán C, Woodward W (2003). Introduction and methods: assessing the environmental burden of disease at national and local levels. Geneva, World Health Organization. (WHO Environmental Burden of Disease Series, No. 1).

Setlow VP, Lawson CE, Woods NF (1998). Gender differences in susceptibility to environmental factors: a priority assessment. Washington, DC, National Academy Press.

Soutar C, Robertson A, Miller B, Searl A, Bignon J (2000). Epidemiological evidence on the carcinogenicity of silica: factors in scientific judgment. *Annals of Occupational Hygiene*, 44:3–14.

Stayner L, Smith R, Thun M, Schnorr T, Lemen R (1992). A dose response analysis and quantitative assessment of lung cancer risk and occupational cadmium exposure. *Annals of Epidemiology*, 2:177–194.

Steenland K, Ward E (1991). Lung cancer incidence among patients with beryllium disease: a cohort mortality study. *Journal of the National Cancer Institute*, 83:1380–1385.

Steenland K, Sanderson W (2001). Lung cancer among industrial sand workers exposed to crystalline silica. *American Journal of Epidemiology*, 53:695–703.

Steenland K, Loomis D, Shy C, Simonsen N (1996). Review of occupational lung carcinogens. *American Journal of Industrial Medicine*, 29:474–490.

Steenland K, Burnett C, Lalich N, Ward E, Hurrell J (2003). Dying for work: The magnitude of US mortality from selected causes of death associated with occupation. *American Journal of Industrial Medicine*, 43(5):461–482.

Stellman JM (1994). Where women work and the hazards they may face on the job. *Journal of Occupational Medicine*, 36:814–825.

Tossavainen A (2000). International expert meeting on new advances in the radiology and screening of asbestos-related diseases. *Scandinavian Journal of Work, Environment and Health*, 26:449–454.

Tossavainen A, Takahashi K (2000). In: Tossavainen A, Lehtinen S, Huuskonen M, Rantonen J, eds. New advances in radiology and screening of asbestos-related diseases. Proceedings of an International Expert Meeting, Espoo Finland, February 2000. FIOH, Helsinki.

Ulvestad B, Kjaerheim K, Martinsen JI, Damberg G, Wannag A, Mowe G, Andersen A (2002). Cancer incidence among workers in the asbestos-cement producing

industry in Norway. *Scandinavian Journal of Work, Environment and Health*, 28(6):411–417.

Ward E, Okan A, Ruder A, Fingerhut M, Steenland K (1992). A mortality study of workers at seven beryllium processing plants. *American Journal of Industrial Medicine*, 22:885–904.

WHO (1999). *International statistical classification of diseases and related health problems (ICD-10) in occupational health*. Geneva, World Health Organization (Occupational and Environmental Health Series, WHO/SDE/OEH/99.11).

WHO (2001). *Electromagnetic fields and public health: Extremely low frequency fields and cancer*. Geneva, World Health Organization (Fact Sheet No. 263. Available at http://www.who.int/inf-fs/en/fact263.html).

WHO (2002). *The world health report 2002*. Geneva, World Health Organization.

World Bank (2001). *World development indicators 2001*. Geneva, World Bank (http://worldbank.com accessed 2003).

Yano E, Wang Z-M, Wang X-R, Wang M-Z, Lan Y-J (2001). Cancer mortality among workers exposed to amphibole-free chrysotile asbestos. *American Journal of Epidemiology*, 154:538–543.

Zwi AB, Reid G, Landau SP, Kielkowski D, Sitas F, Becklake MR (1989). Mesothelioma in South Africa, 1976–1984: incidence and case characteristics. *International Journal of Epidemiology*, 18:320–329.

Annex 1. Evidence for substance-specific relative risk values

A1.1 Carcinogens for lung cancer

The evidence for substance-specific relative risk values, which were used to calculate the overall relative risk for the eight lung carcinogens, is briefly discussed below. A summary relative risk of 1.6 is used for occupational exposure to the set of lung carcinogens considered here (Steenland et al., 1996).

Arsenic

Arsenic is classified as a Category 1 carcinogen (IARC, 1980, 1987a). The six principal epidemiological studies reviewed by Steenland et al. (1996) covered nearly 18 000 workers and indicated a combined relative risk of 3.69, with a range of 1.31–15.2 reported for individual studies, and a clear dose–response relationship. The lowest relative risk came from a study where exposures mostly ranged from 7 to 13 ug/m^3, compared to the Occupational Safety and Health Administration level of 10 ug/m^3 (Enterline et al., 1987). Excess cancers in other studies were probably due to high exposures that occurred largely in the past. A combined relative risk of 3.69 (95% CI: 3.06–4.46) was determined by Steenland et al. (1996), and 3.2 by Nurminen & Karjalainen (2001). This guide uses 3.69 (95% CI: 3.06–4.46).

Asbestos

Both serpentine and amphibole asbestos cause lung cancer in humans, and have a clear dose–response relationship; there is also a synergy between asbestos and tobacco (Lee, 2001). Over 100 cohort studies, many case-referent studies, and animal and cellular studies provide ample evidence for causation. In six cohort studies of nearly 6000 asbestotics, the Standardized Mortality Ratios (SMRs)[1] ranged from 3.5 to 9.1, with a combined relative risk of 5.9. In 20 studies of over 100 000 asbestos workers, SMRs ranged from 1.04 for chrysotile workers to 4.97 for amosite workers, with a combined relative risk of 2.00. It is difficult to determine the exposures involved because few of the studies reported measurements, and because it is problematic to convert historical asbestos measurements in millions of particulates of dust per cubic foot, into gravimetric units. However, little excess lung cancer is expected from low exposure levels. These studies have been the subject of several reviews (IARC, 1977; Steenland et al., 1996; IPCS, 1998; Nurminen & Karjalainen, 2001). The main papers provided a range of relative risks (1.04–7.4), with summary relative risks of 2.0 (Steenland et al., 1996) and 2.3 (Nurminen & Karjalainen, 2001) cited in the two most recent reviews. The lower value (2.0; 95% CI: 1.90–2.11) is selected for this analysis because it is based on a wider range of studies.

[1] See Glossary of terms for a definition of the standardized mortality ratio.

Beryllium

Beryllium is an IARC Category 1 carcinogen (IARC, 1993), although epidemiological evidence is rather limited. A SMR for lung cancer of 2.0 was determined from a registry cohort of 689 women and men (Steenland & Ward, 1991), and an overall SMR of 1.24 was found in a study of 9225 male workers from seven beryllium plants (1.49 at plants with higher exposure) (Ward et al., 1992). Steenland et al. (1996) utilized a smoking-adjusted relative risk of 1.49 (no 95% CI reported), based on a beryllium plant with high exposures, and this value is used in this guide because it appeared the most robust of the available values.

Cadmium

Cadmium is an IARC Category 1 carcinogen (IARC, 1993). The best epidemiological evidence of its relationship to lung cancer comes from a cohort study by Stayner et al. (1992), although the evidence for carcinogenicity is stronger in animals. Its carcinogenicity in humans has recently been questioned (Jarup & Nordberg, 1998). The most recent follow-up study suggests a relative risk of 1.49 (95% CI: 0.96–2.22). (Steenland et al., 1996). Nurminen & Karjalainen (2001) used 1.2, based on a Scandinavian study. This guide uses 1.49 (95% CI: 0.96–2.22).

Chromium

Chromium is an IARC Category 1 carcinogen (IARC, 1990a). There is ample epidemiological evidence that it causes lung cancer, with many cohort studies showing a dose–response relationship. Based on the largest and best-designed studies of chromium production workers, producers of chromate paints, and chromate-plating workers, the overall relative risk is 2.78 (95% CI: 2.47–3.52) (Steenland et al., 1996). Nurminen & Karjalainen (2001) used a lower relative risk of 1.4 from a hospital-based case-referent study. This guide uses 2.78 (95% CI: 2.47–3.52).

Diesel exhaust

Polycyclic aromatic hydrocarbons comprise the main components of diesel exhaust, which contains a mixture of substances. Diesel exhaust is accepted as a Category 2A carcinogen (IARC, 1989) and was scheduled for further review in 2001. It has been difficult to conduct human epidemiology studies, due to limitations in the assessment of exposure to diesel exhaust. However, cohort studies and meta-analyses confirm a relationship between exposure to diesel exhaust and lung cancer, with summary relative risks in the range 1.3–1.5 (Bhatia, Lopipero & Smith, 1998; Lipsett & Campleman, 1999). Based on six relatively consistent recent studies with good documentation of exposure to diesel exhaust, in which the number of cases ranged from 50 to 1256, Steenland et al. (1996) determined a combined relative risk of 1.31 (95% CI: 1.13–1.44). Nurminen & Karjalainen (2001) used the same estimate, as does this guide.

Nickel

Nickel is an IARC Category 1 carcinogen (IARC, 1990a). Based on data from the 1990 report of the International Committee on Nickel Carcinogenesis in Man (ICNCM, 1990), Steenland et al. (1996) calculated a combined relative risk of 1.56 (95% CI: 1.41–1.73). Nurminen & Karjalainen (2001) used an estimate of 1.4 based on a Finnish study. This guide uses 1.56 (95% CI: 1.41–1.73).

Silica

On the basis of detailed reviews, silica has been classified as an IARC Category 1 carcinogen (IARC, 1987b, 1997). Several cohort studies in silica-exposed and silicosis cases show a dose–response relationship between silica exposure and lung cancer relative risk, which has been confirmed by meta-analyses and a pooled study (Steenland & Sanderson, 2001). Animal and cellular studies provide supporting evidence. Controversy remains as to whether silicosis is a necessary precursor for the development of lung cancer, but this does not affect the underlying status of silica as a carcinogen (Hnizdo & Sluis-Cremer, 1991; Checkoway, 2000; Soutar et al., 2000). Steenland et al. (1996) based their combined relative risk of 1.33 (95% CI: 1.21–1.45) on 13 large cohort and case–control studies of silica-exposed workers. These studies included granite workers, stone workers, pottery workers, brick workers, gold miners, and diatomaceous miners, and the population sizes generally numbered from almost 1000 to over 5000. Half of the studies controlled for smoking. Nurminen & Karjalainen (2001) used a slightly higher estimate of 1.4. This guide uses 1.33 (95% CI: 1.21–1.45).

A1.2 Leukaemogens

Leukaemia has been linked to exposures to benzene, ionizing radiation and ethylene oxide, all of which are IARC Group 1 carcinogens (WHO, 1999; IARC, 2001). There is also some evidence that exposure to low-frequency electric fields is leukaemogenic (Nurminen & Karjalainen, 2001; WHO, 2001). However, as this physical agent has not been included in CAREX, it was excluded from consideration in the CRA study (Concha-Barrientos et al., 2004) and also here.

Benzene

The causal relationship between leukaemia and benzene is well recognized. Supporting evidence includes cohort studies in the USA and China that covered workers in chemical plants, refineries, machine production, textile and cloth factories. Excesses of non-lymphocytic leukaemia, myelogenous leukaemia, and acute myeloid leukaemia occurred. There is also limited evidence in mammals (IARC, 1990b; Hayes et al., 1997). A recent review (Lynge, Anttila & Hemminki, 1997) provided the low exposure and high exposure relative risks for this guide, which were 2.0 (95% CI: 1.8–2.2) and 4.0 (95% CI: 3.6–4.4), respectively.

Ionizing radiation

The causal relationship between ionizing radiation and leukaemia is well recognized. There is consistency across numerous studies, strong association between exposure and outcome, and evidence of a dose–response gradient. Excess leukaemia has been observed in survivors of Hiroshima and Nagasaki, and also among patients medically treated with X-rays or γ-rays. The risk of leukaemia increases over five-fold at sufficiently high doses (BEIR V, 1990; ICRP, 1991; IARC, 2000). Two models describing risk have been proposed (BEIR V 1990): the linear relative risk model (1 + 5.5 × dose in Sv), and the quadratic relative risk model (1 + 0.24 × dose + 0.27 × dose^2). A relative risk of 1.22 (95% CI: 1.07–1.70) for low exposure and 1.57 (95% CI: 1.18–2.88) for high exposure (BEIR V, 1990; IARC, 2000) are accepted as the best available estimates, and were used in this study.

Ethylene oxide

Workers are exposed to ethylene oxide, either as a sterilizing agent, or as a chemical intermediary or final product. In a USA study, the use of ethylene oxide as a sterilizing agent was associated with lymphatic leukaemia and non-Hodgkin's lymphoma, with a rate ratio of 1.2 (estimated for a 45-year exposure to 1 part per million). Other studies in Sweden and the United Kingdom showed non-significant excesses of these cancers. Of six studies of chemical plant workers (two in Sweden, the rest in the United Kingdom, Italy, USA and Germany), two found significant excesses, two found non-significant excesses, and two found expected rates (IARC, 1997). Relative risks (arising from varying exposures) ranged from 1.1 to 3.5 (K. Steenland, personal communication), and these were used as the basis of low exposure (1.1) and high exposure (3.5) relative risks in this guide.

A1.3 Malignant mesothelioma

As noted earlier, malignant mesothelioma of the pleura, peritoneum and other mesothelial tissue is virtually uniquely caused by asbestos. Therefore, we do not calculate relative risks as part of the process of calculating AFs. Instead, we outline a different approach (see Section 7.3). Here we offer only some background information about mesothelioma.

Mesothelioma can be caused by all fibre types, although amphiboles are 4–30 times more carcinogenic than chrysotile. Evidence for the causal association between asbestos exposure and malignant mesothelioma comes from animal, cellular and human cohort and case-referent studies (IARC, 1977; IPCS, 1998; Hodgson & Darnton, 2000; Yano et al., 2001). There is a clear dose–response relationship and a latency period of 20–60 years.

Data on national malignant mesothelioma incidence is available for some countries, and there is a relationship between national incidence and historic national per capita asbestos consumption (Tossavainen & Takahashi, 2000).

Malignant mesothelioma incidence is predicted to increase by 50–150% by 2015. Typical incidence rates for Western Europe, USA, Australia, South Africa and New Zealand are 17–35 per million per year (Zwi et al., 1989; Peto et al., 1995, 1999; Burdorf, Swuste & Looman, 1998; Tossavainen, 2000). Sex-specific and age-specific incidences are available for Australia (Leigh, Hendrie & Berry, 2001; Leigh et al., 2001). The current burden is about 10 000 cases per year for Western Europe, USA, Australia and Japan, although the Japan epidemic is probably delayed because the peak use of asbestos in Japan came later than in the West (Nagano, 2002). There are no reliable data for Eastern Europe, Asia, Africa and South America. New use of asbestos is banned in many countries, but it is still used in Africa, India, China and parts of South and Central America.

Annex 2. Country groupings for the WHO Global Burden of Disease study, by WHO subregion[a]

Subregion[b]		WHO Member States
AFR	D	Algeria, Angola, Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Comoros, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Nigeria, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Togo.
AFR	E	Botswana, Burundi, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe.
AMR	A	Canada, Cuba, United States of America.
AMR	B	Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Brazil, Chile, Colombia, Costa Rica, Dominica, Dominican Republic, El Salvador, Grenada, Guyana, Honduras, Jamaica, Mexico, Panama, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela.
AMR	D	Bolivia, Ecuador, Guatemala, Haiti, Nicaragua, Peru.
EMR	B	Bahrain, Cyprus, Iran (Islamic Republic of), Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates.
EMR	D	Afghanistan, Djibouti, Egypt, Iraq, Morocco, Pakistan, Somalia, Sudan, Yemen.
EUR	A	Andorra, Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom.
EUR	B	Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kyrgyzstan, Poland, Romania, Slovakia, Tajikistan, The Former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Uzbekistan, Yugoslavia.
EUR	C	Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine.
SEAR	B	Indonesia, Sri Lanka, Thailand.
SEAR	D	Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Maldives, Myanmar, Nepal, Timor Leste.
WPR	A	Australia, Brunei Darussalam, Japan, New Zealand, Singapore.
WPR	B	Cambodia, China, Cook Islands, Fiji, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam

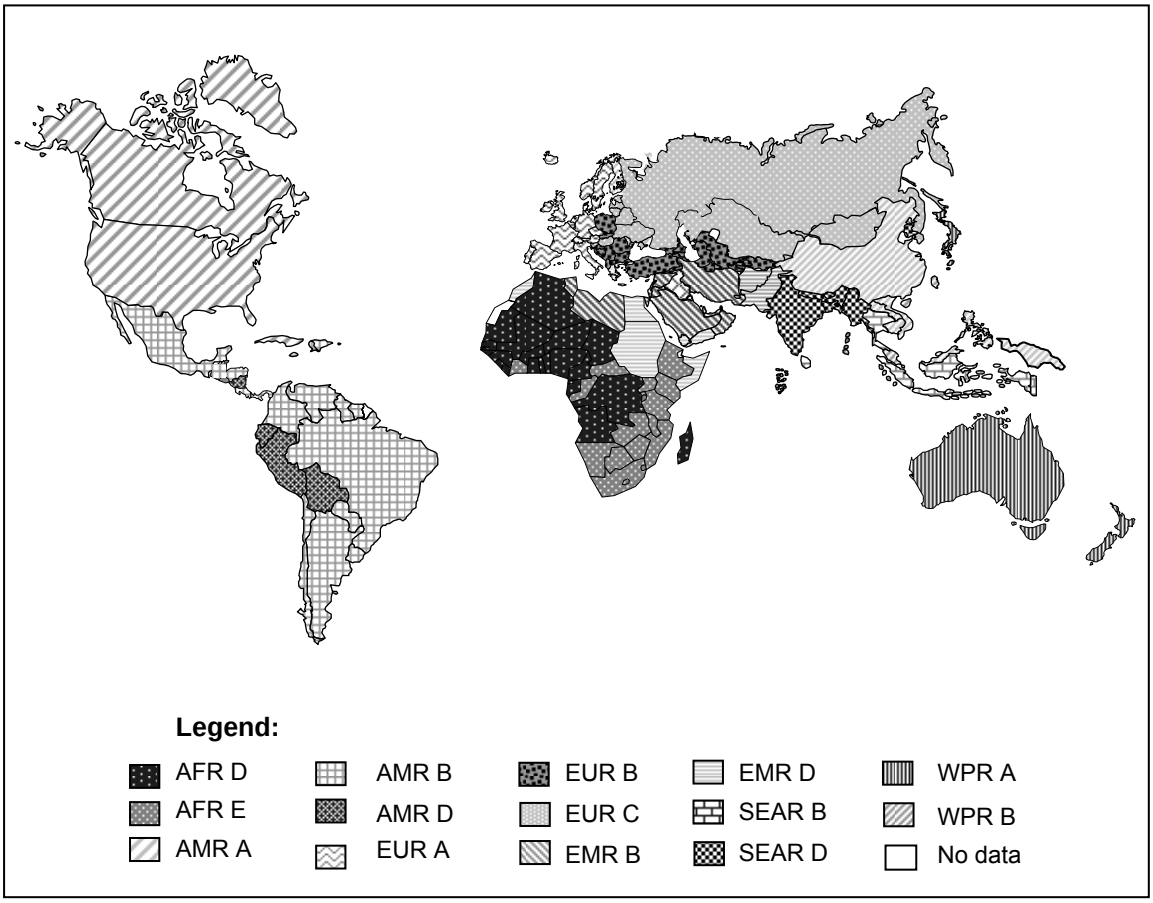
[a] Source: WHO (2002).

[b] Subregions: AFR = Africa; AMR = Americas; EMR = Eastern Mediterranean; EUR = Europe; SEAR = South-East Asia; WPR = Western Pacific; A: Very low child, very low adult mortality; B: Low child, low adult mortality; C: Low child, high adult mortality; D: High child, high adult mortality; E: High child, very high adult mortality.

Annex 3. Assessment of the global disease burden from occupational carcinogens

The approach described in this guide was also used in a global analysis of the disease burden from occupational risk factors, including occupational carcinogens (WHO, 2002; Concha-Barrientos et al., 2004). The analysis assessed the disease burden for the 14 WHO subregions of the world in the year 2000 (Figure A3.1; Annex 2), and by age group and sex.

Figure A3.1 Subregional country groupings for the global disease burden



This is only a schematic representation. The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

To estimate the exposed proportion of the population in each subregion, the Economically Active Population[1] was distributed into nine industry sectors, and worker exposure in each sector was partitioned into high and low levels. Turnover accounted for previous exposures. The primary data sources for estimating exposure included the World Bank (World Bank, 2001); the International Labour Organization (ILO, 1995, 2001, 2002); the European Union CAREX carcinogen exposure database (FIOH, 1999; Kauppinen et al., 2000); published literature on the prevalence and level of exposure to occupational carcinogens; and published literature on the epidemiology of health outcomes linked to occupational carcinogens.

The global analysis included agents classified by the International Agency for Research on Cancer as Group 1 (carcinogenic to humans) and as Group 2A (probably carcinogenic to humans) (IARC, 2002). Work-related malignant conditions considered to be the most common, or that were supported by the strongest evidence, or for which data were available (i.e. lung cancer, leukaemia and malignant mesothelioma) were included in the analysis. The occupational carcinogens included in the global study, and associated outcomes, are shown in Table A3.1

Table A3.1 Occupational carcinogens and health outcomes

Occupational carcinogen	Outcome
Arsenic, asbestos, beryllium, cadmium, chromium, diesel exhaust, nickel, silica	Cancer of the trachea, bronchus or lung
Benzene, ethylene oxide, ionizing radiation	Leukaemia
Asbestos	Malignant mesothelioma

The mean proportions of workers exposed to the selected carcinogens are shown in Table A3.2, and their partitioning into high exposure and low exposure is given in Table A3.3. The values given in these tables were used for the analysis in this guide.

[1] See Glossary of terms for definition.

Table A3.2 Mean proportions of workers in the European Union exposed to selected carcinogens, by industry sector[a]

Carcinogen	Agri-culture	Mining	Manufac-turing	Electrical	Construc-tion	Trade	Transpor-tation	Finance	Services
Silica	0.00372	0.23049	0.02327	0.01415	0.18860	0.00017	0.00476	0.00002	0.00061
Cadmium	0.00000	0.00000	0.00487	0.00287	0.00291	0.00002	0.00065	0.00000	0.00047
Nickel	0.00000	0.02025	0.01680	0.00352	0.00047	0.00007	0.00003	0.00000	0.00043
Arsenic	0.00054	0.00072	0.00400	0.00148	0.00134	0.00006	0.00000	0.00002	0.00011
Chromium	0.00000	0.00346	0.02079	0.00409	0.00237	0.00017	0.00370	0.00000	0.00225
Diesel fumes	0.00646	0.21970	0.01110	0.03358	0.05816	0.00485	0.13438	0.00000	0.00914
Beryllium	0.00000	0.00055	0.00207	0.00070	0.00004	0.00002	0.00011	0.00000	0.00003
Asbestos	0.01248	0.10248	0.00590	0.01702	0.05203	0.00292	0.00684	0.00016	0.00284
Benzene	0.00100	0.00200	0.00300	0.00100	0.00100	0.01000	0.00500	0.00000	0.02000
Ionizing radiation	0.00000	0.01100	0.00000	0.03400	0.00000	0.00000	0.00400	0.00000	0.00000
Ethylene oxide	0.00012	0.00137	0.00060	0.00006	0.00027	0.00000	0.00002	0.00000	0.00057

[a] Source: FIOH (1999).

Table A3.3 Partition factors for high and low exposures to carcinogens, by WHO subregion[a]

Subregions	Low exposure[b]	High exposure
A	0.90	0.10
B, C, D, E	0.50	0.50

[a] See Table A3.1 for country groupings in each subregion.
[b] Low exposure = at or below the PEL; high exposure = above the PEL.

Many sources of exposure–risk information were used to quantify the relationship between exposure and disease. Examples of the main literature sources are provided in Table A3.4. Relative risks differed by cancer, subregion, gender and age group. Summary relative risks are provided in Table A3.5, and additional information can be found in Concha-Barrientos et al. (2004).

Table A3.4 Summary of risk measures for occupational carcinogens

Health outcome	Risk measure	Estimate (95% CI)	Comments	Primary data sources
Cancer of the trachea, bronchus and lung	Relative risk	Low exposure: 1.22 (1.09–1.35) to 1.32 (1.17–1.48) High exposure: 1.79 (1.59–1.97) to 1.93 (1.71–2.16)	Composite relative risk based on individual relative risk of arsenic, asbestos, beryllium, cadmium, chromium, diesel exhaust, nickel and silica.	Steenland et al. (1996).
Leukaemia	Relative risk	Low exposure: 1.67 (1.51–2.00) to 1.93 (1.76–2.17) High exposure: 3.06 (2.64–3.80) to 3.86 (3.48–4.32)	Composite relative risk based on individual relative risk of benzene, ionizing radiation and ethylene oxide.	BEIR V (1990); Lynge et al. (1997); IARC (2000); Steenland et al. (2003).
Malignant mesothelioma	Mortality rate	A subregions, low exposure: 0.000000 (0.000000–0.000001) to 0.000093 (0.000058–0.000145) A subregions, high exposure: 0.000002 (0.000001–0.000003) to 0.000465 (0.000288–0.000724) B, C, D and E subregions, low exposure: 0.000001 (0.000001–000002) to 0.000233 (0.000144–0.000362) B, C, D and E subregions, high exposure: 0.000003 (0.000002–0.000005) to 0.000698 (0.000431–0.00109)	Mortality rates for malignant mesothelioma based on cumulative exposure to asbestos, and age-adjusted for mean duration of exposure.	Hodgson & Darnton (2000).

Table A3.5 Examples of sources used to assess the risk factor–disease relationship for selected occupational carcinogens

Selected risk factor	Health outcome	Evidence of causality
Lung carcinogens	Cancer of the trachea, bronchus or lung	Steenland et al. (1996, 2003); Nurminen & Karjalainen (2001).
Leukaemogens	Leukaemia	BEIR V (1990); IARC (1997); Lynge, Anttila & Hemminki (1997).
Asbestos	Malignant mesothelioma	IARC (1977); IPCS (1998); Hodgson & Darnton (2000); Yano et al. (2001).

The disease burdens for the 14 WHO subregions was calculated from the exposed population and the relative risks for occupational carcinogens. The results are summarized in Table A3.6. Additional details are provided in Tables 5 and 6 of this document. A breakdown of the burden by disease, age group and sex is given in Tables A3.7 and A3.8. No effects specific to the hazards associated with child labour are addressed in this report owing to a lack of data.

Table A3.6 Mortality and DALYs[a] attributable to occupational carcinogens for 14 WHO subregions of the world[b]

Subregion	Attributable mortality (thousands)	Proportion of total mortality attributable to occupational carcinogens (%)	Attributable DALYs (thousands)	Proportion of total DALYs attributable to occupational carcinogens (%)
AFR D	1	0.0	16	0.0
AFR E	2	0.0	24	0.0
AMR A	12	0.4	93	0.2
AMR B	6	0.2	60	0.1
AMR D	0	0.0	5	0.0
EMR B	1	0.1	17	0.1
EMR D	2	0.1	29	0.0
EUR A	19	0.5	152	0.3
EUR B	9	0.5	94	0.2
EUR C	19	0.5	197	0.3
SEAR B	5	0.2	51	0.1
SEAR D	16	0.1	177	0.0
WPR A	5	0.4	37	0.2
WPR B	46	0.4	469	0.2
World	146	0.3	1421	0.1

[a] Abbreviations: DALYs = disability-adjusted life years.
[b] Source: WHO (2002).

Table A3.7 Population attributable fractions for diseases from occupational carcinogens[a]

Disease	Male (%)	Female (%)	Both sexes (%)
Leukaemia	3	2	2
Other malignant neoplasms	2	1	2
Trachea/bronchus/lung cancers	12	6	10

[a] Source: WHO (2002).

Table A3.8 Attributable mortality and DALYs[a] from occupational carcinogens, by age group and sex[b]

	Age group (years)				Sex	
	0-4	**5-14**	**15-59**	**60+**	**Male**	**Female**
Distribution of attributable deaths (% of attributable events)	0	0	28	72	81	19
Distribution of attributable DALYs (% of attributable events)	0	0	52	48	80	20

[a] Abbreviation: DALYs = disability-adjusted life years.

[b] Source: WHO (2002).