European Code against Cancer 4th Edition: Environment, occupation and cancer

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Abbreviations:
AF, attributable fraction; BFRs, brominated flame retardants; DDT, dichlorodiphenyltrichloroethane; ESCAPE, European Study of Cohorts for Air Pollution Effects; EU, European Union; HR, hazard ratio; IARC, International Agency for Research on Cancer; PM₁₀, particulate matter with diameter of 10 micrometres or less; PM₂.₅, particulate matter with diameter of 2.5 micrometres or less; P AHs, polycyclic aromatic hydrocarbons; PFBS, polybrominated dibenzo-p-dioxins and -furans; POPs, persistent organic pollutants; REACH, Registration, Evaluation and Authorisation of Chemicals; TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin; WHO, World Health Organization.

1. Sources of environmental and occupational exposures: An overview

“Environment” is usually defined as the physical, chemical and biological conditions external to the human host, and all related behaviours. People are exposed to a wide range of pollutants from different sources through different pathways and exposure routes (such as inhalation, ingestion or dermal contact). Exposures occur throughout life on multiple occasions and in various settings: at home, at the workplace or in the general environment. There is some evidence that environmental exposures may be more hazardous during gestation and more in children than in adults [1]. Additionally, parental environmental or occupational exposures may increase the risk of cancer in the offspring [2–4]. Environmental contaminants typically affect the general population through exposures that normally cannot be directly controlled...
by the individual. Some exposures are widespread (e.g. air pollution), whereas others are limited to small areas close to, for example, specific industrial sites.

Air pollution, especially outdoors, is a major environmental health problem in Europe [5,6]. Other environmental health exposures derive from consumer products (predominantly man-made) that people are exposed to involuntarily in their daily life: e.g. paints or building materials in households, pesticides applied in gardens or playgrounds, chemicals used for cleaning at home or in schools, and toys. Occupational health risks are directly related to agents occurring in the work environment. The specific types of cancer linked with occupational exposures are mainly cancers of the lung, skin (non-melanoma) and urinary bladder, and mesothelioma [7]. The harmful health effects of environmental exposures usually depend on the carcinogenic potential of the agent, the dose and duration of the exposure, and the susceptibility of the individual.

The International Agency for Research on Cancer (IARC) Monographs programme on the evaluation of carcinogenic risks to humans rigorously evaluates and classifies the carcinogenicity to humans of specific chemicals, groups of related chemicals, complex mixtures, occupational and environmental exposures, cultural or behavioural practices, biological organisms and physical agents [8] into: Group 1 (carcinogenic to humans), 2A (probably carcinogenic to humans), 2B (possibly carcinogenic to humans), 3 (not classifiable as to its carcinogenicity to humans), and 4 (probably not carcinogenic to humans) [9]. The Monographs programme is one of the major sources for the scientific justification of the recommendations related to environment and occupation.

In the framework of the European Code against Cancer [10], the Environment and Occupation Working Group aims to summarise below the current evidence on the main environmental and occupational carcinogens of a chemical nature to which the citizens of the European Union (EU) may be still exposed today.

2. Cancer associated with environmental and occupational chemical exposures

Table 1 presents an overview of chemicals and mixtures, metals, dust and fibres, and occupations classified as carcinogenic (Group 1) to humans, and the cancer sites with sufficient or limited evidence for carcinogenicity. Environmental exposures and occupations with carcinogenic potential may be related to specific compounds, mixtures of exposures, or exposure scenarios where specific carcinogenic agents have yet not been identified. Some environmental and work-related exposures with carcinogenic potential are presented elsewhere in the 4th edition of the European Code against Cancer (Box 1), including second-hand tobacco smoke [11], ionising radiation (radon, radiation-exposed workers) [12] and ultraviolet radiation in outdoor workers [13].

2.1. Environmental exposures

Recently, both outdoor air pollution per se and particulate matter (PM) from outdoor air pollution have been classified as carcinogenic to humans (Group 1) [6]. Outdoor air pollution is a mixture of multiple pollutants originating from a myriad natural and anthropogenic sources such as transport, power generation, industrial activity, biomass burning, and domestic heating and cooking. Exposure levels and contributions from the individual sources of outdoor air pollution vary substantially geographically and over time. Volatile organic compounds, nitrogen-containing and halogenated organic compounds, polycyclic aromatic hydrocarbons (PAHs), toxic metals, and many by-products of incomplete combustion (e.g. dioxins) are all carcinogenic air pollutants. An important contribution to the body of evidence for an association between PM and lung cancer was provided by the European Study of Cohorts for Air Pollution Effects (ESCAPE) – a pooled analysis of data from 17 European countries [14]. ESCAPE reported an increased risk for lung cancer associated with 10 μg/m³ increments of PM₁₀ (hazard ratio (HR): 1.22; 95% CI: 1.03–1.45) and PM₂.₅ (HR: 1.40; 95% CI: 0.92–2.13). These results were apparent even for exposure levels below current European guidelines. The IARC Working Group concluded also that the existing studies have provided some evidence of an increased risk of bladder cancer associated with outdoor air pollution, including occupational and residential exposures to traffic emissions [6], after adjustment for tobacco smoking. Other substances or mixtures contributing to outdoor air pollution have also been classified or reconfirmed as Group 1 by the IARC, including diesel engine exhaust [15], benzene and PAHs [2]. Humans are usually exposed simultaneously to a variety of PAHs which include several potent carcinogens, such as benzo[a]pyrene. Urban populations with high ambient levels of PAHs and other pollutants have exhibited higher rates of lung cancer than rural populations which are independent of tobacco smoking [16]. Benzene is found in refuelling emissions near petrol filling stations and inside vehicles. In occupational studies, sufficient evidence has been established for the association between benzene and acute non-lymphocytic leukaemia, and potentially other haematopoietic malignancies, including acute lymphocytic leukaemia, chronic lymphocytic leukaemia, multiple myeloma and non-Hodgkin lymphoma [2].

In recent decades the European Union has significantly reduced emissions of several air pollutants, such as SO₂, CO, benzene and lead [5]. Emissions of primary PM₁₀ and PM₂.₅ decreased by 14% and 16%, respectively, between 2002 and 2011. Despite these improvements, road transport, industry, power plants, household and agricultural activities continue to emit significant amounts of air pollutants. During 2002–2011, 22–44% of the EU urban population was exposed to concentrations of PM₁₀ above the EU limit for daily air quality, and the PM₁₀ 24-h limit was exceeded in 22 European countries in 2011. Fig. 1 shows the attainment of the PM₁₀ 24-h limit value for all EU member states in 2011. Cross-border pollution – e.g. from intercontinental transport – constitutes a particularly challenging issue since, in many EU countries, more than 50% of the observed PM₂.₅ concentrations derive from outside-border emissions.

Furthermore, overall combustion of fuels for domestic needs has not decreased in the EU in the last decade [5]. Indoor emissions from household combustion of coal, an important source of PM and PAHs, have been classified as carcinogenic to humans with sufficient evidence for increased risk of lung cancer [17]. Another established carcinogen, formaldehyde (Group 1), is also released in combustion processes, and may also be released from particle boards and similar building materials, carpets, paints and varnishes, and during its use as a disinfectant [2]. Second-hand smoke, containing most of the constituents of tobacco smoke including 69 known carcinogens, also contributes to both indoor and outdoor air pollution, as reported elsewhere [11].

Other environmental contaminants are found in water and food. A wide range of compounds – including pesticides, industrial and household chemicals, metals and pharmaceutical products – can reach freshwater bodies in Europe. For instance, non-occupational exposure to arsenic in the general EU population is mainly through contaminated food [18] and water [19], as was shown in a study conducted in Hungary, Romania and Slovakia. Of particular concern are chemical contaminants with persistent and bio-accumulative properties, as well as potentially endocrine-disrupting properties which alter the hormonal and homeostatic systems and thus may be associated with an array of diseases and disorders. Many of these chemicals are used in plastics, textiles,
Table 1
Overview of chemicals and mixtures, metals, dust and fibres, and occupations classified as “carcinogenic to humans” (Group 1) by the IARC and associated cancer sites.

<table>
<thead>
<tr>
<th>Carcinogenic agent</th>
<th>Cancer sites with sufficient evidence in humans</th>
<th>Cancer sites with limited evidence in humans</th>
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</thead>
<tbody>
<tr>
<td><strong>Chemicals and mixtures:</strong></td>
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<tr>
<td>Aromatic amines</td>
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<tr>
<td>4-Aminobiphenyl</td>
<td>Urinary bladder</td>
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<tr>
<td>Benzidine</td>
<td>Urinary bladder</td>
<td></td>
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<tr>
<td>4,4'-Methylenebis(2-chloroaniline) (MOCA)</td>
<td>Strong mechanistic evidence in exposed humans</td>
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<tr>
<td>2-Naphthylamine</td>
<td>Urinary bladder</td>
<td></td>
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<tr>
<td>Ortho-toluidine</td>
<td>Urinary bladder</td>
<td></td>
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<tr>
<td>Diesel engine exhaust</td>
<td>Lung</td>
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<tr>
<td>Indoor emissions from household combustion of coal</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Outdoor air pollution and particulate matter (PM)</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Polycyclic aromatic hydrocarbons (PAH) related</td>
<td></td>
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<tr>
<td>Benz[a]pyrene</td>
<td>Strong mechanistic evidence in exposed humans</td>
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<tr>
<td>Coal tar pitch</td>
<td>Lung; skin</td>
<td></td>
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<tr>
<td>Soot</td>
<td>Lung; skin</td>
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<tr>
<td>Reactive chemicals</td>
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<tr>
<td>Acid mists, strong inorganic</td>
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<tr>
<td>1,3-Butadiene</td>
<td>Larynx</td>
<td></td>
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<tr>
<td>Ethylene oxide</td>
<td>Haematolymphatic organs</td>
<td></td>
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<tr>
<td>Formaldehyde</td>
<td>Leukaemia (particularly myeloid); nasopharynx</td>
<td>Nasal cavity and paranasal sinus</td>
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<tr>
<td>Sulphur mustard</td>
<td>Lung</td>
<td>Liver (angiosarcoma, hepatocellular carcinoma)</td>
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<tr>
<td>Vinyl chloride</td>
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<td>Larynx</td>
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<tr>
<td>Solvents</td>
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<tr>
<td>Benzene</td>
<td>Leukaemia (acute non-lymphocytic)</td>
<td>Leukaemia (acute lymphocytic, chronic lymphocytic, multiple myeloma, non-Hodgkin lymphoma)</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
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<tr>
<td>Bis(chloromethyl)ether; chloromethylmethylether (technical grade)</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Mineral oils, untreated or mildly treated</td>
<td>Skin</td>
<td>Strong mechanistic evidence in exposed humans</td>
</tr>
<tr>
<td>3,4,5,3',4'-Pentachlorobiphenyl (PCB-126)</td>
<td>Strong mechanistic evidence in exposed humans</td>
<td></td>
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<tr>
<td>2,3,4,7,8-Pentachlorodibenzofuran</td>
<td>Skin</td>
<td></td>
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<tr>
<td>Shale oils</td>
<td>All cancers combined</td>
<td>Lung; non-Hodgkin lymphoma; soft tissue sarcoma</td>
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<tr>
<td>2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)</td>
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<tr>
<td><strong>Metals:</strong></td>
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<tr>
<td>Arsenic and inorganic arsenic compounds</td>
<td>Lung; skin; urinary bladder</td>
<td>Kidney; liver; prostate</td>
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<tr>
<td>Beryllium and beryllium compounds</td>
<td>Lung</td>
<td>Kidney; prostate</td>
</tr>
<tr>
<td>Cadmium and cadmium compounds</td>
<td>Lung</td>
<td>Nasal cavity and paranasal sinus</td>
</tr>
<tr>
<td>Chromium (VI) compounds</td>
<td>Lung</td>
<td></td>
</tr>
<tr>
<td>Nickel compounds</td>
<td>Lung; nasal cavity and paranasal sinus</td>
<td></td>
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<tr>
<td><strong>Dust and fibres:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asbestos (all forms)</td>
<td>Larynx; lung; mesothelioma; ovary</td>
<td>Colorectum; pharynx; stomach</td>
</tr>
<tr>
<td>Erionite</td>
<td>Mesotheioma</td>
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<tr>
<td>Leather dust</td>
<td>Nasal cavity and paranasal sinus</td>
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<tr>
<td>Silica dust, crystalline (in the form of quartz or crystobalite)</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Wood dust</td>
<td>Nasal cavity and paranasal sinus; nasopharynx</td>
<td></td>
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<tr>
<td><strong>Occupations:</strong></td>
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<tr>
<td>Aluminium production</td>
<td>Lung; urinary bladder</td>
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<tr>
<td>Auramine production</td>
<td>Urinary bladder</td>
<td></td>
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<tr>
<td>Coal gasification</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Coal tar distillation</td>
<td>Skin</td>
<td></td>
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<tr>
<td>Coke production</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Haematite mining (underground)</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Iron and steel founding</td>
<td>Lung</td>
<td></td>
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<tr>
<td>Isopropyl alcohol production</td>
<td>Nasal cavity and paranasal sinus</td>
<td></td>
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<tr>
<td>Magenta production</td>
<td>Urinary bladder</td>
<td></td>
</tr>
<tr>
<td>Painting</td>
<td>Lung; mesothelioma; urinary bladder</td>
<td>Leukaemia, lymphoma; lung; stomach; urinary bladder</td>
</tr>
<tr>
<td>Rubber production industry</td>
<td></td>
<td></td>
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</tbody>
</table>

Adapted from Cogliano et al. [8].

Cosmetics, dyestuffs, children’s toys and baby-care products, lubricants, pesticides, electronic goods, food packaging, etc., and may also be of concern when discarded as waste, as many chemicals migrate easily to the environment and can be found in wildlife, outdoor air, indoor dust, wastewater and sludge. Although many of these chemicals are considered safe according to regulatory criteria, there is still concern about possible adverse health effects [20,21].
Persistent organic pollutants (POPs) are ubiquitous environmental pollutants, resistant to environmental degradation, that can bioaccumulate and magnify in the food chain. There are thousands of POPs; among the most important are polychlorinated biphenyls (PCBs), brominated flame retardants (BFRs), polychlorinated dibenzo-p-dioxins and -furans (PCDD/Fs), polybrominated diphenyl ethers (PBDEs), organochlorine pesticides or PAHs [22]. POPs are either chemicals produced intentionally, such as the diphenyl ethers (PBDEs), organochlorine pesticides or PAHs [22]. Persistent organic pollutants (POPs) are ubiquitous environmental pollutants, resistant to environmental degradation, that can bioaccumulate and magnify in the food chain. There are thousands of POPs; among the most important are polychlorinated biphenyls (PCBs), brominated flame retardants (BFRs), polychlorinated dibenzo-p-dioxins and -furans (PCDD/Fs), polybrominated diphenyl ethers (PBDEs), organochlorine pesticides or PAHs [22]. POPs are either chemicals produced intentionally, such as the dichlorodiphenyltrichloroethane (DDT) or PCBs, or POPs are either chemicals produced intentionally, such as the diphenyl ethers (PBDEs), organochlorine pesticides or PAHs [22].

Box 1. European Code Against Cancer.

European Code against Cancer

12 ways to reduce your cancer risk

1. Do not smoke. Do not use any form of tobacco
2. Make your home smoke free. Support smoke-free policies in your workplace
3. Take action to be a healthy body weight
4. Be physically active in everyday life. Limit the time you spend sitting
5. Have a healthy diet:
   - Eat plenty of whole grains, pulses, vegetables and fruits
   - Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks
   - Avoid processed meat; limit red meat and foods high in salt
6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention
7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds
8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions
9. Find out if you are exposed to radiation from naturally high radon levels in your home; take action to reduce high radon levels
10. For women:
    - Breastfeeding reduces the mother’s cancer risk. If you can, breastfeed your baby
    - Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT
11. Ensure your children take part in vaccination programmes for:
    - Hepatitis B (for newborns)
    - Human papillomavirus (HPV) (for girls)
12. Take part in organised cancer screening programmes for:
    - Bowel cancer (men and women)
    - Breast cancer (women)
    - Cervical cancer (women)

The European Code Against Cancer focuses on actions that individual citizens can take to help prevent cancer. Successful cancer prevention requires these individual actions to be supported by governmental policies and actions.

2.2. Occupational exposures

Exposures to carcinogens at the workplace are usually much higher than in the general environment. The IARC has classified 44 occupational exposures as human carcinogens: 32 chemicals or physical agents and groups of agents or mixtures to which exposure is mainly occupational, and 12 industrial processes or occupations [8]. Rushton et al. have recently aimed to characterise the specific occupational exposures and their contribution to the burden of cancer in the United Kingdom (UK) [30]. The list (not exhaustive) includes: natural fibres or dust such as asbestos, silica, and wood and leather dust; metals such as arsenic, beryllium, cadmium, chromium VI, or inorganic lead; solvents such as benzene, trichloroethylene or tetrachloroethylene; mineral oils; petrochemicals and combustion by-products such as diesel engine exhaust, PAHs or TCDD; reactive chemicals such as 1,3-butanediene, ethylene oxide, formaldehyde, vinyl chloride, strong inorganic acid mists containing sulphuric acid; aromatic amines; non-arsenical insecticides; and acrylamide; occupational exposures as a painter, hairdresser and barber, steel foundry worker; and within the rubber industry or petroleum refining. Rushton et al. [30] estimated that these occupational exposures accounted for 5.3% of all cancer-related deaths in the UK in 2005.

Many of the occupational exposures were reassessed by the IARC in 2009 to systematically identify tumour sites and mechanisms of carcinogenesis [8]. All forms of asbestos are carcinogenic to humans and account for the largest proportion of occupational cancer in Europe. There is sufficient evidence of a carcinogenic effect of asbestos exposure against mesothelioma and cancers of the lung, larynx, and ovary, and limited evidence for an association with colorectal cancer, pharyngeal cancer and stomach cancer. Although the use of all forms of asbestos has been banned in the EU [31,32], and the level of exposure from previous use of asbestos is decreasing rapidly, compliance with regulations needs to be continuously monitored. For example, workers employed in construction trades, electricians and carpenters can still be exposed to high levels of asbestos through renovations, repairs and demolitions, along with workers exposed to asbestos-containing products e.g. in brake maintenance and repair. In the EU, asbestos is still found in industrial buildings, private homes, ships, heating or cooling systems, and work equipment [33]. In Estonia, for example, the concentration of asbestos fibres in the working environment increased during 2001–2003 due to renovation of cancer and non-Hodgkin lymphoma have also been reported [27].
solid oil-shale-fuelled power plants [34]. Additionally, the general population is also exposed to asbestos when it is released into the environment from the use and deterioration of friable asbestos materials [21,35]. Removal or repair of asbestos-containing products in household maintenance, or contamination of ambient air in the vicinity of deteriorating asbestos-containing products or activities with removal of asbestos represent modes of exposure to the public. Due to the long latency period between exposure to asbestos and the development of manifest mesothelioma, the incidence of this malignancy has not yet peaked in many countries [36] despite the ban; in Germany, for example, the number of deaths from mesothelioma have been predicted to peak in 2020 [37].

Over 2 million workers in the EU are exposed to crystalline silica in mineral, fuel-energy, metal, chemical and construction industries. For example, in Poland, over 50,000 individuals are exposed at work to silica dust exposure exceeding the occupational exposure limit [38]. In 2012, diesel engine exhaust was classified as a Group 1 carcinogen mainly on the basis of robust epidemiological studies of occupational exposure among non-metal miners and railroad and truck workers, showing an excess risk of lung cancer. An increased risk of bladder cancer was also observed in some case–control studies [15]. Maintenance and car repair workers, retail workers, workers using power generators, drivers, delivery and cargo workers, miners, etc. are currently exposed to diesel engine exhaust in the EU [39–41]. Inhalation of arsenic-containing particulates is the primary route of occupational exposure, but exposure due to ingestion and dermal exposure may also be significant in certain settings. Apart from skin cancer, arsenic has been associated consistently with cancers of the lung and urinary bladder, and less consistently with cancers of the kidney, liver and prostate [21]. In 2003, the EU prohibited manufacture and sales of certain azo dyes used in textile and leather articles, which release aromatic amines (Group 1) [2]. Aromatic amines used in the rubber industry have been confirmed to cause cancer of the urinary bladder. In addition, increased occurrences of leukaemia and lymphoma, and cancers of the lung and stomach, have been reported among workers in the rubber-manufacturing industry in relation to a complexity of exposures. Formaldehyde, used in textile and plastic industries, is known to induce nasopharyngeal cancer and myeloid leukaemia. Various PAH-related industries – such as aluminium production, coal gasification or coke production, and other industries involving exposure to PAH-containing mixtures – have been confirmed as causes of e.g. lung cancer and skin cancer (in coal-tar distillation).

In the reassessment of some occupational exposures, the carcinogenic entity has been attributed to specific agents instead of the occupational setting: for example chromium VI and nickel compounds (previously: chromate production and nickel refining) associated with lung cancer and cancers of the lung, nasal cavity and paranasal sinuses, respectively; leather dust (previously: boot and shoe manufacture and repair) associated with cancers of the nasal cavity and paranasal sinuses; or wood dust (previously: furniture and cabinet-making) associated with cancers of the nasal cavity, paranasal sinuses and nasopharynx [8]. Occupational exposure as a painter was recently associated with development of mesothelioma and bladder cancer, in addition to lung cancer. Finally, many of the environmental exposures described above also occur in work settings (Table 1).

Notwithstanding the many established associations, the scientific knowledge of the carcinogenic potential of occupational and environmental chemicals is still incomplete, and some common malignancies have few (or no) identified causal agents: e.g., haematopoietic malignancies, brain tumours, and testicular cancer. Thus, continuous re-evaluation of the evidence for occupational and environmental chemicals is crucial. Recently, increasing attention has been directed toward identification of vulnerable, and “hidden”, groups of workers, such as migrants, part-time workers, sub-contracted staff, women and young workers, who are underrepresented in intervention strategies aimed at reducing occupational exposure to carcinogens [42]. These demographic groups often have hazardous occupations, with exposure to multiple carcinogens, along with inherent low socio-economic status and low awareness of chemical risks.

2.3. Burden of cancer due to occupational and environmental exposures

The cancer burden is easier to quantify for occupational exposures than for environmental exposures. This is due mainly

**Fig. 1.** Attainment situation for PM$_{10}$ in 2011. The graph is based on the 90.41 percentile of daily mean concentration values of PM$_{10}$ corresponding to the 36th highest daily mean for each EU member state; the boxes present the range of concentrations at all station types (in µg/m$^3$) officially reported by the member states and how the concentrations relate to the limit value set by EU legislation (marked by the red line).

to the fact that exposure prevalence in environmental settings is
often unknown or that the magnitude of risk at low doses is not
well established, whereas exposure levels at many workplaces
with possible hazards are regularly monitored and the effects
of high exposures are more easily detectable. Therefore, when
individuals are exposed to certain agents present only at
environmental levels, the evaluation of the cancer burden relies
heavily on whether the effects (even small ones) are assumed to
occur at low levels or only above certain thresholds.

In the early 1990s, an estimated 22–24 million workers in 15 EU
countries were exposed to Group 1 carcinogens [43], including
crystalline silica (3.2 millions), diesel exhaust (3.0 millions), wood
dust (2.6 millions), and benzene (1.4 millions). In their compre-
hensive study based on UK data, Rushton et al. estimated overall
attributable fractions (AF) and numbers of cancer cases occurring
in the UK due to carcinogenic agents, processes and occupations
classified as Group 1 or 2A agents for which evidence of
occupational exposure was either “strong” or “suggestive” for
the specific cancer sites. Overall, cancer death burden in 2005 due
to occupation was estimated to be 8.2% among men and 2.3%
among women, yielding an overall AF of 5.3% [30]. For lung cancer,
the most important occupational cancer, the estimated AF was
>20% among men, similar to the finding in a recent Finnish study
[44]. Fig. 2 presents the most common occupational cancers
(in numbers of cases) with estimated AF > 2%, including cancers of
the lung, nasopharynx, urinary bladder, larynx, oesophagus and
stomach, mesothelioma, sinonasal cancer, non-melanoma skin
cancer and soft-tissue sarcoma [30]; 56% of occupational cancers
were attributable to men employed in the construction industry
(mainly mesothelioma, cancers of the lung, bladder and stomach,
and non-melanoma skin cancer) [30]. The agents responsible for
most occupation-attributable cancers were asbestos, mineral oils,
silica, diesel engine exhaust, PAHs from coal tar and pitches,
dioxins, tetrachloroethylene, arsenic and strong inorganic acid
mists, as well as an occupation as a painter. Also associated with
high numbers of cancer cases and deaths were metal working,
household services, mining, land transport, printing/publishing,
retail/hotels/restaurants, public administration, farming, and sev-
eral manufacturing sectors. In some industry sectors, workers were
exposed to ten or more carcinogenic agents, especially in construc-
tion and many of the manufacturing sectors, and the workers
presented a wide range of cancers [45]. A recent registry-based
follow-up study of 15 million individuals in Denmark, Finland,
Iceland, Norway and Sweden reported associations between
occupational exposures and cancer occurrences similar to those of
the Rushton study in the UK [46].

The combined effects of multiple carcinogens, occupational
agents and environmental factors – including lifestyle habits – may
have additive or synergistic effects. Examples are the combination
of tobacco smoke with radon [47], asbestos, arsenic or alcohol
drinking [48]. Additionally, low-level environmental exposure to
carcinogenic pollutants is a major concern because of the
multiplicity of substances, the involuntary exposure, and the
large numbers of individuals being exposed. The 1981 landmark
publication by Doll and Peto estimated that 2% of cancer deaths
were attributable to pollution worldwide [49]. Recently, the World
Health Organization (WHO) has estimated that the population
attributable fractions from lung cancer due to ambient air and
household air pollution from solid fuels in the 28 EU countries
(including Croatia) in 2012 were 7.27% (95% CI: 1.24–12.99%) and
1.25% (95% CI: 0.57–1.83%), respectively [50]. This corresponds to
20,268 deaths from lung cancer for ambient air and 3482 from
household air pollution.

3. Justification for recommendation

The 4th edition of the European Code against Cancer advocates
for action-oriented recommendations for the general population.
The complexity of the chemical exposures, the corresponding level
of risk for the general population, and the involuntary nature of the
exposure to these agents complicates formulation of layman
statements for recommendations that are otherwise addressed to

![Fig. 2. Attributable numbers (cases) due to occupation. Estimated numbers (cases in men and women together) attributable to occupational exposures by cancer site (and attributable fraction (AF) for men and women together indicated in parenthesis). Data from Rushton et al. [30].](image)
employers or regulators. Since we act on what we know, it is important to raise awareness in the general population about environmental and occupational carcinogens in order to motivate people to be proactive in advocating protection from chemical exposures and supporting initiatives aimed at reducing pollution.

3.1. Management and control of environmental and occupational carcinogens

Exposures to environmental and occupational carcinogens can be reduced or eliminated, and the cancers resulting from these exposures can be prevented through policies promoting healthy working and living environments [51]. There is firm evidence that population-based policies and legislative tools to prevent environmental and occupational carcinogenic risks are feasible and highly effective in reducing cancer burden [52]; some examples are listed in Table 2. At the EU level, the new law REACH (Registration, Evaluation and Authorisation of Chemicals) has been adopted by the Member States and the European Parliament and came into force in June 2007 [53]. This law seeks to improve the protection of human health and the environment through better and earlier identification of intrinsic properties of chemical substances, and placing responsibility on industry to manage risks from chemicals, to provide safety information on the substances, and to progressively substitute the most dangerous chemicals by suitable alternatives. A number of substances, however, do not fall under the REACH regulation, including diesel motor emission, wood dust or welding fumes [42], as well as chemicals marketed before 1981 that have not been adequately tested for safety [20]. These substances and chemicals are regarded as ‘existing substances’ by the current EU legislation, for which the public authorities have the responsibility for identifying hazards, prioritising hazardous substances used in highest volumes for risk assessment and, where needed, developing risk management measures [54].

On the other hand, EU directives on the protection of health and safety at work have had a big impact, laying down basic principles for all sectors of activity, especially general responsibilities of employers. These directives are legally binding and have to be transposed into national laws by the member states [55]. However, continuous surveillance of compliance with protection guidelines is still needed across all EU countries.

3.2. Individual-based interventions to prevent exposures

While for most environmental chemicals the most effective measures are community interventions aimed at reducing or eliminating these substances, rather than personal interventions, there are some personal interventions where the individual can take action. Some examples are listed in Table 3 [56,57]. In discussions of individual-level interventions it is important to acknowledge that population risk perception may differ from the actual risk. For instance, a study in Spain reported that food colouring and other additives were perceived as disease risk factors by the large majority of individuals [58]. Involuntary exposures and events generated the biggest alarm. Interestingly, overweight was a well-known risk factor for most of the public but was conceived as a less important factor than, for example, electromagnetic fields [12]. Furthermore, individuals in the general population living near landfill sites, incinerators, composting facilities and nuclear installations are often concerned about being exposed to carcinogens. This contrasts with the conclusions of a recent review on the waste management practices and their impact on human health stating that the evidence linking waste landfills and incinerators to adverse health effects (notably cancer, reproductive outcomes and mortality) is usually insufficient and inconclusive [59]. Nevertheless, there have been individual situations in which emissions from industries such as smelters, foundries, incinerators, or other sources were of sufficient magnitude to increase cancer risk in nearby populations [60]. Quantitative data on exposures in humans are therefore needed to assess whether a potential risk exists in a particular setting.

3.3. Placing cancer prevention and control in the context of “health in all policies”

With the increasing life expectancy in the EU, the main causes of premature death and disability have become chronic conditions [61]. Since cancer shares many risk factors with other non-communicable diseases such as cardiovascular or respiratory diseases, including some environmental risk factors, it has become increasingly important to address these diseases mutually. Hence, reducing exposure to environmental and occupational carcinogens can produce additional health benefits of huge importance. For example, control measures to reduce outdoor air pollution not only contribute to reduced lung cancer incidence but also to a reduction in the incidence of cardiovascular and respiratory diseases [52]. A recent EU report found evidence that air pollution contributed to an increased occurrence of cancer, heart disease, bronchitis and asthma, and estimated that PM2.5 resulting from

Table 2
Examples of population-based policies and legislative tools to prevent environmental and occupational risks related to cancer.

<table>
<thead>
<tr>
<th>General measures to avoid chemical exposures:</th>
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<tbody>
<tr>
<td>• Hazard identification, risk assessment, risk management and risk communication in all occupational settings</td>
</tr>
<tr>
<td>• Regulations for substitution and phasing out of replaceable processes or carcinogenic substances in the workplace, by replacing them with less dangerous substances</td>
</tr>
<tr>
<td>• Measures aimed at closing industrial facilities in which carcinogens are released, wet processes, ventilation, filtration or cleaning</td>
</tr>
<tr>
<td>• Controlling carcinogen exposure based on threshold limit values</td>
</tr>
<tr>
<td>• Regulating the use of protective equipment for workers and decontamination facilities in industries</td>
</tr>
</tbody>
</table>

Offering incentives to corporations to encourage the elimination of harmful chemicals in their products and processes

Disclosure/labelling laws for identification and classification of chemicals by types of hazard, including safety data sheets

Setting accreditation procedures for labelling industries as health-sensible, and encouraging public administrations to establish preferential contracts with those companies

Promoting effective measures to ensure the safe storage and disposal of recycling of chemicals

Regulations ensuring the safe management of hazardous substances during trade and transport

Raising the overall awareness of workers, employers, and health and safety professionals about work hazards, their recognition and elimination, and ensuring the reporting of cancer cases with a suspected occupational aetiology

Adapted from Espina et al. [52].

Table 3
Examples of individual-based interventions to prevent environmental exposures.

| 1. Ensuring adequate ventilation in private homes, thus reducing indoor air pollution; use energy-efficient household appliances (heating, cooling, etc.) |
| 2. Avoiding open burning of organic matters such as wood or yard debris |
| 3. Limiting the use of and properly maintaining private cars |
| 4. Using bicycle or public transportation, thus helping to reduce outdoor air pollution |
| 5. Properly disposing of household chemicals (e.g. pesticides and paints) or pharmaceuticals, and reducing waste, thus contributing to minimising contamination of drinking water and soil |
| 6. Hiring a professional contractor for asbestos removal and disposal |
| 7. Raising public awareness on healthier environments among the community |

1. 2. 3. 4. 5. 6. 7.
human activities reduces each EU citizen’s life expectancy by an average of 8.5 months [20].

4. Current and future challenges facing control of cancers of environmental and occupational origin

A “safe dose” is a complex concept that depends not only on scientific evidence but also on societal factors. For many carcinogenic substances there is no scientifically established “safe dose”; however, the EU legislation defines “safe” products as any product that does not present “unacceptable risks” under normal or foreseeable conditions of use [53]. The possible combined effects of exposures and mixtures of chemicals occurring at low concentrations in the environment or in consumer goods are receiving increased attention, especially in relation to young children [62]. In that context, it should be noted that an increasing number of diseases occurring during adulthood have been linked to early-life or prenatal exposures [63,64]. Controversies over emerging technologies, such as genetically modified organisms and nanotechnology, are also challenges – being directly related with public perception of risk and scientific uncertainty – which complicate the process of maximizing innovation while minimizing possible individual-level hazards. Nanomaterials and nanotechnology–based products are increasingly used in pharmaceutical and medical applications, water treatment and air filtration, and a great variety of consumer products and materials (from cosmetics to food processing and packaging). Some studies have evaluated the toxicity of some nanomaterials; however, the results are mixed, and the public health implications are unresolved [65].

5. Conclusions and recommendation

Defining individual-level recommendations to reduce cancer risk associated with environmental and occupational exposures had its challenges, being different from many other recommendations that target one particular carcinogen or habit. A general approach to prevention of exposures in the workplace is warranted, since several chemicals, metals, dusts and fibres, and occupations have been established to be causally associated with an increased risk of specific cancers. The number of specific substances is numerous, however, and many of the substances are not yet well defined. Also, for many exposures the relevant dose–response relationships have not been established, rendering it difficult to define “safe” levels. Instead, “acceptable” levels are often introduced, aimed at finding the balance between successful prevention of established cancer risk factors and avoiding false alarms leading to anxiety in the population. Other environmental exposures derive from chemicals used in consumer products, such as those in plastics, textiles, cosmetics, dyestuffs, children’s toys, baby-care products, lubricants, pesticides, electronic goods, or food packaging. As stated above, it has been estimated that the overall cancer burden associated with occupational carcinogens is 5.3% in the UK (one of the most industrial countries in the EU), and 7.27% for ambient air and 1.25% for household air pollution from solid fuels in relation to lung cancer in the 28 EU countries. It should be emphasised, though, that these estimates are likely to change with further identification of carcinogens and cancer sites associated with established carcinogens, better description of dose–response relationships, and identification of additional risk factors for cancers of currently largely unknown aetiology.

The general population has the right to know which substances they have been exposed to in the workplace, home and community, so that they can make informed decisions in relation to their health. A particular challenge is to avoid social inequality in information on safety issues and protection. Information on health-related issues, including potential carcinogenic risks, should be available to the public in layman’s language. This will empower individuals to act as informed consumers and citizens, which may ultimately demand manufactures to use safer substitutes for carcinogens, and industries to reduce the use, disposal and release of hazardous substances. For example, the United States has passed the “Emergency Planning and Community Right-to-Know Act” which makes citizens partners with governments, businesses and public-interest organisations in the management of chemical risks [66].

As regards environmental exposures, the respective frameworks at society level are typically needed to implement successful prevention. While every individual can contribute to a reduction in air pollution, such an initiative will not necessarily reduce the cancer risk of the given individual, but will contribute to a healthier society. The most applicable recommendation at the individual level is to be aware of protective measures and to apply them accordingly, following instructions on how to handle hazardous material at work, avoiding unnecessary exposure, and raising awareness of which relevant exposures occur at work, at home, and in the general environment. In the EU, regulations are not homogeneous across all countries, and protective measures in the workplace are not used consistently by all workers all the time. Taking these issues into account, the European Code against Cancer Environment and Occupation Working Group has developed the following recommendation: “In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.”

Conflict of interest

The authors declare no conflict of interest.

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