

# SECTION OF ENVIRONMENT AND RADIATION (ENV)

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ENVIRONMENT, INCLUDING LIFESTYLE, ENCOMPASSES MANY MAJOR CAUSES OF HUMAN CANCER, INCLUDING TOBACCO USE, ALCOHOL DRINKING, OCCUPATIONAL EXPOSURES, ENVIRONMENTAL POLLUTANTS AND RADIATION. ACCORDINGLY, THE RESEARCH ACTIVITIES OF THE SECTION OF ENVIRONMENT AND RADIATION (ENV) ADDRESS A BROAD SPECTRUM OF RISK FACTORS OF A VARIETY OF CANCERS, EITHER BY FURTHER CHARACTERIZING ESTABLISHED RISK FACTORS IN TERMS OF DOSE-RESPONSE PATTERNS OR IDENTIFYING SPECIFICALLY AFFECTED OR VULNERABLE SUBPOPULATIONS, OR BY INVESTIGATING POSSIBLE BUT NOT ESTABLISHED RISK FACTORS. THE SECTION INVESTIGATES THOSE EXOGENOUS FACTORS WITH THE AIM OF CONTRIBUTING TO THE PRIMARY PREVENTION OF CANCER AND INCREASING OUR UNDERSTANDING OF BIOLOGICAL MECHANISMS OF CARCINOGENESIS. THESE OBJECTIVES ARE ACHIEVED THROUGH COLLABORATIVE, INTERNATIONAL EPIDEMIOLOGICAL STUDIES IN A MULTIDISCIPLINARY APPROACH, WHEN POSSIBLE, OR THROUGH THE INITIATION OF SINGLE EPIDEMIOLOGICAL ANALYTICAL STUDIES. ANOTHER APPROACH USED BY THE SECTION IS THE COORDINATION OF INTERNATIONAL CONSORTIA OF EPIDEMIOLOGICAL STUDIES.

Recent results have emerged from Section projects on lifestyle, environmental, occupational and radiation-related causes of human cancer. They include investigations on tobacco use and cancer and of alcohol

consumption and cancer, a collaboration on a study in hyper-endemic areas of oesophageal cancer in Islamic Republic of Iran, studies on risk factors of head and neck cancer, and an international consortium on occupational risk factors of lung cancer. Recently launched major activities include studying adverse health effects related to pesticide use and the role of pesticides and endocrine-disrupting agents in the etiology of testicular cancer. Two pooling projects examine the impact of the parents' and children's exposure to pesticides and the subsequent risk of childhood cancer. Furthermore, the ENV is involved in projects that address cancer risks among workers in the rubber industry and those exposed to asbestos. Cancer-specific new activities include setting up an oesophageal cancer consortium in Africa, a global initiative on childhood leukaemia and further investigations into causes of brain tumours.

Projects on ionizing radiation include: the effects of protracted low doses of external ionizing radiation from medical diagnostic examinations and from occupational activities; populations exposed to Chernobyl fallout; in utero exposure of children born to workers in nuclear processing plants in the Southern Urals; and the interaction between ionizing radiation and genetic factors.

Non-ionizing radiation research activities include: a case-control study on mobile phone use and the risk of brain tumours, acoustic neuroma and salivary gland tumours; collaboration in a Danish cohort study of mobile phone subscribers; and collaboration in studies on extremely low-frequency magnetic fields and the risk of childhood cancer.

The Section is also about to finalize volume 14 of the IARC Handbooks on Cancer Prevention series on tobacco control. New activities investigate the potential carcinogenicity of another addictive plant, namely qat chewing, and its potential risk of cancer with feasibility studies carried out in East Africa.

## SECTION OF ENVIRONMENT AND RADIATION

### OVERVIEW

To achieve their objectives, the ENV is involved in numerous projects that investigate exogenous factors that lead to human cancer.

**Lifestyle:** A recent analysis embedded in European cohort studies confirmed that cigar and pipe smoking is not a safe alternative to cigarette smoking; the lower cancer risk of cigar and pipe smokers as compared to cigarette smokers was explained by a lesser degree of inhalation and lower smoking intensity (McCormack et al., 2010). Further investigations of head and neck cancer risk revealed that quitting tobacco smoking for 1–4 years already resulted in a 30% risk reduction compared to current smokers, with the risk reduction after  $\geq 20$  years reaching the level of never smokers (Marron et al., 2010). For other lifestyle factors, recent meta-analyses confirmed that oral and pharyngeal, laryngeal and oesophageal cancers are strongly related to alcohol drinking. An inverse association between caffeinated coffee drinking and risk of cancer of the oral cavity and pharynx was observed, whereas tea intake was not associated with head and neck cancer risk. Findings in Golestan, Islamic Republic of Iran, a high-risk area for oesophageal cancer, suggest cigarettes and hookah smoking, nass use, opium consumption, hot tea drinking, poor oral health, low intake of fresh fruit and vegetables and low socioeconomic status to be associated with a higher risk of oesophageal cancer.

**Environment and occupation:** In a study of European asphalt workers, no consistent evidence of an association between indicators of either inhalation or dermal exposure to bitumen and lung cancer risk was found, while a sizable proportion of the excess mortality from lung cancer relative to the general population is likely attributable to high tobacco consumption and possibly to coal tar exposure (Olsson et al., 2010). Investigating occupational risk factors for lung cancer using eastern European multicentre datasets, showed that exposure to polycyclic aromatic hydrocarbons (PAH) did not appear to substantially

contribute to the burden of lung cancer in eastern Europe. To investigate cancer risks in workers in the rubber industry, a new consortium of European cohort studies has been established. In the past two years, the Section commenced a historical cohort study of workers at Uralasbest (Russian Federation), one of the world's largest asbestos mines, to further characterize the effects on cancer of amphibole-free chrysotile, of prolonged low-levels of exposure, and the effect modification of smoking.

**Mammographic density** (percent fibroglandular tissue) is a strong intermediate marker of breast cancer risk. ENV is involved in several studies examining both its heritable and environmental determinants, including studies of determinants of density in young women, of within-woman changes in density and whether these in turn alter breast cancer risk, and a pooling project to examine whether worldwide variations in density underline international variations in breast cancer incidence rates.

**Ionizing radiation:** An international group of experts and advisors within the Agenda for Research on Chernobyl Health (ARCH) project led by IARC, reviewed the current knowledge about the health effects from the accident. They recommended international support for the long-term funding of a Chernobyl Health Effects Research Foundation, involving funding organizations and the three countries most affected by the accident (Williams et al., 2011). Pooling of nuclear workers' (NW) recently updated follow-up data from the US, United Kingdom and French cohorts, previously included in the International NW study, started in 2010. The proposed combined analysis offers the ability to derive more statistically precise risk estimates than any prior epidemiological study of cancer among NW. Evaluation of the contribution of genetic variations in candidate genes potentially relevant to thyroid tumours, and their interaction with ionizing radiation exposure to the thyroid gland, is underway using samples previously collected within the case-control study of thyroid cancer in Belarus. A study to collect and review historical literature discussing radiation dose to the breast was carried out to assess the dose likely received

by the breast during mammography examinations (Thierry- Chef et al., 2011). Cancer risks related to in utero exposure to ionizing radiation are currently being investigated by pooling the Techa River in utero exposed cohort and the Mayak workers' offspring cohort in the Southern Urals, the Russian Federation.

**Non-Ionizing radiation:** The rapid increase in mobile phone use has generated concern about possible health risks related to radiofrequency electromagnetic fields from this technology. In addition to a large international case-control study described below, recent results from the collaboration in a Danish nationwide cohort study of more than 400 000 mobile phone subscribers showed no increased risk of acoustic neuroma; however, heavy mobile phone users could not be studied as a separate group (Schüz et al., 2011). The Section also participates in a study on mobile phone use and risk of brain tumours in teenagers and adolescents (Cefalo) conducted jointly in Denmark, Norway, Sweden and Switzerland. Recently published results did not suggest an increased brain tumour risk in this particular age group (Aydin et al., 2011a). Given the limitations of retrospective studies when reconstructing past exposures, the Section received a grant for investigating the feasibility for running the French component of a European prospective study of mobile phone users. Current activities on extremely low-frequency magnetic fields (ELF- MF) include collaboration in a study on residential ELF-MF and survival after childhood leukaemia and participation in a European study investigating possible mechanisms.

#### IARC HANDBOOK ON TOBACCO PREVENTION

Due to the large proportion of cancer caused by tobacco, the IARC Handbooks of Cancer Prevention series added tobacco control as a topic for review and evaluation. Tobacco smoking is pandemic affecting over a billion people. Tobacco use is the target of control efforts at different jurisdictional levels across nations, and the evaluation of the effectiveness of such policy interventions in the Handbooks is an important contribution for developing cancer

prevention strategies. The last volume of the series, number 14, presents an evidence-based evaluation of the effects of tax and price policies for tobacco control, including the positive outcomes of reduced consumption, increased cessation and decreased initiation. Handbook volume 14 was developed by an interdisciplinary Working Group of experts from 12 countries, who critically reviewed the available evidence. The resulting working drafts were further reviewed during a meeting at IARC on 17–22 May 2010. There were several concluding statements on the effect of taxes on aggregated demand for tobacco, adult tobacco use, use among youth and among the poor, tobacco industry pricing strategies and tax related lobbying, tax avoidance and tax evasion and the economic and health impact of tobacco taxation (Chaloupka et al., 2011; Table 1).

#### OCCUPATIONAL RISK FACTORS OF LUNG CANCER (SYNERGY)

The SYNERGY project (Pooled Analysis of Case-control Studies on the Joint Effects of Occupational Carcinogens in the Development of Lung Cancer) was initiated to identify and estimate joint effects of five selected occupational carcinogens (PAH, asbestos, crystalline silica, chromium and nickel) and tobacco smoking. To date, 14 case-control studies from Europe and North America have been pooled providing lifetime occupational and smoking history from 17 705 cases and 21 813 controls. A unique feature of the SYNERGY project has been the development of SYNJEM – a country, year and job-specific job-exposure matrix with exposure estimates modelled from quantitative exposure measurements from 21 countries.

Additional analyses in the SYNERGY database have been initiated by the study group to address open research questions related to occupational lung cancer; for example diesel motor exhaust and lung cancer (Olsson et al., 2011), and organic dust exposures and lung cancer. Cumulative diesel exposure was associated with a 30% increased lung cancer risk in the highest exposure quartile and showed a significant exposure-response relationship. Those increased risks were confirmed in workers never employed in occupations

with established lung cancer risk, in women and in never-smokers. Organic dust exposure was also associated with increased lung cancer risk in a dose-dependent manner, including in subjects without a history of chronic obstructive pulmonary disease or asthma. Additional analyses on painters, hairdressers, cooks, welders, miners and construction workers are underway. The SYNERGY study group collaborates with the International Lung Cancer Consortium to study alcohol and lung cancer risk, and with the Imperial College in London to develop advanced methods to study multiple interactions.

#### COMPUTER TOMOGRAPHY IN CHILDREN AND THE RISK OF CANCER (EPI-CT)

For paediatric patients, an important innovation in diagnostic radiology has been the development of computerized tomography (CT) scans. However, the growing use of CT in children is a topic of concern in radiological protection. Considerations unique to the paediatric population include increased radiosensitivity, particularly in infancy, a longer lifetime for radiation-related cancer to occur and a lack of size-based adjustments in technique. In light of these considerations, a project coordinated by the Section (CHILD-MED-RAD), demonstrated the feasibility of setting up in Europe a multinational cohort study to evaluate the risks associated with the low doses from CT. Following those recommendations, the EU-funded EPI-CT project started in February 2011. It is a multinational study of paediatric CT patients based on a common core protocol. The work involves pooling of cohort data from nine European countries: Belgium, Denmark, France, Germany, Spain, Sweden, the Netherlands, Norway and the United Kingdom (Figure 1). The study, which is the largest and the most statistically powerful study of paediatric CT undertaken to date, is aiming to: develop knowledge about CT use patterns; accurately quantify doses from these procedures; directly study the long-term health effects of CT, primarily cancer, on paediatric patients; and better understand the balance between risks and benefits of paediatric imaging to optimize the doses delivered from CT.

**Table 1. Evidence for the effectiveness of tax and price policies in tobacco control**

Concluding Statements	Sufficient Evidence	Strong Evidence	Limited Evidence
Increases in tobacco excise taxes that increase prices reduce overall tobacco use, prevalence and consumption in continuing users and induces current tobacco users to quit.	X		
Increases in tobacco excise taxes that increase prices reduce the prevalence of tobacco use and reduce the initiation and uptake of tobacco use among young people, with a greater impact on the transition to regular use.	X		
Tobacco use among young people responds more to changes in tobacco product taxes and prices than does tobacco use among adults.	X		
In high-income countries, tobacco use among lower-income populations is more responsive to tax and price increases than is tobacco use among higher-income populations.		X	
The demand for tobacco products in lower-income countries is more responsive to price than is the demand for tobacco products in higher-income countries.			X
In low- and middle-income countries, tobacco use among lower-income populations is more responsive to tax and price increases than is tobacco use among higher-income populations.			X
Changes in the relative prices of tobacco products lead to some substitution to the products for which the relative prices have fallen.		X	
Tobacco tax increases augment tobacco tax revenues and when tax increases raise prices, population health is improved. Tax avoidance and tax evasion reduce, but do not eliminate, the public health and revenue impact of tobacco tax increases.	X		
A coordinated set of interventions that includes international collaborations, strengthened tax administration, increased enforcement, and swift, severe penalties reduces illicit trade in tobacco products.		X	
Higher and more uniform specific tobacco excise taxes result in higher tobacco product prices and increase the effectiveness of taxation policies in reducing tobacco use.	X		
Tobacco industry price discounting strategies, price-reducing marketing activities, and lobbying efforts mitigate the impact of tobacco excise tax increases.	X		
Tobacco tax increases do not increase unemployment.		X	

**Sufficient Evidence:** An association has been observed between the intervention under consideration and a given effect in studies in which chance, bias and confounding can be ruled out with reasonable confidence. The association is highly likely to be causal.

**Strong Evidence:** There is consistent evidence of an association, but evidence of causality is limited by the fact that chance, bias or confounding have not been ruled out with reasonable confidence. However, explanations other than causality are unlikely.

**Limited Evidence:** There is some evidence of association between the intervention under consideration and a given effect, but alternative explanations are possible.

**Inadequate/No Evidence:** There are no available methodologically sound studies showing an association; the available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between the intervention and a given effect. Alternatively, this category is used when no studies are available.

**Evidence of No Effect:** Methodologically sound studies consistently demonstrate the lack of an association between the intervention under consideration and a given effect.

INTERPHONE is the largest case-control study to date investigating risks related to mobile phone use. Also being explored are other potential risk factors for tumours arising in the tissues most exposed to radiofrequency electromagnetic fields from mobile phones including 2765 glioma, 2425 meningioma, 1121 acoustic neuroma, 109 malignant parotid gland tumour cases and 7658 controls from 13 countries. Overall, no increase in risk of glioma or meningioma was observed with use of mobile phones (INTERPHONE Study Group, 2010). No elevated risk for glioma or meningioma was observed  $\geq 10$  years after first mobile phone use. There were suggestions of an increased risk of glioma at the highest exposure levels, but biases and error prevented a causal interpretation. There was no increase in risk of acoustic neuroma with ever regular use of a mobile phone or for users who began regular use 10 years or more before reference date (INTERPHONE Study Group, 2011). Elevated risks observed at the highest level of cumulative call time could be due to chance, reporting bias or a causal effect. Altogether, the possible effects of long-term heavy use of mobile phones require further investigation.

#### UPCOMING ACTIVITIES

Several of the above described activities have started recently and are still in the phases of demonstrating feasibility, creating the infrastructure for the study, data collection or follow-up. Therefore the scientific results will appear in future years, and for some of the larger projects, perhaps over the next decade or longer. As shown, the Section will continue to be active in all areas: from lifestyle to environmental pollutants, occupational exposures and radiation (both ionizing and non-ionizing), and in areas where key questions on cancer causation are unanswered. With regard to cancer sites, it is particularly lung, oesophageal, testicular, breast and childhood cancers and brain tumours that are addressed by multiple activities and where research collaborations often go beyond environmental and radiation risk factors.

Figure 1. Estimated EPI-CT cohort size for each participating country



A long range goal of the Section is to launch studies on environmental-, occupational- and radiation-related risks in Africa (McCormack & Schüz, 2011). During the ongoing modernization of Africa, there are concerns that environmental exposures to carcinogens, sometimes at high levels, are likely given suboptimal attention in regards to workers' and environmental protection. The use of outdated technologies and lack of hazard awareness, among other concerns, add to the unease.





## EPI-CT: Kick-off meeting, 7 to 8 February 2011, IARC, Lyon



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