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The overall objectives of the Section of Environment and Radiation (ENV) are to investigate environmental, occupational, and lifestyle- and radiation-related causes of cancer and death from cancer in human populations. With this wide remit, ENV focuses its endeavours on three main areas: (i) research in settings where levels of exposure to putative or established carcinogens are high, and research is thus warranted; (ii) studies of common cancer types and of specific exposures that occur in under-researched settings, particularly but not exclusively in low- and middle-income countries (LMICs); and (iii) studies evaluating the role of broader social as well as biological factors throughout the course of the disease. The objectives of ENV are achieved through the conduct of collaborative international

epidemiological studies, including co-ordination of international consortia or through the initiation of targeted individual analytical epidemiological studies. In selecting projects, an effort is made to ensure that the involvement of the Agency makes a specific and substantial difference, by facilitating international collaboration, by overcoming political barriers, by assisting local collaborators in targeted studies with expertise and with increased local visibility and trust in their work, and by using the general expertise, international network, and special function of the Agency as part of the World Health Organization.

With a strong focus on environmental (including occupational and radiation-related) and lifestyle risk factors, ENV fills a major research gap to further

understand the cancer burden attributed to these factors. ENV has steered its research focus to LMICs in particular, a direction that is warranted because in these settings, levels of environmental pollution are often higher. Capacity-building, as well as establishing research platforms, is another vision of IARC to which ENV contributes. Selected examples of ENV projects are described here.

OE SOPHAGEAL CANCER IN EAST AFRICA: THE ESCAPE STUDIES

The incidence of oesophageal cancer, particularly of the histological type oesophageal squamous cell carcinoma (ESCC), has a peculiar spatial distribution worldwide. Similar to the Asian ESCC belt, East Africa has a

high-incidence corridor stretching from Ethiopia to Malawi; in this corridor, ESCC is among the most common cancer types and is a leading cause of cancer death, but its etiology is understudied. ENV initiated the Oesophageal Squamous Cell Carcinoma African Prevention Research (ESSCAPE) study 5 years ago after conducting an extensive review of priority factors requiring investigation in this setting. ESCC case–control studies are continuing in Kenya, Malawi, and the United Republic of Tanzania and represent the largest multi-country African ESCC study, with 1200 cases

and 1200 controls. Investment in biobanking for future molecular studies has been a priority throughout. In a collaboration with Moi University, Kenya, the first results from this country are already providing important clues to the underlying multifactorial etiology. The clear role of alcohol consumption, particularly of traditional brews and distillations, is present and contributes to ESCC incidence more in men than in women (Menya et al., 2019a). Another modifiable risk factor is drinking of very hot tea (Middleton et al., 2019a). ENV has also observed increased risks of

ESCC associated with various indicators of oral health and hygiene, including the first-ever findings for an indicator unique to this setting: dental fluorosis (Menya et al., 2019b). Indoor air pollution from cooking and heating is another concern, and measuring indoor air pollution is the focus of a recently started study extension (Figure 1). Research is continuing into the pathways driving these associations, to inform effective primary prevention avenues. The ESSCAPE studies have opened doors to, and benefited from, capacity-building opportunities for all partners (see text box).

FOSTERING COLLABORATIONS AND CAPACITY-BUILDING IN CANCER RESEARCH

At the heart of the cancer studies of ENV is an extensive network of collaborators across countries, institutions, and disciplines, making research possible and ensuring high-quality scientific insights. Such collaborations are sustained and enriched through capacity-building. The photograph taken at the Oesophageal Squamous Cell Carcinoma African Prevention Research (ESSCAPE) project annual meeting held in October 2018 in Eldoret, Kenya, represents a snapshot of such collaborations.

At this meeting were the ESSCAPE country principal investigators, Dr Diana Menya of Moi University (Kenya), Dr Charles Dzamalala of the College of Medicine (Malawi), and Dr Blandina Mmbaga of the Kilimanjaro Clinical Research Institute (United Republic of Tanzania), and collaborators from Tenwek Hospital (Kenya), the National Cancer Institute (USA), and the University of North Carolina (USA). Researchers from the Section of Mechanisms of Carcinogenesis and the Genetic Epidemiology Group attended the meeting and presented results from mutation and methylation studies. Meeting attendees represented expertise in epidemiology, genetics, surgery, veterinary science, dentistry, endoscopy, and pathology.

The ESSCAPE team benefited from the IARC Summer School in Cancer Epidemiology (seven attendees); two UICC-IARC Development Fellowships (in collaboration with the Union for International Cancer Control), including to Mr Stephen Kararu Maina (Kenya); biobanking support; and pathology training provided by IARC's Dr Behnoush Abedi-Ardekani (Genetic Cancer Susceptibility Group). ESSCAPE has also been the basis of one IARC postdoctoral fellowship and three PhDs. The face-to-face interactions within this collaborative group were rewarding and motivational for all.

Left to right, first row: Odipo Osano, Fatma Some, Stephen Kararu Maina, Margaret Oduor, Winnie Chepkomoi, Betsy Chelangat, and Zdenko Herceg; second row: Charles Dzamalala, Blandina Mmbaga, Jiri Zavadil, Caroline Kibosia, Joachim Schüz, Diana Menya, Valerie McCormack, and Ian Simel; and third row: Esilaba Maina, Steady Chasimpha, Bongani Kaimila, Gissela Maro, Daniel Middleton, Ghislaine Scelo, and Robert Parker. Also present (but not in photograph): Nicholas Kigen.



Figure 1. Indoor air pollution from biomass burning on a traditional cooking stove, Iten, Rift Valley, Kenya, October 2018. © IARC/Jiri Zavadil.



RECOMMENDATIONS ON LONG-TERM THYROID HEALTH MONITORING AFTER NUCLEAR ACCIDENTS

The increasing public awareness and fears about the radiation-related risks of

thyroid cancer and the issues related to overdiagnosis revealed the need for the development of guidelines about whether and how to conduct thyroid health monitoring after nuclear accidents. In 2017, ENV convened an international, multidisciplinary Expert Group to develop respective recommendations on long-term strategies for thyroid health monitoring, on the basis of the scientific evidence and previous experiences (Figure 2). The Expert Group recommended against population thyroid screening after a nuclear accident and that consideration be given to offering a long-term thyroid monitoring programme for higher-risk individuals (defined as those exposed in utero or during childhood or adolescence with a thyroid dose of 100–500 mGy or more) after a nuclear accident. A thyroid monitoring programme is defined as including education to improve health literacy, registration of participants, centralized data collection from thyroid examinations, and clinical management. It is an elective activity offered to higher-risk individuals, who may choose how and whether to undergo thyroid examinations and follow-ups. The choice of a thyroid dose range

of 100–500 mGy for an actionable level reflects the option to be more inclusive (lower actionable levels) or to be more efficient (higher actionable levels) in identifying and monitoring radiation-related thyroid disease in higher-risk individuals. The decision should be made in the broader context of nuclear emergency preparedness and response, such as dosimetry monitoring, protective actions, risk communication, and health monitoring infrastructure, as well as the health-care resources and social values of the affected population. This work was published as IARC Technical Publication No. 46, and a summary was published as a commentary in *The Lancet Oncology* (Togawa et al., 2018).

EPIDEMIOLOGICAL STUDIES ON CANCER RISK AFTER PAEDIATRIC COMPUTED TOMOGRAPHY

EPI-CT is a retrospective European cohort study of almost 1 million children and young adults who underwent at least one computed tomography (CT) examination in the radiology departments of 276 participating hospitals in Belgium, Denmark, France, Germany,

Figure 2. Expert Group on Thyroid Health Monitoring after Nuclear Accidents with colleagues from Japan, second and final meeting in Lyon, 21–23 February 2018. Left to right, first and second rows: Enora Clero, Catherine Sauvaget, Evgenia Ostroumova, Louise Davies, Ausrele Kesminiene, Geraldine Thomas, Christoph Reiners, Kayo Togawa, and Hiroki Shimura; back row: Salvatore Vaccarella, André Ilbawi, Anssi Auvinen, Mykola Tronko, Dominique Laurier, Sergey Shinkarev, Furio Pacini, Joachim Schüz, Catherine Chassin, and Andrew J. Bauer. © IARC.

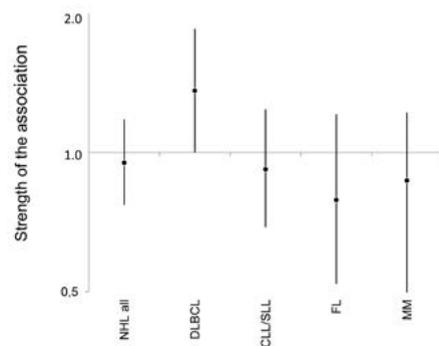


The Netherlands, Norway, Spain, Sweden, and the United Kingdom in 1977–2014 and who were followed up for cancer diagnosis. The absorbed dose to organs of interest was individually calculated using the National Cancer Institute dosimetry system for Computed Tomography (NCICT) software for each CT scan. Mean cumulative doses for various organs ranged from 2.5 mGy to 47.4 mGy. A total of 948 174 participants were identified through the Radiology Information System and were alive and cancer-free before and 1 year after the first CT scan (Bernier et al., 2019). Of those, 658 424 were alive and cancer-free 5 years after their first CT scan and were included in the analyses for brain cancers and other solid cancers. During an average of 7 years of follow-up, 203 brain cancers occurred as well as 1561 other solid cancers at the sites that met the criterion (at least 50 cases overall), chosen to limit bias. A dose–response relationship was observed for cancers of the brain, breast, kidney, and remaining solid cancers in the torso; the excess relative risk at 100 mGy was 2.39 (95% confidence interval [CI], 1.24–4.51), 1.61 (95% CI, 0.35–3.45), 3.47 (95% CI, 0.98–7.61), and 1.37 (95% CI, 0.72–2.21), respectively. These results confirm the importance of the basic principles of radiological protection in the medical setting, namely that the choice of a medical imaging modality with ionizing radiation is justified and that doses to the patient are as low as reasonably possible.

OTHER RECENT FINDINGS

In a pooled analysis from the AGRICOH consortium of three large cohorts of agricultural workers totalling more than 300 000 farmers, ENV investigated the relationship of ever-use of 14 selected pesticide chemical groups and 33 individual active chemical ingredients with non-Hodgkin lymphoma malignancies overall or by major subtypes. An association was seen with terbufos, whereas the broader groups of organochlorine insecticides and phenoxy herbicides showed inverse associations. Deltamethrin and glyphosate were associated with non-Hodgkin lymphoma subtypes but not overall (Figure 3). No associations were seen for most of the pesticides investigated (Leon et al., 2019a). From the same three prospective

Figure 3. Association between occupational use of glyphosate and risk of non-Hodgkin lymphoma (NHL) observed in the AGRICOH pooled study of agricultural cohort studies from France, Norway, and the USA. CLL/SLL, chronic lymphocytic leukaemia/small lymphocytic lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MM, multiple myeloma. © IARC.



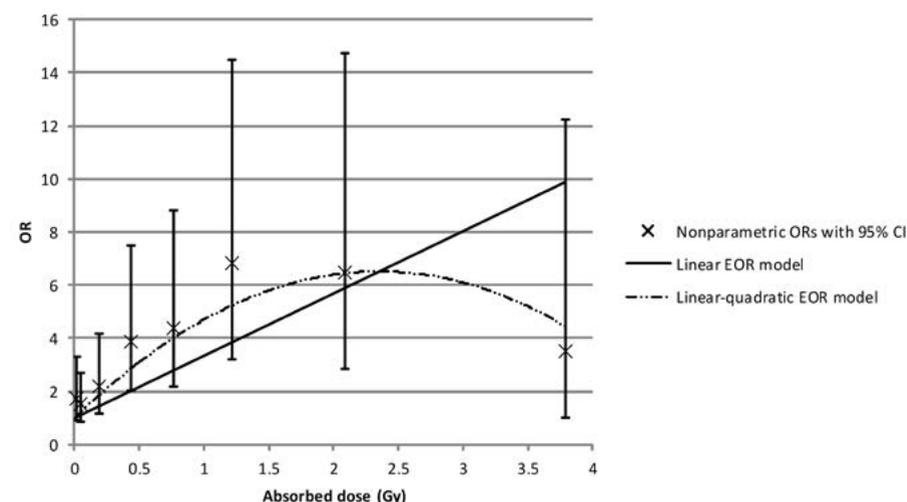
agricultural cohorts, no association was observed between animal farming and risk of lymphohaematopoietic cancer, but a few associations between specific animal species and subtypes of lymphohaematopoietic cancer were observed (El-Zaemey et al., 2019).

To identify host and environmental factors that modify radiation-related risk of thyroid cancers after childhood exposure to iodine-131 (¹³¹I), ENV studied 298 post-Chernobyl thyroid cancer cases and 1934 matched controls from the most contaminated regions of Belarus and the Russian Federation

using advanced dose methodology. The study reconfirmed a significant dose–effect association between exposure and thyroid cancer within thyroid doses of up to 2 Gy and 5 Gy (Figure 4). Stable iodine supplementation in the years after the accident could lower ¹³¹I-related risk of thyroid cancer (Zupunski et al., 2019). In female populations of the most radioactively contaminated areas of Belarus (1978–2010) and Ukraine (1990–2010), no statistically significant increases in risk of breast cancer were observed in association with raion-average accumulated breast dose after adjustment for age, time, and urbanicity (a raion is an administrative region). Because of the limitations of the ecological study design, a detailed analytical study on breast cancer is warranted.

In the ASTRO-RF project, survival among patients with glioma in Denmark, Finland, and Sweden in relation to their mobile phone use at the time of diagnosis was studied. Marginal survival benefits were observed in the mobile phone users among patients; this is likely to be an artificial association explained by prodromal symptoms in cases, resulting in patients not starting to use mobile phones, if it also coincides with poorer survival (Olsson et al., 2019). Not observing any reduction in survival is concordant with the results found in the parallel study in experimental animals of radiofrequency electromagnetic fields (Ouahad et al., 2018).

Figure 4. Association between ¹³¹I thyroid dose and thyroid cancer risk adjusted for self-reported personal history of benign nodules in the study subjects with ¹³¹I thyroid absorbed doses of < 5 Gy. CI, confidence interval; EOR, excess odds ratio; OR, odds ratio. © IARC.



The increased risks of developing vestibular schwannoma (also referred to as acoustic neuroma) with noise exposure related to work and leisure activities were observed in case-control studies conducted in 13 countries. For occupational exposures, duration, time since start of exposure, and a metric combining lifetime duration and weekly exposure showed significant trends of increasing risk with increasing exposure; however, relative risk estimates did not differ markedly by source or other characteristics of noise. Recall bias remains a concern; although a complementary validation study in 111 cases and 217 controls comparing self-reported noise exposure with expert assessments of workplaces showed relatively accurate reporting by study participants, the impact of reporting uncertainties on the risk estimation was non-negligible (Deltour et al., 2019a).

UPDATES ON CONTINUING STUDIES

The African Breast Cancer – Disparities in Outcomes (ABC-DO) study is an ENV-led hospital-based cohort of 2200 women diagnosed with breast cancer across five countries in sub-Saharan Africa, examining multidimensional barriers to improving breast cancer survival. In 3-year survival analyses, lagging survival was found for the cohort as a whole, but with large between-setting differences. ENV also observed within-setting survival deficits associated with late stage, lower education level, undertreatment, and being HIV-positive. High proportions of women who remained untreated within 1 year of diagnosis (up to one third in some settings), particularly women in groups with lower socioeconomic status, were documented (Foerster et al., 2019).

ENV reached a milestone in its occupational cohort study of workers exposed to chrysotile in mines and processing facilities in Asbest, Russian Federation (Asbest Chrysotile Cohort), carried out in collaboration with the Federal State Budgetary Scientific Institution Izmerov Research Institute of Occupational Health in Moscow. The cohort includes 35 837 individuals, 37% of whom are women. Exposure was estimated from more than 90 000 measurements of airborne dust concentrations made since the 1950s

across the mines and processing mills. The cohort was followed up for mortality from 1975 to 2015 with vital status obtained from original death certificates and official records of the Sverdlovsk oblast, which included information on migration from the oblast. Risk analysis began in autumn 2019.

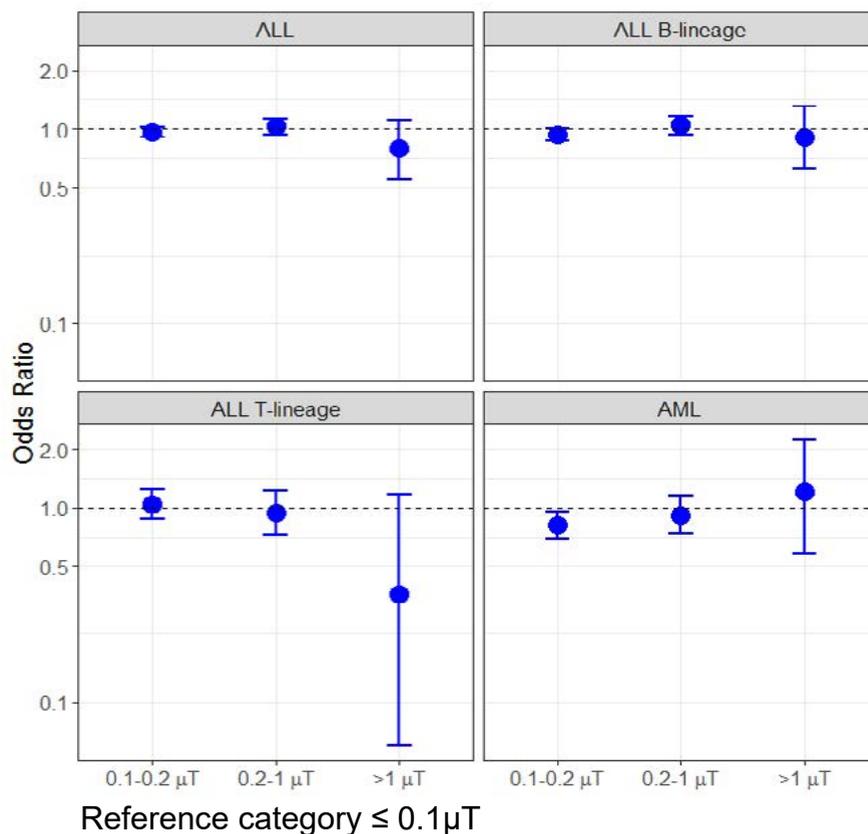
ENV hosts the Data Coordination Center of the Childhood Leukemia International Consortium of more than 20 case-control studies around the world, from which data are pooled to obtain further insight into the etiology of childhood leukaemia. In an ENV-led project, no association was seen between parents' exposure to extremely low-frequency electric and magnetic fields at their workplace before conception or during pregnancy and the risk of leukaemia in their offspring (Talibov et al., 2019a) (Figure 5). However, a modestly increased risk of acute myeloid leukaemia was seen in children whose mothers consumed more than

1 cup of coffee per day (Karalexi et al., 2019). Advanced parental age was positively associated with the risk of lymphoblastic leukaemia (Petridou et al., 2018), but results were inconsistent for acute myeloid leukaemia (Panagopoulou et al., 2019).

The Cohort Study of Mobile Phone Use and Health (COSMOS) is a prospective cohort of mobile phone users addressing the open question of whether radiofrequency electromagnetic fields emitted during the use of mobile phones or other wireless technologies have adverse health effects. ENV completed the major recruitment of the French branch of COSMOS, in collaboration with the large French cohort Constances, in early 2019, enrolling approximately 18 000 participants.

In the large-scale collaboration between ENV and the Cancer and Environment Unit of Centre Léon Bérard, Lyon, on the

Figure 5. Association between paternal occupational exposure to extremely low-frequency magnetic fields (ELF-MF) in the months before conception and the subsequent risk of leukaemia in the offspring; results displayed for all leukaemia combined and major subtypes acute lymphoblastic leukaemia (ALL) of B-lineage or T-lineage and acute myeloid leukaemia (AML). Courtesy of Madar Talibov.



causes of testicular cancer (TESTIS), including components to better measure and predict people's occupational and domestic exposure to pesticides, the

fieldwork of the core case–control study has been completed, and analysis is under way. From the methodological ancillary studies, it was found that domestic use

and the persistence of banned pesticides may contribute substantially to indoor pesticide contamination in France (Béranger et al., 2019).