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The overall objectives of the Section of Environment and Radiation (ENV) are to investigate environmental, lifestyle, occupational, and radiation-related causes of cancer and death from cancer in human populations. With this wide remit, ENV focuses its endeavours in 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 cancers and of specific exposures occurring in under-researched settings, particularly but not exclusively in low- and middle-income countries (LMICs); (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 coordination 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 WHO.

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. Although estimates vary, in developed countries up to 50% of cancers are potentially preventable. The remaining half, with an unknown etiology to date, may have a larger contribution

from environmental factors than current research has established. 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 and occupational protection regulations are often lacking or not adhered to. Capacity-building as well as establishing research platforms is another vision of IARC to which ENV contributes through its conduct of research in under-researched settings.

Key questions currently studied in ENV involve asbestos and other lung carcinogens, pesticides, uranium, ionizing radiation (environmental, occupational, and medical), and non-ionizing radiation (electromagnetic fields) as main exposures, as well as cancer types with unusual geographical occurrence in relation to the environmental or lifestyle-related contribution to causes or prognosis, such as breast cancer, oesophageal cancer, childhood cancer, testicular cancer, and thyroid cancer. Selected examples are described here.

In utero irradiation and subsequent risk of cancer

Two cohorts from the Southern Urals – offspring of female workers of one of the country's largest nuclear facilities (Mayak Production Association, Ozyorsk) and of women living in areas along the Techa River (Figure 1) contaminated by nuclear accidents and nuclear waste dumping – were analysed to estimate the lifetime risk of cancer related to in utero exposure to irradiation (Deltour et al., 2016; Krestinina et al., 2017). The combined cohort had a total of about 20 000 subjects, and follow-up lasted to the maximum age of 61 years. The highest in utero exposures were more than 1 Gy. A weak positive association was observed with incidence of haematological malignancies (Schüz et al., 2017), whereas for solid cancers no association was seen (Akleyev et al., 2016). Postnatal exposure to ionizing radiation showed an association with solid cancer but not with haematological malignancies. Because the cancer peak in the cohort is expected to occur in the next 10 years, a new project with further follow-up of this unique cohort is recommended.

Figure 1. The Techa River as seen from the highway between Yekaterinburg and Chelyabinsk in the Southern Urals, Russian Federation. In the 1950s, nuclear waste from the nearby Mayak Production Association – one of the country's biggest nuclear facilities – was dumped into the river, leading to major radioactive contamination of residents of the riverside villages, including irradiation of the fetus in women who were pregnant during that time. ENV, together with colleagues from the Urals Research Center of Radiation Medicine (URCRM), Chelyabinsk, and the Southern Urals Biophysics Institute (SUBI), Ozyorsk, has analysed the cancer risk of offspring exposed in utero. © IARC/Joachim Schüz.

Changes in breast density with age seen internationally

Breast density, a measure of the amount of dense tissue compared with fatty tissue in the breast, is a strong marker of breast cancer risk. Determinants of breast density have been studied in high-income countries but not in women worldwide. ENV initiated the International Consortium of Mammographic Density (ICMD), with the collection of images to centrally assess mammographic density based on almost 12 000 mammograms from 27 studies in 22 countries (Burton et al., 2016) (Figure 2). One aim was to study how breast density differed by age and menopausal status. Regardless of the country and ethnic group, breast density was much lower in postmenopausal women than in premenopausal women of the same age (Burton et al., 2017). In addition, as a relative proportion of breast area, breast density was lower in older women among both premenopausal and postmenopausal women. Among premenopausal women, breast density changed with age without an increase in breast area, but among

Figure 2. Mammograms used in the International Consortium of Mammographic Density (ICMD) project, coordinated by ENV. For the joint analyses, three readers evaluated almost 12 000 mammograms, i.e. indicating on the image the dense area of the breast and breast edges, for the calculation of dense area, non-dense area, breast area, and percentage density. © IARC/Valerie McCormack.
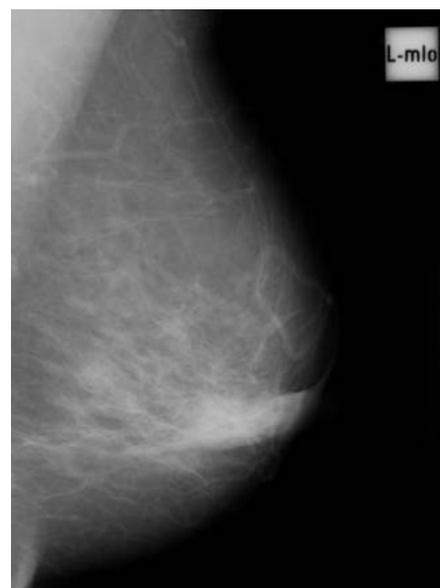
postmenopausal women, there was also an increase in breast area. The consistency of these changes in breast density with age internationally suggests that the change is due to a universal biological mechanism inherent to all women. If cumulative breast density is a key determinant of breast cancer risk, younger ages may be the more critical exposure periods for primary prevention research efforts to identify lifestyle modifications aimed at reducing breast density and later breast cancer risk.

High occurrence of oesophageal squamous cell carcinoma in East Africa

Oesophageal squamous cell carcinoma (ESCC) is among the three most common cancers in most of East Africa. However, the etiology in this African ESCC corridor is little understood and has hardly been studied. ENV has initiated a spectrum of ESCC research in Africa, including Kenya, the United Republic of Tanzania, Malawi, and Ethiopia, with the perspective of investigating a broad range of factors, prioritizing factors that have been identified as established or probable ESCC carcinogens, and interpreting findings from both a local and an Africa-wide perspective (McCormack et al., 2016). Candidate risk factors include consumption of hot beverages (Figure 3), nutrient deficiencies, and alcohol consumption and tobacco use, the roles of which may have been underestimated in some of the settings. The ENV-led African consortium initiated for these epidemiological studies (ESCCAPE) is a prominent example of research coupled with capacity-building, training, knowledge transfer in both directions, and fostering collaboration (see text box).

Figure 3. Consumption of hot tea, especially milky tea, may be an important and modifiable risk factor for oesophageal squamous cell carcinoma (ESCC) in the United Republic of Tanzania. The contribution of this habit to the risk of ESCC needs to be evaluated in this setting, jointly with that of the many risk factors that act synergistically in this multifactorial disease. A cross-sectional study initiated by ENV showed that participants started drinking at a mean temperature of 70.6 °C, which exceeds that in all previous studies. © IARC/Valerie McCormack.

The ESCCAPE project

Oesophageal squamous cell carcinoma (ESCC) in East Africa is a neglected research area, despite the fact that it is the most common cancer in some of Africa's oesophageal cancer hot spots. Extremely poor prognosis makes primary prevention through modification of risk factors essential, in addition to screening for early disease. However, in Africa, there are no robust data to inform either of these efforts.

ENV initiated the Oesophageal Squamous Cell Carcinoma African Prevention Research (ESCCAPE) consortium of unified case–control studies on risk factors in Eldoret (Kenya), Moshi (United Republic of Tanzania), Blantyre (Malawi), and Ethiopia (pilot stage), which is in the process of merging and expanding with other activities on ESCC in sub-Saharan Africa. In addition to the core work, effects on

Participants in the kick-off meeting of the oesophageal squamous cell carcinoma study as part of the ESCCAPE project, held in October 2015 at the Kilimanjaro Clinical Research Institute (KCRI), Moshi, United Republic of Tanzania. © Mr Kennedy Ngowi, KCRI.

capacity-building, training, and international collaboration were of equal importance and beneficial to all partners. Short-term fellowships at ENV enabled training of African partners in methodology, joint analytical work, and building up of international research partnerships. Regular visits of ENV personnel to Africa enabled the training of local staff in methodology and fieldwork in these settings. Pathology training by an IARC senior pathologist was held for local pathologists. Creating the network, including clinicians, fostered exchange in matters of diagnostics, dealing with patients, and palliative care, creating a platform to learn from each other.

Enabling follow-up studies in Africa with the implementation of mHealth technologies

Breast cancer is the most common cancer in women in sub-Saharan Africa, with the burden projected to double between 2012 and 2030 as a result of population ageing and expansion. Prognosis is poor, and an understanding is needed of the determinants of breast cancer outcomes. ENV aims to fill this knowledge gap by conducting, across multiple African settings, a comprehensive study of a woman's entire journey with and after breast cancer: the African Breast Cancer–Disparities in Outcomes (ABC-DO) study (McKenzie et al., 2016a). The study aims to provide information about when and how to implement strategies to improve breast cancer survival, through an understanding of context-specific societal, health systems, and individual-level barriers to early detection, diagnosis, and appropriate treatment.

ENV has embraced the use of modern technologies for the implementation of epidemiological studies, especially those involving fieldwork, by using mobile health (mHealth) technologies throughout (Figure 4). The first of these was ABC-DO, which is an almost paperless mHealth implemented study. Mobile phones are used for face-to-face immediate data input and also to conduct follow-up and batch-send text messages to participants. This has several significant advantages, which all lead to improved efficiency, speed, and quality. Notably, ENV and local investigators have real-time access to live data, and thus quality control can be conducted immediately and any issues resolved in a very short time frame. The app also improves data completeness. Because researchers can monitor recruitment in real time, they are up to date with study progress and can contact local collaborators with any queries. Finally, the app also acts as a pre-programmed study protocol to implement study management uniformly across sites. For example, for the regular follow-up calls that need to be made to all women in the ABC-DO study, the app automatically sends an alert to the site's phone with a reminder of who to call.

Another major advantage is the close interaction between the teams, which

Figure 4. Screenshot of the app developed for the African Breast Cancer–Disparities in Outcomes (ABC-DO) study, coordinated by ENV in five countries in sub-Saharan Africa: Namibia, Nigeria, South Africa, Uganda, and Zambia. © IARC/Valerie McCormack.
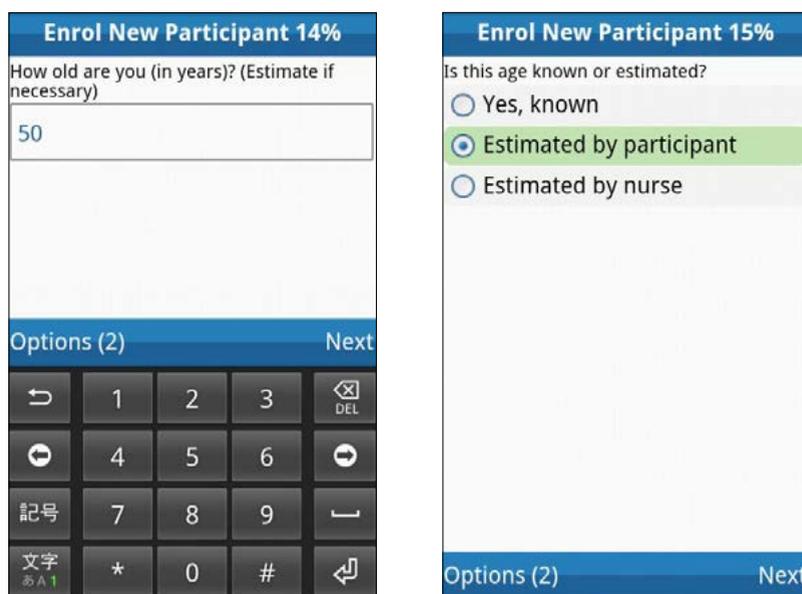
is highly motivating for those doing the fieldwork, especially in settings where experience in larger-scale fieldwork is lacking (Figure 5). Finally, mHealth is a breakthrough for the first population-based study in Africa of this kind, because no other means of communication exist, and for women who do not return to the hospital, the course of disease would otherwise not be known.

Low impact of parental exposures to chemicals on risk of testicular cancer in the offspring

The incidence of testicular cancer has increased rapidly and has shown temporal and geographical variations, suggesting an etiological role of environmental factors. Parental occupational exposure before the child's birth or maternal

Figure 5. Research nurses in Uganda enjoying the interviewer training using the app developed for the African Breast Cancer–Disparities in Outcomes (ABC-DO) study. The real-time data assessment enables a closer link between the local collaborators and their ENV partners thousands of miles away. © IARC/Fiona McKenzie.

exposure during pregnancy may play a role, in particular exposures to agents with potential endocrine-disrupting capabilities. In a registry-based linkage study in the Nordic countries with almost 10 000 cases of testicular cancer, no overall association was observed between paternal or maternal exposure to pesticides and the risk of testicular cancer in their offspring. For solvents, no association was seen with paternal exposure, but maternal exposure to aromatic hydrocarbon solvents was associated with a modest increase in risk (Le Cornet et al., 2017). Furthermore, the study provided little evidence of associations between parental exposures to heavy metals or welding fumes and testicular cancer risk, with the potential exception of high paternal exposure to chromium (Togawa et al., 2016). Overall, this study cannot exclude weak associations between parental occupational exposures and testicular cancer risk in the offspring, but if those associations were causal, they would explain only a small proportion of cases.