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The main programme of work of the Section of Environment and Radiation (ENV) encompasses environmental, occupational, and radiation-related cancer, and lifestyle and cancer etiology and prognosis in low- and middle-income countries (LMICs), as well as the implementation of cancer prevention research. With the start of the new IARC Medium-Term Strategy 2021–2025 and the new organizational structure as of 1 January 2021, ENV was renamed as the Environment and Lifestyle Epidemiology Branch, to better capture its broad scope of activities.

ENV focuses its endeavours on four main areas: (i) research in settings where levels of exposure to putative or established carcinogens in the environment, in the workplace, or related to people's lifestyles are high, and research is thus warranted; (ii) studies of common cancer types and of specific environmental, occupational, or lifestyle exposures that occur in underresearched settings; (iii) studies evaluating the role of broader social and biological factors throughout the course of the disease and its prognosis; and (iv) catalysing all new knowledge on lifestyle, environmental, occupational, and radiation-related risk

factors, and on screening and vaccination with the respective collaborators, into recommendations at the individual and population level. The objectives of ENV are achieved through the conduct of collaborative international epidemiological studies, including coordination of international consortia or through the initiation of focused individual and multicountry analytical epidemiological studies. In selecting programmes of research, an effort is made to ensure that the involvement of the Agency serves a specific and substantial function, by facilitating international collaboration, by overcoming political barriers, by

initiating new studies through assisting local collaborators with IARC's unique expertise in and beyond ENV and increasing 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 (WHO).

With a strong focus on environmental (including occupational and radiation-related) and lifestyle risk factors, ENV fills a major research gap to further identify factors and to understand the cancer burden attributed to these factors. ENV

has steered its research focus to LMICs in particular, a direction that is consistent with the Agency's international remit and is warranted because in these settings, levels of environmental pollution are often higher and protection measures are often less developed. Another focus of ENV is to identify and investigate previously unstudied lifestyle habits and exposures unique to LMICs and other settings that may affect carcinogenesis. Capacity-building, as well as establishing research platforms, is another mission of IARC to which ENV contributes extensively. ENV also plays

a key role in the translation of research findings into applied cancer prevention by, for example, informing the respective international and national authorities on worker protection, especially against radiation. Most directly, ENV is conducting cancer prevention research through the World Code Against Cancer initiative, which is developing sets of regional recommendations on primary and secondary prevention of cancer, and by chairing the newly established Cancer Prevention Europe platform, which had an influential role in shaping Europe's Beating Cancer Plan.

*MANUS SORDIDAE, MENS PURA* (DIRTY HANDS, BUT A CLEAN MIND)

At the heart of the cancer studies carried out by ENV is the conduct of fieldwork in underresearched areas of the world, in particular in low-income countries that have a scarcity of available data but unique and never-studied exposures (many not yet even identified as candidates) and combinations of exposures, higher exposures in workplaces and in the environment, and less protection of workers, communities, and environments compared with high-income countries. High-quality studies in these settings can be initiated only if the collaboration between the local and international scientists is respectful and is driven by shared scientific curiosity and open-mindedness and addresses questions, exposures, and exposure circumstances relevant to the local setting. This requires not only a mutual understanding of each group's expertise and how it contributes to the joint success of the project but also an appreciation of how epidemiological methods from

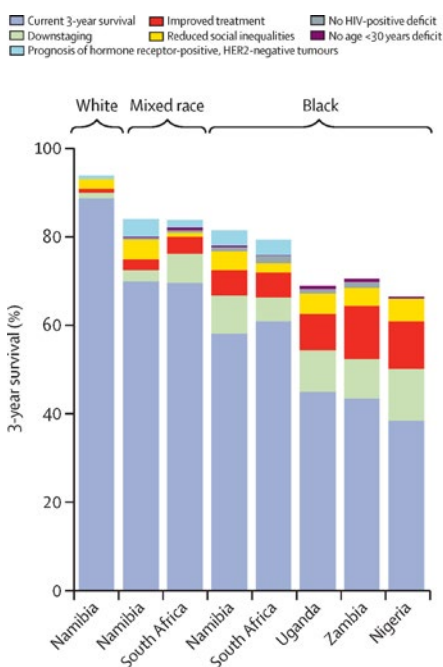
**A scene from ESCCAPE fieldwork, illustrating the challenge of percentage ethanol estimation in local distillations. This is an artisanal *kachasu* (maize-based) distillation setup in Malawi. The ethanol content of this unregulated spirit varies according to the distillation process and between distillers, and differs between the regular and *mutu* (strong) *kachasu*. Although the first research implicating the role of *kachasu* in the incidence of oesophageal cancer was published in 1969, evidence of its contribution to the oesophageal cancer burden in East Africa is only now beginning to emerge. © IARC.**



textbooks are put into practice and, for the international scientists, an appreciation of the local context, culture, and environment. The setting up of protocols, including methods of study conduct and interpretation of results, is full of pitfalls and barriers. However, more than 50 years of experience has shown IARC that such barriers can be minimized by regular and frequent mutual visits and joint explorations, which no virtual platform in the world can replace. With such a focus on hands-on studies, ENV is closely following Geoffrey Rose's motto of *manus sordidae, mens pura* ("dirty hands, but a clean mind"; <https://www.bmj.com/content/bmj/2/6143/1006.full.pdf>). The continuing COVID-19 pandemic has had a large impact on such activities. ENV pledges to make all efforts to enable fieldwork research that is informative and scientifically sound, and not diluted and misleading.

The African Breast Cancer – Disparities in Outcomes (ABC-DO) study is an ENV-initiated programme of work aimed at addressing multiple dimensions of a major cause of cancer death in women in sub-Saharan Africa: low breast cancer survival. This common cancer type in women has a very good prognosis in high-income settings; therefore, improving survival should be a priority in cancer control plans in all LMICs. To examine the major barriers to improving

**Figure 1. Three-year overall survival (%) of patients with breast cancer in sub-Saharan Africa. Observed survival (blue) and predicted survival if the following improvements had been made, by site and race: downstaging to improved distributions of earlier stage at diagnosis (green), improved treatment so that all women receive surgery and systemic therapy (red), reduction in survival deficits attributed to social inequalities (orange), and elimination of survival deficits attributed to increased mortality in HIV-positive women (dark grey), being young (< 30 years) (purple), and not having estrogen receptor (ER)-positive or progesterone receptor (PR)-positive, human epidermal growth factor receptor 2 (HER2)-negative tumour subtypes (light blue). Reproduced from McCormack et al. (2020), Copyright Elsevier (2020).**



breast cancer survival, ENV set up a five-country breast cancer cohort (<https://abc-do.iarc.who.int>), which continues to follow up 2200 women who were newly diagnosed with breast cancer during 2014–2017. Mobile-health (mHealth) real-time data collection and follow-up protocols were uniquely adopted in this study, ensuring few losses to follow-up (Foerster et al., 2020a). Recent findings showed that breast cancer survival is alarmingly low in Black African women (Figure 1). At 3 years after diagnosis, survival was 90% in White Namibian women, 58% in Black Namibian and Black South African women, 46% in Ugandan and Zambian women, and 36% in Nigerian women (McCormack et al., 2020). The largest contributors to low survival were late stage at diagnosis and a lack of access to surgery and systemic therapy, which particularly affected women in lower socioeconomic groups. In contrast, the relatively high proportions of young-onset breast cancer (age < 30 years at diagnosis), HIV-positive women, and more aggressive tumour subtypes made only a small contribution to low overall survival (McCormack et al., 2020).

The drivers of late stage at diagnosis have also been identified and include extensive delays between presentation at a first-line health provider and diagnosis (Foerster et al., 2021), as well as the geospatial element driving later stage at diagnosis in women living farther away from diagnostic centres (Togawa et al., 2021a). ABC-DO has also, for the first time, revealed the extent of the inter-generational effect of such high patient mortality rates by quantifying the number of maternal orphans associated with each breast cancer death (Galukande et al., 2021). The ABC-DO cohort continues to be followed up, and current research is studying the impact of additional morbidities (hypertension, HIV, and obesity) on survival (Ayeni et al., 2021). The comprehensive multidimensional insights gained through ABC-DO are helping to show the impact of breast cancer deaths and to shed light on the most effective pathways to improving survival, as part of WHO's 2021 launch of the Global Breast Cancer Initiative.

The European Code Against Cancer was launched in 1986, and IARC was mandated to lead the development of its fourth edition. The IARC methodology to develop the cancer prevention recommendations has been refined and expanded to include information on successful interventions, as described in a roadmap laid out within the European Union (EU) Innovative Partnership for Action Against Cancer (iPAAC); this roadmap now forms the basis for the development of the fifth edition within Europe's Beating Cancer Plan (Espina et al., 2021). The need for better dissemination across Europe was identified from surveys showing that too few Europeans are well informed on how to reduce their risk of cancer (Ritchie et al., 2021). The strengthening of primary, secondary, and tertiary cancer prevention has also been achieved through the newly established Cancer Prevention Europe network, chaired by ENV, and its role in shaping the EU Cancer Mission and Europe's Beating Cancer Plan (Berns et al., 2020).

Inspired by the European Code Against Cancer, IARC called for this model to be extended to other world regions to achieve a World Code Against Cancer. In 2021, this process has begun with the preparation of the first Latin American and Caribbean Code Against Cancer, in collaboration with the Pan American Health Organization and several regional partners. In parallel, the use of more modern technologies (mHealth) to spread knowledge on cancer prevention through mobile phone messages has been explored in this region through dissemination research. The importance of, and barriers to, cancer prevention were discussed in a Special Issue of the journal *Molecular Oncology*, coordinated by guest editors in ENV (Schüz and Espina, 2021).

RECENT RESEARCH FINDINGS

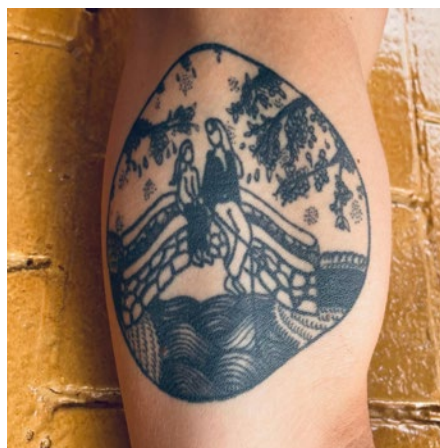
Whether and to what extent the increasing use of pesticides contributes to the global cancer burden remains a major environmental health concern, and ENV is involved in several activities to study cancer risk in relation to pesticide

use. A study of the incidence of cancer in farmers and agricultural workers, compared with the general population, in eight countries within the AGRICOH consortium (<https://agricoh.iarc.fr/>) has illustrated that these occupational groups generally have reduced incidence rates, in particular for cancer types associated with unhealthy lifestyle factors such as smoking or physical inactivity (Togawa et al., 2021b); increased incidence rates were found only for skin melanoma and multiple myeloma in women, and for prostate cancer. These findings confirm the challenges of studying a factor such as exposure to pesticides in an otherwise relatively healthy population. In other pesticide-related research, there was little evidence that the exposure of parents to pesticides increases the subsequent risk of testicular cancer in their male offspring, perhaps with the exception of fungicides (Danjou et al., 2021), as seen in a large-scale case-control study in France. A systematic review confirmed concerns that the exposure of parents to pesticides increases the risk of leukaemia in their offspring (Karalexi et al., 2021).

Lung cancer is the most common occupationally related cancer type. An analysis by the ENV-coordinated SYNERGY consortium of 16 case-control studies of lung cancer confirmed that working as a painter, which is among the jobs that require respective preventive measures, was associated with a 30% increase in the risk of lung cancer (Guha et al., 2021). Using the same data source for an advanced dose-response analysis showed the critical roles of diesel motor exhaust (Ge et al., 2020a) and respirable crystalline silica (Ge et al., 2020b) in causing occupationally related lung cancers. In a different occupational cancer study, ENV determined that four well-known lung carcinogens (asbestos, respirable crystalline silica, chromium VI, and nickel) also increase the risk of laryngeal cancer (Hall et al., 2020).

Another large employment sector worldwide is the petroleum industry; a systematic review by ENV highlighted the limited scientific knowledge on cancer risks because of the lack of systematic epidemiological studies, both on a global scale (Onyije et al., 2021) and within major oil-producing countries such as the Islamic

**Figure 2. Although tattoos are common, public awareness of the possible related health hazards and risks is low. In addition to the possibility of skin irritation, the potential threat from subcutaneous exposure to chemicals in the tattoo ink, which have proven to be carcinogenic by dermal or respiratory uptake, remains widely neglected. Lymphatic accumulation of such toxins could pose an unknown risk of immune-related cancers, particularly the group of non-Hodgkin lymphomas. © IARC.**



Republic of Iran (Hosseini et al., 2021). In further occupational studies, valuable insights for worker protection are expected to be gained from the large-scale historical cohort study of almost 36 000 miners and millers exposed to chrysotile (asbestos) in the Russian Federation, working in the world's largest active chrysotile mine and enrichment factory; fieldwork was completed in late 2019 (Schüz et al., 2020a), and reports on measures to ensure high data quality have been published (Olsson et al., 2020; Schüz et al., 2020b). Finally, many substances used in the traditional art of tattooing, a practice that has increased substantially in popularity, are established occupational carcinogens. Therefore, an increased risk of some cancer types, in particular lymphomas, is not implausible (Figure 2), and ENV has just started the first prospective investigations with collaborators in France and Germany (Foerster et al., 2020b).

Another example of a collaborative focused research programme where fieldwork studies were needed is the case of oesophageal cancer in East

Africa and southern Africa. Through the Oesophageal Squamous Cell Carcinoma African Prevention Research (ESCAPE) study, ENV and a network of African institutions (Figure 3) completed case-control studies in Kenya, Malawi, and the United Republic of Tanzania in 2021. The findings so far indicate the presence of multiple risk factors, notably the considerable role of tobacco use and alcohol consumption in men and of consumption of hot beverages in both sexes. Poor oral health and hygiene are also implicated, and studies of the pathways driving these associations, such as constituents of the oral microbiome, are under way. The ESCAPE study also includes investigations of the impact of geophagia, the intentional consumption of non-food items (typically soil, a very common practice during pregnancy, potentially causing irritation to the mucosa), an example of a never-studied factor. This habit was not found to increase risk of oesophageal squamous cell cancer (Narh et al., 2021).

Protection from radiation at low doses still needs to be optimized, and data from the aftermath of nuclear accidents remain the most informative source. Therefore, ENV researchers observed with concern a lack of funding for previously developed research strategies related to the Chernobyl nuclear accident, which should have been implemented with urgency, given that the affected populations are ageing and the possibility of their participation in studies is decreasing (Ostroumova et al., 2020). Recent IARC-led research on Chernobyl showed no statistically significantly increased risk of breast cancer in association with district-averaged accumulated breast radiation dose after adjustment for age, time, and urbanicity in female populations of the most radioactively contaminated areas of Belarus (1978–2010) and Ukraine (1990–2010) (Zupunski et al., 2021) (Figure 4), but detailed analytical studies on breast cancer are warranted. The gold mine tailings in South Africa are also of concern, because of their contamination with uranium; a study of hair samples confirmed elevated levels in residents of various neighbourhoods, highlighting the need for studies of possible adverse health effects in humans.

Figure 3. Meeting of the Oesophageal Squamous Cell Carcinoma African Prevention Research (ESCAPE) study team of collaborators from IARC, Kenya (Moi University, Eldoret), Malawi (College of Medicine, Blantyre), the United Kingdom (University of Liverpool), and the United Republic of Tanzania (Kilimanjaro Clinical Research Institute/Kilimanjaro Christian Medical Centre, Moshi), held in Blantyre, Malawi, in February 2020. © IARC.



Because mobile phone use is ubiquitous and technologies change regularly, the monitoring of potential adverse health effects associated with their use remains important. ENV has compared the incidence rates of the most common type of brain tumour – glioma – in men in the Nordic countries with projections of increased risk scenarios related to mobile phone use; the results suggest that if there is a risk, it is very small. These recent population findings are not compatible with the results of previous case-control studies, indicating that the

effects have at least been overestimated. Continued monitoring is warranted, and ENV is participating in the multinational prospective cohort study of mobile phone users (Cohort Study of Mobile Phone Use and Health [COSMOS]; Tettamanti et al., 2020).

Childhood cancer remains a priority research area of ENV. In 2021, ENV coordinated a Special Issue of the journal *Cancer Epidemiology* describing the situation with respect to awareness, diagnosis, referral, and treatment of

childhood cancer around the world, showing disparities between high- and low-income countries of greater magnitude than for most adult cancer types (Schüz and Roman, 2021). An assessment of the impact of the COVID-19 pandemic on paediatric oncology diagnoses in Germany in 2020 revealed a significantly higher incidence of all childhood cancers and in all childhood age ranges (Erdmann et al., 2021); the underlying reasons for this increase are not known, and close monitoring is warranted.

Figure 4. Breast cancer relative risk (RR) estimates by 5-year-lagged cumulative absorbed breast dose categories compared with the reference category (< 5.0 mGy; RR = 1.00) adjusted for attained age and urban or rural status, and stratified by 5-year intervals in (a) Belarus and (b) Ukraine. Reproduced with permission from Zupunski et al. (2021), © John Wiley & Sons.

