Latin America and the Caribbean Code Against Cancer

Main risk factors and cancer prevention actions recommended at each life stage

	Infancy	Childhood	Adolescence	Young adulthood	Adulthood	Older adulthood
	age 0 to 5 years	age 6 to 11 years	age 12 to 18 years	age 19 to 29 years	age 30 to 64 years	age 65 years or older

Do not smoke

Avoid second-hand smoke

Achieve a healthy weight

Get physical activity

Eat a healthy diet

Avoid drinking alcohol

Breastfeed

Protect yourself from direct sun exposure

Avoid the build-up of smoke inside your home

Avoid exposure to air pollution

Prevent occupational risks

Detect and treat *Helicobacter pylori*

Vaccinate against HBV

Vaccinate against HPV

Detect and treat HBV and HCV

Detect and treat HIV

Use condoms

for menopause

al cancer

t cancer

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at which these recommendations apply.
s a possible wider age range.

HIV: Human Immunodeficiency Virus | HPV: Human Papilloma Virus | HBV: Hepatitis B Virus | HCV: Hepatitis C Virus

PAHO

Environment and Lifestyle Epidemiology Branch (ENV)

Branch head
Dr Joachim Schüz

Deputy branch head
Dr Valerie McCormack

Scientists
Dr Isabelle Deltour
Dr Carolina Espina
Dr Milena Foerster
Dr Florence Guida
Dr Ann Olsson
Dr Evgenia Ostroumova
Dr Ljubica Zupunski

Staff
Ms Christine Bassier
Mr Liacine Bouaoun
Ms Catherine Chassin

Mr Gilles Ferro
(until November 2022)
Ms Véronique Luzon
Ms Monika Moissonnier
Mr David Ritchie

Visiting scientists
Dr Roya Dolatkhah
Dr Friederike Erdmann
(until September 2022)
Dr Ausrele Kesminiene
Dr Clement Tetteh Narh
Dr Kayo Togawa
Dr Hajo Zeeb

Postdoctoral fellows
Dr Shukrullah Ahmadi
(until August 2022)
Dr Wendy Bijoux

Dr Pauline Boucheron
Dr Amandine Busson
(until August 2023)
Dr Aurélie Danjou (until June 2022)
Dr Ariadna Feliu Josa
Dr Milena Foerster
(until August 2022)
Dr Bayan Hosseini
Dr Joanne Kim
Dr Michele Matta
Dr Melitah Motlhale
Dr Felix Onyije
Dr Hannah Simba
Dr Ljubica Zupunski
(until December 2022)

Students
Ms Chanelle Bodnar (until June 2023)
Mr Lucas Dufour (until April 2022)
Ms Elsa Lubart (until August 2023)

The overall objectives of the Environment and Lifestyle Epidemiology Branch (ENV) are to investigate environmental, lifestyle, occupational, and radiation-related causes of cancer and death from cancer in human populations. ENV focuses its endeavours on three 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; and

(iii) studies evaluating the role of broader social and biological factors throughout the course of the disease.

The inclusion of ENV in the IARC scientific pillar From Understanding to Prevention reflects that the Branch's etiological research is tailored to directly inform prevention, such as for workers' protection or radiation protection through other United Nations institutions such as WHO, the International Labour Organization (ILO), and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), and for the translation of study findings

into applicable recommendations for health decision-makers, such as an assessment of completion of curative treatment for breast cancer (Foerster et al., 2022) and, in Namibia, identifying phases of the journey to and beyond breast cancer diagnosis that need to be strengthened to improve survival (Boucheron et al., 2023a). Furthermore, a major objective of ENV is to enable cancer prevention and control through translation of research evidence. Its main projects are the World Code Against Cancer Framework and its regional projects in Europe, Latin America and the Caribbean (see below), and Asia,

the coordination of Cancer Prevention Europe, and the coordination of the IARC Evidence Summary Briefs series. Figure 1 shows ENV's five objectives.

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. Some examples are studies on occupational cancer in the Islamic Republic of Iran (Hosseini et al., 2022, 2023a), major environmental contamination in South Africa (Zupunski et al., 2023), and the development of tools to assess tattoo exposures (Foerster et al., 2023).

With its strong focus on environmental and lifestyle risk factors, ENV fills a major research gap to further understand the cancer burden attributed to these factors. Selected highlights of ENV's work during the 2022–2023 biennium are described in more detail here.

Disentangling the effects of multiple exposures to lung carcinogens and smoking

Occupational carcinogens represent a significant threat to the health of workers, notably when they are simultaneously exposed to several carcinogens and if they smoke. Single epidemiological studies often have limited statistical power to investigate joint effects of carcinogens, because of a too-low prevalence of exposure to combinations of agents. The SYNERGY project, which includes 14 case–control studies on lung cancer, was established to overcome this limitation of individual studies. The quantitative job-exposure matrix SYN-JEM was used to assign occupational exposures to asbestos, respirable crystalline silica, chromium(VI), nickel, and polycyclic aromatic hydrocarbons (PAHs) (by using benzo[*a*]pyrene as a proxy) to 37 866 workers' lifelong occupational histories. The study showed that most co-exposures to the selected

Figure 1. The five objectives of the Environment and Lifestyle Epidemiology Branch (ENV). © IARC.
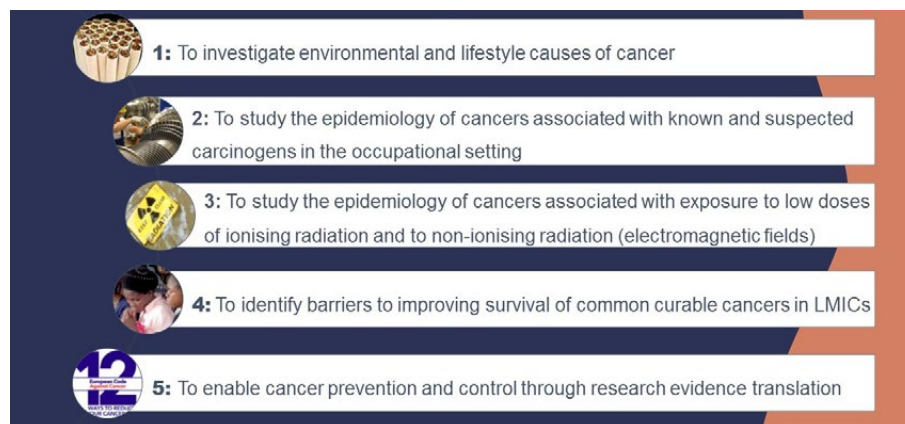

lung carcinogens result in higher risk compared with individual exposures; small or no deviations from additive or multiplicative effects were observed. This means that additive calculation for creating compensation schemes for workers exposed to these carcinogens would be pragmatic. These results highlight the importance of reducing and controlling exposures to carcinogens in workplaces, and of preventing smoking and promoting smoking cessation among workers. Joint effects of occupational exposure to chromium(VI) and nickel with smoking were, in general, greater than additive (Behrens et al., 2023); the same was found for PAHs and smoking (Olsson et al., 2022), silica and smoking, and asbestos and smoking. ENV recently obtained funding to further investigate the joint effects of smoking and occupational exposures in greater detail, for example whether the joint effect persists in former smokers and at different levels of smoking. These forthcoming new results will inform the design of targeted public health interventions.

Alcohol consumption, tobacco use, consumption of hot beverages, and risk of oesophageal squamous cell carcinoma in the African oesophageal cancer corridor

ENV has invested almost a decade of research into the poorly understood high incidence rates of oesophageal squamous cell carcinoma (ESCC) in the African oesophageal cancer corridor. These Oesophageal Squamous Cell Carcinoma African Prevention

Research (ESCCAPE) studies comprise complementary case–control studies and cross-sectional exposure characterization studies and contribute to international genomic studies of somatic mutation signatures within tumours. During the 2022–2023 biennium, ENV examined the associations of several lifestyle and behavioural factors in more than 1200 patients with oesophageal cancer in Kenya, the United Republic of Tanzania, and Malawi, compared with the same number of controls. In Kenya and the United Republic of Tanzania, increased risks of ESCC were found to be associated with consumption of alcohol, based on a detailed assessment of the habitual intake of multiple commercial alcohols and traditional brews and distillations (Middleton et al., 2022). A substantial contribution of alcohol to the ESCC burden was present in men in these two countries; associations in Malawi need further investigation. Another sex-patterned habit in this setting is tobacco use. Tobacco smoking is more common in men, whereas the prevalence of smokeless tobacco use is higher in women. Both forms of tobacco use, in combination and in exclusivity, were found to be associated with risk of ESCC (Figure 2) (Simba et al., 2023a). Increased ESCC risk was also observed with consumption of hot beverages and food, as assessed by a 12-point thermal injury exposure score (Masukume et al., 2022). ENV is now embarking on a pooling of African ESCC case–control studies within the African Esophageal Cancer Consortium (AfrECC).

Figure 2. In the African oesophageal cancer corridor, tobacco smoking and smokeless tobacco use, in combination and in exclusivity, were found to be associated with risk of oesophageal squamous cell carcinoma. Reproduced with permission from Simba et al. (2023a), John Wiley and Sons.
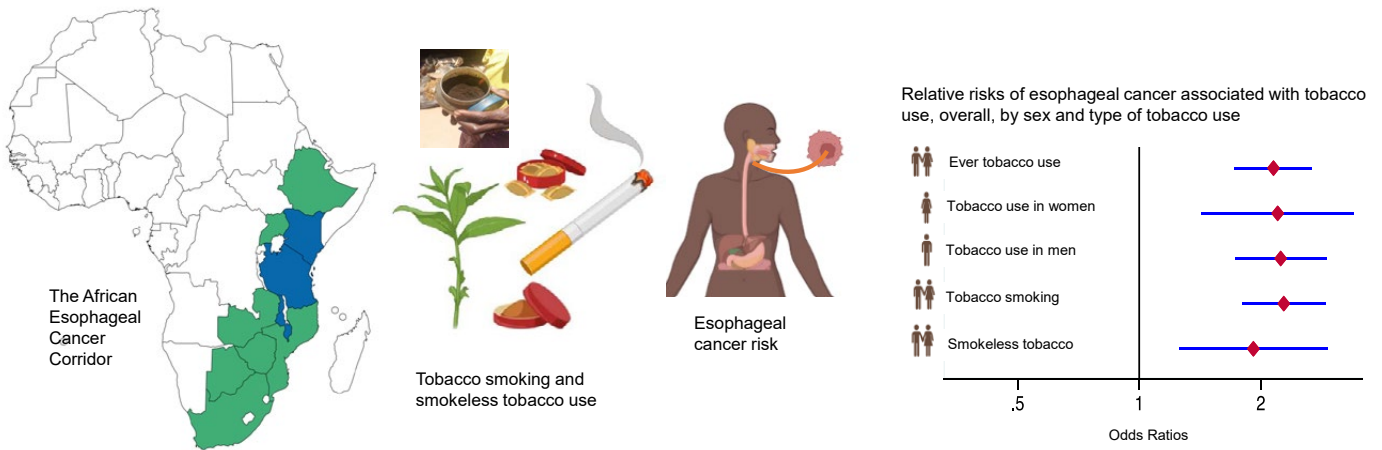

Mobile phone use and risk of brain tumours

Since 2011, when radiofrequency electromagnetic fields (RF-EMF) were classified by the *IARC Monographs* programme as possibly carcinogenic to humans, RF-EMF have remained a research priority in ENV, given the ubiquitous exposure from mobile phones, their base station antennas, and other wireless applications, all over the world in all populations, and the constant technological development, with the recent launch of the 5G networks. ENV is participating in the major multinational prospective study of mobile phone users (Cohort Study of Mobile Phone Use and Health [COSMOS]), designed to investigate adverse health effects, including cancer, in mobile phone users, but because the repeat questionnaire in France is scheduled for late 2023, ENV contributed expertise but no data to the first follow-up. Other RF-EMF research projects were completed. Comparing the incidence rate time trends of glioma in the Nordic countries with projected trends of hypothesized risks confirmed that the few case–control studies that observed strong risks are in conflict with reality and should be excluded from future risk assessments (Deltour et al., 2022); the data were reassuring that ordinary mobile phone use would not pose any increase in risk of glioma. The same conclusions

were derived from an update of the UK Million Women Study, which showed no increased risks of any brain tumours in both long-term users and daily users, including when specifically looking at the most exposed areas of the brain (Schüz et al., 2022a) (Figure 3). An open question remained on very heavy mobile phone use, but a recent ENV simulation study, using validation study results on reporting errors in case–control studies, demonstrated that the nature of bias in categorical risk analyses (higher error variance in cases) would create a J-shaped exposure–response pattern with a spuriously increased risk among heavy users. This adds strong evidence that the previously observed glioma risks in only heavy mobile phone users are probably also a result of recall bias.

Figure 3. Relative risks (RRs) for brain tumours in users versus never-users of cellular telephones in median year 2011, sensitivity analysis, UK Million Women Study. [a] Stratified by year of birth, year of answering the baseline survey, and region only. [b] Excluding women who completed the questionnaire in 1999–2000. [c] Excluding the first 2 years of follow-up. RRs are plotted as squares; the area of each square is inversely proportional to the variance of the log RR. Error bars represent the 95% confidence intervals (CIs). Reproduced from Schüz et al. (2022a), © Schüz et al., 2022. Published by Oxford University Press.
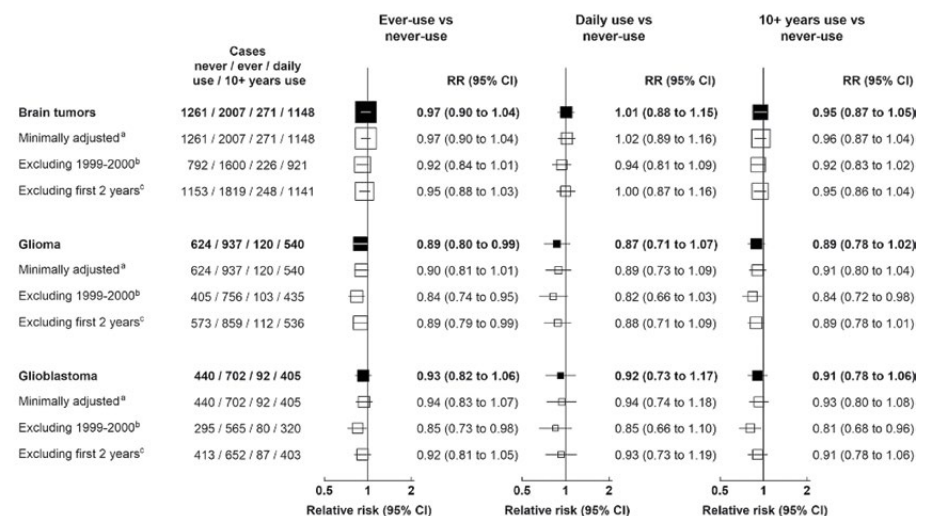
In the African Breast Cancer – Disparities in Outcomes (ABC-DO) study cohort, the inability to link to death registers necessitated active follow-up with women or their next of kin. This in-person conversation with the family member afforded a unique opportunity to enquire about the impact of the woman's death on her family, which revealed concerns about the care and education of the children who had then become maternal orphans. This poignant observation of the devastating impact of cancer deaths led to the realization that global estimates of the number of orphans due to cancer had never been made. Using the IARC GLOBOCAN estimates of cancer death (from the IARC Global Cancer Observatory) and fertility data from the United Nations World Population Prospects, ENV estimated the global number of orphans due to maternal deaths from cancer in 2020 for 185 countries and territories. Globally, there were an estimated 1 047 000 new maternal orphans due to cancer (Guida et al., 2022) (Figure 4). Almost half (48%) of these children were in Asia, and more than one third (35%) were in Africa. In terms of contributing cancer sites, deaths from breast cancer were the single largest cause of new maternal orphans globally (25%), followed by cervical cancer (20%) and upper gastrointestinal cancers (13%). This novel work gained high-level attention: it was highlighted at a press conference during the Union for International Cancer Control (UICC) World Cancer Congress 2022, was the main theme of the WHO Director-General's videos for World Cancer Day 2023, and was reported in several media outlets, including the American Association for Cancer Research (AACR) journal *Cancer Discovery*. Continuing work includes following up the children of mothers included in the ABC-DO cohort and making estimates of paternal orphans due to cancer.

Figure 4. An infographic depicting the estimated global number of new orphans due to maternal deaths from cancer in 2020. © IARC.
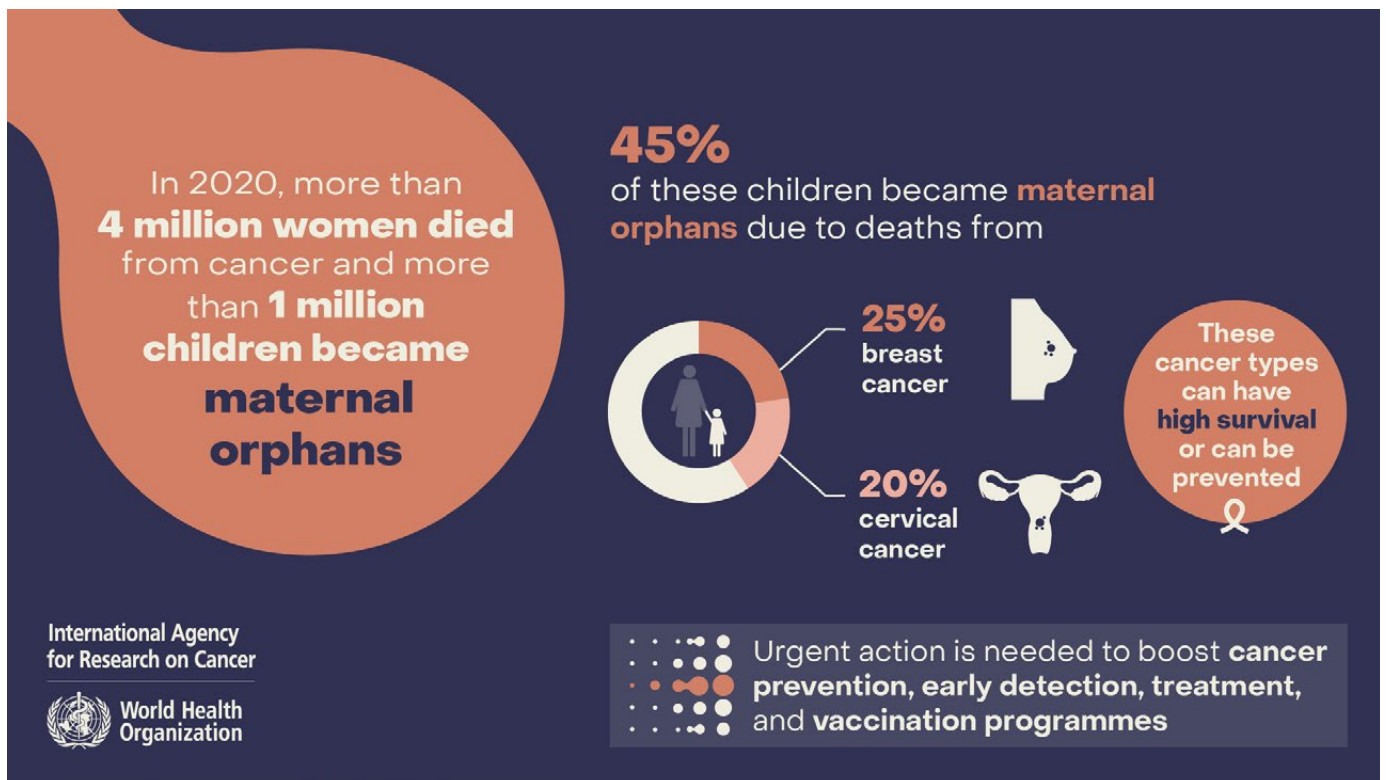
On 17 October 2023, the 1st edition of the Latin America and the Caribbean (LAC) Code Against Cancer was launched as the first Regional Code developed under the World Code Against Cancer Framework (Espina et al., 2023). The LAC Code Against Cancer, 1st edition, consists of 17 evidence-based recommendations for the public, based on the most recent solid evidence on lifestyle, environmental, occupational, and infectious risk factors, and medical interventions (Figure 5). Each recommendation is accompanied by recommendations for policy-makers to guide governments in establishing the infrastructure needed to enable the public to adopt the recommendations. All recommendations are tailored to the context and needs of the LAC region, considering specific risk factors, the cancer burden, social inequalities, economic barriers, and health-care systems' portfolio of services. The development process entailed collecting, analysing, and evaluating the most recent scientific evidence, with the objective of supporting the recommendations and anticipating challenges in implementing

the recommended policies and innovations (Aburto et al., 2023; Baena et al., 2023a; Blanco et al., 2023; Herrero et al., 2023; Reynales-Shigematsu et al., 2023). In addition, a multicountry mixed-methods study aimed at testing the comprehension and persuasiveness of the draft recommendations of the LAC Code was carried out among the general public of five LAC countries (Lemos et al., 2023), and a free, user-friendly comprehensive online competency-based microlearning programme for primary health-care professionals, to be hosted in the Pan American Health Organization (PAHO) Virtual Campus for Public Health, was developed to expand on the recommendations of the LAC Code (Feliu et al., 2023). For the development and endorsement of the LAC Code, more than 60 independent experts in epidemiology, cancer prevention, health promotion, behavioural change, public health, and public policies, and institutions and representatives of civil society and medical associations from the LAC region, were convened in several committees and working groups and led by IARC and PAHO. The LAC Code offers an exceptional tool for cancer prevention education and public health, developed by the experts of the LAC region and for the region.

Figure 5. The Latin America and the Caribbean (LAC) Code Against Cancer, the first Regional Code developed under the World Code Against Cancer Framework. © IARC.

Latin America and the Caribbean Code against Cancer

*Learn how to help prevent cancer
in yourself and your family*

Specialists on the subject and civil society representatives from Latin America and the Caribbean, convened by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) and the Pan American Health Organization (PAHO), have reviewed the scientific evidence and recommend the following 17 actions people can take to help prevent cancer:

1. Don't smoke or use any type of tobacco. If you do, quitting is possible, with professional help if needed. Don't use e-cigarettes either, as they lead to tobacco use.
2. Make your home a smoke-free place. Respect and promote laws that ensure smoke-free spaces to protect our health.
3. Achieve or maintain a healthy weight throughout your life to help prevent several types of cancer.
4. Get daily physical activity throughout your life and limit the time you spend sitting. Being a physically active person helps prevent several types of cancer.
5. Eat a healthy diet:
   - Eat as many fruits and vegetables as possible at each meal, and regularly include legumes such as beans and lentils.
   - Eat whole grains, such as whole-grain bread, corn tortillas, and brown rice, rather than refined grains such as white bread or rice.
   - Avoid sugar-sweetened beverages, drink water instead.
   - Limit your consumption of ultra-processed foods, such as sweets, sweetened breakfast cereals, salty snacks, pastries, and cookies, among others. Instead, eat natural foods or foods prepared at home.
   - Avoid processed meats, such as deli meats, sausages, or cured meats, and limit your consumption of red meat.
   - Limit your consumption of very hot beverages, such as tea, coffee, and *mate*. Wait a few minutes until the liquid no longer feels hot enough to burn your lips or tongue.
6. Avoid drinking alcoholic beverages. This helps prevent several types of cancer.
7. Breastfeed your baby—the more months the better—to help prevent breast cancer and excess weight in your baby.
8. Protect yourself from direct sun exposure during peak sunlight hours to help prevent skin cancer.
9. If you cook or heat your home with coal or firewood, make sure smoke doesn't build up inside your home.

10. If air pollution is high where you are, limit your time outdoors.
11. Find out if your job exposes you to substances that can cause cancer, and request and adopt the recommended protective measures.
12. Infection from *Helicobacter pylori* bacteria can cause stomach cancer. Check with health professionals to find out if you might benefit from screening and treatment for this bacterial infection.
13. Infection with viruses such as hepatitis B and C, human papillomavirus (HPV), and human immunodeficiency virus (HIV) can also cause cancer. Therefore:
   - Vaccinate children for hepatitis B virus in their first 24 hours of life. Vaccinate yourself and your family at any age if you have not yet done so.
   - Vaccinate girls and teens against the human papillomavirus (HPV), primarily to help prevent cervical cancer, as well as other types of cancer. Take this preventive measure at the ages recommended in your country. If available, vaccinate boys as well.
   - Talk to health professionals to see if you might benefit from screening and treatment for hepatitis B and C viruses to help prevent liver cancer.
   - Get tested for human immunodeficiency virus (HIV), and ask about the prevention and treatment programs available in your country.
   - Make sure to use condoms consistently and correctly, especially with new or casual partners.
14. Do not use hormone replacement for menopause unless directed to do so by your healthcare provider. Hormone replacement can cause breast cancer.

Cancer can be controlled and cured if it is detected and treated early:

15. If you are between the ages of 50 and 74, visit a health care provider and ask for an early detection test for colon and rectal cancer (fecal occult blood test or colonoscopy). Based on the results, follow your health professional's recommendations promptly.
16. If you are 40 years of age or older, visit a health care provider every two years for a clinical breast exam. From age 50 to 74, get a mammogram every two years. Based on the results, follow your health professional's recommendations promptly.
17. If you are between the ages of 30 and 64, visit a health care provider and ask for a molecular human papillomavirus (HPV) test at least every 5–10 years for early detection of cervical cancer. Ask if you can collect the sample yourself. If you don't have access to the HPV test, ask for the exam that is available in your country. Based on the results, follow your health professional's recommendations promptly.

CAPACITY-BUILDING FOR GLOBAL CANCER RESEARCH

Capacity-building is an integral part of ENV's research, and in every research programme, ENV aims to match the cancer capacity investment with the needs of the setting where the research is being conducted. Thus, reflecting the international profile of research, the ENV team originates from 18 countries: nine in Europe (France, Germany, Ireland, Lithuania, the Russian Federation, Serbia, Spain, Sweden, and the United Kingdom), four in Africa (Botswana, Ghana, Nigeria, and Zimbabwe), two in the Americas (Canada and Haiti), and three in Asia (the Islamic Republic of Iran, Japan, and Lebanon).

Dr Clement Tetteh Narh. Courtesy of Dr Clement Tetteh Narh.

An exemplary success story illustrating the emerging next generation of international cancer leaders is that of Dr Clement Narh. After defending his PhD dissertation in Mainz (Germany) in 2020, Dr Narh joined ENV for one year in November 2020, working on the ESCCAPE oesophageal cancer studies. Two years later, he returned to the Fred Binka School of Public Health at the University of Health and Allied Sciences in Ghana. Through a unique competitive global mentoring grant scheme introduced by the United States National Cancer Institute, Dr Narh and ENV were awarded an opportunity to lead an extension to the ABC-DO African breast cancer cohort – a cohort that has already provided ample insights into the survival gaps for breast cancer in the continent. This award, mentored by ENV and Ghanaian institutions, is providing Dr Narh with valuable experience as the principal investigator for the ABC-DO Ghana study. Dr Narh is coordinating all aspects of study management, supervision, fieldwork, and analyses. This experience is pivotal in shaping his future independent career as a cancer leader in West Africa. Through ENV, IARC is also proudly supporting the Research and Excellence in African Capacity to Control and Treat Cancer (REACCT-CAN) African network for capacity-building in cancer science, a six-country US$ 4 million investment led by Addis Ababa University (Ethiopia) and supported through the Science for Africa Foundation.