International Agency for Research on Cancer

World Health Organization

Biennial Report

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International Agency for Research on Cancer 2022–2023

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Table of Contents

Introduction – from the IARC Director

This Biennial Report showcases a selection of the work conducted by the International Agency for Research on Cancer (IARC) during the period 2022–2023. It reflects the everyday efforts of IARC personnel, in collaboration with the Agency's global network of experts, to provide cancer research for cancer prevention. IARC continued its work on cancer research priorities identified in the IARC Medium-Term Strategy 2021–2025 and took a step closer towards fulfilling its mission of "cancer research that matters".

This Biennial Report is accompanied by a webpage (https://www.iarc.who.int/biennial-report-2022-2023web/) that showcases key facts and figures on IARC and scientific highlights during the 2022–2023 biennium.

Cancer is an immense threat for sustainable development and for our societies. The cancer burden continues to rise globally. IARC estimated that cancer will become the leading cause of premature death worldwide over the course of this century and the single most important barrier to further gains in life expectancy. The cancer burden is not equally distributed across countries, within countries, and between different groups within societies. IARC showed that the greatest increases in the cancer burden by 2040 will affect mainly low- and middle-income countries with low levels of the Human Development Index (HDI). Such inequalities can only be expected to grow unless resource-dependent, effective, and cost-effective interventions are considered as greater priorities in low- and middle-income countries and are urgently implemented.

An additional challenge is to reduce social inequalities in cancer. IARC and partners revealed that cervical cancer mortality in Europe is driven largely by levels and trends of cancer mortality rates in groups with lower education levels. This primarily reflects inequalities in the availability of, access to, and uptake of effective screening programmes, which can detect and remove precancerous lesions and thus reduce incidence and mortality. The immediate implication is that reducing cancer mortality rates among the most disadvantaged groups within countries is a crucial step to lowering the national average cancer mortality rates and the overall burden of cancer. Therefore, cancer prevention measures will depend on action on the social determinants of health, considering socioeconomic, cultural, and geographical conditions.

To improve the implementation of cancer prevention interventions globally, IARC strongly endorsed further intensifying the coordination and collaboration with the World Health Organization (WHO), to enable more effective links between science and policy. In 2022–2023, IARC and WHO finalized a joint strategic work plan for 2023–2025, which is now being implemented, and intensified the coordination of technical activities. As examples, IARC-led research on breast cancer survival in sub-Saharan Africa has informed key indicators to support the implementation of the WHO Global Breast Cancer Initiative, and for cervical cancer prevention, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) used IARC-led research to conclude that single-dose human papillomavirus (HPV) vaccination delivers solid protection against infection.

For IARC, 2022 was an unprecedented year because of the preparation for the move to its new headquarters building, which brought the Agency many challenges. IARC personnel showed impressive and unwavering commitment and resilience to adapt and rise to these challenges as the situation evolved. After 50 years in the tower building in the

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Grange Blanche district, IARC successfully moved into its new headquarters in the Gerland Biodistrict of Lyon at the end of 2022. With its iconic shape, the new building embodies the Agency's vision for Open Science and international collaboration in cancer research. I am convinced that our new building will become a beacon for cancer research and a catalyst to strengthen collaboration between scientists, health professionals, and the general public.

On 12 May 2023, IARC held an official inauguration ceremony for the new building, which was attended by the French Minister of Health and Prevention, local government officials, members of the IARC Governing Council, dignitaries from IARC Participating States, representatives of WHO, national and international collaborators, and the principal funders of the construction project.

China joined IARC as a Participating State in May 2021. This new membership will further strengthen our collaboration in key research areas and will enable China to join the network of countries that are shaping global research priorities in cancer control and prevention. IARC welcomed a delegation from China to an in-person session of the IARC Governing Council for the first time in May 2023. In keeping with the tradition for incoming Participating States, the flag of China was raised on its pole next to the flags of the other Participating States.

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As described in this Biennial Report, IARC has launched several new initiatives in recent years, such as the IARC Research Teams framework, the development of the fifth edition of the European Code Against Cancer, the IARC Cross-Cutting Working Group on Cancer Prevention Knowledge Translation and Transfer, and the IARC Equity and Diversity Advisory Group. The Equity and Diversity Advisory Group was formed because gender equality in science is essential for IARC to achieve its mission. As we work towards a world where fewer people develop cancer, we also ensure that IARC remains diverse, equitable, and inclusive.

The global scale of IARC's research activities provides a truly unparalleled example of cancer research informing policies and practice related to cancer worldwide. As an international public health organization, IARC is uniquely positioned and plays a critical role in supporting national and international efforts to reduce the global cancer burden, and is a vital resource for governments, researchers, trainees, and health professionals around the world.

I am deeply honoured to have been re-elected as Director of IARC for a second term. I take this opportunity to thank all IARC personnel, who have contributed tremendously to the success of our organization. Together, we have made significant progress in advancing cancer research, prevention, and control, as reflected in this Biennial Report, and I am proud of our collective achievements. As I embark on my second term as Director, I am committed to building on our successes and continuing to advance the Agency's mission with the ultimate goal of reducing the global cancer burden, avoiding unnecessary suffering, and saving as many lives as possible.

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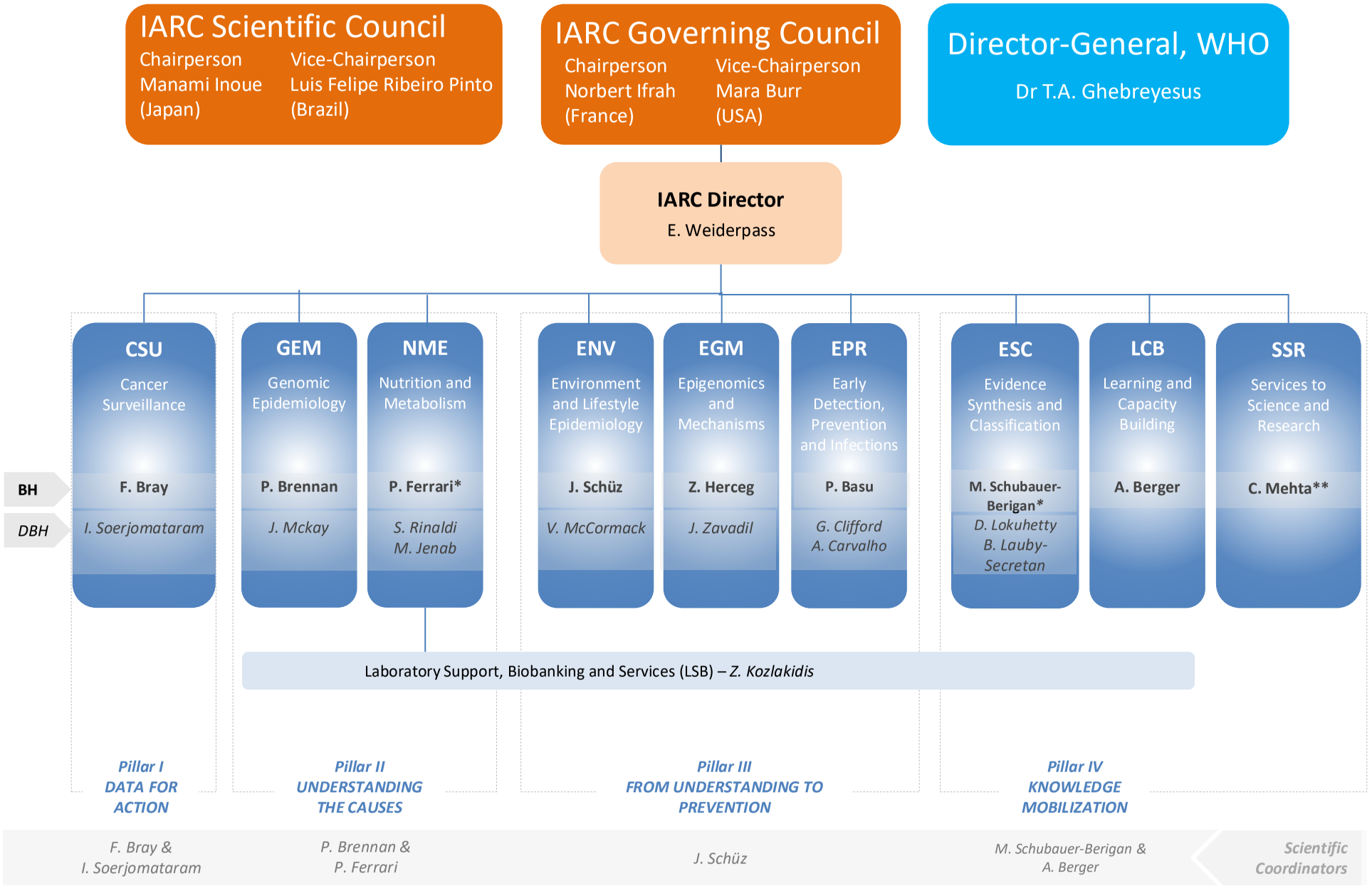
1 November 2023



BH = Branch Head (*Acting / ** Ad interim)
DBH = Deputy Branch Head

IARC Lectures

In 2022 and 2023, IARC was honoured and delighted to host seminars that were delivered by some of the world's most eminent speakers in the fields of cancer research, prevention, implementation science, and health inequalities, as well as cancer initiatives currently under way at both the European and global levels.

IARC Distinguished Speaker Series

These distinguished speakers were invited to present topics of interest within the framework of regular Town Hall meetings, which were generally broadcast online.

January 2022	Elio Riboli (Imperial College London, United Kingdom) – The role of nutrition and metabolic factors in cancer causation and prevention: lessons learned from EPIC and other large population cohort studies
February 2022	Bente Mikkelsen (WHO headquarters, Switzerland) – Cancer prevention and control in the SDG era: progress, priorities and actions
March 2022	Brad Reisfeld (Colorado State University, USA and IARC Senior Visiting Scientist Awardee, IMO) – Are we there yet? The long road to realizing the promise of in silico approaches in toxicology
March 2022	Thomas Dubois (National Cancer Institute, France) – France 10-year cancer control strategy 2021–2025 roadmap
April 2022	Verna D.N.K. Vanderpuye (National Center for Radiotherapy, Oncology and Nuclear Medicine, Korle Bu Teaching Hospital, Ghana) – Cancer in Africa: a focus on women – surveillance through the cancer care continuum
June 2022	Satish Gopal (National Cancer Institute Center for Global Health, USA) – Pursuing cancer research that matters in Malawi and at the NCI
July 2022	Hans Kromhout (Utrecht University, The Netherlands) – What do we need for informative epidemiological studies on pesticides?
September 2022	Eric Solary (Gustave Roussy Cancer Center, France) – UNCAN.eu, a European platform to UNderstand CANcer
October 2022	Paolo Vineis (Imperial College London, United Kingdom) – Environmental crisis and human health
October 2022	Lauren E. McCullough (Emory University, USA) – Epidemiology beyond its limits – leveraging population data to address breast health equity
November 2022	Béatrice Fervers (Centre Léon Bérard, France) – French Cancer Primary Prevention Research Network CANCEPT: accelerating the translation of actionable knowledge into innovative cancer prevention

January 2023	Sarah De Saeger and Marthe De Boevre (Ghent University, Belgium) – Mycotoxins and the exposome
February 2023	Suzette Delaloge (Gustave Roussy Cancer Center, France) – Towards building risk-based cancer interception
March 2023	Montserrat García-Closas (National Cancer Institute, USA) – Polygenic risk scores for cancer: can they be useful for precision prevention?
March 2023	Iordanis Arzimanoglou (European Innovation Council, Belgium) – Current state of the Health and Biotech portfolio at European Innovation Council (EIC)
April 2023	Mary Beth Terry (Columbia University, USA) – Cancer epidemiology study designs and cancer susceptibility: rethinking population-based approaches to confront global challenges
June 2023	Núria Malats (Spanish National Cancer Research Centre - CNIO, Spain), Making precision prevention of pancreatic cancer possible
June 2023	Cyrille Delpierre (Centre for Epidemiology and Population Health Research - CERPOP, France) and Sébastien Lamy (CERPOP, France and IARC Visiting Scientist, CSU) – How do the social environment and social determinants influence the risk of cancers, their management, and their development?
July 2023	Marc Van Den Bulcke (Cancer Centre - Sciensano, Belgium) – The Europe's Beating Cancer Plan and Mission on Cancer: a country perspective on opportunities and challenges for a cooperative multi-state implementation in cancer healthcare and research
September 2023	Gian-Paolo Dotto (Cutaneous Biology Research Center, USA) – Dual role of androgen receptor signalling in skin cancer

IARC Award for Women in Cancer Research seminars

The IARC Award for Women in Cancer Research recognizes outstanding contributions in the field of cancer prevention research by scientists who identify as women.

May 2022	Cristina Stefan (Institute of Global Health Equity Research, Rwanda) – The journey of an oncologist: past, present, and predicting the future
October 2023	Neerja Bhatla (All India Institute of Medical Sciences, India) – The long winding road of cervical cancer prevention research

Professor Neerja Bhatla. © IARC.


NATIONAL CANCER REGISTRY
AT THE FOREFRONT OF COMBATING CANCER

GICR–IARC Collaborating Centre inauguration event in South Africa, 22 November 2022. © IARC

Cancer Surveillance Branch (CSU)

Branch head
Dr Freddie Bray

Deputy branch head
Dr Isabelle Soerjomataram

Professional staff
Dr Melina Arnold (until July 2022)
Mr Morten Ervik
Mr Jacques Ferlay
(until December 2022)
Mr Les Mery
Dr Eileen Morgan
Dr Marion Piñeros-Petersen
Dr Eva Steliarova-Foucher
Dr Salvatore Vaccarella
Dr Ariana Znaor

Technical and administrative staff
Ms Aude Bardot
Ms Murielle Colombet
Ms Anastasia Dolya
Ms Maria Fernan
Mr Frédéric Lam
Mr Mathieu Laversanne
Ms Fatiha Louled
Mr Eric Masuyer (until May 2023)
Ms Katiuska Veselinović
Mr Jérôme Vignat

Visiting scientists
Dr Hadrien Charvat
(until December 2023)
Dr Ophira Ginsburg
(until February 2022)
Dr Louisa Gordon (until July 2023)
Dr Sébastien Lamy
(until December 2023)
Dr Valentina Lorenzoni
Dr Max Parkin (until December 2023)
Dr Margherita Pizzato
Dr Rama Ranganathan
(until November 2023)
Dr Mark Rutherford
(until December 2023)
Dr Kamal Seneviratne
(until July 2022)

Postdoctoral fellows and doctoral students
Dr Manushak Avagyan
(until February 2023)
Dr Diego Capurro Fernandez
Dr Neimar de Paula Silva
Dr Marzieh Eslahi
Ms Hanna Fink
Dr Andrea Gini (until October 2023)
Dr Maxime Large
Mr Oliver Langselius
Dr Ganfeng Luo
Dr Allini Mafra da Costa
(until August 2022)
Dr Eileen Morgan
(until October 2022)
Dr Jean Niyigiba (until October 2023)
Dr Sampath Pitchaimuthu
(until November 2023)
Dr Adeylson Guimarães Ribeiro
(until March 2023)
Dr Harriet Rumgay
Dr Richa Shah
Dr Deependra Singh (until July 2023)
Dr Patumrat Sripan (until April 2022)
Dr Robabeh Ghodssighassemabadi
(until May 2023)
Dr Andras Weber (until May 2023)
Dr Mariam Zahwe

Students
Ms Dagrun Daltveit
(until December 2023)
Ms Eline de Heus (until April 2023)
Ms Nermin Osman (until April 2022)
Ms Asimina Papadimitriou
Ms Julia Rey Brandariz
(until July 2023)

The Cancer Surveillance Branch (CSU) systematically collects, analyses, interprets, and disseminates cancer data and statistics worldwide, as per its mandate from WHO. CSU builds on long-standing expertise in cancer registration and descriptive epidemiology, aligning its activities with the evolving global cancer agenda. The key priorities of CSU include:

- ensuring that locally recorded high-quality cancer data are available to governments in transitioning countries, thus informing priorities for national cancer control;
- serving as a reference to the global cancer community in the provision of national cancer indicators;
- describing and interpreting the changing magnitude and the transitional nature of cancer risk profiles around the world; and
- advocating the health, social, and economic benefits of preventive interventions, through a systematic quantification of their future impact.

Some highlights across CSU's six dedicated programmes during the 2022–2023 biennium are provided here.

Cancer registry support and collaboration

The Global Initiative for Cancer Registry Development (GICR, https://gicr.iarc.who.int) brings partners together to improve cancer surveillance worldwide. Capacity-building is a key objective, and one important milestone was the launch of an e-learning series of 14 modules developed in partnership with Vital Strategies and the African Cancer Registry Network (AFCRN) and supported by Bloomberg Philanthropies. Available in English, French, and Spanish, the freely available course offers the staff of population-based cancer registries (PBCRs) formal certification as International Cancer Registrars.

As well as a series of consultancies to PBCRs (Figure 1), virtual courses were held during the biennium on cancer registration (in collaboration with the Quito Cancer Registry in Ecuador and the Pan American Health Organization, and in the Lao People's Democratic Republic with the National Cancer Institute of Thailand), on CanReg5 (in collaboration with the National Cancer Institute of Colombia), and on cancer coding (in collaboration with the National Cancer Institutes of Argentina and Colombia). The annual IARC–GICR Summer School with the National Cancer Center of the Republic of Korea was held virtually in 2022 and in person in 2023.

The GICR continued to bring innovation to registry operations. The E-NNOVATE partnership piloted the linkage of electronic medical records to PBCRs via the world's largest health information management system, the District Health Information Software version 2 (DHIS2). Continuing the model of strengthening regional capacity, in late 2022 three IARC–GICR Collaborating Centres in sub-Saharan Africa were officially launched, in Côte d'Ivoire, Kenya, and South Africa, in collaboration with Vital Strategies.

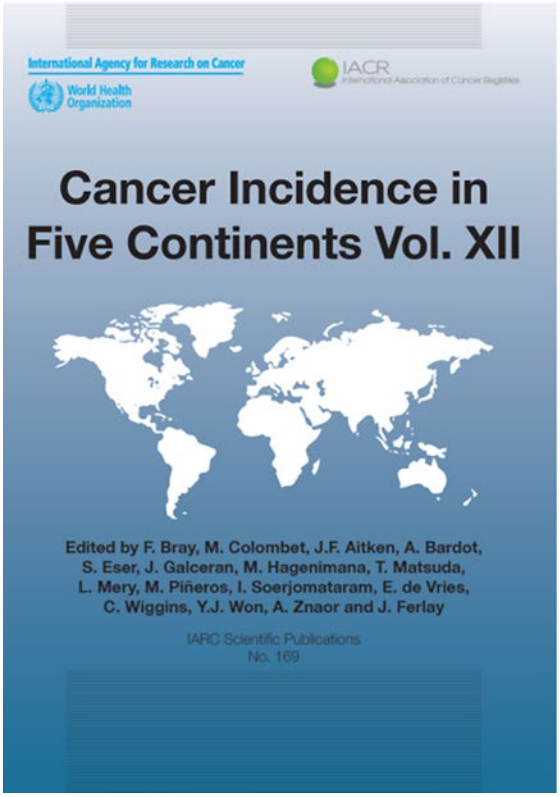
Working closely with the GICR, CSU serves as the Secretariat for the International Association of Cancer Registries (IACR, http://www.iacr.com.fr), the professional body dedicated to fostering the aims of PBCRs worldwide. After online meetings held during the COVID-19 pandemic, an in-person scientific conference was hosted in Granada (Spain) in partnership with the European Network of Cancer Registries (ENCR).

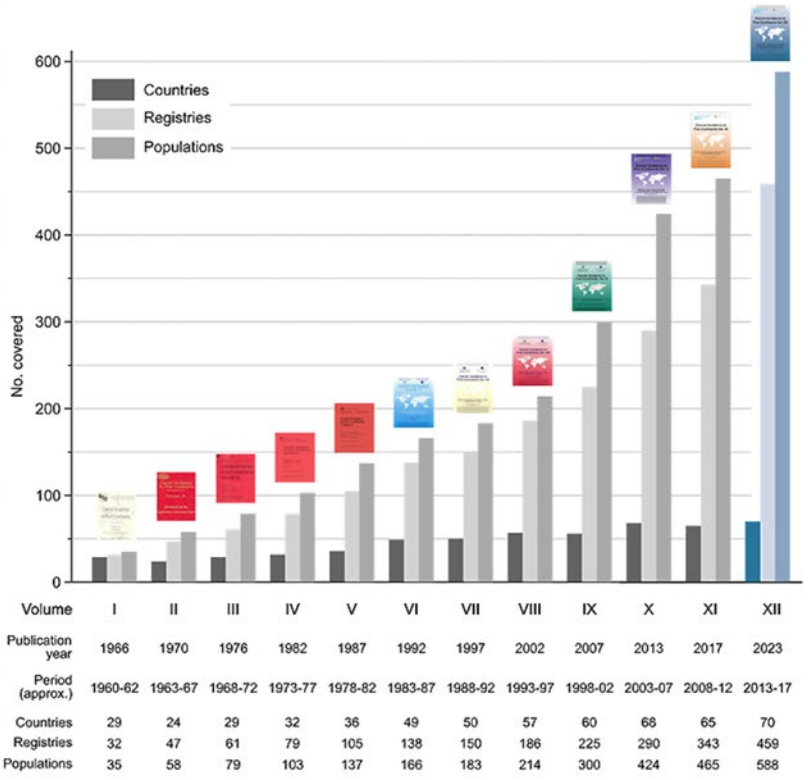
Disseminating cancer data and statistics

Two of IARC's flagship global goods were disseminated online in 2023. *Cancer Incidence in Five Continents* (CI5) is a compendium of comparable data on cancer incidence in different subpopulations and a reference source for studies that explore cancer variations worldwide. The 12th iteration of CI5 (Volume XII), which includes high-quality information on cancers diagnosed in 2013–2017, has an increase of one third in the number of registries included, compared with Volume XI (Figure 2). With 812 submissions from PBCRs responding to the call for data, Volume XII includes 588 populations from 459 registries in 70 countries. The updated website provides utilities to examine cancer incidence patterns in different populations (https://ci5.iarc.who.int/CI5-XII/); it is being transitioned to the repurposed

Figure 1. Consultancies to (left) San Salvador population-based cancer registry (El Salvador), 13–25 July 2022, and (right) Chiang Mai population-based cancer registry (Thailand), 1 March 2023. © IARC.

Figure 2. ***Cancer Incidence in Five Continents*** **Volume XII and the increasing number of countries, registries, and populations included in each of the quinquennial Volumes I to XII. © IARC.**





Volume	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
Publication year	1966	1970	1976	1982	1987	1992	1997	2002	2007	2013	2017	2023
Period (approx.)	1960-62	1963-67	1968-72	1973-77	1978-82	1983-87	1988-92	1993-97	1998-02	2003-07	2008-12	2013-17
Countries	29	24	29	32	36	49	50	57	60	68	65	70
Registries	32	47	61	79	105	138	150	186	225	290	343	459
Populations	35	58	79	103	137	166	183	214	300	424	465	588

IACR website to enable geographical and temporal analyses of individual data sets across the 12 volumes of CI5.

Second, updated national estimates (GLOBOCAN) of the cancer burden in 185 countries or territories for 2022 were developed, largely from the CI5 Volume XII data submissions, and the European estimates were co-developed with the ENCR. National incidence, mortality, and prevalence in 2022 were made available on the Cancer Today and Cancer Tomorrow subsites of the IARC Global Cancer Observatory platform (GCO, http://gco.iarc.who.int); the Cancer Tomorrow subsite provides tools to predict the future cancer burden up to 2050. An accompanying article documenting the cancer variations by world region will be published in *CA: A Cancer Journal for Clinicians* in 2024. Updates of attributable fractions for infection were disseminated, on the Cancer Causes subsite (https://gco.iarc.who.int/causes/), as were survival estimates (https://gco.iarc.who.int/survival/) based on CSU's survival benchmarking programmes Cancer Survival in Countries in Transition (SURVCAN), now in its third edition, and the International Cancer Benchmarking Partnership (ICBP SURVMARK-2). An article presenting and discussing global estimates of lung cancer for the main histological subtypes was also published (Zhang et al., 2023c).

Descriptive studies

As the COVID-19 pandemic evolved, CSU moved towards evidence synthesis of the direct impact of the pandemic on risk factors, cancer services, and excess mortality (Carle et al., 2022; Freeman et al., 2022; Luo et al., 2022b; Sarich et al., 2022). CSU co-led the International Partnership for Resilience in Cancer Systems (I-PARCS) in providing tools to mitigate future crises and support health system resilience. The IARC Scientific Council and Governing Council supported the IARC COVID-19 and Cancer Initiative (IARC-C19) to undertake deep dives on selected cancer types, including the development of a dynamic evidence-based decision-making platform that incorporates mitigation strategies adapted to national contexts.

Several studies provided an evidence base for cancer prevention. A European study estimated that 1.3 million cancers could be prevented if prevention policies in the best-performing countries were implemented across the region (Cabasag et al., 2022c). CSU also quantified the long-term impact of implementation of tobacco control measures in Japan, the role of human papillomavirus (HPV) in anal squamous cell carcinoma (Deshmukh et al., 2023a), and the importance of lifestyle factors in head and neck cancer (Budhathoki et al., 2023). Cardiovascular disease and cancer are now the leading causes of death in greater Europe. Several combined assessments of mortality transitions in cardiovascular disease and cancer were undertaken to measure progress in their control (Wéber et al., 2023a; Znaor et al., 2022a).

Through SURVCAN and ICBP SURVMARK-2, CSU coordinated survival studies to improve data quality, standards, and local capacity to produce cancer survival data in-house (Andersson et al., 2022a, 2022b; Gil et al., 2022).

Benchmarking studies revealed large survival inequalities in female breast cancer, prostate cancer, colorectal cancer, and cervical cancer (Figure 3) (Soerjomataram et al., 2023). In-depth analyses performed in countries with local investigators in Colombia (Bravo et al., 2022), Thailand (Maláková et al., 2022), the Islamic Republic of Iran (Nemati et al., 2022a, 2022b), and Brazil (Mafra et al., 2023) evaluated the effectiveness of cancer policies, including the role of universal health coverage. Across seven high-income countries, persistent disparities were observed by stage, sex, or age, with the quality of cancer care and health system factors influencing survival (Araghi et al., 2022; Arnold et al., 2022a; Cabasag et al., 2022a, 2023).

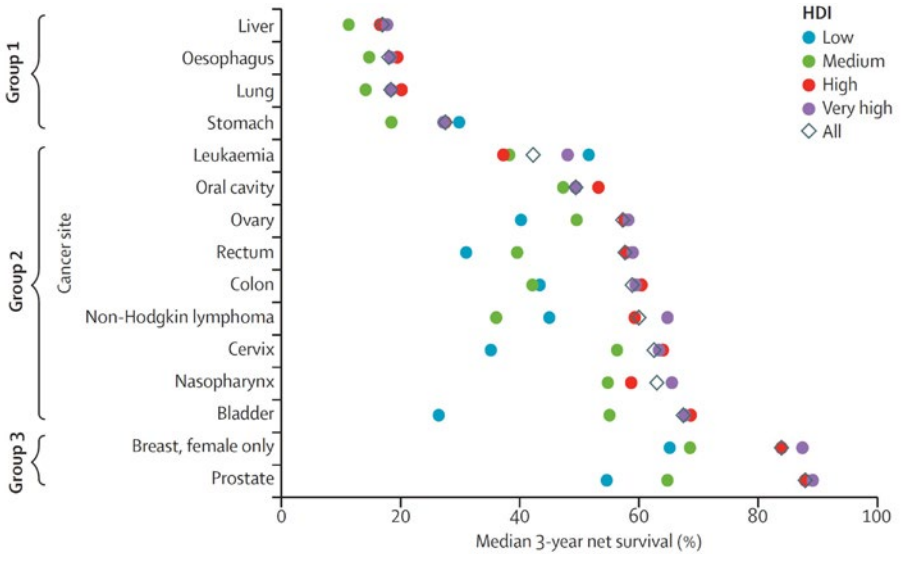
CSU also provided assessments of the current and future burden from specific cancer types, including cancers of the gastrointestinal tract (Morgan et al., 2023; Rumgay et al., 2022a, 2022b), urinary tract (Bukavina et al., 2022; Jubber et al., 2023; Znaor et al., 2022b), lung (Wéber et al., 2023b), skin (Arnold et al., 2022b), ovary (Cabasag et al., 2022b), and thyroid (Pizzato et al., 2022a) and non-Hodgkin lymphoma (Mafra et al., 2022), as well as overviews by age at diagnosis (Pilleron et al., 2022; Wang et al., 2022a). In addition, CSU developed baseline estimates for the WHO global cancer initiatives, including cervical cancer elimination (Singh et al., 2023), and population-level analyses of breast cancer stage (Piñeros et al., 2022a). At the regional level, CSU presented situation analyses in Latin America and the Caribbean (Piñeros et al., 2022b) and in sub-Saharan Africa (Bray et al., 2022), and there were numerous country overviews (Ghasemi-Kebria et al., 2023a, 2023b; Leal et al., 2022; Luo et al., 2022a, 2022b; Mafra da Costa et al., 2022; Maláková et al., 2022; Pierannunzio et al., 2022), including a series of papers highlighting cancer inequalities in the municipalities of the State of São Paulo, Brazil (Guimarães Ribeiro et al., 2023; Ribeiro et al., 2023a, 2023b).

Childhood cancer

CSU developed a framework for streamlining the collection and validation of routine data on childhood cancer from PBCRs and other sources, in consideration of data sharing policies. The quality-assured data compiled in the International Incidence of Childhood Cancer (IICC-3, https://iicc.iarc.who.int/) study were used to examine childhood cancer incidence in Latin America. Data standards were promoted through a revised third edition of the International Classification of Childhood Cancer (https://iicc.iarc.who.int/classification/). A standardized set of teaching materials was developed within the framework of the ChildGICR programme (https://gicr.iarc.who.int/childgicr/) in collaboration with St. Jude Children's Research Hospital (USA), and the ChildGICR Masterclass participants were trained to disseminate knowledge on childhood cancer registration. Subsequently, 90 students from 17 transitioning countries were trained in partnership with the Viet Nam National Cancer Institute, the Cancer Institute in Chennai (India), and the National Center for Disease Control and Public Health in Georgia.

In collaboration with 150 PBCRs worldwide, CSU assembled data to analyse risk of second primary neoplasms in childhood cancer survivors. In work carried out within the Cancer Risk in Childhood Cancer Survivors (CRICCS, https://criccs.iarc.who.int) study, a novel method of estimating the prevalence of childhood cancer survivors, based on grouped data, was developed.

Figure 3. Median age-adjusted 3-year net survival across population-based cancer registries by the four-tier 2019 Human Development Index (HDI) and cancer site in 2008–2012, from SURVCAN-3. The HDI is divided into low (< 0.55), medium (0.55–0.69), high (0.70–0.79), and very high (0.80–1.00). Groups were identified on the basis of strength of association with HDI and median 3-year net survival across registries. Group 1 has no association with HDI and very low median net survival, group 2 has a moderate association with HDI and moderate median net survival, and group 3 has a strong association with HDI and high median net survival. Reprinted from Soerjomataram et al. (2023). Copyright 2022, with permission from Elsevier.



The economic burden of cancer

A research focus in CSU has been the monetary valuation of productivity lost due to premature mortality from cancer. CSU estimated that half of the total productivity loss in Europe was due to unpaid work, with a particularly high proportion among women (Ortega-Ortega et al., 2022). Although ongoing declines in premature cancer mortality imply lower future productivity losses, CSU estimated that the cumulative costs of cancer would be €1.3 trillion over the next two decades, amounting to 0.43% annually of total GDP (Ortega-Ortega et al., 2022). Novel methods (Hanly et al., 2022), country-specific analyses (De Camargo Cancela et al., 2023), and economic evaluations of alcohol reduction strategies (Rumgay et al., 2023) were all published during the 2022–2023 biennium. Within ChildGICR, a systematic review of financial hardship in childhood cancer proposed a data-driven methodological framework to

inform effective policies to address the economic impact on families (Ritter et al., 2023).

Within the *Lancet* Commission on Women, Power, and Cancer (Figure 4), CSU analysed the economic impact of cancer diagnosis among women, evaluating women's contribution to the cancer health workforce, setting the investment case and standards for a responsive health system refocused to the needs of women in all their diversity (Ginsburg et al., 2023). An analysis from eight Asian countries found that almost three quarters of women spent more than 30% of their annual household income on cancer-related expenses in the year after the diagnosis. Another study showed that the value of women's unpaid caregiving work ranged from 2.0% of national health expenditure in Mexico to 3.7% in India.

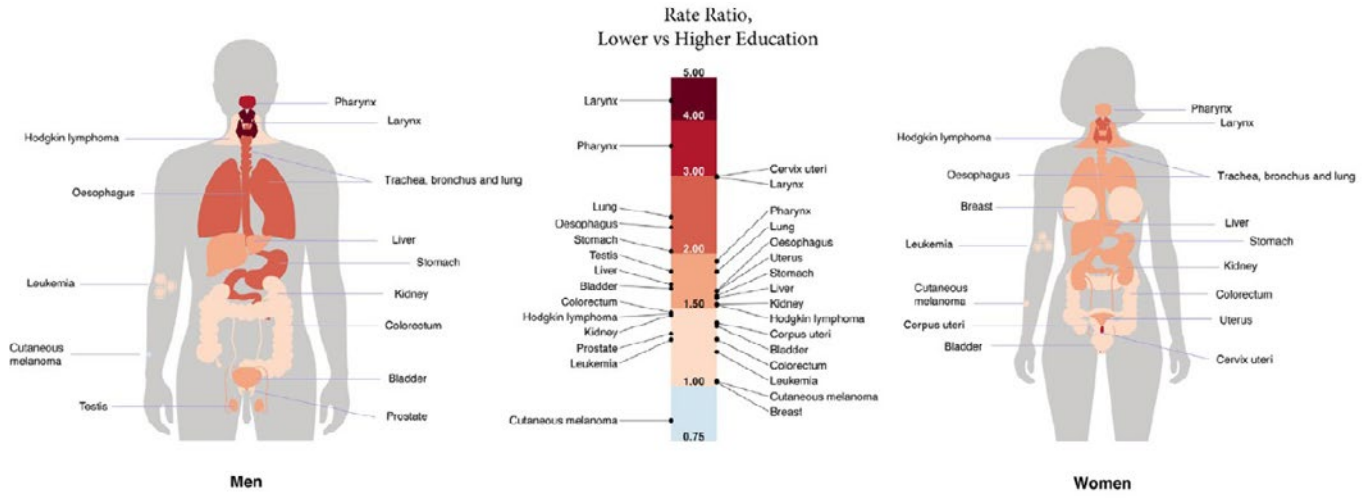
Figure 4. *Lancet* Commission on Women and Cancer meeting, Istanbul (Türkiye), 3 March 2023. © IARC.

Social inequalities and cancer

Arguing that policy-makers still need to prioritize cancer inequities on the global stage (Ali et al., 2023), one of CSU's major contributions was to show that socioeconomic inequalities in cancer mortality persist across Europe and for every cancer type (Figure 5) but that the extent of these inequalities varies considerably across countries (Vaccarella et al., 2022). Other contributions to the field included an assessment of social inequalities in cancer incidence and mortality in Brazil (Ribeiro et al., 2023a, 2023b), global estimates of the number of maternal orphans due to cancer (Guida et al., 2022), and socioeconomic inequalities in lung cancer in the Nordic countries (Pizzato et al., 2022b). CSU research indicates that socioeconomic factors are the single most important factor explaining the distribution of cancer between and within countries.

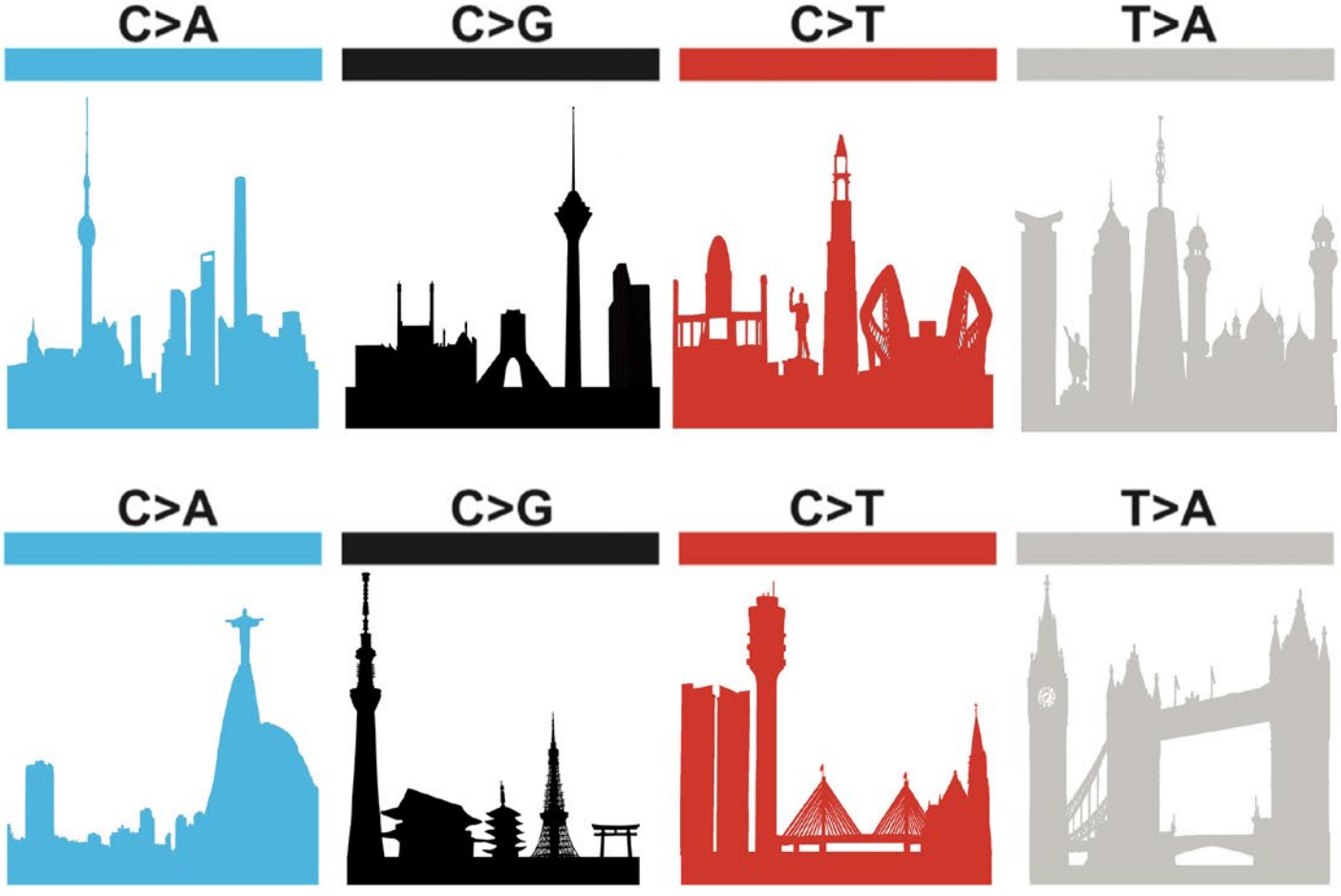
Inefficiencies in the provision of healthcare services are crucial drivers of cancer inequalities. CSU has shown that the management of thyroid cancer is both a public health and an economic challenge in many high-income countries. CSU research in France estimated the substantial costs associated with overdiagnosis and associated treatments in disease management (Li et al., 2023a).

Figure 5. Relative inequalities in cancer mortality between lower and higher education levels in 18 European countries, by cancer site and sex in 1998–2015. Reprinted from Vaccarella et al. (2022). Copyright 2022, with permission from Elsevier.



Volume 100 August 2021

nature genetics



Mutational Signatures in esophageal squamous cell carcinoma from eight countries

Courtesy of Joshua Atkins. Reproduced from Moody et al., Mutational signatures in esophageal squamous cell carcinoma from eight countries with varying incidence, *Nature Genetics* volume 53, issue 11, 2021, Springer Nature

Genomic Epidemiology Branch (GEM)

Branch head
Dr Paul Brennan

Deputy branch head
Dr James McKay

Scientists
Dr Behnoush Abedi-Ardekani
Dr Nicolas Alcala
Dr Shaymaa AlWaheidi
Dr Ievgeniia Chicherova
Dr Ana Carolina De Carvalho Peters
Dr Lynnette Fernandez-Cuesta
Dr Aida Ferreiro-Iglesias
Dr Matthieu Foll
Dr Mattias Johansson
Dr Florence Le Calvez-Kelm
Dr Sandra Perdomo Velasquez
Dr Hilary Robbins
Dr Mehrnaz Shamalnasab
Dr Mahdi Sheikh
Dr Shama Virani

Secretariat
Ms Juliette Prazak
Ms Isabelle Rondy
Ms Andreea Spanu-Bermond

Research assistants
Ms Karine Alcala
Mr Thomas Cattiaux
Ms Valérie Gaborieau
Ms Hélène Renard (until March 2023)
Dr Sergey Senkin
Dr Catherine Voegele

Project assistants
Ms Natalia Alves de Oliveira Vaz
Ms Laurène Bouvard (until November 2022)
Ms Sandra Moreno Ayala

Laboratory technicians
Ms Amélie Chabrier
Ms Priscilia Chopard
Ms Nathalie Forey

Postdoctoral fellows
Dr Joshua Atkins (until July 2022)
Dr Ricardo Cortez Cardoso Penha
Dr Claudia Coscia-Requena (until April 2023)
Dr Allison Domingues
Dr Wellington Dos Santos
Dr Rafii Fadoua (until January 2022)
Dr Xiaoshuang Feng
Dr Ryan Langdon
Dr Daniela Mariosa (until September 2023)
Dr Emilie Mathian
Dr Michael Olanipekun
Dr Justina Onwuka
Dr Han La Park
Dr Apiwat Sangphukieo
Dr Sergey Senkin (until March 2022)
Dr Alexandra Sexton-Oates
Dr Laura Torrens Fontanals

Students
Mr Sébastien Calvet (until July 2022)
Dr Gabrielle Drevet
Ms Elmira Ebrahimi
Ms Lipika Lipika (until November 2023)
Ms Laurane Mangé
Ms Fannie Martin (until August 2023)
Mr Simon Niceron (until August 2022)
Mr Eric Rucogoza (until August 2023)
Ms Hana Zahed

Visiting scientists
Dr Anvari Seyd Omid
Dr Patrice Avogbe
Dr Giovanni Centonze (until July 2022)
Dr Eleonora Lauricella (until October 2023)
Dr Delfin Lovelina Francis (until November 2023)
Dr Maike Morrison (until April 2023)
Dr Dariush Nasrollahzadeh Nesheli (until October 2022)
Dr Saeed Nemati
Dr Arash Nikmanesh (until October 2023)
Dr Simon Pahnke
Ms Fatemeh Shafighian (until October 2023)
Dr Jifang Zhou

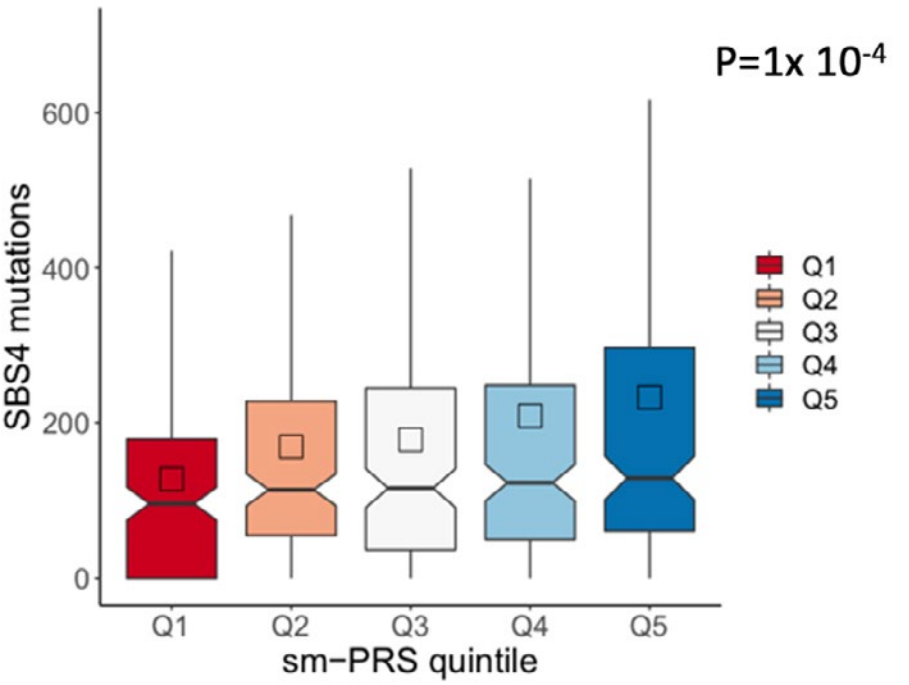
The over-arching goals of the Genomic Epidemiology Branch (GEM) are to further the understanding of cancer prevention and early detection using a combination of genomic and traditional epidemiology methods. This is done by bringing together six broad areas of work, as described here.

Area 1: Understanding the genetic susceptibility to cancer

GEM has continued to explore how genetic variation influences cancer susceptibility, with a focus on large international consortia to assemble expanded genetic data sets of lung cancer, head and neck cancer, renal cancer, and lymphomas. GEM's genetic studies are now on the order of 70 000 for lung cancer, close to 60 000 for lymphomas, 15 000 for head and neck cancer, and 30 000 for kidney cancer. GEM is now working with genotyping laboratories to undertake the genotyping and quality control analysis.

Through this continued expansion, GEM has identified novel susceptibility loci, implicating genetic loci containing genes such as *CHRNA4, CHRNB2, DBH, POLI, CHEK1, ERCC2, CYP1A1,* and *HLA*, and further implicated genes related to additive behaviour, DNA repair, telomere length, metabolic processes, and immune response in the carcinogenic process. GEM has continued to explore how germline genetic variants influence cancer susceptibility. For example, GEM has combined its germline analysis with its genomic analysis of the somatic material to demonstrate that the genetic variants related to aspects of nicotine addiction are also associated with the presence of mutational signatures associated with tobacco exposure in the patient's tumour (Figure 1). This appears consistent with the notion that genetic variants influence individuals' smoking behaviour, which in turn influences the degree of carcinogenic exposure in their lung tissue and, consequently, their somatic mutation burden (Gabriel et al., 2022).

Figure 1. GEM has combined its germline analysis with its genomic analysis of the somatic material to demonstrate that the genetic variants related to aspects of nicotine addiction are also associated with the presence of mutational signatures associated with tobacco exposure in the patient's tumour. sm-PRS, polygenic risk score for smoking; Q, quintile. Reproduced from Gabriel et al. (2022). © Gabriel et al., 2022. Published by Oxford University Press.



GEM used a similar approach to explore the influence of telomere length on susceptibility and lung adenocarcinoma tumour expression profiles (Cortez Cardoso Penha et al., 2023) and to implicate mutations in *BRCA2* in susceptibility to oesophageal squamous cell carcinomas. GEM also made important contributions to facilitate the efforts of these consortia, hosting an online conference during the travel restrictions imposed during the COVID-19 pandemic, and more recently hosting in-person meetings at IARC that also include online participation through hybrid meeting formats using the up-to-date facilities in the new IARC building. GEM continues to embrace technological advances, by developing consortia frameworks that enable data sharing of the consortia resources in a safe and efficient manner while supporting researchers from around the world (Figure 2).

Figure 2. The annual meeting of the International Lymphoma Epidemiology Consortium (InterLymph), at IARC in France in June 2023. © IARC.

Area 2: Identifying novel causes of cancer through genomics studies

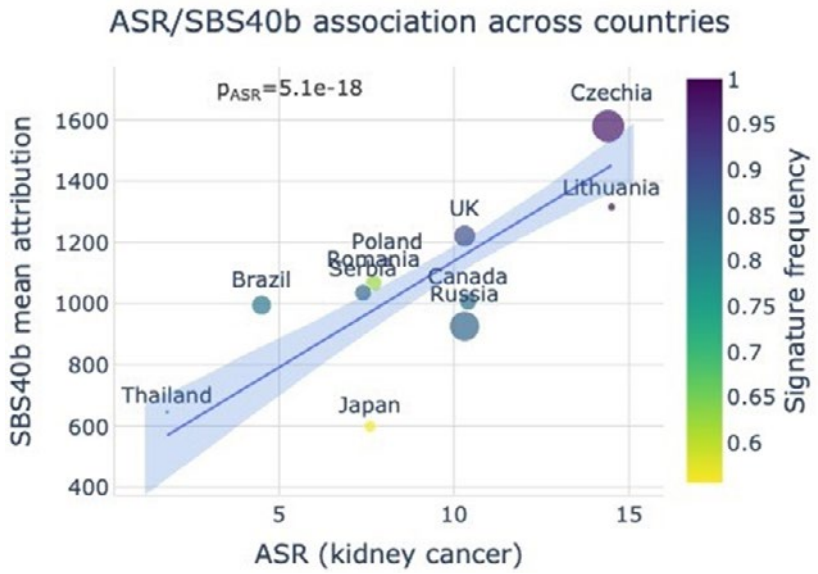
Mutographs

Mutographs is a Cancer Grand Challenges project that aims to understand the causes of five different cancer types across five continents by generating mutational signature profiles. The initial recruitment of about 6000 cases has been completed, and samples from 4000 cases have been successfully processed at IARC and sent to the Wellcome Sanger Institute (United Kingdom) for whole-genome sequencing. Genomic, exposure, and clinical data will be publicly available through the International Cancer Genome Consortium Accelerating Research in Genomic Oncology (ICGC ARGO) platform. The analysis of 552 cases of oesophageal cancer from eight countries with varying incidence was reported in 2021 and illustrated the importance of non-mutagenic causes of oesophageal cancer in high-incidence regions. Analysis of about 1000 kidney cancers across 11 countries has been completed, and the results are shedding light on the contribution of environmental causes to the high risk of kidney cancer in central Europe. In particular, the results highlighted a novel signature (SBS40b) that correlates strongly with incidence of kidney cancer (Figure 3). Understanding the cause of this signature could help to understand why incidence of kidney cancer is particularly high in central Europe.

Other results included the presence of a signature (SBS22) in south-eastern Europe that is linked to the mutagen aristolochic acid, and a separate signature (SBS12) that was present in Japan. These results raise the possibility that many millions of people in these regions are exposed to common mutagens.

The emerging results from the Mutographs project are changing the thinking about how environmental agents cause common cancers, and they have led to two large additional projects: (i) PROMINENT (see the text box) and (ii) DISCERN.

Figure 3. The results from the Mutographs project highlighted a novel signature (SBS40b) that correlates strongly with incidence of kidney cancer. ASR, age-standardized incidence rate. Reproduced from Senkin et al. (2023). Geographic variation of mutagenic exposures in kidney cancer genomes. medRxiv, 2023.06.20.23291538.



DISCERN

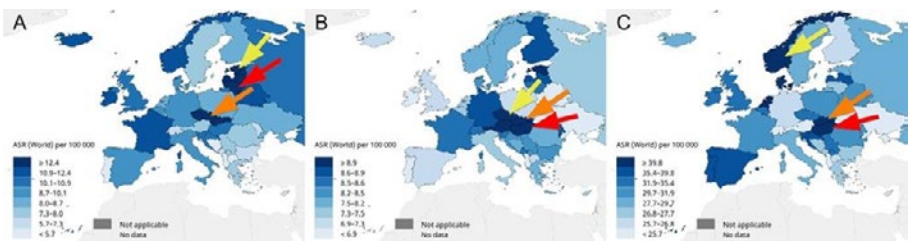
The Discovering the Causes of Three Poorly Understood Cancers in Europe (DISCERN) project was started in 2023 and is funded as part of the European Commission Cancer Mission initiative. The overall goal of DISCERN is to understand the causes of three poorly understood cancers in Europe – renal cancer, pancreatic cancer, and colorectal cancer – and to help explain the geographical distribution of these cancer types, including their high incidence in central and eastern Europe (Figure 4).

This will be achieved by combining large-scale European biorepositories comprising population-based cohorts and tumour case series with state-of-the-art exposomics and proteomics, as well as genomics technologies that analyse both normal and tumour tissue. DISCERN will provide the critical evidence base required to develop new prevention strategies for these cancer types in Europe. DISCERN builds on ongoing pan-European initiatives, including the European Human Exposome Network (EHEN), the Partnership for the Assessment of Risks from Chemicals (PARC), the Exposome-Powered Tools for Healthy Living in Urban Settings (EXPANSE) project, and the Mutographs project.

Area 3: Early cancer detection to reduce mortality and morbidity

Over the past few years, GEM has invested substantially in research aiming

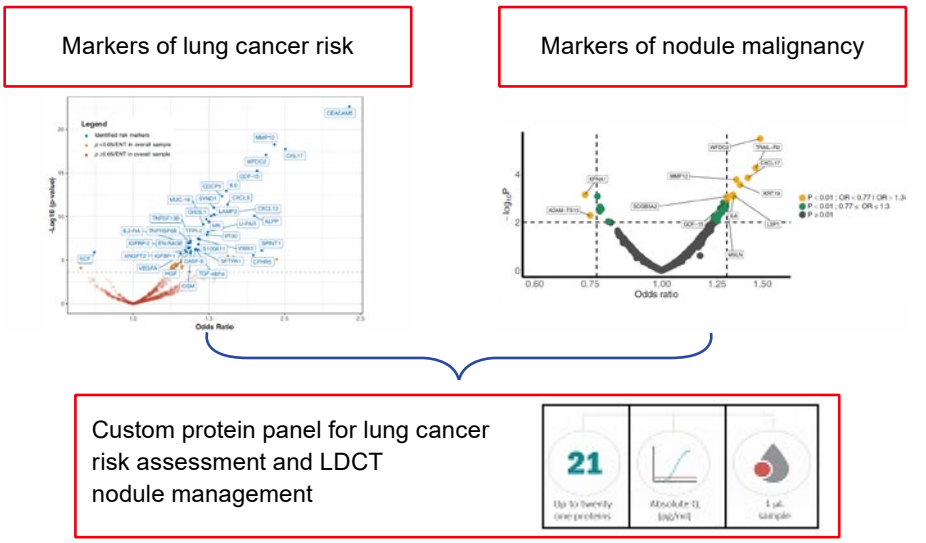
Figure 4. The overall goal of DISCERN is to understand the causes of three poorly understood cancers in Europe – (A) renal cancer, (B) pancreatic cancer, and (C) colorectal cancer – and to help explain the geographical distribution of these cancer types, including their high incidence in central and eastern Europe. From Ferlay et al. (2020). Global Cancer Observatory: Cancer Today. Lyon, France: IARC. Available from: https://gco.iarc.who.int/today.



to improve early detection of cancer. GEM's approach has focused on three research domains: (i) developing and evaluating risk models to inform the identification of individuals who may benefit from screening, (ii) identifying novel risk biomarkers that may improve existing risk models for use in determining screening eligibility, and (iii) developing minimally invasive early cancer biomarkers that may indicate an early undetected cancer.

In early detection of lung cancer, GEM research has been carried out in the context of screening with low-dose computed tomography (LDCT). LDCT screening has been shown to reduce lung cancer mortality in individuals who are at high risk, which is defined as having a history of heavy tobacco exposure. The current screening criteria only consider former and current smokers and typically involve a pack-year threshold (e.g. ≥ 20 or 30 pack-years of smoking exposure), time since quitting (e.g. 15 years), and an age range (e.g. 50–75 years). The use of risk models that provide absolute risk estimates based on individual risk profile data is also being evaluated in different settings. The choice of screening eligibility criteria will have a different impact depending on the setting, and GEM recently carried out an analysis that compared different strategies in Brazil. A major issue is that all commonly used screening eligibility criteria will leave many individuals who are destined to develop lung cancer ineligible for screening, and GEM has carried out extensive research aiming to develop biomarkers that can improve existing risk models. This research has been carried out using resources from the Lung Cancer Cohort Consortium (LC3), a major initiative coordinated by GEM since 2011 that involves 24 population cohorts from around the world with almost 3 million research participants followed up over time (Robbins et al., 2023). Based on these resources, GEM recently identified 36 robust protein biomarkers of lung cancer risk (Lung Cancer Cohort Consortium (LC3), 2023) that were able to substantially improve on traditional risk models (Feng et al., 2023a). Together with collaborators (Khodayari Moez et al., 2023), GEM is now developing a protein-based tool that can inform both the eligibility criteria for lung cancer screening and the management of nodules detected on LDCT screening (Figure 5).

Figure 5. A custom protein panel for assessment of lung cancer risk and management of nodules detected on low-dose computed tomography (LDCT) screening. (left) Reproduced from Lung Cancer Cohort Consortium (LC3) (2023). © Springer Nature. (right) Reproduced from Khodayari Moez et al. (2023), by permission of Oxford University Press.



For several years, GEM has organized research aiming to develop early biomarkers of human papillomavirus (HPV)-associated cancers. A seminal observation was a study in 2013 that observed frequent blood positivity for antibodies against the HPV16 E6 oncoprotein, several years before diagnosis of oropharyngeal cancer. The study also determined that this biomarker is rarely seen in healthy controls, opening up the possibility of using it as an early detection tool for HPV-associated cancer. This work stimulated the initiation of the HPV Cancer Cohort Consortium (HPVC3), which involves many population cohorts from around the world. One important question was to quantify the risk of oropharyngeal cancer that an individual would have after a positive HPV16 E6 blood test; a GEM study based on HPVC3 estimated the 10-year risk of oropharyngeal cancer in an HPV16 E6-seropositive individual at age 60 years to be 27.1% in men and 5.5% in women (Robbins et al., 2022a). This high level of risk may warrant periodic, minimally invasive surveillance after a positive HPV16 E6 serology test, particularly for men in high-incidence regions. However, an appropriate clinical protocol for surveillance remains to be established.

Bladder cancer is the 10th most common cancer type worldwide, and no urinary test has demonstrated sufficient performance to be useful for early detection purposes. Somatic mutations in the promoter of the telomerase reverse transcriptase (*TERT*) gene are common in urothelial cancer, and previous GEM research has demonstrated that it is possible to detect such mutations (TERTpm) in urine. Therefore, GEM scientists have developed a sensitive assay (uTERTpm) based on droplet digital PCR (ddPCR) with the view to use it as a non-invasive biomarker for early detection and monitoring of bladder cancer. The protocol for this ddPCR assay was recently published with step-by-step instructions for use in *TERT* mutation screening, including recommendations for sample preparation (Zvereva et al., 2023). GEM recently evaluated the ddPCR-based uTERTpm assay in a high-risk population in Kerman Province in the Islamic Republic of Iran, where bladder cancer is the most common cancer type in men (Pakmanesh et al., 2022). The uTERTpm assay detected 100% of primary bladder cancers, with a low false-positivity rate (12%) based on control subjects. The test was less sensitive (50%) for recurrent bladder cancer. Overall, this study shows promise for using the ddPCR uTERTpm assay as a non-invasive urinary marker of bladder cancer.

Area 4: Building global capacity for cancer science

GEM has made significant strides in promoting international collaboration in cancer research by addressing key challenges posed by data sharing and protection laws, such as the General Data Protection Regulation (GDPR). With the prime objective of ensuring enhanced access to harmonized genetic and epidemiological data for cancer studies, GEM supported the successful launch of the IARC Scientific IT platform in close collaboration with the Information Technology Services (ITS) team and the DAF Office. This centralized platform securely manages and stores data and enables remote data access without the need to transfer individual-level data. This approach not only streamlines data sharing but also aligns with the stringent data protection standards set by international laws.

Crucially, the project established an efficient administrative framework to manage data access requests. It leveraged existing consortium protocols and introduced a Data Use Agreement, thereby simplifying data sharing processes. Critical consortium studies have been integrated into the platform, including the European Prospective Investigation into Cancer and Nutrition (EPIC), the Lung Cancer Cohort Consortium (LC3), and the International Lymphoma Epidemiology Consortium (InterLymph). The success of this endeavour will undoubtedly fast-track global cancer research collaborations in the future and has also demonstrated a potential model for other scientific research networks.

The importance of data integration and sharing is exacerbated for the study of rare cancers. The ground-breaking efforts of the Rare Cancers Genomics Team (RCG) with the MESOMICS project underscore this principle. By meticulously integrating the largest whole-genome sequencing data set for malignant pleural mesothelioma with previous multi-omics studies (Mangiante et al., 2023), RCG has created an unparalleled resource. This endeavour does not stop at data sharing; by making the data accessible via the TumorMap web portal, RCG ensures interactive visualization and hypothesis generation without the need for intricate computational expertise (Di Genova et al., 2022). By democratizing access to high-quality data sets, ensuring reproducibility through shared bioinformatics pipelines (https://github.com/IARCbioinfo), and providing intuitive visualization tools, RCG is setting new benchmarks in advancing the collective knowledge of rare cancers.

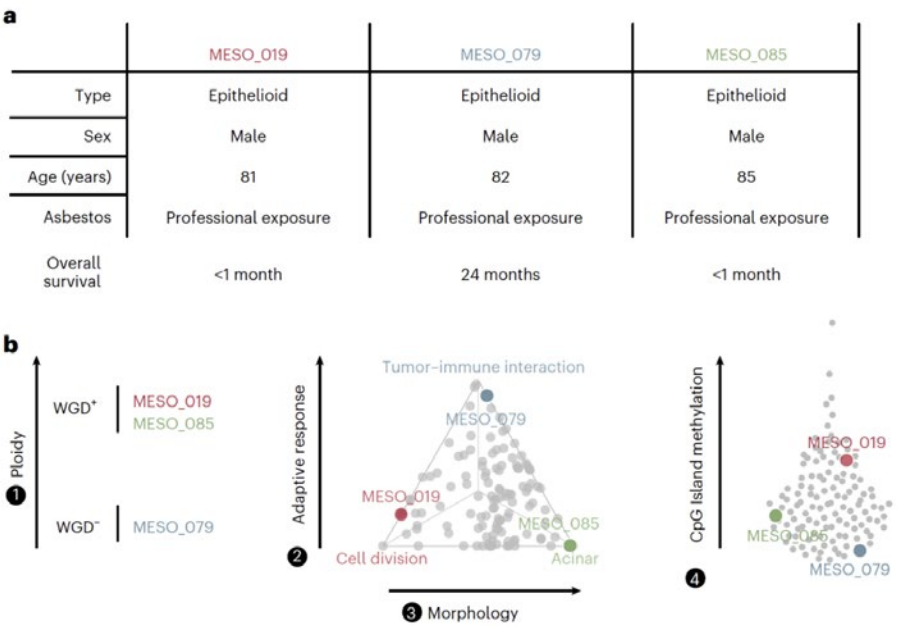
Large-scale biorepositories and databases are essential to generate equitable, effective, and sustainable advances in cancer prevention, early detection, and surveillance. The Mutographs project has created a large genomic data set and biorepository of more than 7800 cancer cases from 30 countries across five continents with extensive demographic, lifestyle, environmental, and clinical information. This collection has resulted in more than 85 000 biological samples currently stored in the IARC Biobank. Whole-genome sequencing data are being generated for nearly 4400 cancer cases.

Area 5: Somatic cancer genomics

The Rare Cancers Genomics Team (RCG) aims at the molecular characterization of rare cancers (https://rarecancersgenomics.com/; https://www.iarc.who.int/teams-rcg/), including malignant pleural mesothelioma (MESOMICS) and lung neuroendocrine neoplasms (lungNENomics). For MESOMICS, RCG has lifted the curtain on molecular differences between malignant pleural mesotheliomas (Figure 6) through the identification of molecular axes and specialized tumour profiles driving the intertumour heterogeneity (Mangiante et al., 2023). RCG has also generated a molecular phenotypic map of this disease (Di Genova et al., 2022). For lungNENomics, RCG has worked on developing a new anomaly-detection deep-learning algorithm, HaloAE, to identify patterns in images that could help to discriminate regions for tumour proliferation or aggressiveness.

RCG has also contributed to review the current biological and clinical knowledge on lung neuroendocrine neoplasms (Fernandez-Cuesta et al., 2023), to unveil that changes in *OTP* gene DNA methylation are responsible for its differential expression in lung neuroendocrine tumours (Moonen et al., 2022), and to better understand the mechanisms

Figure 6. The utility of a four-criteria classification of mesothelioma. (a) Three patients with mesothelioma (identified as MESO_019, MESO_079, and MESO_085) had similar clinical characteristics yet different outcomes. (b) The three patients have vastly different tumour profiles based on the four-criteria classification. Arrows are directed from low to high values for each criterion (e.g. from ploidy of 1 to ploidy of 4), and grey dots represent mesothelioma tumours. WGD, whole-genome doubling (ploidy > 2). Reproduced from Mangiante et al. (2023). © Mangiante et al., 2023. Published by Springer Nature.



behind the transformation of epidermal growth factor receptor *(EGFR)*-mutant lung adenocarcinomas into small-cell lung cancers (Mc Leer et al., 2022). RCG's contribution has also recently expanded to developing mathematical models for cancer evolution (Alcala and Rosenberg, 2022; Morrison et al., 2022).

RCG's projects have a strong computational biology component, particularly for the analysis and integration of –omics data (whole-genome and transcriptome sequencing, methylation arrays, single-cell and spatial transcriptomics data), the interpretation of histopathological images with deep-learning algorithms, and the modelling of cancer evolutionary processes. RCG actively shares these tools as open-source packages (https://github.com/IARCbioinfo), ultimately building capacity for cancer genomics (https://rarecancersgenomics.com/datasets/) and strongly contributing to research in Area 4.

Area 6: Understanding variations in cancer incidence and survival in diverse populations

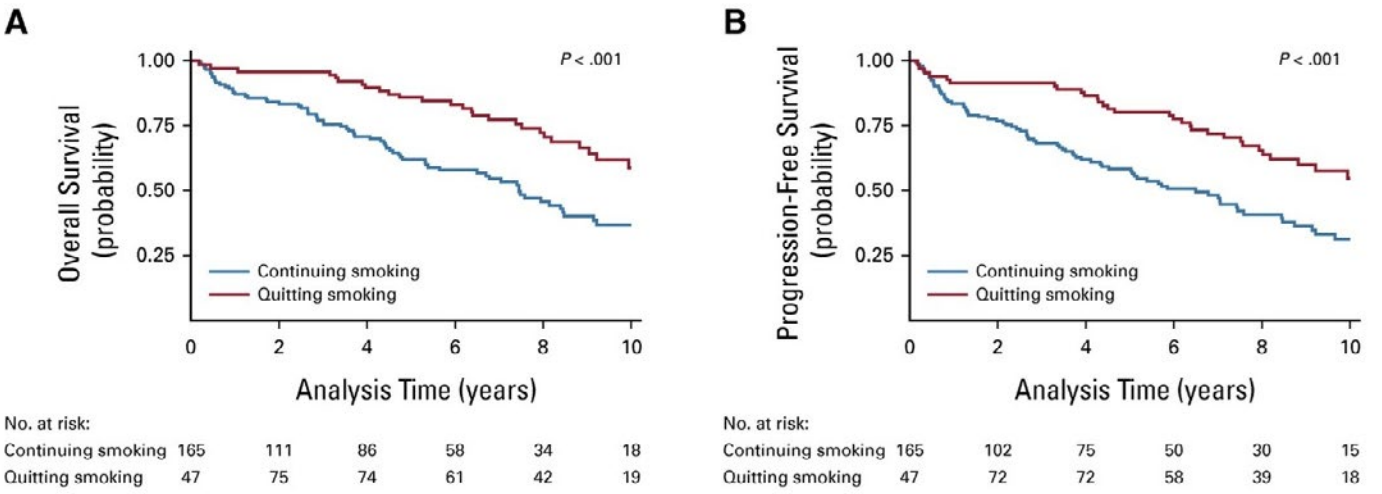
Two GEM initiatives are assessing variations in cancer incidence. The Opioid Cohort Consortium (OPICO) study is generating a single database with detailed individual-level information on opioid use, cancer incidence, and confounders, as well as exploring Mendelian randomization methods, to evaluate the association between regular opioid use and cancer incidence and mortality (Sheikh et al., 2023a). The Latin American Study of Hereditary Breast and Ovarian Cancer (LACAM) has started to describe how both germline pathogenic variants and modifiable lifestyle risk factors influence the risk of breast cancer and ovarian cancer (Díaz-Velásquez et al., 2023) in high-risk individuals in six countries in Latin America.

Additional studies between GEM and external collaborators show the effect of modifiable risk factors on cancer survival. GEM and collaborators from nine centres in the Russian Federation, Poland, Serbia, Czechia, and Romania concluded a survival analysis of 2052 patients with stage I–IIIA non-small cell lung cancer diagnosed and followed up in 2007–2016 (Sheikh et al., 2023b). The results revealed an overall 5-year survival rate of 50%. In patients from central and eastern Europe, higher risk of death and disease progression was observed in individuals with higher-stage tumours (hazard ratio [HR] for stage IIIA vs stage I, 5.54; 95% confidence interval [CI], 4.10–7.48), those who were current smokers (HR, 1.30; 95% CI, 1.04–1.62), and those who were alcohol drinkers (HR, 1.22; 95% CI, 1.03–1.44).

Another study, in collaboration with the N.N. Blokhin National Medical Research Center of Oncology (Russian Federation), recruited 212 patients with primary renal cell carcinoma in 2007–2016 and showed that quitting smoking after diagnosis of renal cell carcinoma may significantly improve survival (HR, 0.51; 95% CI, 0.31–0.85) and reduce the risk of disease progression (HR, 0.45; 95% CI, 0.29–0.71) and of cancer mortality (HR, 0.54; 95% CI, 0.31–0.93) in patients who smoke (Sheikh et al., 2023c) (Figure 7).

Two other projects are exploring variations in survival in diverse populations. The Translational Studies of Head and Neck Cancer in South America and Europe (HEADSpAcE) study is investigating the causes of late-stage diagnosis and the effect on survival of head and neck cancer cases in Europe and South America. The uTERTpm study is evaluating the use of non-invasive biomarkers for monitoring of bladder cancer recurrence.

Figure 7. Extended Kaplan–Meier curves illustrating the probability of (A) overall survival and (B) progression-free survival among smoker patients with renal cell carcinoma during the quitting smoking versus continuing smoking periods. Quitting smoking after diagnosis of renal cell carcinoma may significantly improve survival (hazard ratio [HR], 0.51; 95% confidence interval [CI], 0.31–0.85) and reduce the risk of disease progression (HR, 0.45; 95% CI, 0.29–0.71) and of cancer mortality (HR, 0.54; 95% CI, 0.31–0.93) in patients who smoke. Reproduced from Sheikh et al. (2023c). © 2023 by the American Society of Clinical Oncology.



PROMINENT: Discovering the molecular signatures of cancer PROMotion to INform prevENTion

In 2022, GEM received a Cancer Grand Challenges award from Cancer Research UK and the United States National Cancer Institute for the PROMINENT project. This project is co-led by GEM in collaboration with the Nutrition and Metabolism Branch (NME), along with 10 other partners in five countries (France, the United Kingdom, the USA, Spain, and Sweden). PROMINENT brings together a diverse team of experts who will use advanced high-throughput genomic, proteomic, and functional methods to uncover the main factors and processes that drive the transformation of normal cells into cancer cells.

This project builds on a unique collection of several thousand human samples – both normal and matched tumour samples – collected from more than 20 countries and stored in the IARC Biobank. These samples come from regions with varying levels of cancer risk, and detailed exposure information is available. Analysis of these samples, together with intervention studies in human populations, mouse models, and human organoids, will enable the development of a roadmap of tumour promotion, from individual normal cells with driver mutations all the way to full malignant progression.

PROMINENT team leads and members at the announcement of the awarded Cancer Grand Challenges teams at the 2022 Cancer Grand Challenges Summit in Washington DC, USA. © IARC.

Nutrition and Metabolism Branch (NME)

Branch head
Dr Marc Gunter (until January 2023)
Dr Pietro Ferrari (acting)

Deputy branch heads
Dr Mazda Jenab
Dr Sabina Rinaldi

Scientists
Dr Laure Dossus
Dr Heinz Freisling
Dr Inge Huybrechts
Dr Pekka Keski-Rahkonen
Dr Neil Murphy
Dr Augustin Scalbert (until July 2022)
Dr Vivian Viallon

Senior visiting scientists
Dr Marc Gunter
Dr Elio Riboli (until September 2022)
Dr Guri Skeie

Visiting scientists
Dr Kristin Benjaminsen-Borch (until June 2022)
Dr Sheila Coelho Soares Lima (until June 2022)
Dr Elodie Faure
Dr Agnès Fournier
Dr Mohamed Khalis
Dr Tomohiro Matsuda
Dr Norie Sawada

Research assistants
Dr David Achaintre (until June 2022)
Ms Carine Biessy
Ms Corinne Casagrande (until March 2023)
Mr Bertrand Hémon
Ms Vanessa Neveu
Ms Geneviève Nicolas
Ms Nivonirina Robinot
Ms Béatrice Vozar

Laboratory technicians
Ms Audrey Gicquiau (until September 2022)
Ms Anne-Sophie Navionis

Secretariat
Ms Sally Moldan (until February 2023)
Ms Karine Racinoux
Ms Sarah Sherwood
Ms Tracy Wootton
Ms Karina Zaluski

Postdoctoral fellows
Dr Adam Amara (until December 2022)
Dr Jessica Blanco Lopez
Dr Felix Boekstegers
Dr Manon Cairat (until July 2022)
Dr Chrysovalantou Chatziioannou (until August 2023)
Dr Emeline Courtois
Dr Charlotte Debras (until September 2023)
Dr Niki Dimou
Dr Esther Gonzalez Gil
Dr Rhea Harewood
Dr Mathilde His (until December 2022)
Dr Inarie Jacobs
Dr Rola Jaafar
Dr Anna Jansana Riera
Dr Ruhina Laskar (until September 2023)
Dr Matthew Lee
Dr Azam Majidi
Dr Shiny Lizia Manohar
Dr Komodo Matta
Dr Ana-Lucia Mayen-Chacon (until September 2022)
Dr Mira Merdas
Dr Yahya Mahamat Saleh
Dr Sabine Naudin
Dr Nikolaos Papadimitriou
Dr Jodi Rattner (until June 2023)
Dr Martina Recalde (until July 2022)
Dr Sanam Shah
Dr Daniel Tolossa
Dr Sabrina Wang
Dr James Yarmolinsky (until May 2022)

Doctoral students
Ms Inmaculada Aguilero (until May 2023)
Ms Aline Al Nahas
Mr Christian Antoniussen (until August 2023)
Mr Jeroen Berden
Ms Marie Breeur
Ms Carlota Castro-Espin (until June 2023)
Mr Alberto Catalano (until June 2023)
Ms Bernadette Chimera
Ms Emma Fontvieille
Mr Quan Gan
Ms Emine Koc Camak (until November 2023)
Ms Kim Maasen (until June 2022)
Ms Alessandra Macciotta (until June 2023)
Mr Pablo Marcos Lopez (until January 2023)
Ms Maria Matias de Pinho (until July 2022)
Ms Fernanda Morales Berstein (until May 2022)
Ms Julie Neau (until November 2022)
Ms Laia Peruchet-Noray
Ms Martina Recalde (until June 2022)
Ms Fanélie Vasson
Ms Diana Wu
Ms Yuhan Zhang (until August 2023)
Ms Yadi Zheng

Trainees
Mr Loïc Abed (until July 2022)
Mr Pablo Marcos Lopez (until July 2022)
Ms Fanélie Vasson (until August 2023)
Mr Maxime Vincent (until March 2022)
Mr Wendyam Yameogo (until August 2023)
Ms Julie Neau (until August 2022)

The Nutrition and Metabolism Branch (NME) places a strong emphasis on the implementation and coordination of epidemiological studies on cancer to identify causal relationships between nutrition, metabolism, and cancer and inform on cancer prevention. The activities of NME largely focus on three major research themes: (i) understanding the role of obesity and metabolic dysfunction in cancer development; (ii) research on the role of diet and lifestyle factors in cancer, including identification of biomarkers of diet and nutrition and their application within studies of cancer etiology; and (iii) multimorbidity and biological pathways common to cancer, diabetes, and cardiovascular diseases.

Research in NME aims to exploit methodological advances in molecular profiling techniques, epidemiology, and biostatistics to implement an integrated, multidisciplinary programme of research. Given the potential for advances in molecular profiling to help overcome methodological challenges in nutrition and cancer research and to discover the underlying biological pathways, emphasis has been placed on conducting molecular epidemiological research that integrates –omics data (see the text box), including metabolomics, hormone measurements, and genomics, within population-based cohorts and intervention studies. In addition to NME's work within established cohorts such as the European Prospective Investigation into Cancer and Nutrition (EPIC) and the UK Biobank and across cohort consortia, NME has devoted considerable resources to the development of studies in low- and middle-income countries, such as South Africa and Morocco, and in Latin America where, because of the epidemiological transition, cancers linked to diet and lifestyle are increasing in incidence. Over the past 5 years, NME scientists have also initiated small-scale intervention studies, primarily focused on biomarker discovery or to understand mechanisms linking obesity, diet, and cancer.

NME's studies are inherently multidisciplinary and typically involve collaborations with multiple partners. Significant cancer research activities from the six NME teams are reported here.

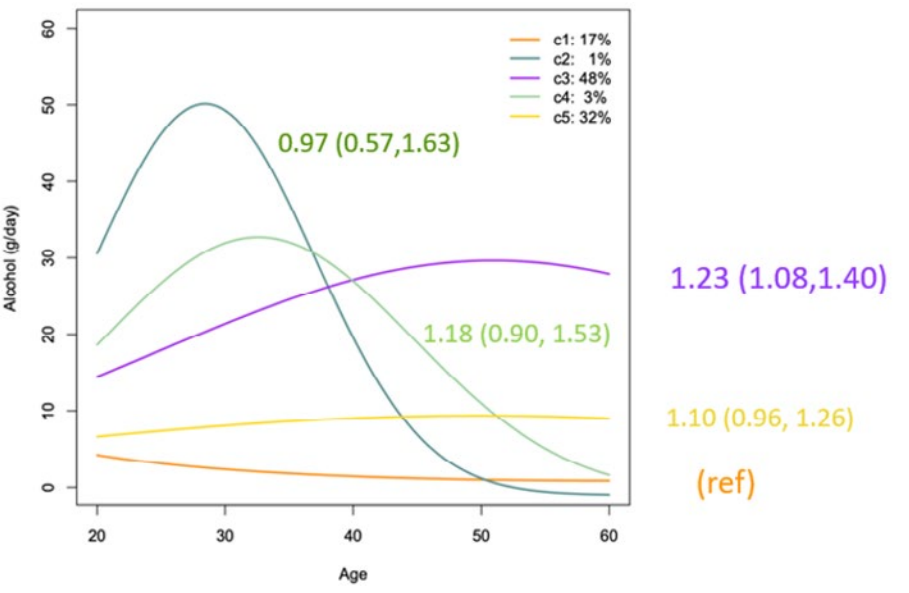
Biostatistics and Data Integration Team (BDI)

Data are at the core of cancer epidemiology, and tasks related to (i) data management, including data centralization, harmonization, and dissemination, and (ii) application of cutting-edge statistical methods are essential. During the 2022–2023 biennium, BDI continued the centralization and harmonization of laboratory data acquired within EPIC. BDI was in charge of the dissemination of EPIC data and data available in recently funded large-scale projects, such as Discovering the Causes of Three Poorly Understood Cancers in Europe (DISCERN) and PROMINENT: Discovering the molecular signatures of cancer PROMotion to INform prevENTion, co-led by the Genomic Epidemiology Branch (GEM). In line with recommendations for international data protection regulations, data dissemination and analysis have been seamlessly conducted via the IARC Scientific IT platform, which was developed by the Information Technology Services (ITS) team to follow the Open Science principle that data should be "as open as possible and as closed as necessary".

Methodological developments were conducted to assess and improve the performance of several statistical methods, including extensions of the lasso and dimension-reduction techniques, which are valuable for the analysis of –omics data in cancer epidemiology (Etiévant and Viallon, 2022a; Ballout et al., 2023). A data-shared lasso analysis of pre-diagnostic metabolite concentrations measured in blood in several nested case–control studies identified nine metabolites associated with cancer risk across multiple cancer sites (Breeur et al., 2022).

Leveraging the availability of longitudinal exposure assessments within EPIC participants, a research programme was developed to investigate the impact of changes in modifiable lifestyle factors on cancer risk and mortality. Adherence to the healthy lifestyle index, a composite score based on smoking, alcohol consumption, obesity, and physical activity, was inversely associated with risk of colorectal cancer (Botteri et al., 2023), risk of lifestyle-related cancers, and all-cause mortality. Trajectory profiles of alcohol intake during early and mid-adulthood showed that consistent moderate to elevated exposures to alcohol intake throughout adulthood were associated with risk of colorectal cancer (Mayén et al., 2022) (Figure 1).

Figure 1. Trajectory profiles of alcohol intake (c1 to c5) during adulthood in men in the European Prospective Investigation into Cancer and Nutrition (EPIC), and associated estimates of colorectal cancer hazard ratio (95% confidence interval). Reproduced from Mayén et al. (2022), © 2022, Springer Nature.



Lifestyle Exposure and Intervention Team (LEI)

New dietary and lifestyle indicators were generated and validated in cohort studies, enabling the investigation of novel diet–cancer associations. Databases on dietary fatty acid isomers were compiled in cohort and case–control studies (Huybrechts et al., 2022). Fatty acid isomers and industrial trans fatty acids were positively associated with colorectal cancer risk in the Iran Opium and Cancer (IROPICAN) study (Seyyedsalehi et al., 2022a, 2022b) and in the NutriNet-Santé cohort (Wendeu-Foyet et al., 2023). In addition, food processing was investigated in relation with cancer risk via the NOVA classification. Results in EPIC showed inverse relationships between the consumption of fresh or minimally processed foods and overall cancer risk, whereas consumption of processed and ultra-processed foods was positively related to the risk of several cancer types (Kliemann et al., 2023).

In collaboration with scientists in the Hormones and Metabolism Team (HorM), the role of food processing in breast cancer etiology was evaluated in countries in epidemiological transition. Consumption of ultra-processed foods was positively associated with colorectal cancer risk in a study conducted in Morocco (El Kinany et al., 2022). Results from the PRECAMA study (525 case–control pairs) indicated that consumption of ultra-processed foods may be related to the risk of breast cancer in young women in Latin America (Romieu et al., 2022). Results from a study in Black women in Soweto, South Africa (the South Africa Breast Cancer [SABC] study) (396 case–control pairs) indicated that the intake of unprocessed or minimally processed foods may reduce the risk of breast cancer (Jacobs et al., 2022a). Food processing may play a role in breast cancer etiology in these populations.

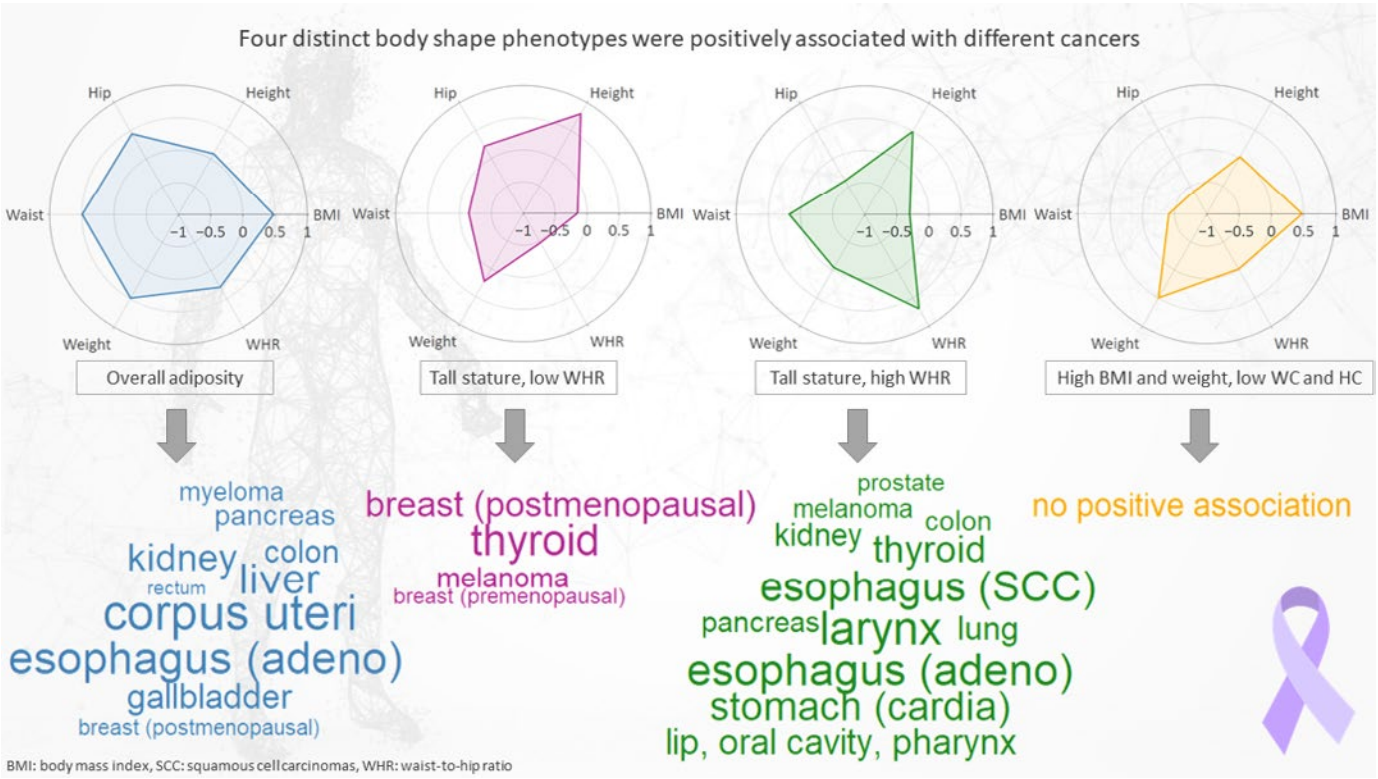
An intervention study to promote changes in lifestyle behaviours was designed within the colorectal cancer screening programme in France (ClinicalTrials.gov identifier: NCT05273931). The Lifestyle Intervention After Colonoscopy (LIFE-SCREEN) study involved 30 hospitals (15 in the control arm and 15 in the intervention arm), and 20 participants were recruited in each hospital.

Nutrition, Cancer, and Multimorbidity Team (NCM)

In a large prospective study in 2 645 885 Catalonian individuals, using the Information System for Research in Primary Care (SIDIAP) electronic health record database, body mass index (BMI) across the participants' lifetime was investigated. Anthropometric indicators, such as overweight and obesity duration, intensity, and onset age, were found to be linked with 18 cancer types, five more than previously thought. Some of the novel cancer types that were identified are leukaemia, non-Hodgkin lymphoma, and bladder cancers, particularly in people who never smoked (Recalde et al., 2023a).

To investigate the role of anthropometry in a more comprehensive way beyond BMI, a multivariate dimension-reduction technique was used to derive participants' body shapes from height, weight, BMI, waist circumference, hip circumference, and waist-to-hip ratio. Four distinct body

Figure 2. Cancer risk associations with four distinct body shape phenotypes derived in the European Prospective Investigation into Cancer and Nutrition (EPIC). Reproduced from Sedlmeier et al. (2023). © 2023, Sedlmeier et al.



shapes were identified and captured the heterogeneous distribution of adiposity compared with single anthropometric traits. In an EPIC study of 340 152 men and women from nine European countries, the four distinct body shapes were positively associated with the risk of overall cancer and 17 site-specific cancers (Sedlmeier et al., 2023) (Figure 2). Using genetic variants related to these body shapes, associations with breast cancer risk were reported (Peruchet-Noray et al., 2023). In a study of 159 045 European adults, among 1045 patients with colorectal cancer and 1620 patients with breast cancer, both cumulative BMI and cardiometabolic diseases had a direct link to survival outcomes, independently of each other (Kohls et al., 2022).

Metabolic Epidemiology Team (MET)

Studies leveraging genetic and tumour marker data were conducted to investigate associations of body size and diabetes with colorectal cancer. In a pooled observational analysis that included more than 11 000 colorectal cancer cases with tumour molecular marker data, BMI was positively associated with colorectal cancer risk for cases with Jass types 1–4 colorectal cancer but not for cases with Jass type 5 colorectal cancer (considered familial-like/Lynch syndrome) (Murphy et al., 2023) (Figure 3). The lack of association observed for Jass type 5 suggests that BMI is not a risk factor for the development of colorectal cancer for individuals with Lynch syndrome.

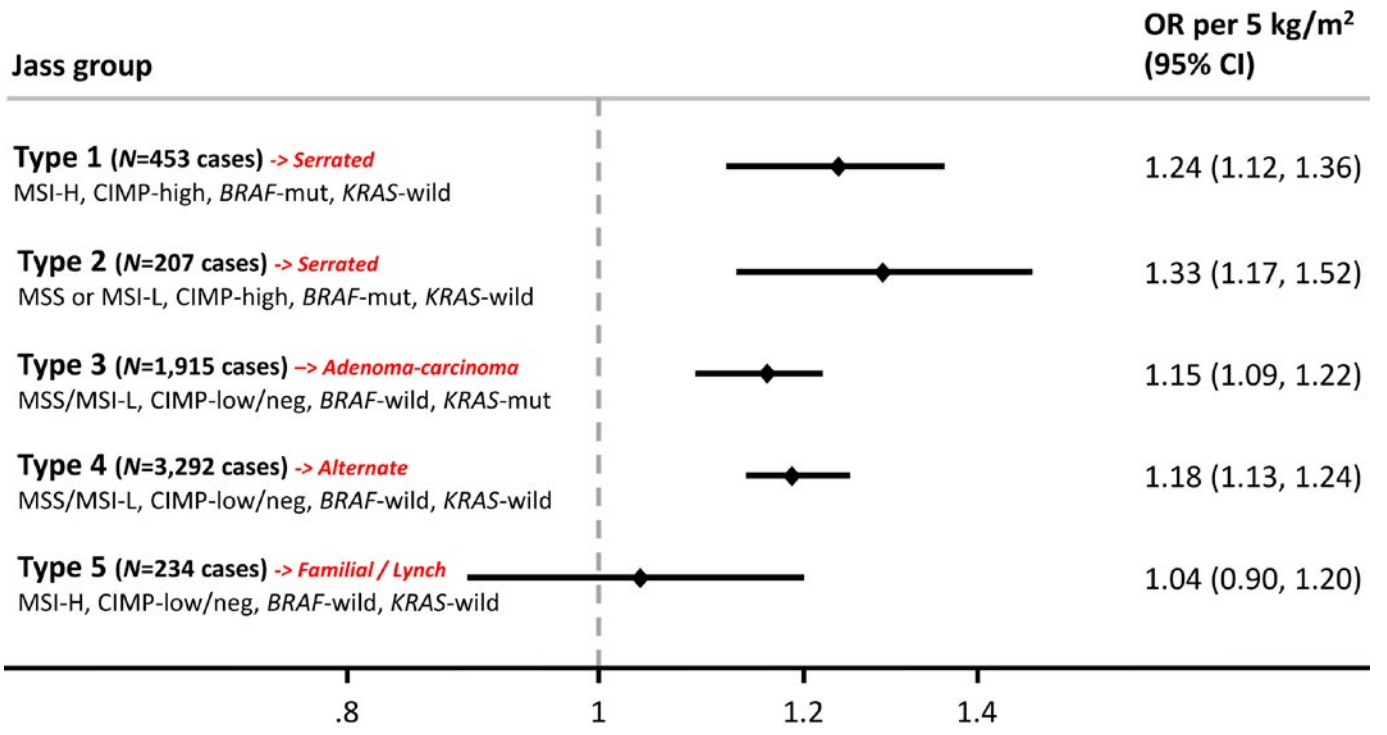
Mendelian randomization was used to separate the effects of early-life and later-life adiposity on colorectal cancer risk (Papadimitriou et al., 2023). Genetically predicted early-life body size was estimated to increase the odds of colorectal cancer. However, after accounting for adult body size using multivariable Mendelian randomization, effect estimates for early-life body size were attenuated towards the null. These findings suggest that the influence of early-life body size on colorectal cancer development is largely mediated through later-life body size.

In a genome-wide gene–environment interaction (GxE) analysis including 31 318 colorectal cancer cases and 41 499 controls, a significant interaction was found between diabetes status and the variants rs3802177 in *SLC30A8*, a gene that regulates phosphorylation of the insulin receptor and phosphatidylinositol 3-kinase (PI3K) activity, and rs9526201 in *LRCH1*, a gene that regulates T-cell migration, with colorectal cancer risk (Dimou et al., 2023). These results suggest that variation in genes related to insulin signalling and immune function may modify the relationship between diabetes and colorectal cancer.

Hormones and Metabolism Team (HorM)

The associations of inflammatory biomarkers with breast cancer risk were evaluated in the EPIC study (1600 case–control pairs) and in the Molecular Subtypes of Premenopausal Breast Cancer in Latin American Women (PRECAMA) study (453 case–control pairs). Inflammatory biomarkers were measured in the NME laboratory. In EPIC, leptin, the leptin-to-adiponectin ratio, and C-reactive protein (CRP) levels were borderline inversely associated with breast cancer risk in premenopausal women, and positively associated with risk in postmenopausal women (Cairat et al., 2022). In PRECAMA, levels of interleukin 6 (IL-6) and tumour necrosis factor alpha (TNF-α) were positively associated with breast cancer risk overall, with some

Figure 3. Observational associations between body mass index and Jass classified types and inferred pathways (in red) of colorectal cancer. CI, confidence interval; OR, odds ratio. © IARC.



evidence of heterogeneity by estrogen receptor status and according to tumour size (Fontvieille et al., 2022) (Figure 4). The findings suggested that systemic inflammation may play a modest role in breast cancer development.

Onco-Metabolomics Team (OMB)

Leveraging the acquired expertise in the high-throughput profiling of biospecimens from population-based studies within the NME laboratories, research conducted by OMB indicated that metabolic signatures expressing adherence to the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) recommendations were inversely associated with colorectal cancer in EPIC (Rothwell et al., 2022b). These results indicate the potential of metabolic profiling for risk stratification. Also, metabolic syndrome, a marker of poor metabolic health, was positively related to the risk of gastrointestinal cancers (Rothwell et al., 2022a). A metabolomics study focusing on early-life obesity, which is a candidate risk factor for several cancer types, examined the mediating role of metabolites measured in cord blood between different prenatal exposures and postnatal growth and propensity towards childhood overweight (Alfano et al., 2022). The results suggested a mediating role of cholestenone, a microbial catabolite of cholesterol, in the relationship between maternal exposures and postnatal growth.

Higher total blood concentrations of bile acids, particularly taurine- and choline-conjugated bile acids, were positively linked to risk of hepatocellular carcinoma in a nested case–control study in EPIC, indicating a role of bile acid metabolism and liver function in this cancer type (Stepien et al., 2022).

In a study of the metabolic impacts of metformin treatment versus placebo in 373 randomized breast cancer survivors who were overweight or obese (Bellerba et al., 2022), metformin increased levels of branched chain amino acids, proline, 3-methyl-2-oxovalerate, 4-methyl-2-oxovalerate, alanine, and indoxyl sulfate, and reduced levels of long-chain unsaturated phosphatidylcholines, among others (Bellerba et al., 2022) (Figure 5). OMB scientists wrote a review on the role of the gut microbiome and microbiome-derived metabolites in hepatobiliary cancer development.

Figure 4. Associations between inflammatory biomarkers and breast cancer, by estrogen receptor (ER) status and in triple-negative (TN) tumours. Odds ratios (ORs) are per standard deviation (SD) increase in log-transformed biomarker concentration. P-homogeneity ER compares ER-negative and ER-positive tumours. P-homogeneity TN compares TN and non-TN tumours. CI, confidence interval; IFN, interferon; IL, interleukin; TNF, tumour necrosis factor. Reproduced from Fontvieille et al. (2022). © 2022, Fontvieille et al.

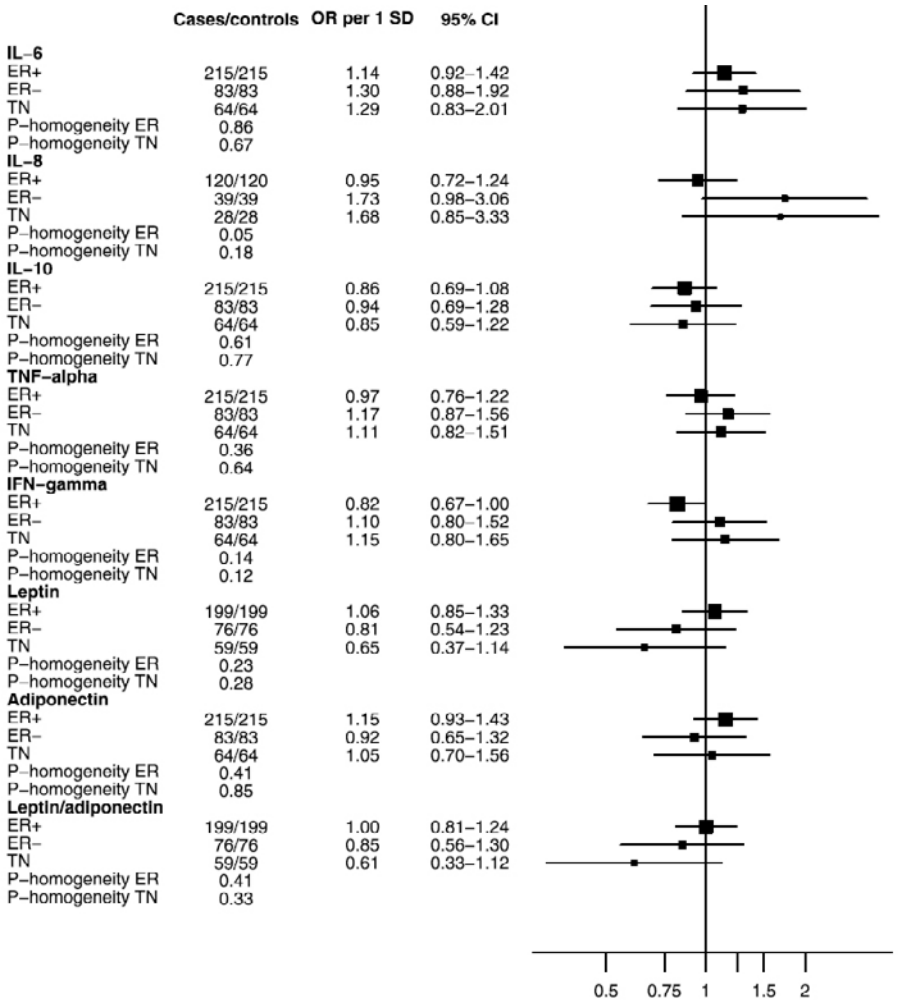
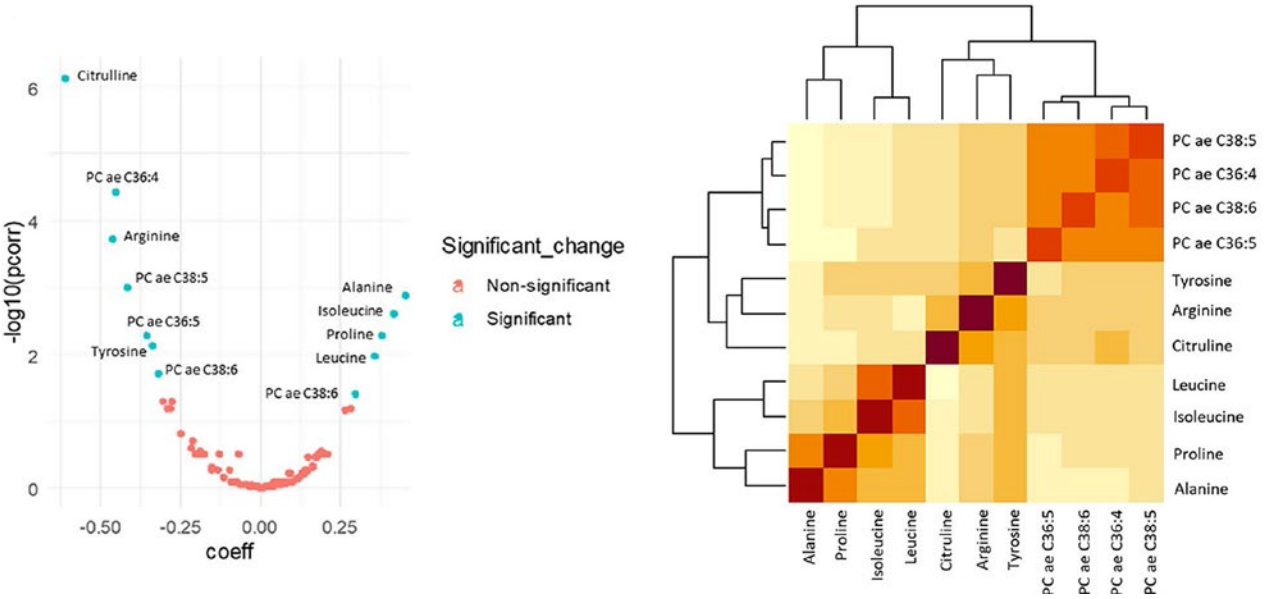
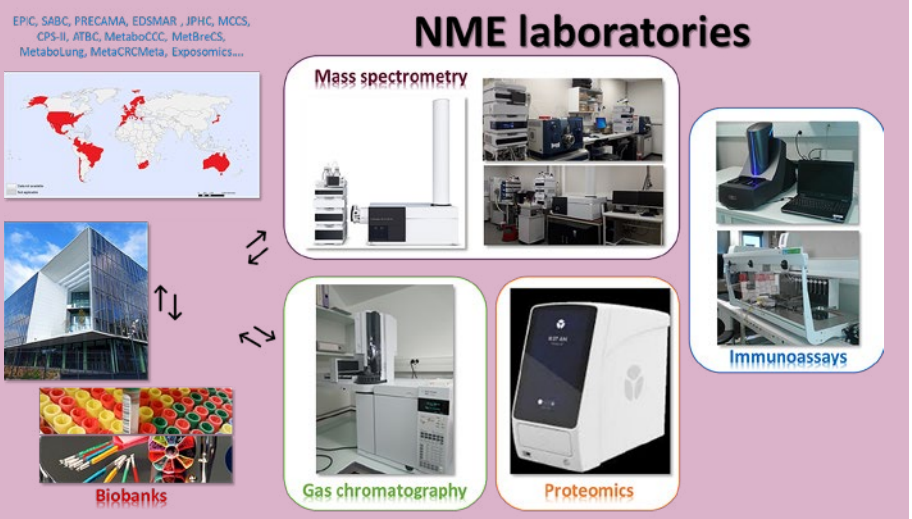


Figure 5. A volcano plot (left) and a heatmap (right) showing changes in plasma metabolite concentrations after metformin treatment in breast cancer survivors who were overweight or obese (Biocrates AbsoluteIDQ p180 targeted metabolomics; *n* = 194 metformin, *n* = 197 placebo). The volcano plot shows the beta regression coefficients of the treatment effect on the horizontal axis and the $-\log_{10}$(false-discovery rate [FDR]-corrected *P* values) on the vertical axis. PC, phosphatidylcholine. Reproduced from Bellerba et al. (2022). © 2022, Bellerba et al.



NME laboratory activities

The laboratories of NME have been set up to suit the needs of epidemiological studies. Analytical methods have been specifically developed to be applicable to large series of samples, to be fast, and to need low sample volume, because the quantity of samples in biobanks is often limited. This specificity of NME laboratories has enabled the Branch to work with many collaborators and projects worldwide. © IARC. Building: © Kevin Buy.



Over the past few years, the NME laboratories have made relevant investments in methodology and technological capabilities. As a result, state-of-the-art biochemical profiling techniques were effectively applied to a large number of biological samples collected in cohort, case–control, and intervention studies. The NME laboratories are equipped with cutting-edge technology analytical instruments, including four liquid chromatography-mass spectrometry systems (SCIEX QTRAP 5500, Triple Quadrupole 4500, Agilent Q-TOF 6550, and Thermo Q Exactive), all coupled to ultra-high-performance liquid chromatographs, a multiplexing electrochemiluminescence reader (Meso Scale Discovery), two gas chromatographs with flame ionization detectors (FID) (Agilent), and, very recently, the Signature Q100 machine from Olink for targeted proteomics. Automated liquid handling systems are also available to speed up sample preparation for applications to large-scale projects. Major applications include untargeted and targeted (Biocrates AbsoluteIDQ p180 kit) metabolomics, analyses of hormones (including sex steroids), biomarkers of inflammation, fatty acids, and polyphenols. Plasma, serum, and urine samples were mainly analysed. During the 2022–2023 biennium, this technology was used to analyse about 20 000 biospecimens, originating from more than 20 different countries, and created invaluable opportunities for scientific collaborations with several local and international partners.

Laboratory Support, Biobanking, and Services (LSB)

Group head
Dr Zisis Kozlakidis

Secretary
Ms Tracy Wootton

Biobank process management assistant
Dr Elodie Caboux

Laboratory services management assistant
Dr Stéphanie Villar

Senior biobank technician
Mr Christophe Lallemand

Biobank technicians
Ms Elodie Colney
Mr Henri Cordier
Ms Sophie Guillot
Ms Gertrude Tchoua

Students and visiting scientists
Mr Anis Abboute (until August 2023)
Ms Ruzica Biga (until July 2022)
Professor Io Hong Cheong (until May 2023)
Ms Mbayame Diop (until July 2022)
Ms Julie Grataloup (until September 2022)
Dr Kouamé Kintossou (until July 2023)
Ms Estelle Morel (until July 2023)
Ms Sandra Nanyonga (until September 2023)
Mr Jiaao Yu

Laboratory Support, Biobanking, and Services (LSB) (Figure 1) works with the IARC Administrative Services Office (ASO) and research Branches to provide core laboratory and biobanking services to support the Agency's research activities. LSB's technical and safety advice was crucial for the design, installation, and restarting of the laboratories and the IARC Biobank at the new IARC headquarters building. LSB also leads national and international research projects on biobanking and medical research infrastructure, in alignment with the IARC Medium-Term Strategy 2021–2025.

Figure 1. Laboratory Support, Biobanking, and Services (LSB) team photo. © IARC.

Laboratory services

LSB ensures that optimal laboratory services are available, including a laboratory store that provides consumables, glass-washing facilities, mycoplasma testing and quarantine for cell cultures, pipette checking, and the freezing and/or retrieval of cell lines in liquid nitrogen gas. In conjunction with the Laboratory Steering Committee (LSC), LSB oversees the common laboratory platforms and ensures that equipment is well maintained. Interaction between laboratory-based and epidemiological research is enhanced through the upgrading, updating, and acquisition of state-of-the-art scientific instruments and the provision of sample storage capacity.

Health and safety

Health and safety issues are managed in collaboration with the Occupational Health and Safety Committee (OHSC). The IARC safety manual, a key document, is now available online; it has been regularly updated and is aligned with the latest national and international guidelines. A new safety manual is being developed for the new IARC building, describing the role of personnel and services involved in safety and security at IARC, access conditions, emergency procedures, and medical services, as well as laboratory safety, including IARC general safety guidelines in the laboratories and emergency procedures in case of an accident or incident in the laboratories. Other information on personal and collective protection guidelines, management of equipment, laboratory services offered, good laboratory practice, and biological and chemical risks, including risks related to the handling of carcinogens, liquid nitrogen, and laboratory waste, will be available in a separate document.

IARC authorizations for the restricted use of genetically modified organisms (GMOs) are handled by LSB. Radionuclide experimentation has ceased entirely, and the relevant authorizations have not been renewed; the old site was successfully validated as cleared by the relevant authorities before the handover. LSB initiated the declaration of the biological collections stored at IARC and the authorization to import and/or export biological samples in accordance with CODECOH rules and constraints provided by the French Ministry of Higher Education and Research. The authorizations to import and export are valid for 5 years. Furthermore, LSB is an active participant in the working group for the dematerialization of the import and export authorization procedure, by invitation of the French government.

During the 2022–2023 biennium, LSB provided 91 safety briefings for newcomers until the move to the new IARC building, 17 training sessions for newcomers working in laboratories, and four theoretical trainings and three practical trainings of 47 people to ensure the transfer of the liquid nitrogen tanks. LSB gave several presentations and a training session on laboratory safety during the Twinning for the Armenian Research Infrastructure on Cancer Research (ARICE) project conference and training workshop in Armenia. LSB made more than six online presentations to more than 100 laboratory personnel in total, covering new guidelines linked to COVID-19 constraints, working with liquid nitrogen, working with carcinogens, working in the L3 or L2+ laboratories, and completing the Electronic Laboratory Notebook. LSB also published a report on biosafety, specifically on the immunological considerations for laboratory staff and COVID-19 biosafety (Kintossou et al., 2023).

Biobank services

The IARC Biobank maintains biological sample collections from international studies and operates a service platform for sample retrieval, inventory, aliquoting, DNA extraction and quantification, and reception or shipment of biological material worldwide.

The IARC sample management database (SAMI) stores information on more than 6 million biological specimens. During the biennium, information on more than 423 000 new samples was imported into SAMI, as a result of a huge effort made by all IARC groups before the move to the new IARC building, and more than 150 000 samples were accessed for collaborators. SAMI is continuously being upgraded; version 2.0 was launched in 2020 and was fully integrated operationally during the 2022–2023 biennium. In addition, the information from older samples is being updated and incorporated into the database.

The new sample disposal policy was implemented, and requests by scientists for the disposal of 68 defunct collections were serviced in 11 batches (totalling more than 100 000 samples). During the 2022–2023 biennium, 86 Material Transfer Agreements for incoming and outgoing samples were technically validated. LSB supervised the replacement of obsolete equipment and the purchase of new units to increase cold storage capacity to meet future needs as well as provide adequate back-up facilities. A new freezer-temperature monitoring system, which had already been validated, was installed on all cold storage equipment, and the remote, real-time temperature monitoring system was fully implemented within the new IARC building.

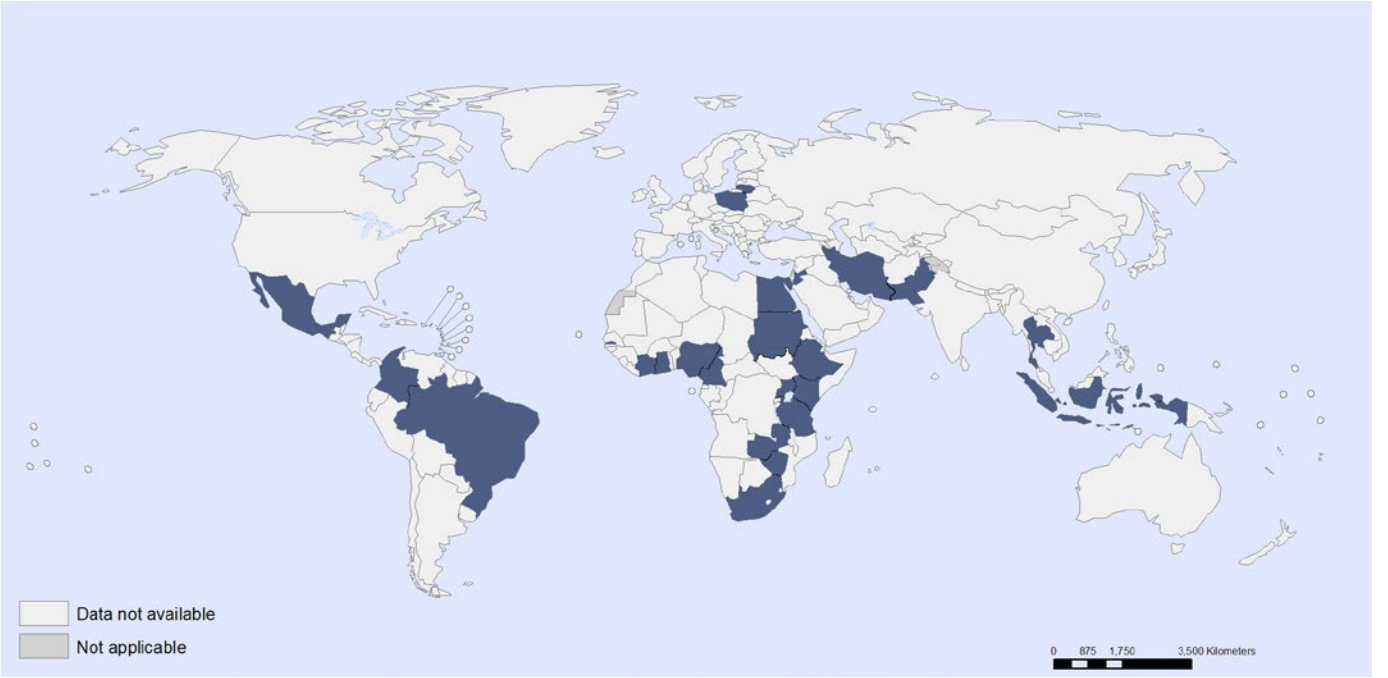
The Biobank continues to provide pre-analytical services, charging collaborators only the consumables costs incurred. During the 2022–2023 biennium, 20 projects were serviced, all of which related to requests from international institutions. This resulted in more than 33 000 sample retrievals from liquid nitrogen, 3043 DNA extractions, 5106 DNA aliquots, 23 300 plasma and serum aliquots, and 123 receptions and 111 shipments of samples from or to 48 countries worldwide. The Biobank inventoried more than 123 000 individual samples and provided support across the continuum, from reception to data upload into SAMI.

The Biobank continues to participate in international proficiency testing schemes, and after the move to the new IARC building, the new facilities have applied for the IBiSA accreditation programme (to be initiated in 2024).

BCNet

LSB participates in several research programmes, in line with IARC's mission of cancer research for cancer prevention. To address the underrepresentation of biological resources in low- and middle-income countries (LMICs) in research, the LMICs Biobank and Cohort Building Network (BCNet; https://bcnet.iarc.who.int/) was established

Figure 2. Map of BCNet member countries, July 2023. © IARC.



by IARC in 2013. Currently, 46 institutions in 24 countries are members of BCNet (Figure 2). During the 2022–2023 biennium, BCNet delivered seven presentations to external collaborators (in Egypt, Germany, Guatemala, Indonesia, Malaysia, the Philippines, and the United Republic of Tanzania) and published several seminal articles (Ezzat et al., 2022; Kozlakidis et al., 2022a; Ngwa et al., 2022; Simeon-Dubach and Kozlakidis, 2022). Collaborations continue, with a particular focus on South-East Asia (Association of Southeast Asian Nations [ASEAN] Member States) and countries in sub-Saharan Africa.

BCNet direct funding is provided by the Center for Global Health, National Cancer Institute, National Institutes of Health, USA. LSB gratefully acknowledges all the members of BCNet and their active discussions and exchanges, which have enriched our scientific world as well as our contextual understanding of global research.

Collaborations

With regard to infrastructure research, LSB represents IARC at the International Organization for Standardization (ISO; https://www.iso.org/), at the Biobanking and BioMolecular resources Research Infrastructure–European Research Infrastructure Consortium (BBMRI-ERIC; https://www.bbmri-eric.eu/) (Figure 3), and at the European Open Science Cloud (EOSC). LSB participated in infrastructure research from the perspective of operational readiness and responsiveness (Aisyah et al., 2022a, 2022b; Al Knawy et al., 2022, 2023; Casati et al., 2022; Shirakashi et al., 2022). LSB also contributed to the development of further recommendations and guidelines (Kozlakidis, 2023a, 2023b; Kozlakidis et al, 2022b; Matharoo-Ball et al., 2022; Medina et al., 2022), with a particular emphasis on data sharing and artificial intelligence (Aisyah et al., 2023; Kozlakidis and Struelens, 2022; Schmid et al., 2023).

Figure 3. The Biobanking and BioMolecular resources Research Infrastructure–European Research Infrastructure Consortium (BBMRI-ERIC), together with IARC, launched canSERV, a European Union-funded project under the Horizon Europe programme that provides cutting-edge, interdisciplinary, and customized oncology services across the entire cancer continuum. © canSERV.eu.

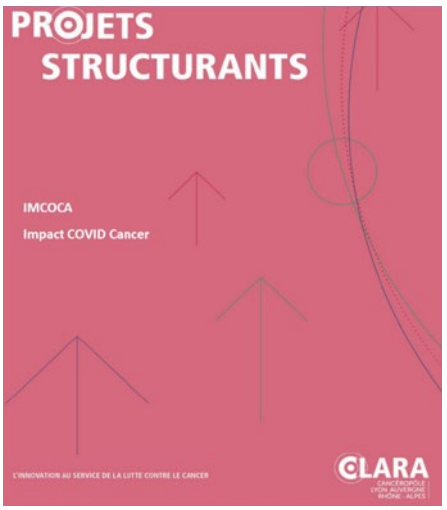
Furthermore, LSB is leading the WHO Academy course on "Managing Research Infrastructures", expected to be completed in early 2024. As part of the EOSC "Upskilling Countries" Task Force, LSB has contributed to the recommendations on digital health research (to be published in early 2024). Dr Kozlakidis has also edited a book titled *Digitisation of Healthcare in Low- and Middle-Income Countries*, which contains contributions by several LSB staff members, to be published in early 2024 by Springer Nature.

During the 2022–2023 biennium, LSB investigated the impact of the COVID-19 pandemic on infrastructures and patients with cancer (Bogaert et al., 2022, 2023). This research will continue as part of the regional project "Impact of COVID-19 on Cancer" (IMCOCA), a *Projet Structurant* funded by Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA; https://www.canceropole-clara.com/), awarded jointly to Centre Léon Bérard (CLB; https://www.centreleonberard.fr/en) and LSB (Figure 4). Further work on the impact of COVID-19 has been published in a series of eight publications in a

collaboration with Loma Linda University and Patton State Hospital, USA (Sfera et al., 2022a, 2022b, 2023a, 2023b).

LSB participates in projects funded by the European Commission: the Human Exposome Assessment Platform (HEAP) project (grant no. 874662) (https://heap-exposome.eu/), the ARICE project (grant no. 952417) (https://www.arice.am/), the Providing Cutting-Edge Cancer Research Services Across Europe (canSERV) project (grant no. 101058620) (https://www.canserv.eu/), and the European Union COST Action INTercEption of oRal CancEr develoPmenT (INTERCEPT; https://www.cost.eu/actions/CA21140/) (grant no. CA21140). Further ad hoc funding is provided by BBMRI-ERIC for the European Paediatric Translational Research Infrastructure (EPTRI; https://eptri.eu/) and the Center of Excellence in Biobanking and Biomedical Research at the University of Cyprus (https://biobank.cy/).

Figure 4. The "Impact of COVID-19 on Cancer" (IMCOCA) *Projet Structurant* is funded by Cancéropôle Lyon Auvergne Rhône-Alpes (CLARA) and was awarded jointly to Centre Léon Bérard (CLB) and LSB. Courtesy of CLARA.




Latin America and the Caribbean
Code Against Cancer
Main risk factors and cancer prevention actions
recommended at each life stage
Infancy
age 0
to 5 years
Childhood
age 6
to 11 years
Adolescence
age 12
to 18 years
Young adulthood
age 19
to 29 years
Adulthood
age 30
to 64 years
Older adulthood
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
cer
at which these recommendations apply.
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.

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

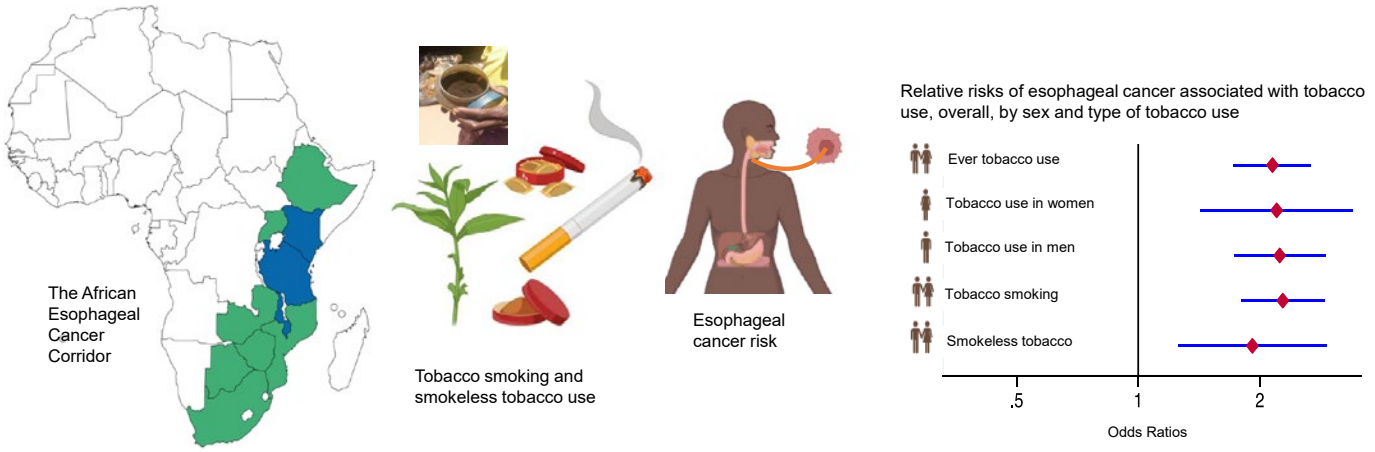
Disentangling the effects of multiple exposures to lung carcinogens and smoking

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 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).

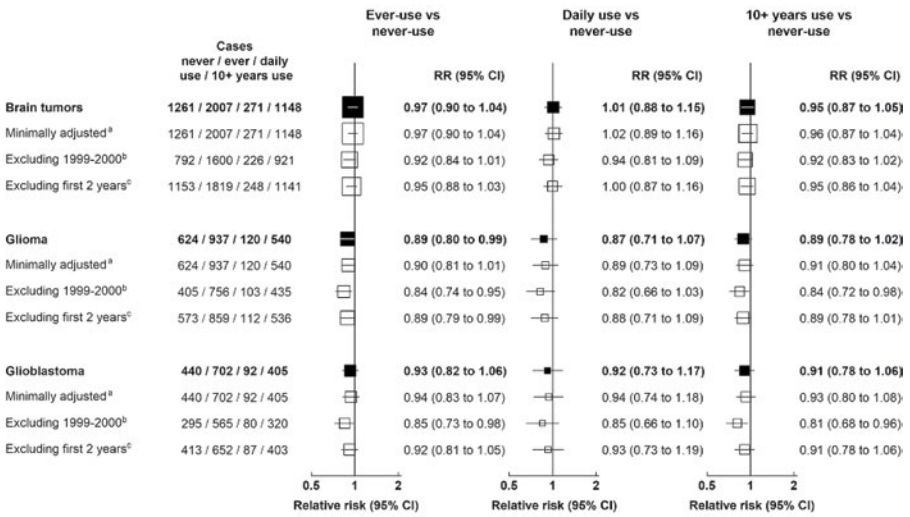
Figure 2. In the African oesophageal cancer corridor, tobacco smoking and smokeless tobacco use, in combination and in exclusivity, were found to be associated with risk of oesophageal squamous cell carcinoma. Reproduced with permission from Simba et al. (2023a), John Wiley and Sons.



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.

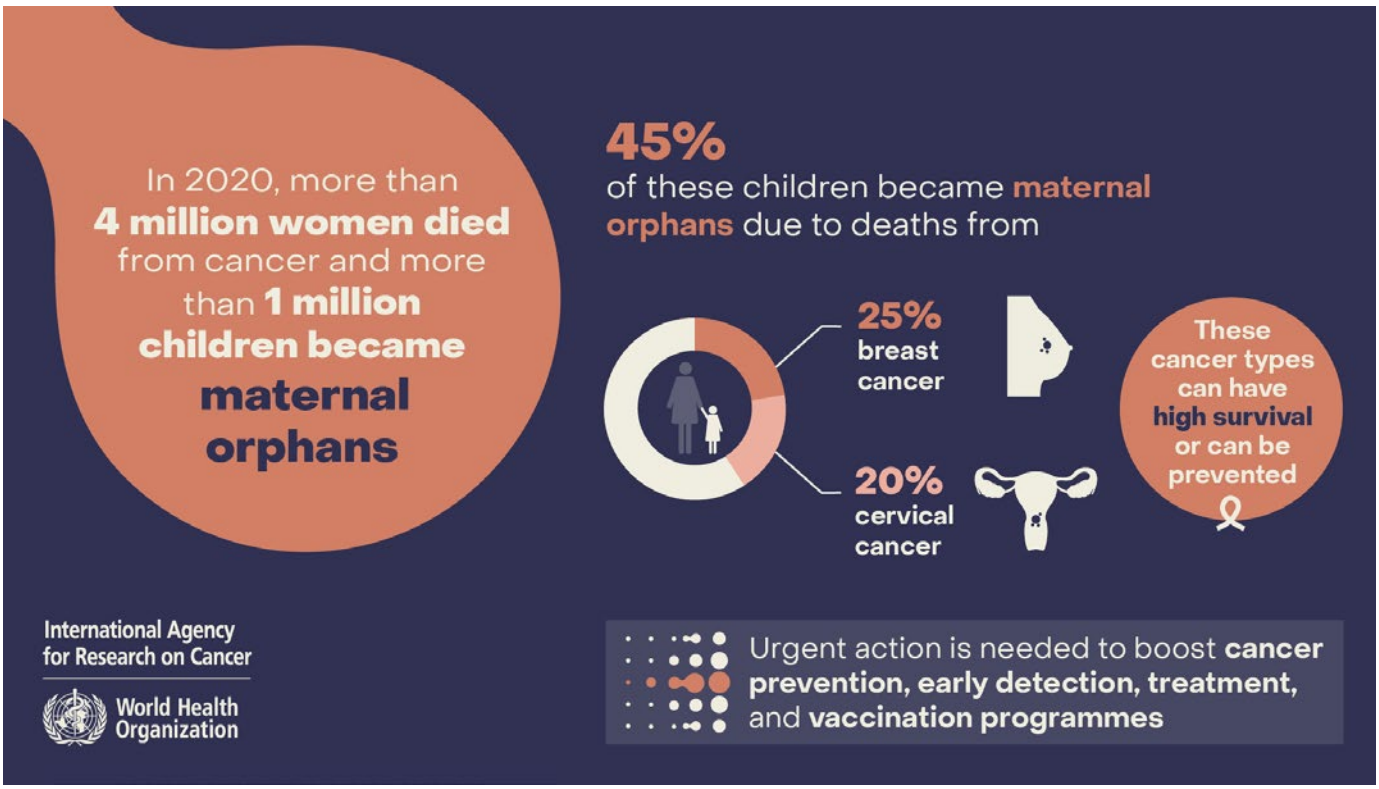
Figure 3. Relative risks (RRs) for brain tumours in users versus never-users of cellular telephones in median year 2011, sensitivity analysis, UK Million Women Study. [a] Stratified by year of birth, year of answering the baseline survey, and region only. [b] Excluding women who completed the questionnaire 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.



Global estimation of maternal orphans due to cancer

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.



Launch of the 1st edition of the Latin America and the Caribbean Code Against Cancer

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.


RADIATION THERAPY
DRINKING ALCOHOL
REPRODUCTIVE HISTORY
HORMONES
OVERWEIGHT
PHYSICAL INACTIVITY
FAMILY HISTORY
BREAST DENSITY
MAMMOGRAPHY
BIOMARKERS
UNDERSTAND BREAST CANCER RISK
EXERCISE REDUCE RISK

Epigenomics and Mechanisms Branch (EGM)

Branch head
Dr Zdenko Herceg

Deputy branch head
Dr Jiri Zavadil

Scientists
Dr Akram Ghantous
Dr Tarik Gheit
Dr Rita Khoueiry
Dr Michael Korenjak

Senior research assistants, data management/analyst
Mr Vincent Cahais
Dr Claire Renard

Research assistants
Ms Sandrine Chopin
Mr Cyrille Cuenin
Ms Aurélie Salle
Ms Cécilia Sirand

Secretariat
Ms Elizabeth Page
Ms Nicole Suty

Postdoctoral fellows
Dr Zainab Awada (until July 2023)
Dr Julia Bruno
Dr Samrat Das
Dr Luisa Galati
(until December 2022)
Dr Farah Nassar
Dr Grace Odongo
Dr Caroline de Aguiar Pires Poubel
Dr Natalia Spitz Toledo Dias

Doctoral students
Ms Bérénice Chavanel
Ms Veronica Fertitta
(until September 2022)
Ms Mariana Gomes da Silva Araujo
Ms Hanna Krynska
(until November 2022)
Ms Francesca Manara
(until January 2023)
Mr Athanasios Mouchtaris Michailidis
Ms Shefali Thakur (until June 2022)
Ms Tereza Turkova (until June 2022)

Master's students
Mr Pierre Bertrand (until July 2023)
Ms Pauline Goddard
(until September 2023)
Mr Julien Ledig
(until September 2022)

Trainees
Ms Jeliyah Clark (until August 2022)
Mr Stéphane Keita (until July 2022)
Ms Taja Lozar (until June 2023)
Mr Recep Uyar (until April 2022)

Visiting scientists
Dr Assunta Venuti (until August 2022)
Dr François Virard

The overarching aim of the Epigenomics and Mechanisms Branch (EGM) is to advance the understanding of the role of (epi)genetic changes and pathways induced by environmental factors and endogenous processes in cancer causation, underpinning studies of etiology, carcinogen evaluation, and prevention. This is achieved by exploiting conceptual and technological advances in laboratory science and molecular epidemiology as well as by capitalizing on IARC's unique role in international cancer research (Figure 1) (Chung et al., 2023; Das et al., 2022; Herceg et al., 2022; Karimi et al., 2023; Talukdar et al., 2022a; Vicente et al., 2022). Key elements of EGM's strategy include developing innovative state-of-the-art molecular and cell biology and functional epigenomics research methodologies and bioinformatics and biostatistics tools, which are applicable to experimental cancer models and human samples from biobanks associated with population-based and case–control studies. EGM's ambition is to place increased emphasis on contributions to translational studies, through the discovery of mechanism-based biomarkers of exposure and risk stratification. Some highlights of EGM's work during the 2022–2023 biennium are described here.

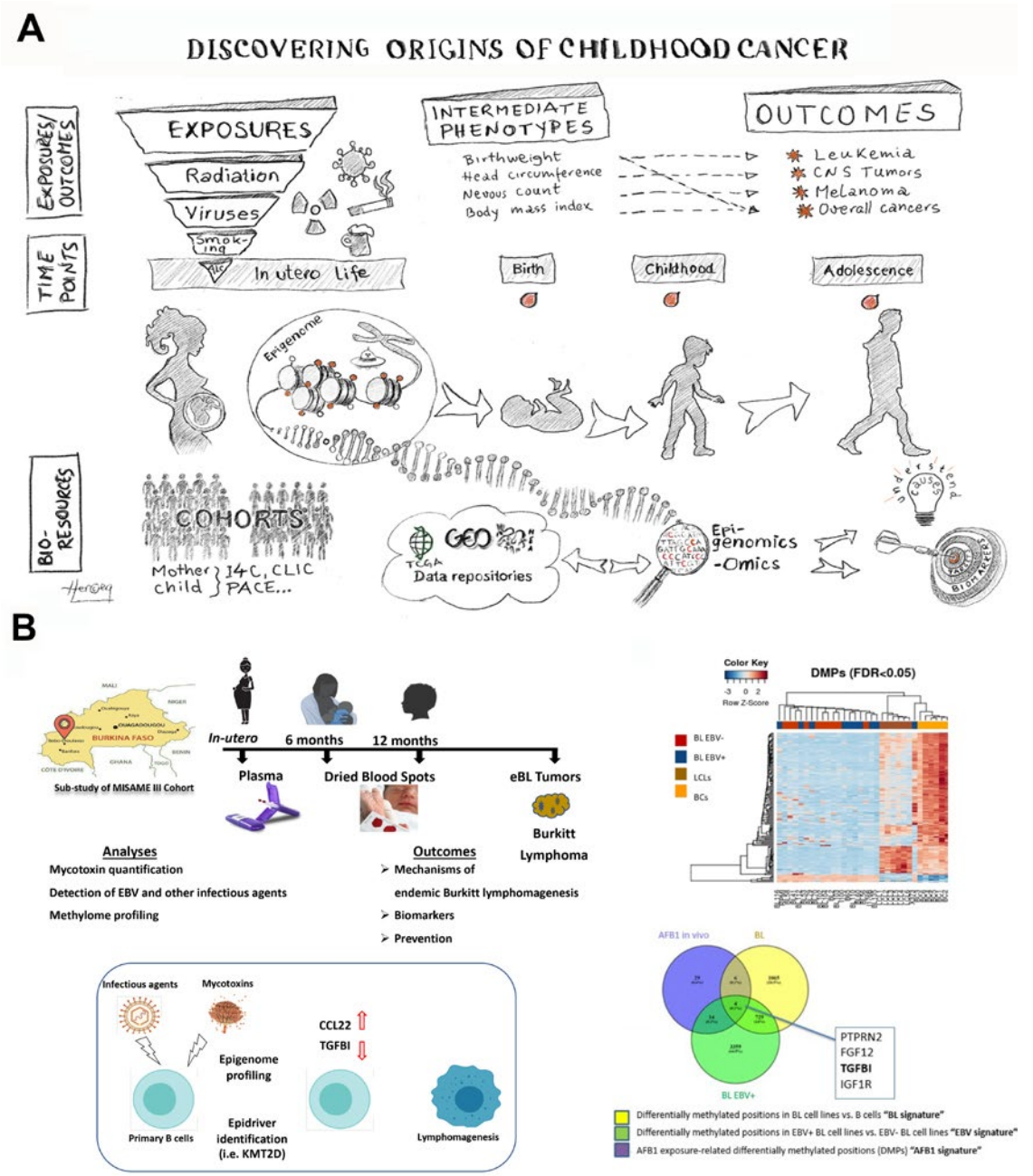
Figure 1. Research aims, collaborators, technological platforms, and resources of the Epigenomics and Mechanisms Branch (EGM). The Branch combines molecular epidemiology and mechanistic studies aimed at investigating the role of (epi)genetic changes and deregulated molecular pathways induced by environmental factors and identifying biomarkers of exposures and cancer risk. EGM also implements (epi)genomic methodologies, profiling strategies, and bioinformatics tools, which are applicable to population-based cohorts (molecular epidemiology studies coordinated by IARC and external collaborators) as well as state-of-the-art in vitro models. EGM's programme is carried out in close collaboration with IARC scientists and epidemiologists as well as external collaborators, many of which are part of international networks established to share technological platforms and biological resources. The emphasis is on enhancing interdisciplinarity and creating synergy within the Branch, thus facilitating the synthesis of scientific evidence from disciplines within the Branch, as well as the development of important transferrable skills between IARC and collaborators in low- and middle-income countries. © IARC.

Identifying epigenetic origins and markers of childhood cancer risk

Epigenome-wide alterations precede diagnosis since birth and affect prognosis of paediatric acute lymphoblastic leukaemia

Paediatric cancer is the leading cause of disease-related mortality in children and adolescents, with increasing incidence worldwide and lifelong sequelae in survivors. The causes of leukaemia, which is the most common form of paediatric cancer, are largely unknown. Growing evidence points to an origin in utero, when global redistribution of the epigenome (DNA methylation) modifications occurs, driving tissue differentiation (Figure 2A). Epigenome-wide DNA methylation was profiled in neonatal blood, with follow-up to paediatric pre-B acute lymphoblastic leukaemia (pre-B ALL), using double-blind analyses between prospective cohorts (from the International Childhood Cancer Cohort Consortium, I4C) extending from birth to diagnosis and retrospective studies backtracking from clinical disease to birth. Validation was done using an independent technology and population (totalling 317 cases and 483 controls) and complemented with pan-tissue methylation-stability (n = 5023 tissues; 30 types) and methylation-expression (n = 2294 tissues; 26 types) analyses. At diagnosis (n = 644 patients with pre-B ALL), methylation analysis was performed in leukaemia tissues from patients with pre-B ALL with at least 10 years of follow-up. Genomic imprinting was found to play a major role among identified loci, and an imprinted immunomodulating tumour suppressor gene was significantly hypermethylated at birth in nested cases relative to controls in all tested populations, including European and Hispanic ancestries. Specific differentially methylated regions (DMRs) were found to be stable over follow-up years after birth and across surrogate blood and target bone marrow tissues. Differential methylation was found to be associated with a change in gene expression and with survival of patients with pre-B ALL, supporting a functional and translational role for epigenetic markers. This study provides a proof of concept to detect epigenetic alterations at birth as potential precursors predisposing to

Figure 2. Identifying origins and causes of childhood cancer. (A) The hypothetical model. Exposure from external sources (general and specific factors) and internal biological processes may induce stable and mitotically heritable changes in the epigenome, which may result in alterations in the gene expression programme of stem and progenitor cells, leading to cancer in childhood and in later life and to cancer-predisposing intermediate phenotypes, which occur during the latency period between the exposure time and disease onset. The intermediate phenotypes, such as birth weight, head circumference, and naevus count, are positively associated with childhood leukaemia or lymphoma, brain tumours, and melanomas (in children, adolescents, and adults), respectively. EGM's studies identify epigenetic (DNA methylation) markers of specific exposures such as tobacco smoking, air pollution, ultraviolet radiation, and infections, as well as general exposures such as socioeconomic status, season of birth, and parental body mass index. (B) In utero and early-life epigenome profiling to decipher the multifactorial origins of endemic Burkitt lymphoma (eBL) in Africa. (left panel) Study design of the cohort-based analyses (top) and in vitro mechanistic analyses aiming to dissect the in utero and early-life epigenome–exposome interplay to decipher the multifactorial origins of eBL in Africa. (right panel) Heat map of differentially methylated positions (DMPs) in the genome of Epstein–Barr virus (EBV)-positive and EBV-negative BL-derived cell lines, primary B cells (BCs), and lymphoblastoid cells (LCLs) (top). Genes commonly affected by methylation changes identified from the comparative analysis of methylome profiles associated with B-cell transformation (BL signature), EBV (EBV signature), and aflatoxin B1 exposure (AFB1 signature) (bottom). The mechanistic analyses confirmed DNA methylation-dependent transcriptional silencing of TGFBI involving the recruitment of DNMT1, which is associated with an activation of the NF-κB pathway. The results revealed a potential common mechanism of B-cell transformation shared by the main risk factors of eBL (EBV and AFB1), suggesting a key determinant of disease that could enable the development of more efficient targeted therapeutic strategies. (A) © IARC/Z. Herceg. (B) (left panel) © IARC, (right panel) Reproduced from Manara et al. (2022). © 2022 by the authors. Licensee MDPI, Basel, Switzerland.



childhood leukaemia, reproducible in three continents and two ethnicities.

Assessment of in utero and early-life epigenome profiles to decipher the multifactorial origins of endemic Burkitt lymphoma in Africa

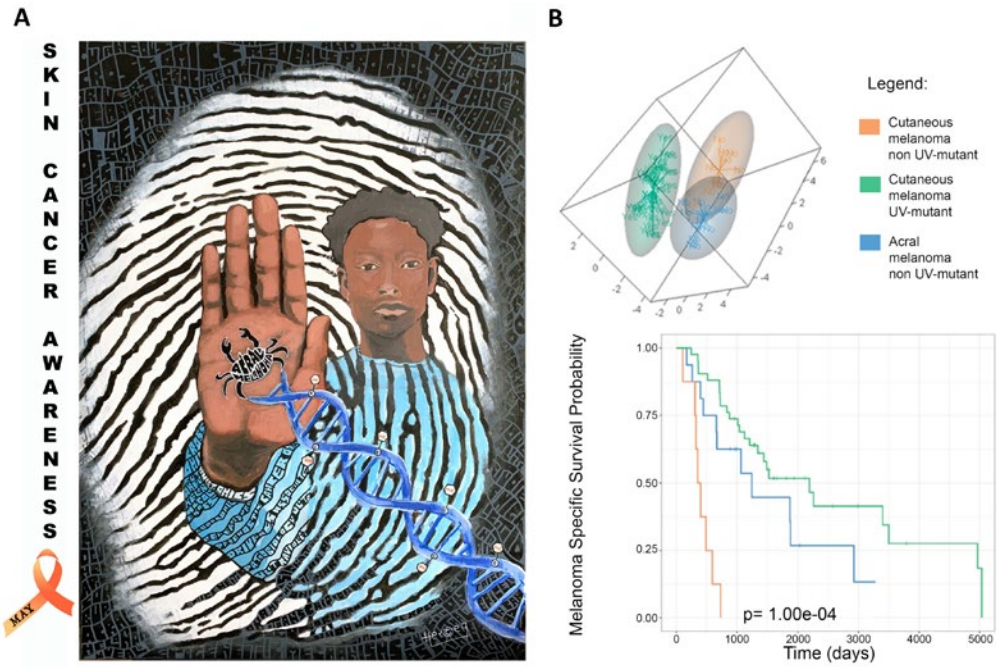
Endemic Burkitt lymphoma (eBL) is the most prevalent childhood cancer in sub-Saharan Africa. Although infection with Epstein–Barr virus (EBV) is necessary and is associated with eBL, it is not sufficient to induce lymphoma; this strongly suggests the multifactorial etiology of eBL. To gain insights into the synergistic impact of co-infections and exposure to mycotoxins on the epigenome, which may underpin eBL development, EGM built on a well-established mother–children cohort from Burkina Faso (the MISAME-III cohort, coordinated by Dr Carl Lachat at Ghent University), an eBL tumours cohort, and state-of-the-art established in vitro approaches (Figure 2B). Using biospecimens collected during pregnancy (mothers) and early in life (children at age 6 months and 12 months) and eBL tumour samples, EGM is performing methylome profiling complemented with in vitro mechanistic analyses to identify biomarkers of exposures, reveal eBL risks, and decipher early mechanisms of eBL development (Figure 2B). The data obtained so far suggest a synergistic impact of the mycotoxin aflatoxin B1 and EBV on immunoregulatory cytokine profiles of B cells and the expression of several cancer-related genes, and revealed putative epigenetic drivers ("epidrivers") of (e)BL among epigenetic regulator genes (Manara et al., 2022). Continuing work should provide a better understanding of environmental factors and mechanisms that underpin eBL carcinogenesis and reveal early biomarkers of the disease, relevant to prevention in low- and middle-income countries.

Cutaneous and acral melanoma cross-omics reveals prognostic cancer drivers associated with pathobiology and ultraviolet exposure

Exposure to ultraviolet (UV) radiation is causally linked to cutaneous melanoma, which occurs mainly in fair-skinned people, but the underlying epigenetic mechanisms, known as molecular sensors of exposure, have not been characterized in clinical biospecimens. EGM integrated clinical, epigenome (DNA methylome), genome, and transcriptome profiling of cutaneous melanoma from two multi-ethnic cohorts (the Barretos Cancer Hospital cohort, in Brazil, and The Cancer Genome Atlas/Skin Cutaneous Melanoma cohort, TCGA/SKCM). The study identified UV-related alterations in immunological pathways, with multi-omics cancer driver potential affecting patient survival. The top hits were validated by targeted sequencing, providing cost-effective opportunities for clinical application.

The study, published in *Nature Communications* (Vicente et al., 2022), also revealed important features of melanomas that are not associated with UV exposure (Figure 3). A subset of cutaneous melanomas did not harbour UV molecular signatures, and their molecular landscape and clinical prognosis not only were different from those of UV-exposed melanomas but also resembled those of the pathologically distinct acral melanoma. Acral melanoma

Figure 3. (A) Molecular fingerprints can infer exposure to ultraviolet (UV) radiation and distinguish between melanoma types, including acral melanoma, which develops in skin areas that are not often exposed to sunlight, such as the palms (as shown), and is the most common type of melanoma in darker-skinned people. (B) (top) Epigenomic maps demonstrating that non-UV-mutant cutaneous melanoma more closely resembles (i.e. overlaps with) acral melanoma rather than UV-exposed cutaneous melanoma. (bottom) Melanoma-specific survival, showing that patients with non-UV-mutant cutaneous melanoma, similarly to those with acral melanoma, have worse survival than patients with UV-exposed cutaneous melanoma. The *P* value was from the log-rank test. (A) © IARC/Z. Herceg. (B) Reproduced from Vicente et al. (2022).



develops in skin areas that are not often exposed to sunlight, such as the palms and soles, and is the most common type of melanoma in darker-skinned people.

By including patients with different skin colours, this study widened the resolution spectrum to various forms of melanoma and gained a better understanding of the origins of this cancer type, which is not necessarily triggered by UV exposure. These gene–environment interactions reveal translationally impactful mechanisms in melanomagenesis (Vicente et al., 2022).

Integrated multi-omics investigations of aristolochic acid-associated urothelial cancers

Aristolochic acids (AAs), natural compounds in Aristolochiaceae plants, pose grave risks of severe nephropathy and urological, hepatobiliary, and other cancers. The tumours arising after exposure to AA-containing herbal medicines or AA-contaminated foods bear a unique mutational signature, a marker of exposure to AA. The ARISTOCANCERS project (https://aristocancers.iarc.who.int/), led by EGM, explored the role of AA in upper tract urothelial carcinoma (UTUC) occurring in southern European regions with prevalent AA nephropathy (Karanović et al., 2022). In this case-series study, EGM and collaborators performed multi-omics analysis of UTUC tumours and patient urine samples, which revealed intricate cancer development processes, including specific DNA adduct formation, multitier gene regulatory network remodelling, and characteristic mutational fingerprints in both the genomic DNA and messenger RNA (mRNA). A microRNA (miRNA)-based urine test for cancer presence and recurrence was devised (Figure 4A). Inadequate regulations have allowed global sales of AA-containing herbal medicines, and environmental exposure routes remain neglected. To raise awareness, EGM published a comprehensive review in *Nature Reviews Cancer*, detailing the mutagenic and carcinogenic effects of AA (Das et al., 2022) and emphasizing the need to eliminate AA exposure sources to reduce cancer rates. The study highlights challenges in assessing AA-induced nephrotoxicity and carcinogenicity worldwide (Figure 4B) and proposes coordinated global actions to limit AA exposure, to prevent far-reaching adverse effects on AA-associated cancers and other pathologies.

Figure 4. The ARISTOCANCERS project on the role of aristolochic acid (AA) in human cancers. (A) The roadmap for multi-omics analysis of AA mutagenicity and carcinogenicity in upper tract urothelial cancers and of biomarkers of tumour presence and recurrence. (B) The global distributions of AA-containing *Aristolochia* plants, AA-associated cancers, reports of AA-associated mutagenesis, and occurrence of AA nephropathy (AAN), as reviewed in Das et al. (2022). mRNA, messenger RNA; miRNA, microRNA. (A) © IARC. (B) Reprinted from Das et al. (2022).

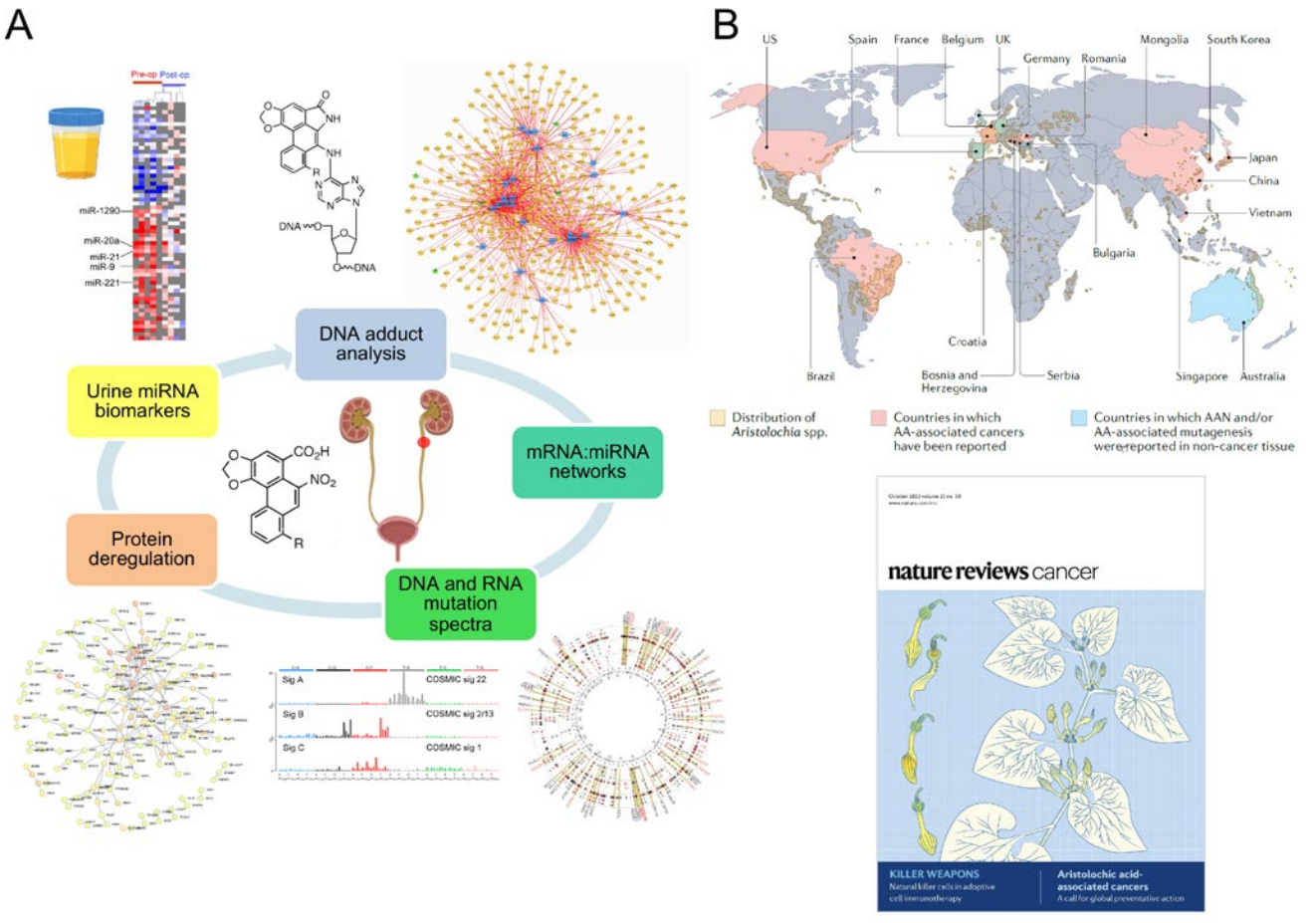
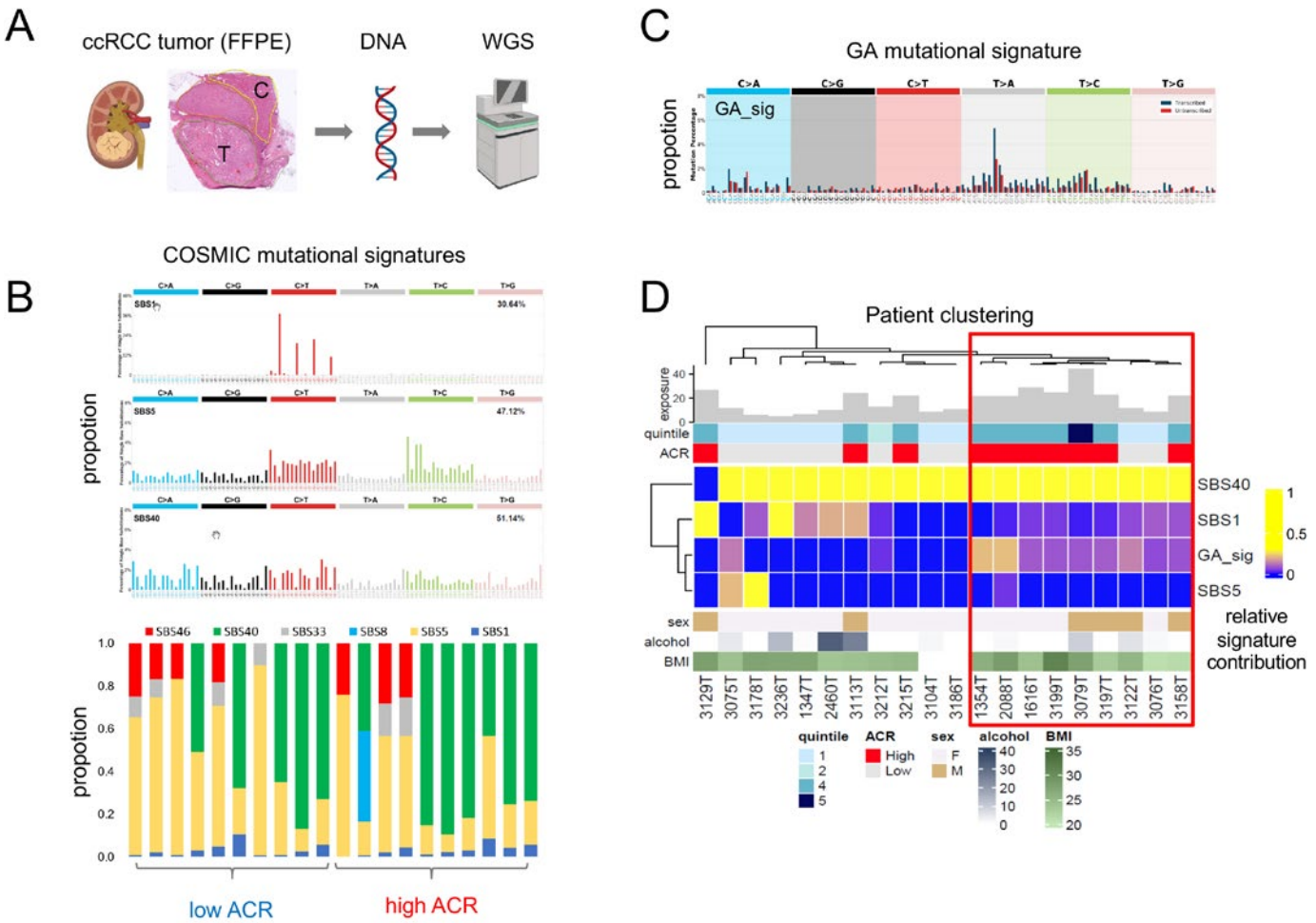


Figure 5. The MODARC project on mutational signatures in renal cancer after dietary exposure to acrylamide (ACR). (A) Schematic of the analysis of genome-scale mutational signatures in tumours of the patients with clear-cell renal cell carcinoma (ccRCC) in the Netherlands Cohort Study on Diet and Cancer (NLCS). T, tumour tissue area; C, non-tumour control tissue. (B) COSMIC mutational signatures identified in NLCS ccRCCs, and their distribution in samples of each ACR exposure group. (C) The mutational signature of glycidamide (GA), the reactive metabolite of ACR. (D) Hierarchical clustering of NLCS ccRCC samples based on mutational signatures reveals a relative enrichment of the presence of the GA signature (GA_sig) in the group with high dietary ACR exposure (red rectangle). BMI, body mass index; FFPE, formalin-fixed, paraffin-embedded; SBS, single-base substitution; WGS, whole-genome sequencing. © IARC.



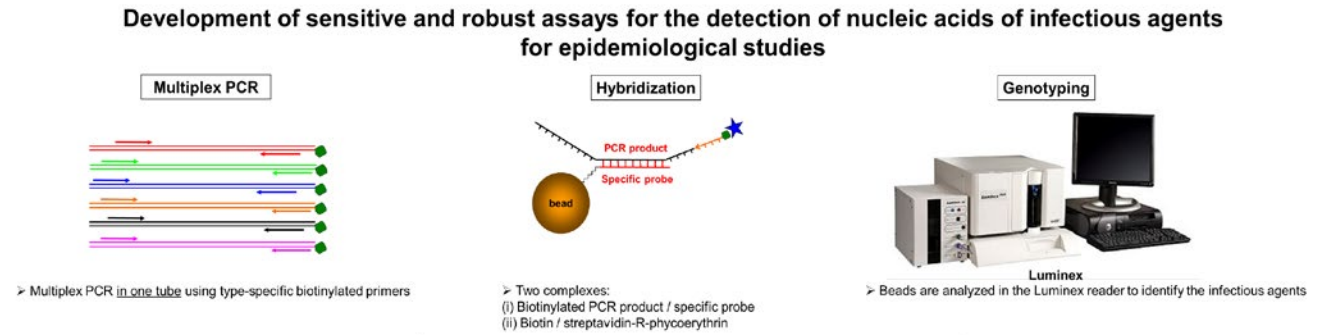
Mutational signatures of dietary acrylamide in renal cancer

Acrylamide, which was classified by the *IARC Monographs* programme as probably carcinogenic to humans (in 1994), is found in heated starchy foods and tobacco smoke. Previous studies on dietary acrylamide exposure and cancer yielded inconclusive results, although a potential elevated acrylamide-associated risk of clear-cell renal cell carcinoma (ccRCC) in non-smokers was proposed. EGM's MODARC project, a World Cancer Research Fund International-funded collaboration between EGM, Maastricht University, and the United States Food and Drug Administration National Center for Toxicological Research, investigates a molecular link between dietary acrylamide intake and ccRCC in the Netherlands Cohort Study on Diet and Cancer (NLCS), which involved 120 852 participants, including 480 with renal cancer. EGM's genomic investigations revealed the presence of endogenous COSMIC mutational signatures in all tumour samples, regardless of the dietary acrylamide exposure history (Figure 5A, B). However, an optimized in silico signature attribution approach showed a 2-fold enrichment of the mutational signature of glycidamide, a reactive metabolite of acrylamide, previously described by EGM (Figure 5C), in the cases with high acrylamide exposure (Figure 5D). This indicates a possible link between glycidamide-induced mutagenesis and ccRCC development, warranting further investigations on a larger scale. Furthermore, the findings can inform measures aiming to reduce acrylamide exposure and prevent related cancer formation.

Laboratory tools for epidemiological studies on virus-induced cancers

The IARC platform has established highly sensitive Luminex-based assays that enable the identification of viral biomarkers in body fluids, including circulating human papillomavirus DNA (HPV ctDNA) (Galati et al., 2022a)

Figure 6. Development of sensitive and robust assays for the detection of nucleic acids of about 250 infectious agents, including viruses, parasites, and bacteria. The assays combine two different steps: (i) multiplex polymerase chain reaction (PCR) using type-specific primers for the amplification of DNA, and (ii) bead-based hybridization for the identification of the infectious agents (Luminex technology). © IARC.



Infectious agents detected by the Luminex platform

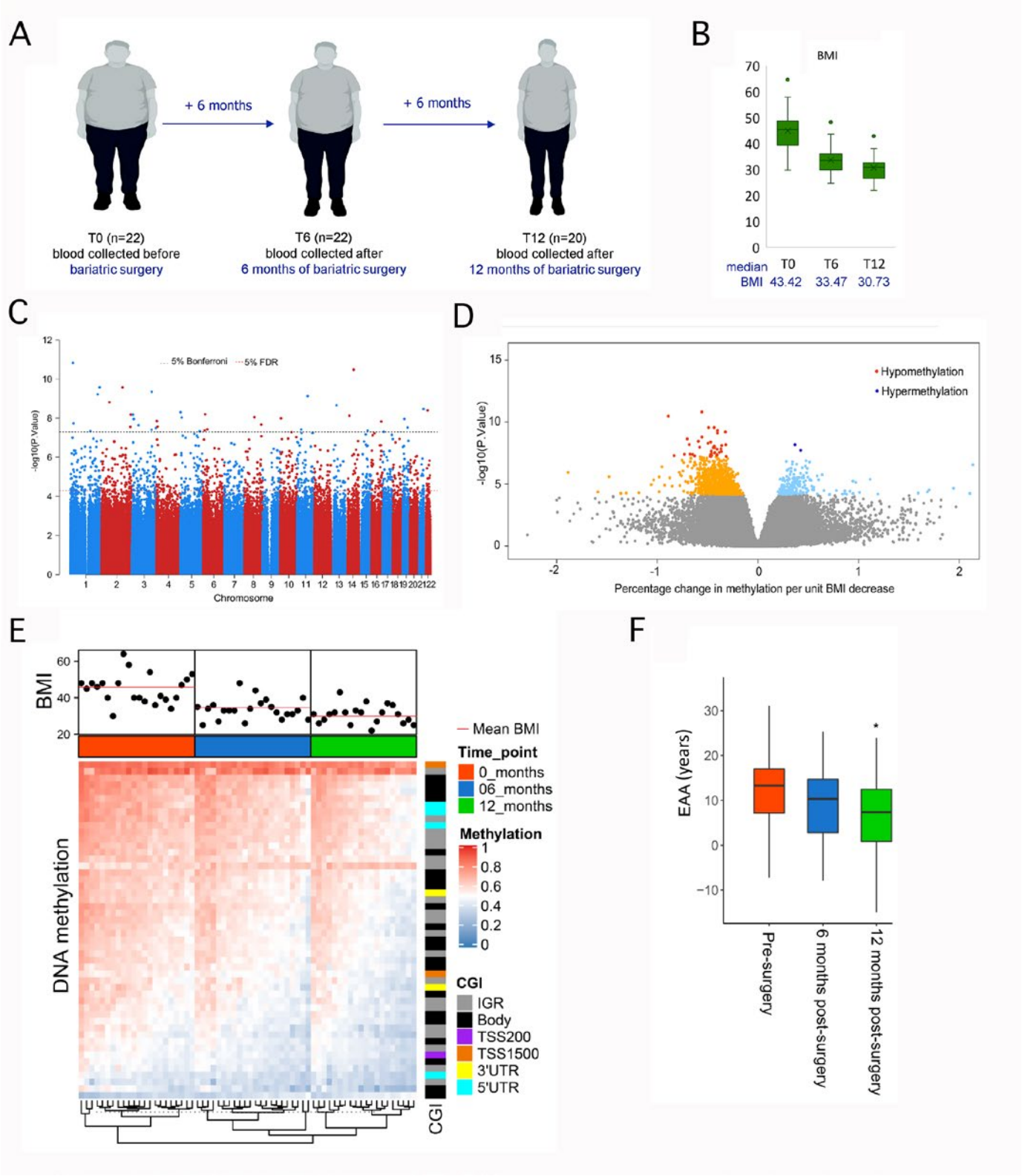
Infectious agents	No. of infectious agents
High-risk and two Low-risk (HPV6 and 11) alpha HPV types	21
Low-risk alpha HPV types	29
gamma HPV types	52
beta HPV types	46
Polyomaviruses	12
Herpesviruses	8
Adenoviruses	17
Other infectious agents (Chlamydia T., HBV, MMTV, Schistosoma (haematobium, mansoni, japonicum), HPV1, Bocavirus)	8
Microbiome (bacteria suspected to be involved in human cancer and other diseases)	50
	Total = 241

(Figure 6). Potential advantages of the use of body fluid-based assays include reduced time and easier management of patients, especially for early diagnosis and disease monitoring (Karimi et al., 2023). In collaboration with the European Institute of Oncology (Italy), a proof-of concept biomarker study was designed to compare several non-invasive diagnostic approaches to identify HPV-associated head and neck squamous cell carcinomas (HNSCC) using a combination of HPV ctDNA in plasma and HPV DNA in oral samples from patients with HNSCC (n = 132) and non-SCC HNC (n = 10). EGM found that oral HPV DNA and, slightly more, HPV16 ctDNA in plasma represent highly sensitive and reliable biomarkers for the identification of HPV-positive oropharyngeal squamous cell carcinoma (OPSCC). The use of combined biomarkers, such as HPV16 ctDNA and oral HPV16 DNA in gargle, resulted in the identification of 100% of HPV16-related OPSCCs (15 of 15; 95% confidence interval, 76.14–100.00), even at earlier cT stages. This proof-of-concept study, which complements and extends the work described by Robbins et al. (2022), indicates that non-invasive body-fluid biomarkers could be adjunctive tools, which can be easily applied together with the available methods, in a diagnostic algorithm of HPV-driven OPSCCs.

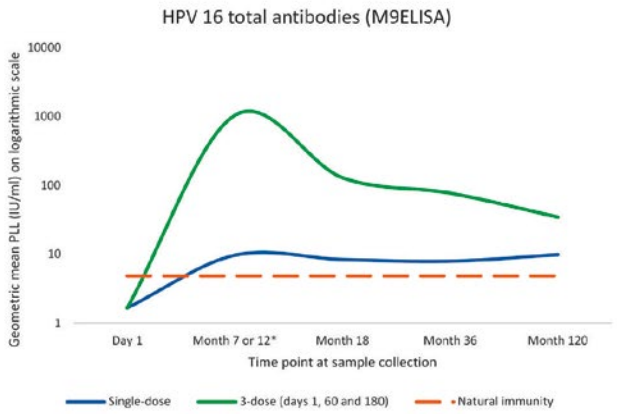
Bariatric surgery-induced weight loss and associated genome-wide DNA methylation alterations in obese individuals

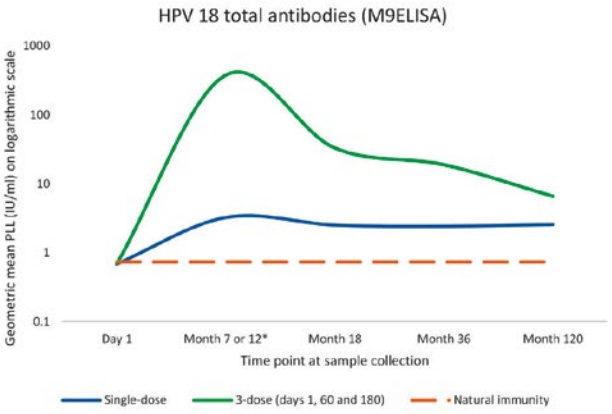
Obesity is a multifactorial and chronic disease that adversely affects human health, including cancer risk. EGM took advantage of intervention studies (including the ISS-Rome bariatric surgery and caloric restriction cohort) to investigate the effects of bariatric surgery-induced weight loss on clinical parameters and epigenome alterations in individuals with severe obesity (Figure 7). The study collected blood samples and follow-up data, based on which EGM performed DNA methylome analysis to identify differentially methylated genes and pathways linked to weight loss. To substantiate the results, a replication set of samples from body mass index (BMI)-discordant monozygotic twins was included. The obese twins in the replication set lost weight due to caloric restriction, thus serving as a control group that did not undergo bariatric surgery. The analysis revealed 41 significant (Bonferroni $P < 0.05$) and 1169 suggestive differentially methylated positions (DMPs) associated with weight loss due to bariatric surgery. Among the significant DMPs, the top hits were replicated in an independent cohort of BMI-discordant monozygotic twins (where the heavier twin underwent diet-induced weight loss). Pathway enrichment analysis of the DMR-associated genes showed that functional pathways related to immune function and type 1 diabetes were significant. Weight loss due to bariatric surgery also significantly decelerated epigenetic age 12 months after the intervention (Figure 7) (Talukdar et al., 2022a). EGM's findings provide evidence that weight loss brings about an improvement in biological (epigenetic) age and in the clinical/metabolic profile of obese individuals. Continuing studies are aimed at addressing whether specific epigenetic changes that occur as early events in response to weight loss may contribute to the reduction of obesity-associated cancer risk.

Figure 7. Weight loss and associated genome-wide DNA methylation alterations in obese individuals. (A) Study design with participant details and collection time points. (B) BMI-change trajectory at 6 months and 12 months after bariatric surgery. (C) Manhattan plot showing all differentially methylated positions (DMPs) across autosomes after weight loss. (D) Volcano plot showing hypermethylated and hypomethylated DMPs. (E) Heat map showing DNA methylation patterns of DMPs with weight loss. (F) Epigenetic age acceleration (EAA) at different time points during the course of weight loss. EAA analysis was performed using the Hannum method by taking the residual from the regression of epigenetic age (based on β values of 71 CpG probes) on chronological age. Positive EAA values suggest that the epigenetic age is greater than expected based on chronological age. Reproduced with permission from Talukdar et al. (2022a).



IARC's Indian HPV vaccine study has shown that the efficacy of a **single dose** against persistent **HPV 16 and 18** infections was as high as that of three doses due to high and durable antibody response in the single dose recipients 10 years post-vaccination



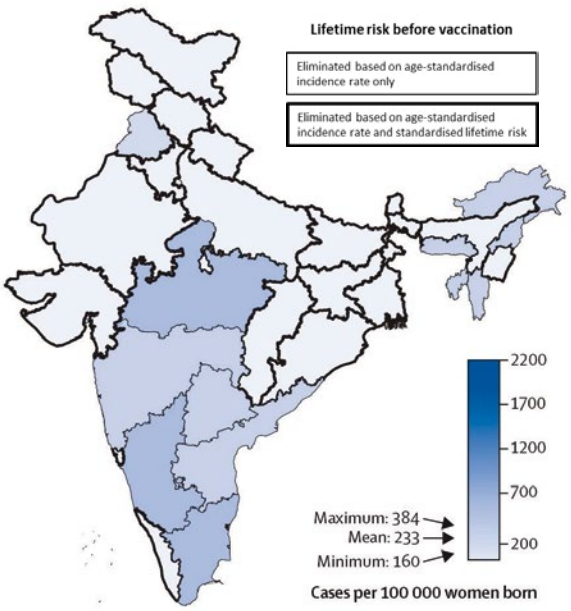


Efficacy of HPV vaccine against persistent HPV 16/18 infections in IARC India trial:

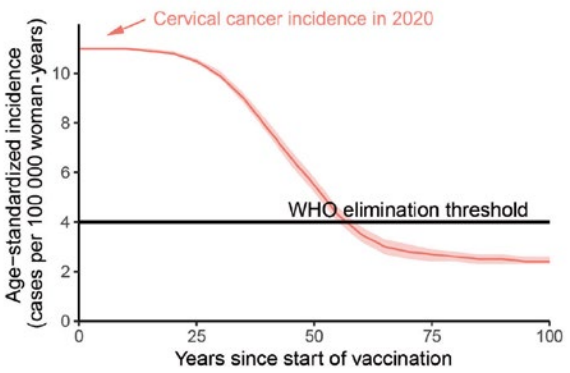
90.1% **92.7%** **90.1%**

India alone contributes to one fifth of global burden of cervical cancers

If **HPV vaccination** is introduced now in India, it could **prevent almost 1 million** cervical cancer cases among the birth cohort currently aged 10 years or younger



The introduction of single dose HPV vaccination is expected to **eliminate cervical cancer** as a public health priority in India **in 50 years**



Early Detection, Prevention, and Infections Branch (EPR)

Branch head
Dr Partha Basu

Deputy branch heads
Dr Andre Carvalho
Dr Gary Clifford

Scientists
Dr Maribel Almonte Pacheco
Dr Armando Baena-Zapata
Dr Iacopo Baussano
Dr Arunah Chandran
Dr Jean-Damien Combes
Dr Catherine de Martel
Dr Nadya Dimitrova
Dr Mathilde Forestier
Dr Irene Man
Dr Isabel Mosquera Metcalfe
Dr Richard Muwonge
Dr Jin Young Park
Dr Mary Luz Rol
Dr Catherine Sauvaget
Dr Farida Selmouni
Dr Patricia Villain

Health information systems specialist
Mr Eric Lucas

Data managers
Mr Damien Georges
Ms Vanessa Tenet

Secretaries
Ms Nadia Akel
Ms Karima Bendeddouche
Ms Lobna Boulegroun
Ms Susan Gamon
(until January 2023)

Project assistants
Ms Philippine Gason
Ms Viktoria Knaze
Ms Cécile Le Duc

Information assistant
Ms Krittika Guinot

Postdoctoral fellows
Dr Indira Adhikari
Dr Catharina J. Alberts
(until July 2022)
Dr Beatriz Cordeiro Jardim
Dr Jyoshma D'Souza
Dr Ahmad Fuady (until June 2023)
Dr Andrea Gini
Dr Mayo Hirabayashi
(until August 2022)
Dr Ahmadaye Ibrahim-Khalil
(until December 2022)
Dr Marta Iljaba Martinez
(until May 2023)
Dr Irene Man (until November 2022)
Dr Keitly Mensah
Dr Tolani Musliu Adetola
Dr Kunal Oswal (until June 2022)
Dr Arianis Tatiana Ramirez Pineda
Dr Deependra Singh
Dr Mwiza Singini
Dr Tamar Skhirtladze
(until June 2022)
Dr Katayoun Taghavi
Dr Rayana Toyé (until August 2023)
Dr Daniela Vázquez Juárez
(until April 2023)
Dr Feixue Wei (until June 2023)
Dr Li Zhang (until December 2022)

Students
Ms Raquel Aguirra de Moraes
(until February 2023)
Dr Nidhi Bhatnagar (until May 2022)
Dr Maxime Bonjour
Dr Sreeya Bose (until July 2022)
Ms Séphora Campoy
(until October 2022)
Ms Maomao Cao (until July 2023)
Ms Esther Chanakira
Ms Laura Downham
Mr Lucas Dufour (until August 2022)
Mr Mattis Eynard (until July 2023)
Ms Laura Gil Sanchez
(until August 2023)
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(until July 2023)
Dr Meritxell Mallafré
(until August 2022)
Dr Asmita Rana (until March 2022)
Dr Manikandanesan Sakthivel
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Dr Pia Kirkegaard
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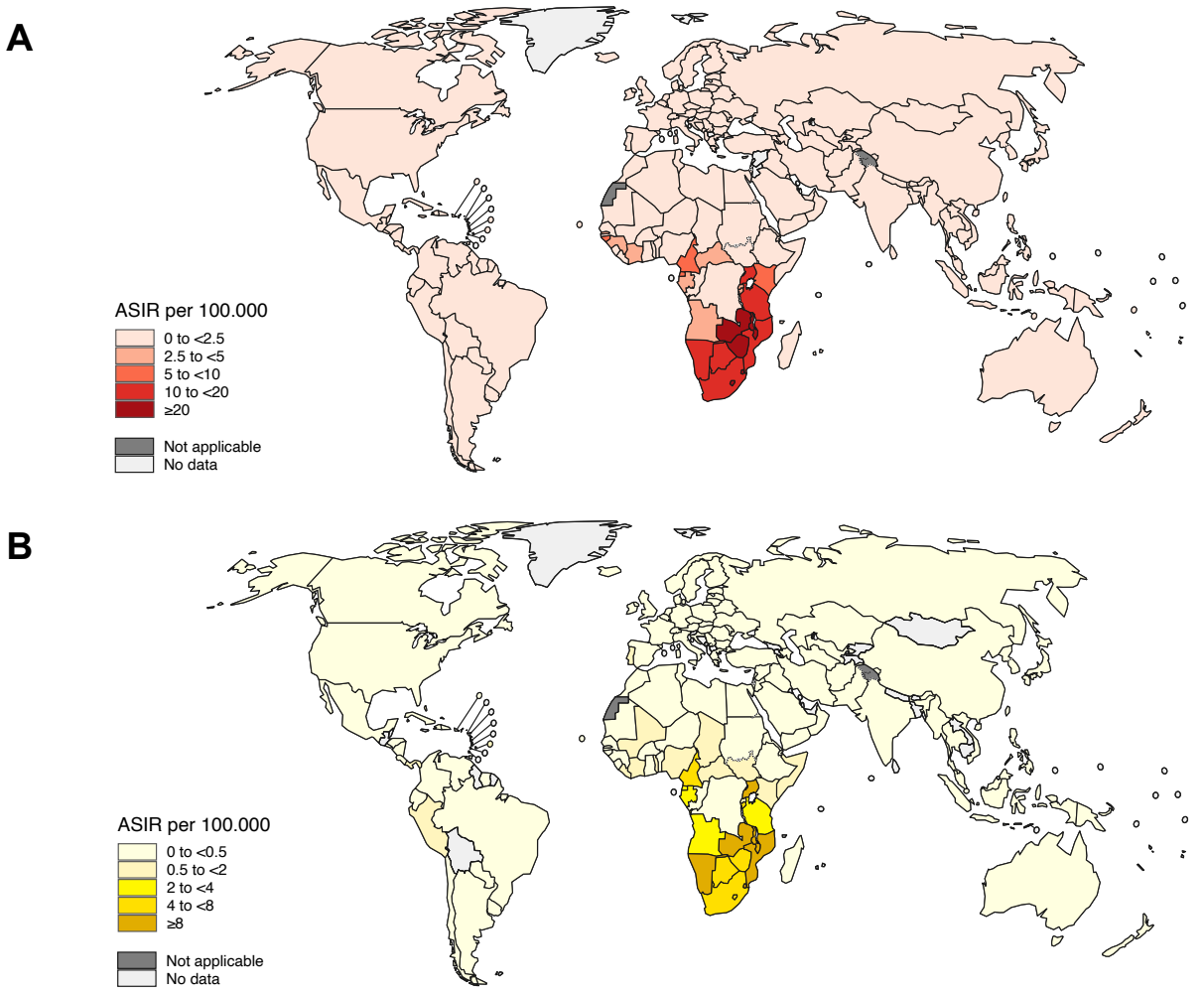
During the 2022–2023 biennium, the Early Detection, Prevention, and Infections Branch (EPR) contributed significantly to the priority research areas of the Agency to support countries to implement evidence-based interventions in cancer prevention and early detection, tailored to the local context.

Given the amenability of infections to preventive interventions, EPR continued to improve global, regional, and country-level estimates with new data and methodology, most notably expanding the cancer types considered to be causally associated with Epstein–Barr virus (EBV). In a meta-analysis of 220 studies including more than 68 000 cases of gastric adenocarcinoma, EBV prevalence in tumour cells was 7.5%, suggesting the occurrence of 81 000 EBV-associated gastric cancers worldwide annually (Hirabayashi et al., 2023a). In another meta-analysis, EBV prevalence was 11.0% in gastric diffuse large B-cell lymphoma (DLBCL) (Hirabayashi et al., 2023b). EPR's studies on the prevalence of EBV in large, representative tumour series of patients diagnosed with all types of lymphoma in France (Donzel et al., 2022) and in Rwanda (Mpunga et al., 2022) suggested an important etiological involvement of EBV in DLBCL, in addition to well-characterized associations with Hodgkin lymphoma, Burkitt lymphoma, and natural killer/T-cell lymphoma subtypes. A meta-analysis of 520 studies estimated 42% of cirrhosis globally to be attributable to hepatitis B virus and 21% to hepatitis C virus (Alberts et al., 2022); this will inform policies towards the elimination of viral hepatitis.

EPR also addressed the cancer burden attributable to HIV. For cervical cancer, 5% of the global burden was estimated to be attributable to HIV; this percentage was more than 40% in southern Africa, where the contribution of HIV was much higher in younger women (Ibrahim Khalil et al., 2022a). An estimated 19 560 HIV-attributable cases of Kaposi sarcoma are diagnosed annually in sub-Saharan Africa (~80% of the worldwide burden) versus 5064 cases of non-HIV-attributable (classic or endemic) Kaposi sarcoma (~60% of the worldwide burden) (Figure 1) (Ibrahim Khalil et al., 2022b).

Figure 1. Age-standardized incidence rates (ASIR) in 2020 by country of (A) HIV-attributable cervical cancer and (B) HIV-attributable Kaposi sarcoma, using the entire female population (for cervical cancer) or the entire population (for Kaposi sarcoma) as a denominator. (A) Reproduced from Ibrahim Khalil et al. (2022a). © 2022 World Health Organization; licensed by UICC. International Journal of Cancer published by John Wiley & Sons Ltd on behalf of UICC. (B) Reproduced from Ibrahim Khalil et al. (2022b). © 2022 World Health Organization. International Journal of Cancer published by John Wiley & Sons Ltd on behalf of UICC.

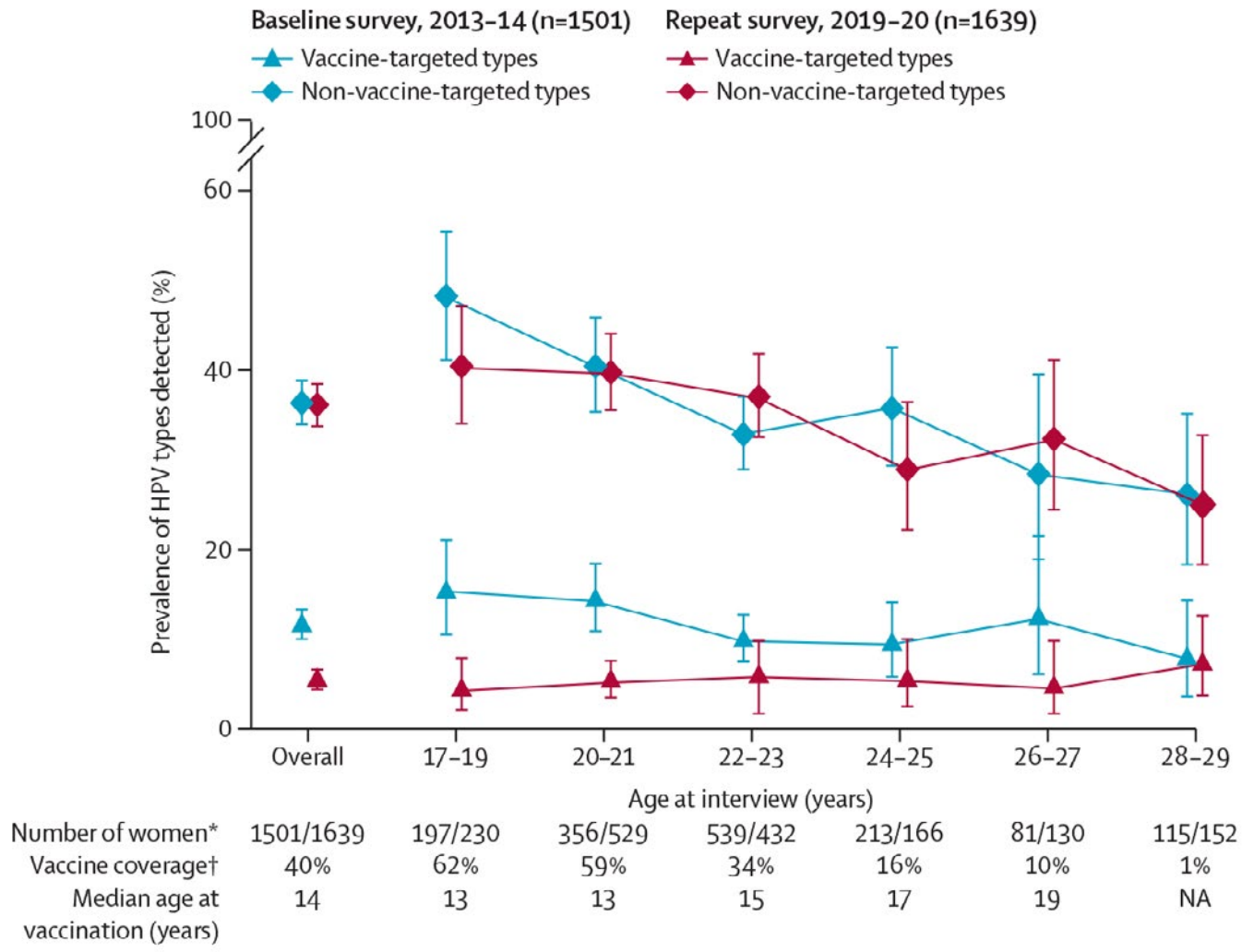


EPR studies generated valuable evidence to support the WHO advice in 2022 to opt for a single dose of human papillomavirus (HPV) vaccine. Yearly follow-up of a large cohort of females (*n* = 17 729) who received different numbers of doses of quadrivalent vaccine in India demonstrated robust immune response in single-dose recipients 10 years after vaccination and high efficacy against persistent HPV16/18 infections equivalent to that of two or three doses (Joshi et al., 2023a). By comparing antibody titres from girls aged 9–14 years in the United Republic of Tanzania who received a single dose of nonavalent vaccine with those from girls aged 10–18 years in the IARC study in India who received a single dose of quadrivalent vaccine, the Dose Reduction Immunobridging and Safety Study (DoRIS) randomized controlled trial demonstrated equivalent and sustained protection in the young Tanzanian girls (Baisley et al., 2022).

Quantifying the effectiveness of HPV vaccination is essential to reinforce the political and financial commitment of health authorities (Schulte-Frohlinde et al., 2022). Studies conducted by EPR have demonstrated the favourable impact of HPV vaccination on HPV burden at a population level in low- and middle-income countries (LMICs). Rwanda was the first African country to implement a national HPV vaccination programme, in 2011. To assess the population-level effectiveness of vaccination on HPV prevalence, cross-sectional surveys were done in 2013–2014 (baseline) and 2019–2020 (repeat) in sexually active women aged 17–29 years in Kigali, Rwanda (Figure 2) (Sayinzoga et al., 2023). Vaccine-type HPV prevalence in participants decreased from 12% in the baseline survey to 5% in the repeat survey, with an adjusted overall vaccine effectiveness of 47% (95% confidence interval [CI], 31–60%) and an adjusted indirect (due to herd protection) vaccine effectiveness of 32% (95% CI, 9–49%).

The large global burden of gastric cancer and its known principal cause, chronic infection with *Helicobacter pylori,* which is treatable, make gastric cancer a logical target for global action. EPR continues to investigate factors (e.g. salt intake) that may potentially explain regional and ethnic variations in gastric

Figure 2. Human papillomavirus (HPV) prevalence in baseline and repeat surveys in Rwanda by HPV type and age. Error bars show 95% confidence intervals. Vaccine-targeted types: HPV6, HPV11, HPV16, and HPV18. Non-vaccine-targeted types: 40 types detected by general primer (GP5+ or GP6+)-mediated polymerase chain reaction (PCR), other than the 4 vaccine-targeted types. NA, not applicable. * Baseline survey/repeat survey. † Repeat survey. Reproduced from Sayinzoga et al. (2023). © 2023 World Health Organization. Published by Elsevier Ltd.



cancer risk, using the IARC global survey, the Epidemiological Investigation of Gastric Malignancy (ENIGMA), and using biomarkers and standardized methods (Knaze et al., 2023). The GISTAR study, a collaboration with the University of Latvia, showed high compliance with the *H. pylori* test-and-treat and upper endoscopy examination among those who agreed to participate in the study, and reasons for refusal have been documented in detail, urging efforts to raise awareness (Leja et al., 2022). GISTAR also provided essential information on antibiotic resistance in those who received *H. pylori* eradication therapy, suggesting that the clarithromycin-containing regimen, unlike the amoxicillin/bismuth-containing treatment, should be avoided in a population-based setting, because the gut resistome remained increased. Correlations and temporal changes between gastric cancer and oesophageal cancer across populations worldwide were compared to inform on etiological similarities and differences (Li et al., 2023b).

As members of the WHO Guidelines Development Group for cervical cancer screening and treatment, EPR researchers identified the priority implementation research questions in the population-level introduction of the new screening algorithms, including primary HPV DNA and messenger RNA (mRNA) testing with or without triage (Broutet et al., 2022). EPR studies continued to generate evidence to inform the WHO living guidelines. The performance of visual inspection after application of acetic acid (VIA) and colposcopy as triage techniques was assessed in the ESTAMPA multicentre study in Latin America, in which more than 40 000 women aged 30–64 years were screened with HPV testing. Although the results varied greatly between examiners and study sites, both triage methods showed high sensitivity for the detection of cervical intraepithelial neoplasia grade 2 or 3 (CIN2/3) (84.5% for VIA and 91.2% for colposcopy), with an almost 50% reduction in referrals (Baena et al., 2023b; Valls et al., 2023). A longitudinal study involving 9526 women in China demonstrated that women with positive results on self-sampled HPV tests could be very effectively triaged with a combination of HPV16/18 genotyping and human gene methylation testing (with HPV16/18-positive women referred for colposcopy and non-HPV16/18-positive women tested for methylation). Such a triage strategy had a sensitivity of 96.6% and a specificity of 58.3% to detect CIN2+ lesions, and the colposcopy referral rate was reduced by half (Zhang et al., 2022a). Genotyping of cervical samples from 1252 participants (including 398 women with CIN2+ lesions) in the ESTAMPA study demonstrated that genotypic diversity (the prevalence of multiple infections of HPV types) gradually decreased with higher grade of lesions: 43% for ≤ CIN2, 28% for CIN3, and 8% for cancers (Basiletti et al., 2022; Correa et al., 2022).

Based on a longitudinal follow-up of 1153 women living with HIV (WLHIV) in India, EPR demonstrated that the women with persistent HPV infection had a 138-fold increased risk of CIN2+ lesions compared

Figure 3. Essential criteria to be fulfilled by a screening programme to be considered as organized. Through a systematic review and an expert consensus, 16 essential criteria were identified. Reproduced from Zhang et al. (2022b). © Zhang et al., 2022.

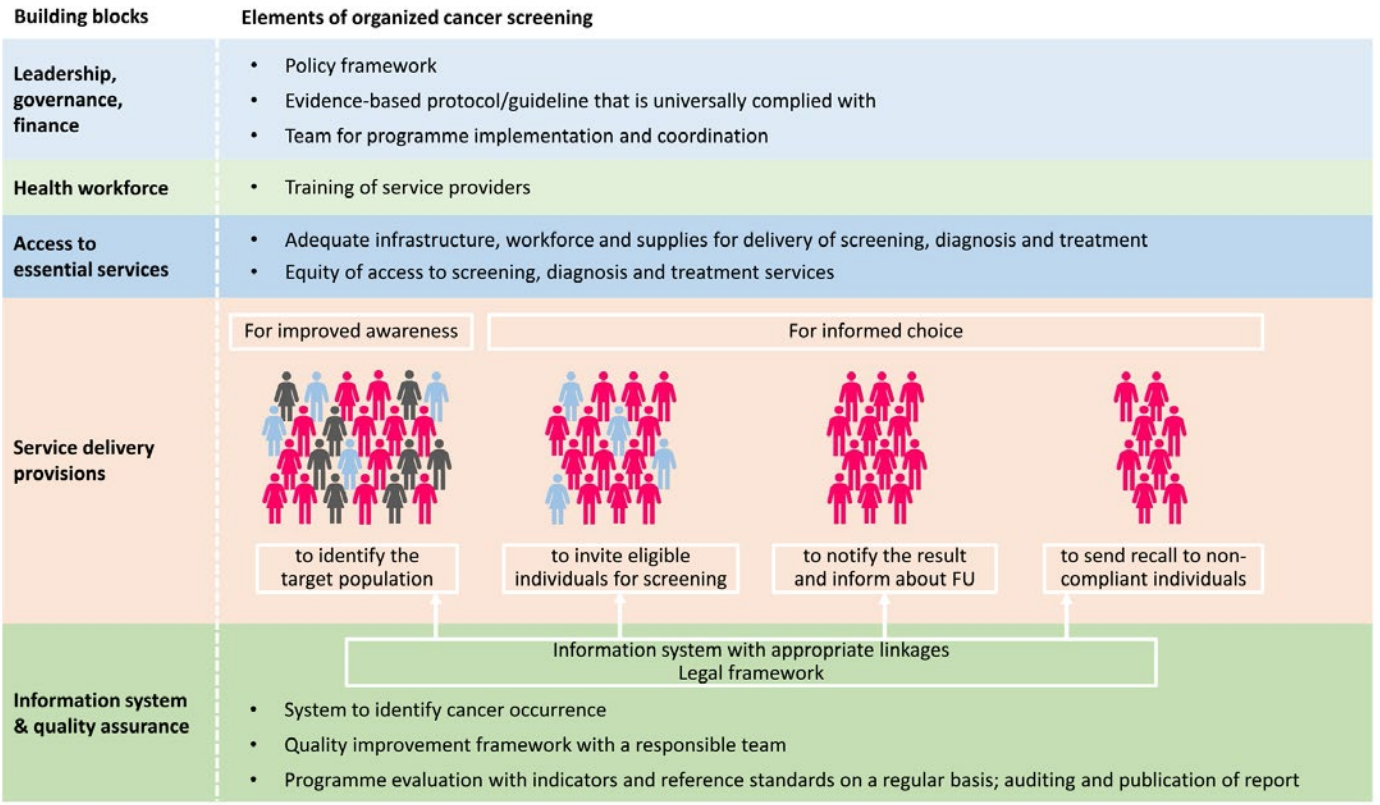


Figure 4. In collaboration with the Department of Health and the Health Service Executive of Ireland, EPR defined the key issues in the practice of cancer audits in cervical screening programmes. © IARC.

with the HPV-negative women. The HPV-negative WLHIV have nearly zero risk of developing CIN2+ in the next 3.5 years, thus providing supporting evidence to the WHO recommendation to extend the screening interval to 3–5 years in WLHIV despite their significant risk of developing cervical cancer (Joshi et al., 2023b).

The efficacy and safety of thermal ablation and cryotherapy for cervical precancers were studied in a large randomized trial in Zambia (Mwanahamuntu et al., 2022), and a systematic review of the evidence was performed (Zhang et al., 2023a). Another study, conducted in Benin, Cote d'Ivoire, and Senegal, demonstrated the feasibility of screening a large number of women opportunistically through primary care settings and the high acceptance (88%) of same-day ablative treatment. The most significant implementation challenge was low compliance (66.1%) of the women referred to higher-level facilities for excisional treatment or for further investigation due to suspected cancer (Selmouni et al., 2022a).

Studies are continuing in EPR to evaluate the effectiveness of screening for cancer sites other than the cervix (breast, colorectum, lung, prostate, and stomach). Clinical breast examination was evaluated as a screening test for women aged 35–69 years in a randomized controlled trial in India. Long-term (14-year) follow-up of 115 290 participants demonstrated a significantly higher age-standardized incidence rate of early-stage cancers (relative risk [RR], 1.4; 95% CI, 1.1–1.8) in the screened women compared with the unscreened women, without any difference in the mortality rate (RR, 1.1; 95% CI, 0.8–1.5) (Ramadas et al., 2023).

A demonstration project implemented in Morocco in collaboration with the Ministry of Health screened 10 000 men and women aged 50–75 years for colorectal cancer with the faecal immunochemical test (FIT) through primary health care (Selmouni et al., 2022b). Among the 4.7% FIT-positive individuals, compliance with colonoscopy was only 62.6%, which was directly linked with the lengthening of the waiting time as endoscopy services became overwhelmed. The detection rate of colorectal cancer was low (0.5 per 1000 screened).

An EPR study reported quantitative estimates of the impact of the COVID-19 pandemic on cancer screening programmes in selected LMICs (Argentina, Bangladesh, Colombia, Morocco, Sri Lanka, and Thailand). Compared with 2019, there was a significant reduction in 2020 in the volume of tests (the reduction ranged from 14.1% in Bangladesh to 72.9% in Argentina for cervical screening), the number of diagnostic evaluations of screen-positive individuals, and the detection rates of precancers (e.g. a reduction of 45.4% in the detection rate of CIN2/3 in Argentina) and cancers (e.g. a reduction of 19.1% in breast cancer detection in Morocco) (Lucas et al., 2023).

Providing evidence-based guidance to countries to implement cancer screening programmes with high quality remained one of the key research focuses of EPR (Figure 3 and Figure 4).

Cancer Screening in Five Continents (CanScreen5) (Zhang et al., 2023b) is a global cancer screening data repository, which reported the status and

Table 1. Comparison of organization, protocol, and quality assurance mechanisms of the cervical cancer screening programmes by continent, based on information collected by the CanScreen5 project. Reproduced from Zhang et al. (2023b). © Zhang et al., 2023.

Question	Response	Percentage by continent					*P* value
		Africa (*n* = 15)	Americas (*n* = 22)	Asia (*n* = 8)	Europe (*n* = 27)	Oceania (*n* = 1)	
Organization of screening							
Is there a person responsible for management or coordination of the cancer screening activities?	Yes	86.7	77.3	100	74.1	100	0.423
Does the health authority allocate a budget to cancer screening?	Yes	53.3	63.6	100	85.2	100	**0.001**
Is there a policy document that recommends cancer screening?	Yes	100	100	100	96.3	100	0.733
What is the type of the policy document?	Law	0	13.6	25.0	25.9	0	**< 0.001**
When was the screening programme initiated?	Before 2000	6.7	40.9	25.0	33.3	100	**0.042**
Are the screening tests available free of charge?	Yes	80.0	90.9	87.5	88.9	100	0.542
Are the diagnostic tests available free of charge?	Yes	46.7	63.6	50	74.1	0	0.056
Information system and data collection							
Are the screening-related data collected on an individual basis?	Yes	20.0	59.1	75.0	70.4	100	**0.001**
Are screening data linked with population-based cancer registries?	Yes	0	9.1	25.0	66.7	0	**< 0.001**
Screening protocol							
What is the primary screening method?	VIA	93.3	46.7	20.0	0	0	NA
	Cytology	26.7	95.5	62.5	100	0	
	HPV	26.7	27.3	25.0	11.1	100	
	Co-test	0	18.2	0	0	0	
Invitations for screening and further assessment							
Is there a system to send individual invitations to the eligible population?	Yes	0	27.3	62.5	77.8	100	**< 0.001**
Are the screen-positive individuals actively contacted for further assessment?	Yes	73.3	50.0	87.5	51.9	100	0.197
Quality assurance of screening activities							
Is there a documented guideline or policy for quality assurance?	Yes	46.7	63.6	75.0	55.6	100	**< 0.001**
Is there a person responsible for quality assurance?	Yes	53.3	50.0	87.5	66.7	100	0.083
Are there specified performance indicators?	Yes	73.3	77.3	100	55.6	100	**< 0.001**
Were the performance reports published?	Yes	33.3	31.8	75.0	59.3	100	**0.074**

HPV, human papillomavirus; NA, not applicable; VIA, visual inspection after application of acetic acid.

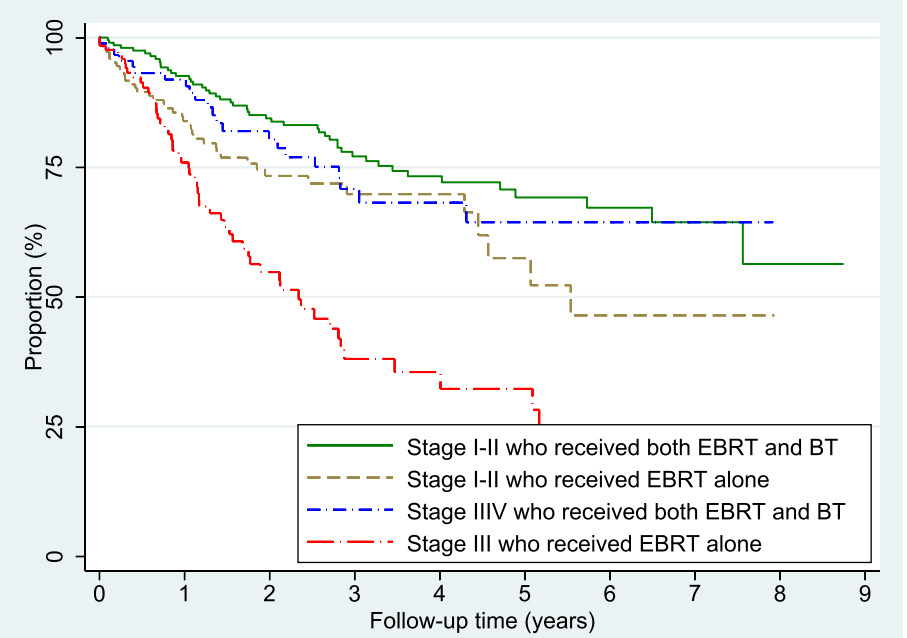
performance of breast cancer (*n* = 57), cervical cancer (*n* = 75), and colorectal cancer (*n* = 51) screening programmes in 84 countries in 2023 (Table 1). Data collected mainly from the ministry of health in each country, using a harmonized set of criteria and indicators, were made publicly available through a web-based portal (https://canscreen5.iarc.fr/).

The cancer burden, prevalence of cancer risk factors, existing national cancer control plans, and health system capacities of fragile states were reviewed in a collaborative study with WHO (Mosquera et al., 2022). Countries with a Fragile States Index (FSI) score of ≥ 90.0 for at least 10 years during the period 2006–2020 (*n* = 31) were included. The proportion of cancers attributable to infections was significantly higher in these 31 states than in non-fragile states. Despite the growing prevalence of risk factors and cancer burden, only 6 of the 31 states had implemented more than one of the WHO MPOWER measures for tobacco control, and only half had an updated cancer control plan.

EPR scientists have strongly advocated for implementation research studies to improve cancer control (Basu et al., 2022). Such studies conducted by EPR are aimed at identifying context-appropriate solutions to improve participation in cancer screening, especially of socio-economically disadvantaged populations (Oommen et al., 2023). Some of these solutions include having dedicated policies to improve coverage among disadvantaged populations and using innovative methods to minimize the structural barriers. As part of one such study in the European Union, a survey was conducted among 31 screening programme managers from 22 countries to identify existing policies focused on improving participation of vulnerable women in cervical screening. The results of this survey suggested that although many countries identify lower coverage among vulnerable population subgroups as a public health problem, few have developed dedicated policies to broaden coverage in these subgroups (Mallafré-Larrosa et al., 2023).

EPR studied the effectiveness of patient navigation to improve access to cancer screening through a systematic review of evidence (Mosquera et al., 2023a). The review found that patient navigation could increase screening participation by up to 250% compared with usual care. However, only one of the 44 studies included in the review was conducted in LMICs. Patterns-of-care studies reported the impact of delays and abandonment of cancer care in selected LMICs (Figure 5).

Figure 5. In a patterns-of-care study on patients with cervical cancer in Morocco, EPR demonstrated that more than half of the patients did not have a full course of radiation (external-beam radiotherapy [EBRT] and brachytherapy [BT]), and they had significantly lower survival compared with patients with the same stage of disease who completed the full course of radiation. Reproduced from Benider et al. (2022). © Benider et al., 2022.



	2-year		5-year	
	No. at risk	Survival proportion (%)	No. at risk	Survival proportion (%)
Radiotherapy type by stage at diagnosis				
EBRT and brachy therapy among stage I-II patients	133	84.4	46	69.2
EBRT alone among stage I-II patients	61	73.3	12	57.5
EBRT and brachy therapy among stage III patients	51	80.4	18	64.4
EBRT alone among stage III patients	35	54.8	9	32.3

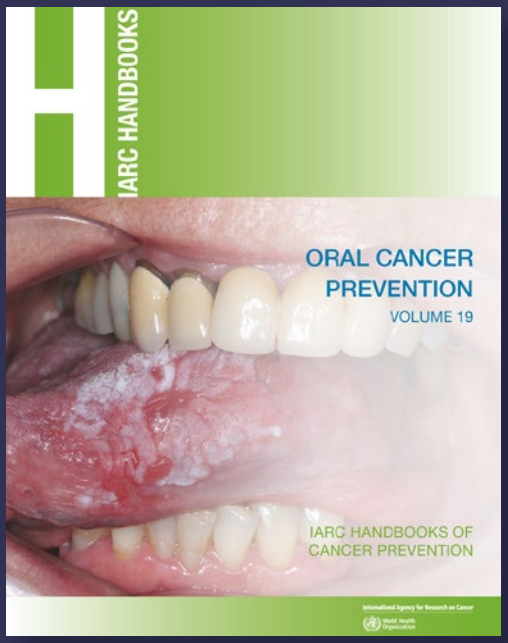
CanScreen5

Capacity-building is at the core of developing and upholding the CanScreen5 network. In the short term, it assists public health officials and researchers in understanding how to evaluate and ensure quality assurance of screening programmes. Over time, it stimulates countries to collect and share precise information about their cancer screening initiatives. These data are subsequently used to review and enhance the quality improvement of these programmes.

The CanScreen5 framework involves a training programme organized by IARC, geared towards imparting foundational cancer screening principles and quality improvement. Training of Trainers was provided to 44 countries (17 in Africa and 27 in the Community of Latin American and Caribbean States [CELAC]), with participants nominated by the health authorities of each country.

The next step involves helping Master Trainers to spread the training to health-care providers and screening managers in their respective countries. To ensure the long-term sustainability of the CanScreen5 capacity-building initiative, EPR is proposing to establish training hubs worldwide, managed by regional organizations or institutions. These hubs will encompass a customized Training of Trainers programme rooted in the regional and local context. This vision ensures the sustainability and lasting impact of the CanScreen5 capacity-building programme.

Participants in the in-person session of the CanScreen5 Training of Trainers Learning Programme in Sharjah (United Arab Emirates), 17–19 May 2022. © IARC.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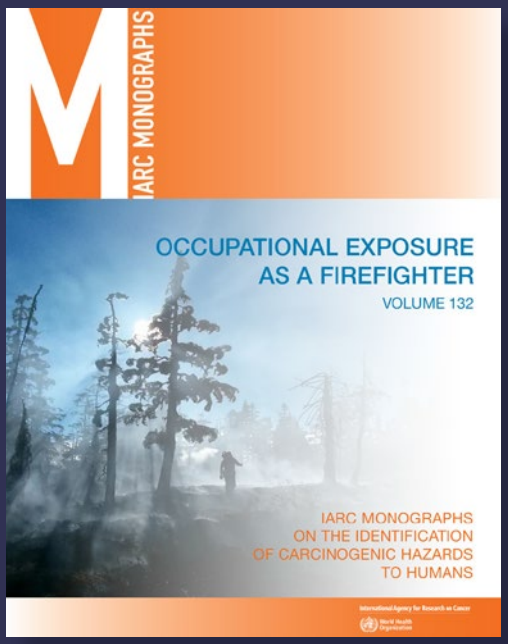
VOLUME 19
IARC HANDBOOKS OF CANCER PREVENTION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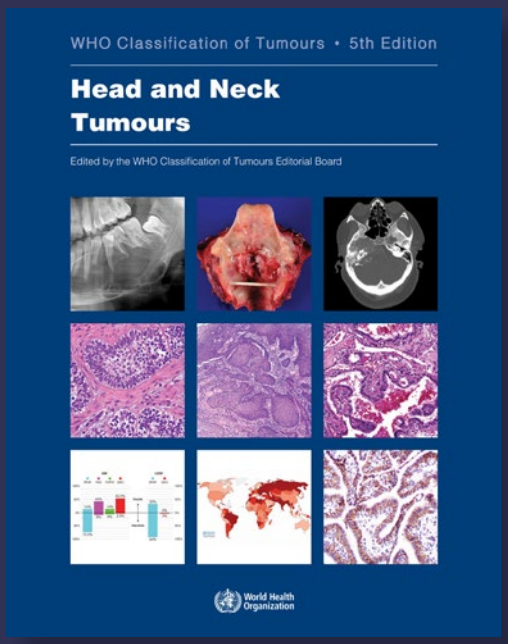
WHO Classification of Tumours • 5th Edition
Head and Neck Tumours
Edited by the WHO Classification of Tumours Editorial Board
World Health Organization

Evidence Synthesis and Classification Branch (ESC)

Branch head
Dr Ian A. Cree (until July 2023)
Dr Mary Schubauer-Berigan (acting)

Deputy branch heads
Dr Béatrice Lauby-Secretan
Dr Dilani Lokuhetty
Dr Mary Schubauer-Berigan
(until July 2023)

Secretary
Ms Anne-Sophie Bres

IARC Monographs Programme (IMO)

Programme head
Dr Mary Schubauer-Berigan

Scientists
Dr Lamia Benbrahim-Tallaa
Dr Aline De Conti
Dr Nathan DeBono (until March 2023)
Dr Fatiha El Ghissassi
(until August 2023)
Dr Caterina Facchin
Dr Yann Grosse
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Dr Elisa Pasqual
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(until September 2022)
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Student
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(until August 2023)

IARC Handbooks Programme (IHB)

Programme head
Dr Béatrice Lauby-Secretan

Scientists
Dr Véronique Bouvard
(until August 2023)
Dr Daniela Mariosa

Secretary/technical assistant
Ms Marieke Dusenberg

Technical assistants
Ms Noëmi Joncour
Ms Niree Kraushaar
Ms Solène Quennehen
(until March 2023)

Postdoctoral fellow
Dr Nahid Ahmadi

Visiting scientists
Dr Susan Gapstur
Dr Suzanne Nethan
Dr Irena Duš-Ilnicka (until June 2023)

WHO Classification of Tumours Programme (WCT)

Programme head
Dr Ian A. Cree (until July 2023)
Dr Dilani Lokuhetty

Scientists
Dr Gabrielle Goldman-Lévy
(pathologist)
Dr Iciar Indave (systematic reviewer)
(until January 2022)
Dr Nick Myles (systematic reviewer)

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Ms Anne-Sophie Bres

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Mr Ramon Cierco Jiménez

Trainees
Ms Valeria Baldassarre
(until April 2022)
Mr Nicolás Rosillo Ramírez
(until February 2022)

The Evidence Synthesis and Classification Branch (ESC) comprises three programmes: the IARC Handbooks Programme, the IARC Monographs Programme, and the WHO Classification of Tumours Programme.

The IARC Handbooks Programme produces the *IARC Handbooks of Cancer Prevention*, a series of systematic scientific reviews that identify interventions and strategies that may reduce the risk of cancer or mortality from cancer. The programme also runs collaborative projects on topics related to recent *Handbooks* volumes.

The IARC Monographs Programme produces the *IARC Monographs on the Identification of Carcinogenic Hazards to Humans*, a series of systematic scientific reviews that identify environmental factors that may cause cancer in humans. The programme also organizes advisory groups and international scientific workshops on key issues pertaining to the assessment of carcinogens and their mechanisms.

The WHO Classification of Tumours Programme produces the *WHO Classification of Tumours* series (also known as the WHO Blue Books). Now in its fifth edition as a series of 14 volumes, this series provides the definitive and internationally accepted standards for the diagnosis of tumours.

For each volume of the *WHO Classification of Tumours*, the *IARC Monographs*, and the *IARC Handbooks*, IARC convenes international, interdisciplinary groups of expert scientists and physicians to systematically review the pertinent scientific literature and to develop consensus evaluations and classifications. IARC selects these experts on the basis of their knowledge and experience as well as the absence of conflicting interests.

IARC Monographs Programme (IMO)

The IARC Monographs Programme (IMO) is responsible for producing the *IARC Monographs on the Identification of Carcinogenic Hazards to Humans*. The *IARC Monographs* are fundamental to the Agency's mission of identifying the preventable causes of cancer in humans. Since the inception of the *Monographs* in 1971, 1046 agents have been evaluated for carcinogenicity. This international, interdisciplinary endeavour provides an authoritative reference for researchers, health authorities, and the public. Health agencies worldwide rely on the *Monographs* for scientific support of actions to control exposures and prevent cancer. In addition to producing this important resource, the scientific personnel of IMO contribute to the scientific literature on topics related to the methodology and contents of the *Monographs*.

Major accomplishments

The IARC Monographs Programme organized five Working Group meetings and two Scientific Workshops during the 2022–2023 biennium. The meeting for Volume 131 was held fully remotely, because of the travel restrictions put in place during the COVID-19 pandemic. The other meetings were held as hybrid meetings, incorporating lessons learned from the remote meetings. The agents evaluated at the five Working Group meetings included a range of agents that had been recommended as priorities for evaluation:

- Volume 131: Cobalt, Antimony Compounds, and Weapons-Grade Tungsten Alloy (2–18 March 2022)
- Volume 132: Occupational Exposure as a Firefighter (7–14 June 2022)
- Scientific Workshop on Epidemiological Bias Assessment in Cancer Hazard Identification (17–21 October 2022)
- Volume 133: Anthracene, 2-Bromopropane, Butyl Methacrylate, and Dimethyl Hydrogen Phosphite (28 February–7 March 2023)
- Volume 134: Aspartame, Methyleugenol, and Isoeugenol (6–13 June 2023)
- Scientific Workshop on Key Characteristics-associated End-points for Evaluating Mechanistic Evidence of Carcinogenic Hazards (25–28 July 2023)
- Volume 135: Perfluorooctanoic Acid (PFOA) and Perfluorooctanesulfonic Acid (PFOS) (7–14 November 2023)

The focus and results of these meetings (Table 1) illustrate the unique ability of the *Monographs* to evaluate the carcinogenicity of diverse agents. These agents range from chemicals that have been tested only in animal bioassays to complex exposures, such as occupational exposure as a firefighter, which have been evaluated in epidemiological and mechanistic studies.

The evaluations achieved in these meetings comprised 19 classifications, including 7 agents never before evaluated by IARC, and re-evaluations of 12 agents considered previously.

A concise summary of each evaluation with the classification, accompanying rationale, and key references is published in *The Lancet Oncology* within several weeks of each meeting. Full details and supporting data are provided in the complete *Monographs* volume, which is expected to be published about a year after each meeting. Both are available to download for free from the IARC Publications website (https://publications.iarc.who.int/).

Table 1. Summary of evaluations from the five *Monographs* meetings held in 2022–2023

Agent (Volume)	Overall classification	Strength of evidence of cancer in humans (tumour type provided for *limited* or *sufficient* evidence)	Strength of evidence of carcinogenicity in experimental animals	Strength of mechanistic evidence (key characteristics of carcinogens with *consistent and coherent* evidence[a])
Cobalt, Antimony Compounds, and Weapons-Grade Tungsten Alloy (Volume 131)				
Cobalt metal without tungsten carbide or other metal alloys	Group 2A	*Inadequate*	*Sufficient*	*Strong* (2, 5, 6, 10)
Soluble cobalt(II) salts	Group 2A	*Inadequate*	*Sufficient*	*Strong* (2, 5, 7, 10)
Cobalt(II) oxide	Group 2B	*Inadequate*	*Sufficient*	
Cobalt(II,III) oxide	Group 3	*Inadequate*	*Inadequate*	
Cobalt(II) sulfide	Group 3	*Inadequate*	*Limited*	
Other cobalt(II) compounds	Group 3	*Inadequate*	*Inadequate*	
Trivalent antimony	Group 2A	*Limited* (lung)	*Sufficient*	*Strong* (2, 5, 6, 10)
Pentavalent antimony	Group 3	*Inadequate*	*Inadequate*	
Weapons-grade tungsten (with nickel and cobalt) alloy	Group 2B	*Inadequate*	*Sufficient*	
Occupational Exposure as a Firefighter (Volume 132)				
Occupational exposure as a firefighter	Group 1	*Sufficient* (mesothelioma, bladder) *Limited* (colon, prostate, testis, melanoma of the skin, non-Hodgkin lymphoma)	*Inadequate*	*Strong* (2, 4, 5, 6, 8)
Anthracene, 2-Bromopropane, Butyl Methacrylate, and Dimethyl Hydrogen Phosphite (Volume 133)				
Anthracene	Group 2B	*Inadequate*	*Sufficient*	
2-Bromopropane	Group 2A	*Inadequate*	*Sufficient*	*Strong* (2, 5, 7)
Butyl methacrylate	Group 2B	*Inadequate*	*Sufficient*	
Dimethyl hydrogen phosphite	Group 2B	*Inadequate*	*Sufficient*	
Aspartame, Methyleugenol, and Isoeugenol (Volume 134)				
Aspartame	Group 2B	*Limited*	*Limited*	(5)
Methyleugenol	Group 2A	*Inadequate*	*Sufficient*	*Strong* (1, 2)
Isoeugenol	Group 2B	*Inadequate*	*Sufficient*	
Perfluorooctanoic Acid (PFOA) and Perfluorooctanesulfonic Acid (PFOS) (Volume 135)				
Perfluorooctanoic acid (PFOA)	Group 1	*Limited* (renal cell carcinoma and testicular cancer)	*Sufficient*	*Strong* (4, 5, 7, 8, 10)
Perfluorooctanesulfonic acid (PFOS)	Group 2B	*Inadequate*	*Limited*	*Strong* (4, 5, 7, 8, 10)

N/A, not applicable.
[a] Numbers correspond to one or more of the 10 key characteristics of carcinogens, as identified by Smith et al. (2016; https://www.ncbi.nlm.nih.gov/pubmed/?term=26600562) and described in the Preamble to the *IARC Monographs* (https://monographs.iarc.who.int/iarc-monographs-preamble-preamble-to-the-iarc-monographs/).

A summary of the results of the Scientific Workshop on Epidemiological Bias Assessment in Cancer Hazard Identification was published in the scientific journal *Occupational and Environmental Medicine*, ahead of the publication of a new volume in the IARC Scientific Publications series *Statistical Methods in Cancer Research*. The new volume, expected in the first half of 2024, will summarize methods for bias assessment to support cancer hazard identification, illustrate these methods with examples, and discuss how these methods could also be incorporated into future published studies to better inform cancer hazard and risk assessments.

The discussions during the Scientific Workshop on Key Characteristics-associated End-points for Evaluating Mechanistic Evidence of Carcinogenic Hazards will result in the publication of an *IARC Monographs* Technical Report. The report, expected in the first half of 2024, will provide insights into the mechanistic evaluation of cancer hazards and highlights on the furtherance of the application of the key characteristics of carcinogens. In addition, it is expected that the report will be accompanied by research articles addressing specific topics stemming from the discussions relative to the main themes of the workshop.

Publications

During the 2022–2023 biennium, the following *IARC Monographs* volumes were published:

- Volume 129: Gentian Violet, Leucogentian Violet, Malachite Green, Leucomalachite Green, and CI Direct Blue 218
- Volume 130: 1,1,1-Trichloroethane and Four Other Industrial Chemicals
- Volume 131: Cobalt, Antimony Compounds, and Weapons-Grade Tungsten Alloy
- Volume 132: Occupational Exposure as a Firefighter

IARC Handbooks Programme (IHB)

The IARC Handbooks Programme (IHB) is responsible for producing the *IARC Handbooks of Cancer Prevention*. The *IARC Handbooks* evaluate interventions and strategies for primary and for secondary cancer prevention. Recent volumes have covered screening (for cancers of the cervix and the oral cavity), individual-level and population-level interventions, and preventive strategies.

Major accomplishments

Volume 19: Oral Cancer Prevention (September–December 2021)

This three-in-one *Handbook* of oral cancer prevention provides evaluations of primary and secondary prevention interventions and strategies: (i) the impact of cessation of exposure to the established risk factors (tobacco smoking, alcoholic beverage consumption, smokeless tobacco use, chewing of areca nut with or without tobacco) in reducing oral cancer incidence or mortality; (ii) behavioural and pharmacological interventions aimed at reducing the prevalence of use of smokeless tobacco or areca nut products; and (iii) screening by clinical oral examination (Figure 1).

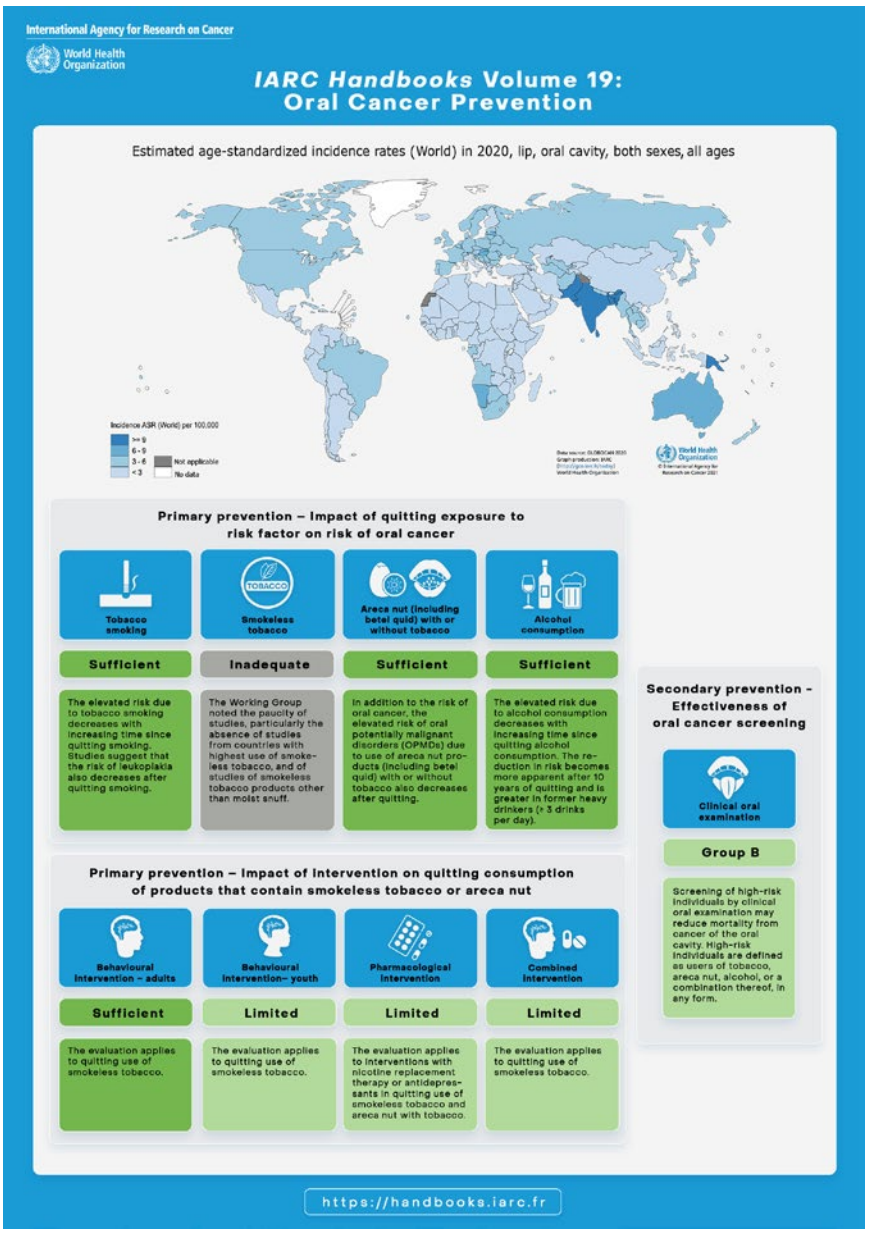
Volumes 20A and 20B: Alcohol Control

Alcoholic beverages have been classified by the *IARC Monographs* as carcinogenic to humans (Group 1), causing cancers of the oral cavity, pharynx, larynx, oesophagus, liver, colorectum, and female breast. At the World Health Assembly in 2010, Resolution WHA63.13 was adopted, on a global strategy to reduce the harmful use of alcohol. Therefore, similar to the series on tobacco control (Volumes 11–14), the *IARC Handbooks* Programme is currently developing a two-part volume on alcohol control.

Volume 20A: Reduction or Cessation of Alcoholic Beverage Consumption (February 2023–May 2023)

The *IARC Handbooks* Programme reviewed and evaluated evidence from epidemiological and mechanistic studies on cessation or reduction of alcoholic beverage consumption. Overall, there is *sufficient evidence* that reduction or cessation of alcoholic beverage consumption reduces alcohol-associated risk of oral cancer and oesophageal cancer, *limited evidence* for laryngeal cancer, colorectal cancer, and breast cancer, and *inadequate evidence* for pharyngeal cancer and liver cancer. Moreover, there

Figure 1. *IARC Handbooks* Volume 19: Oral Cancer Prevention. © IARC.



is *sufficient evidence* that cessation of alcoholic beverage consumption reduces alcohol-related carcinogenesis, based on *strong evidence* for three mechanisms: (i) cessation results in the elimination of alcohol-related local exposure of the upper aerodigestive tract and colon to acetaldehyde; (ii) in the context of chronic heavy alcohol consumption, cessation leads to a decrease in DNA chromosomal aberrations and micronuclei in peripheral blood mononuclear cells within a few months to several years, and in a rapid reduction or elimination of acetaldehyde–DNA adduct formation in cells of the oral cavity; and (iii) among individuals with alcohol use disorders, cessation reverses increased intestinal permeability and microbial translocation.

Volume 20B: Alcohol Control Policies

This volume, prepared in close collaboration with the WHO Regional Office for Europe, aims to evaluate how individual-level and population-level interventions may reduce the prevalence of alcohol consumption. A scoping meeting for Volume 20B took place in November 2023, to identify scientific priority areas for review, define the relevant experts to invite, and discuss the outline of the book. Subgroup sessions are planned in June 2024 (remotely), and plenary sessions will be held in October 2024 (in person).

Publications

- *IARC Handbooks* Volume 18: Cervical Cancer Screening was published online in May 2022 and in print in October 2022.
- *IARC Handbooks* Volume 19: Oral Cancer Prevention was published online in November 2023.

WHO Classification of Tumours Programme (WCT)

The work of the WHO Classification of Tumours Programme (WCT) encompasses the *WHO Classification of Tumours* series (also known as the WHO Blue Books), the *IAC-IARC-WHO Cytology Reporting Systems* series, the IARC histopathology laboratory, and the International Collaboration for Cancer Classification and Research (IC^3R) including the Evidence Gap Map project, which is funded by a European Union Horizon grant (grant number HORIZON-HLTH-2021-CARE05 PROJECT 101057127).

WHO Classification of Tumours series

Tumour classification is a major scientific endeavour of considerable importance, underpinning the diagnosis of all cancers worldwide. In recent years, the adoption of a relational database approach for the series and a hierarchical classification format according to Linnaean principles has vastly improved the standardization of tumour classification across anatomical sites, requiring authors to consider all characteristics of each tumour and highlighting the increasingly multidisciplinary nature of cancer diagnosis.

During the 2022–2023 biennium, the following volumes were published in print (these are also available on the WHO Classification of Tumours Online website; https://tumourclassification.iarc.who.int/):

- *Central Nervous System Tumours*, fifth edition (2022)
- *Urinary and Male Genital Tumours*, fifth edition (2022)
- *Paediatric Tumours*, fifth edition (2023) (Figure 2).

The following volumes were made available on the WHO Classification of Tumours Online website as beta versions:

- *Head and Neck Tumours*, fifth edition
- *Endocrine Tumours*, fifth edition
- *Haematolymphoid Tumours*, fifth edition
- *Skin Tumours*, fifth edition
- *Eye and Orbit Tumours*, fifth edition
- *Genetic Tumour Syndromes*, fifth edition

These six web-based volumes are in various stages of print production. *Head and Neck Tumours* and *Haematolymphoid Tumours* are intended to be produced by early 2024 and the rest during 2024. The books and the accompanying website have both been very well received, and use of the classification is expanding in the wider biomedical community (e.g. among epidemiologists, radiologists, researchers, oncologists, molecular pathologists, and geneticists). Production of the *WHO Classification of Tumours* series continues to be funded by book sales and website subscriptions alone. Special discounts are provided for readers in low- and middle-income settings and for trainees.

IAC-IARC-WHO Cytopathology Reporting Systems series

Cytopathology is important as a discipline for early cancer detection or diagnosis, especially in low- and middle-income settings. It also provides a pathway to molecular and cellular diagnosis. In keeping with the IARC objective of promoting international collaboration in cancer research, WCT initiated a dialogue with the International Academy of Cytology (IAC) in 2019, to develop IAC-IARC-WHO reporting systems for cytopathology. The aim of this series is to harmonize cytopathology reporting across different body sites at a global level. The first two volumes – for lung cytopathology and pancreaticobiliary cytopathology – have been published. These will be followed by reporting systems for lymph node, spleen, and thymus cytopathology and soft tissue cytopathology. In 2023, work started on the upcoming volumes for breast cytopathology, liver cytopathology, and kidney and adrenal cytopathology. After all major sites have been covered, the reporting

Figure 2. *Paediatric Tumours*, fifth edition, Part A. © IARC.

systems will be revised regularly with new and emerging research evidence. These new reporting systems are designed to be a helpful addition to the *WHO Classification of Tumours* series.

During the 2022–2023 biennium, the following volumes were published in print (these are also available on the WHO Classification of Tumours Online website; https://tumourclassification.iarc.who.int/):

- *WHO Reporting System for Lung Cytopathology*, first edition (2023)
- *WHO Reporting System for Pancreaticobiliary Cytopathology*, first edition (2023)

Histopathology laboratory

The histopathology laboratory provides pathology expertise and support across the Agency through four WCT pathologists and a research assistant. It also provides a histopathology service to other IARC groups, including providing whole slide images for the WHO Blue Books. The histopathology imaging needs of the WHO Blue Books are critical to their future success, and close links with pathology provision within IARC are facilitated by WCT's leadership of the histopathology laboratory. This is also an essential service to the laboratory groups and others engaged in studies involving human tissue.

The histopathology laboratory has modernized its equipment, with a corresponding increase in capacity and capability. The laboratory is increasingly involved in all aspects of digital and computational pathology. Its capacity to produce high-quality immunohistochemistry for research projects has been enhanced by the acquisition of an automated immunostainer and a cryostat, which is used to produce slides and frozen sections. It is now a state-of-the-art research laboratory located within the new IARC building. Collaborations conducted with Centre Léon Bérard and other institutions worldwide continue to expand.

International Collaboration for Cancer Classification and Research (IC^{3}R)

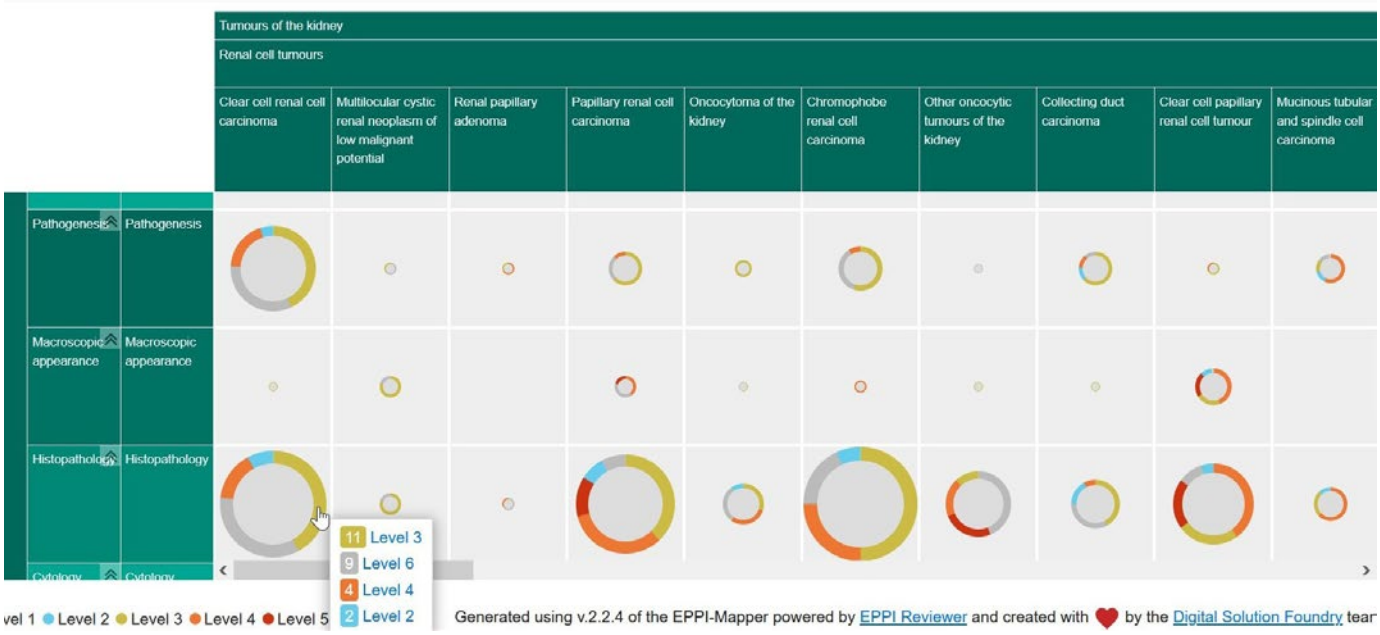
The translation of research findings into practice is never easy, and the sheer volume of information produced each year can be daunting for those involved. Crucially, scientific information must be of high quality to be of use. Unlike in other branches of medicine, the translation of cancer research into diagnostic practice is largely in the hands of its users, through incorporation into the WHO Classification of Tumours.

The International Collaboration for Cancer Classification and Research (IC^{3}R; https://ic3r.iarc.who.int/) was established by WCT to bring cancer research institutions together to improve research quality and to meet the need for evaluation and synthesis of research findings. Currently, 22 institutions are involved in IC^{3}R, and it is funded by membership dues. IC^{3}R aims to promote evidence-based practice in pathology and to set standards for tumour classification and cancer research harmonization to underpin successful translation of cancer pathology research into tumour classifications and clinical practice. The formation of inter-professional research teams, including pathologists, epidemiologists, systematic reviewers, and cancer researchers, under the IC^{3}R umbrella was further enhanced by securing a large innovative European Union Horizon grant for the WCT Evidence Gap Map project in 2022.

Evidence Gap Map (EVI MAP) project

Mapping the Evidence for the WHO Classification of Tumours: a Living Evidence Gap Map by Tumour Type (EVI MAP) includes an international consortium of five European institutions and one additional international partner, coordinated by WCT. The initiative will enable the identification of evidence gaps, strengths, and weaknesses in the entire spectrum of human tumour classifications, to build a solid framework for future evidence-based pathology practice and research on tumour classification. It aims to inform the WCT editorial process for the upcoming editions of the WHO Blue Books, by creating dynamic interactive evidence maps for human tumours. A sample evidence gap map is shown in Figure 3.

Figure 3. A sample evidence gap map from the EVI MAP project. Generated using v.2.0.1 of the EPPI-Mapper, powered by EPPI Reviewer and created with the Digital Solution Foundry team. Digital Solution Foundry and EPPI Centre (2023), EPPI-Mapper, Version 2.2.4. EPPI Centre, UCL Social Research Institute, University College London.



Learning and Capacity-Building Branch (LCB)

Branch head
Ms Anouk Berger

Assistant, IARC research training and fellowship programme
Ms Isabelle Battaglia

Assistant, IARC courses programme
Ms Sandrine Montigny

Project assistants
Ms Heather Coombs
Ms Dominique Meunier
(until July 2023)

Multimedia and e-learning assistant
Ms Amélie Labaume

Secretary
Ms Mira Delea

Administrative clerks
Ms Elke Niehaus
Ms Nadia Ben Amara
(until July 2023)
Ms Erika Ferrand-Cooper
(until July 2023)

Master's student
Ms Julie Chrétien (until July 2023)

Consultants
Ms Amélie Labaume
(until June 2022)
Ms Julie Cwik (until July 2022)
Ms Dominique Meunier

Affiliated staff
Dr Andre Carvalho (Scientific director, Summer School module on Implementing Cancer Prevention and Early Detection)
Dr Arunah Chandran (Scientific director, Summer School module on Implementing Cancer Prevention and Early Detection)
Dr Isabel Mosquera (Scientific director, Summer School module on Implementing Cancer Prevention and Early Detection)
Dr Laure Dossus (Scientific director, Summer School module on Introduction to Cancer Epidemiology)
Dr Pietro Ferrari (Scientific director, Summer School module on Introduction to Cancer Epidemiology)
Dr Valerie McCormack (Scientific officer, fellowship programme)

As a core function of the Agency, IARC's education and training programmes have made a substantial contribution to the development of human resources for cancer research worldwide and have also helped to widen the Agency's network of collaborators.

Key achievements of IARC's education and training programmes during 2022–2023 are presented here. Whereas the Learning and Capacity-Building Branch (LCB) coordinates the Agency's activities in these areas, many initiatives are led by the research Branches.

Research Training and Fellowship Programme

The programme offers researchers at different stages of their career (collectively referred to as Early Career and Visiting Scientists) opportunities to receive training at IARC by participating in collaborative research projects. These Early Career and Visiting Scientists are supported either by project funds from IARC Branches or by IARC Fellowships. A total of 296 Early Career and Visiting Scientists from 66 different countries were hosted at IARC during the biennium. This represents a 16.5% increase compared with the previous biennium (2020–2021), which is directly related to increased mobility resulting from the lifting of travel and entry restrictions imposed during the COVID-19 pandemic. Furthermore, a comparison of the 2022–2023 figures with those for the 2018–2019 biennium shows that the number of Early Career and Visiting Scientists joining IARC is back to pre-pandemic levels.

Hosting environment and career growth

The internal programme of generic skills courses, jointly managed by LCB and the Human Resources Office, offered more than 40 instructor-led training courses to Early Career and Visiting Scientists in 2022–2023 (Table 1), which were attended by more than 300 participants. Because of the preparation for the move to the new IARC building and the period of transition after the move, the courses offered were mostly held online until the second half of 2023. In addition, Early Career and Visiting Scientists accessed more than 80 online learning resources on the WHO/IARC ilearn learning platform.

LCB continued to work closely with the Early Career Scientists Association (ECSA). Among other activities, ECSA organized its annual Scientific Days, to showcase the work of IARC students and postdoctoral scientists, and held career panels and workshops for professional development, as well as social and networking activities (Figure 1).

Postdoctoral Fellowships

During the biennium, the Agency awarded nine IARC Postdoctoral Fellowships to candidates from low- and middle-income countries (LMICs) for projects in line with the IARC Medium Term Strategy 2021–2025.

Table 1. Generic instructor-led courses for Early Career Scientists, 2022 and 2023. © IARC.

Research skills development	**Writing skills**
FAIR data principles in practice	Effective scientific posters
Fundamentals of implementation, by the University of Washington	European Commission (EC) grants: insights from an expert evaluator
Introduction to Bayesian statistics	Grant writing: fundamental considerations
Introduction to multiple imputation for missing data	Publishing in scientific journals
Learn R facilitated training	PubMed: search efficiently
Science implementation vs intervention: basic considerations	Predatory publishing
R Shiny for beginners	Systematic reviews search methodology
	Writing competitive grant applications
IT skills	**Communication skills**
Meeting rooms – audiovisual equipment	Effective interpersonal communication techniques
REDCap for surveys	Information is beautiful
REDCap for data collection	Science communication
SAMI (SAmple Management at IARC) training sessions: beginner and advanced	The power of visual storytelling
Take IT Easy: 10 sessions on Microsoft Teams, OneDrive, Office 365, OneNote	
Career management and development	**Leadership and management**
Creating your personal brand (WHO)	Creating and sustaining high performance
Emotional intelligence in the workplace – masterclass series (WHO)	Giving and receiving feedback
WHO Emotional Intelligence (EQ) Café	"No excuse" webinar series related to sexual misconduct (WHO)
Networking for results (WHO)	Research leadership training course
Motivation and focus	Time management workshop (WHO)
Motivation and well-being	Values-based decision-making and communication
Working together remotely	Bystander training in the workplace (WHO)
Workshop on CV skills and competency-based interviews (WHO)	Workshop on preventing and addressing abusive conduct (WHO)

"First aid at work" sessions in French and English were offered throughout 2023.

Figure 1. Early Career Scientists Association (ECSA) Day 2022. © IARC.

In addition, as part of efforts to identify complementary sources of funding for the programme, negotiations with Children with Cancer UK led to a renewed agreement enabling the awarding of two fellowships to scientists wishing to carry out research on paediatric cancers or cancer in teenagers and young adults.

Budget decisions in May 2023 had an impact on the total number of 2-year fellowships funded on the regular budget, which decreased from seven to six. Consequently, and to maintain the opportunities for the most excellent candidates, (i) one candidate who had been awarded another competitive 1-year fellowship, which could not be postponed, was only awarded a 1-year fellowship by IARC, and (ii) the remaining funding was combined with available extrabudgetary funding at the host Branch level to award a 2-year fellowship to the first candidate on the waiting list.

Mid-Career Visiting Scientist Award

The former Senior Visiting Scientist Award evolved into several awards for mid-career scientists from LMICs to develop collaborative research projects with IARC, contribute to enhancing their career prospects, and build the capacity of their institution through longer-term collaborations initiated or strengthened through the fellowship. Three such fellowships were awarded.

Courses Programme

The courses programme is designed to enhance the capacity of the global research community, in particular in LMICs, through lifelong learning in the areas of the Agency's expertise.

Learning events

The Agency organized 69 courses or webinars targeting researchers and health professionals from many countries, in particular LMICs (Table 2). Because of the COVID-19 pandemic and the move to the new IARC building, most courses during 2022–2023 were offered online. When on-site options were not possible, courses were redesigned to combine live sessions with facilitated self-learning. They lasted from a few days, such as the three ChildGICR Childhood Cancer Registration online courses (in Georgia, India, and Viet Nam) and the Codificación de Tumores ICD-O-3 course, to several weeks, such as the Training of Trainers on quality assurance for cancer screening for Georgia, Latvia, and Slovakia, or even months, such as the Research Leadership training. Some events also combined a face-to-face component to focus on practice and networking, such as the IARC Summer School 2023 (see the text box) or the Cancer Screening in Five Continents (CanScreen5) Train the Trainers course (Figure 2). More than 3800 scientists and health professionals benefited from these learning events during the biennium.

Self-learning and teaching resources

As a key complement to live events, IARC continued to produce self-learning resources. A video series on managing data according to FAIR principles (Findable, Accessible, Interoperable, and Reusable) was developed through the Human Exposome Assessment Platform (HEAP) project (https://www.youtube.com/playlist?list=PL-Hb2W9K8uzrRrKYRrXYOZFj7_o6RXQvt). A new self-paced learning programme, Introduction to Cancer Prevention and Early Detection, based on a combination of IARC learning material, was launched in 2022 (https://learning.iarc.fr/edp/courses/sp-intro-cancer-prevention-and-early-detection/). This introductory learning path was a

Table 2. Learning events, 2022 and 2023. © IARC.

Course title	Location	Number of participants	External collaborations
Cancer surveillance			
CanReg5 training course for Japan, the Republic of Korea, Barbados, and Trinidad and Tobago (2022)	Online	25	
ChildGICR Childhood Cancer Registration for India, Bangladesh, Bhutan, Nepal, and Sri Lanka (2022)	Online	31	St. Jude Children's Research Hospital, Memphis, USA; Cancer Institute (WIA), Chennai, India
ChildGICR Childhood Cancer Registration for Viet Nam, Brunei Darussalam, Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Myanmar, the Philippines, Singapore, and Thailand (2022)	Online	32	St. Jude Children's Research Hospital, Memphis, USA; Viet Nam National Cancer Institute, Hanoi, Viet Nam
ChildGICR Childhood Cancer Registration for Armenia, Azerbaijan, Georgia, the Republic of Moldova, Türkiye, and Ukraine (2023)	Online	31	St. Jude Children's Research Hospital, Memphis, USA; National Center for Disease Control and Public Health (NCDC), Tbilisi, Georgia
GICR Basic Cancer Registration Course for Ecuador, El Salvador, Guatemala, Panama, Paraguay, and Peru (2022)	Online	22	Sociedad de Lucha Contra el Cáncer (SOLCA), Quito, Ecuador; Pan American Health Organization (PAHO) Virtual Campus for Public Health
GICR CanReg5 training course for Latin America (2022)	Online	41	National Cancer Institute, Colombia
GICR Codificación de tumores de mama y de tracto genital femenino for Latin American countries (2023)	Online	78	National Cancer Institute, Colombia
GICR Codificación de tumores ICD-O-3 for Latin America: Argentina, Chile, and Uruguay (2023)	Online	24	National Cancer Institute, Argentina
Joint IARC–National Cancer Center of the Republic of Korea Summer School on Cancer Registration: Principles and Methods (2022 and 2023)	Blended; online and Republic of Korea	29 + 23	GICR, National Cancer Center of the Republic of Korea and its Graduate School of Cancer Science and Policy (GCSP)
IARC-WHO EMRO Workshop on cancer data use to inform cancer control planning in the Eastern Mediterranean Region countries (2023)	Egypt	30	WHO Regional Office for the Eastern Mediterranean
Cancer prevention and early detection			
CanScreen5 Train the Trainers – African Region – Face-to-face (2022)	United Arab Emirates	20	American Cancer Society (ACS), United Kingdom Medical Research Council (MRC), Friends of Cancer Patients (FoCP)
CanScreen5 Train the Trainers – Community of Latin American and Caribbean States (CELAC); Three groups: A and C Spanish, B English (2023)	Blended; online and Miami (USA) and Panama	18 + 35 + 30	American Cancer Society (ACS), United Kingdom Medical Research Council (MRC)
CIRC Série d'échanges « Cancer de la bouche : quels facteurs de risque ? comment le prévenir ? » (2023)	Online	40	Centre Léon Bérard, Lyon, France
Colposcopy training programme (2022)	India	15	Nargis Dutt Memorial Cancer Hospital, India
IARC Summer School: Implementing Cancer Prevention and Early Detection (2023)	Blended; online and IARC, Lyon	35	
IARC Summer School – 12 public events (2023)	Online	1597	
IFCPC-IARC Training course in Colposcopy and the Prevention of Cervical Cancer – OSCE (2022–2023)	Online	50	International Federation of Cervical Pathology and Colposcopy (IFCPC)
Pre-conference workshop of the European Public Health Conference – Cancer prevention for a sustainable future: an interactive workshop for public health specialists (2023)	Face-to-face	20	Cancer Prevention Europe including Cancer Research UK
The World Code Against Cancer – for Youth Ambassadors for the European Code Against Cancer – Digital Summer School (2022)	Online	60	Association of European Cancer Leagues (ECL)
Theoretical and hands-on training in study protocol, ethical considerations, and procedures (cervical cancer screening) for the EASTER Project (2023)	Zimbabwe	20	EASTER Project partners
Training and quality assurance on colposcopy (2022)	Zambia	16	International Federation of Cervical Pathology and Colposcopy (IFCPC)
Training of Trainers on quality assurance for cancer screening for Georgia, Latvia, and Slovakia (2023)	Online	24	
Training on clinical breast examination for the State of Libya (2023)	Tunisia	6	
Training on use of portable breast ultrasound for the detection of breast abnormalities (2022 and 2023)	Blended; online and India	10 + 45	Bhabha Atomic Research Centre (BARC) Hospital, Mumbai, India

Table 2. Learning events, 2022 and 2023 (continued). © IARC.

Course title	Location	Number of participants	External collaborations
World Cancer Report Updates webinar series: Polygenic scores for cancer prevention (2022)	Online	391	European Society for Medical Oncology (ESMO)
World Cancer Report Updates webinar series: The present and future of lung cancer screening (2022)	Online	166	European Society for Medical Oncology (ESMO)
World Cancer Report Updates webinar series: Liquid biopsy-based biomarkers for cancer detection and monitoring (2023)	Online	243	European Society for Medical Oncology (ESMO)
Cancer research infrastructure and methods			
Environmental and occupational cancer	Online	15	School of Public Health of Yale University, USA
Epidemiology of breast cancer – 5th International Course on Breast Cancer, by Institut Curie (2022)	France	25	Institut Curie, France
Epigenomics and Mechanisms of Human Carcinogens for the EMGS, webinar and online workshops (2023)	Online	60	Environmental Mutagenesis and Genomics Society (EMGS); Education, Student, and New Investigator Affairs (ESNIA)
Evidence Gap Maps training programme (online series), WHO Classification of Tumours Evidence Gap Map (EVI MAP) Project (2022–2023)	Online	25	University of Newcastle, United Kingdom
IARC Summer School: Introduction to Cancer Epidemiology (2023)	Blended; online and IARC, Lyon	35	
Precision Oncology Summer School – Liquid biopsy biomarkers: rationale, technological developments, and clinical applications (2022)	France	35	European Scientific Institute (ESI), Archamps, France
Precision Oncology Summer School – Optimizing personalized cancer diagnosis and treatment (2023)	France	35	European Scientific Institute (ESI), Archamps, France
Training for pathology laboratory technicians (2022)	India	16	Cachar Cancer Hospital, India
Training on biobanking best practices (2023)	Online	30 + 25	Mansoura University, Egypt; University of Alessandria, Italy
Training on biobanking best practices and pre-analytical factors for the Annual Egyptian Biobanking Conference (2023)	Online	32	BCNet
Training on biobanking best practices and pre-analytical factors (2022 and 2023)	Czechia, Armenia, and IARC, Lyon	8 + 20 + 5	ARICE study
Training on biobanking best practices and pre-analytical factors (2023)	China	12	Chinese Center for Disease Control and Prevention, China
Training on biobanking best practices and pre-analytical factors for the ASEAN Biobank Feasibility Study (2023)	The Philippines	12	BCNet
Training on biobanking best practices and pre-analytical factors (2022 and 2023)	Guatemala and United Republic of Tanzania	8 + 8	IIPAN/NICHE Study; BCNet
Training on biobanking in relation to pathology and clinical practices at the AORTIC conference (2023)	Senegal	5	BCNet
Training on laboratory safety for the University of Shanghai (2023)	Online	45	Shanghai Jiao Tong University, School of Public Health, China
Training on laboratory safety for the ASEAN Biobank Feasibility Study/The Philippines (2023)	Online	12	BCNet
Training on laboratory safety and toxicology (2023)	Online	25	National Quality Control Laboratory of Drug and Food, Indonesia
Training on untargeted metabolomics for non-laboratory scientists (2022)	Online	40	Mount Sinai School of Medicine, USA; Columbia University, USA; and Imperial College London, United Kingdom
Training on urine sample collection in HPV study protocol (2022)	Zimbabwe	35	University of Zimbabwe Clinical Trials Research Centre
Training on urine sample collection in HPV study protocol (2023)	Lao People's Democratic Republic	15	Mother and Child Health Center, Ministry of Health, Lao People's Democratic Republic
Research leadership			
Research Leadership Training Programme (twice in 2022)	Online	21 + 29	Mobilize Strategy Consulting

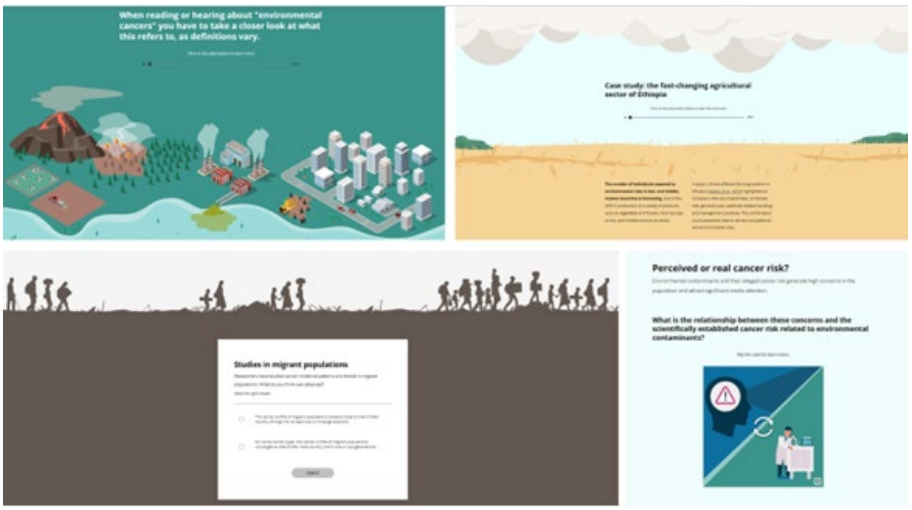
Figure 2. Cancer Screening in Five Continents (CanScreen5) Train the Trainers face-to-face sessions in Sharjah, United Arab Emirates. © IARC.

prerequisite to apply for the corresponding module of the IARC Summer School 2023 (see the text box). Another self-paced learning module, Introduction to Research on Pollution and Cancer, was released in 2023 as part of the collaboration with the European Society for Medical Oncology (ESMO) (https://learning.iarc.fr/wcr/courses/module-1-pollution/) (Figure 3). Also as part of the *World Cancer Report* Updates learning platform, IARC launched a Teaching Toolkit on Cancer Research for Cancer Prevention, designed to support anyone involved in transmitting knowledge and skills on cancer research for cancer prevention. In line with IARC's commitment to open science, the first module of the toolkit, Rationale and Scope of Cancer Research for Cancer Prevention, was published under a Creative Commons licence, Attribution-NonCommercial-ShareAlike 3.0 IGO (CC BY-NC-SA 3.0 IGO), which allows reuse, adaptation or translation, and publication under the same licence.

Learning portal

Launched in 2019, the IARC Learning portal (https://learning.iarc.who.int/) enables access to several thematic learning platforms (Biobanking, Cancer Prevention and Early Detection, and *World Cancer Report* Updates). It also provides access to IARC WebTV, including the IARC Summer School video channel, as well as to the websites of other IARC-led projects with learning materials on cancer

Figure 3. Self-paced e-learning module, Introduction to Research on Pollution and Cancer. © IARC.



surveillance and on the exposome (the HEAP project). The IARC Learning portal continues to attract an increasing audience. Since November 2019, about 4500 professionals (2806 during 2022–2023) have created an account on the portal to freely access learning resources. About half of the users of the IARC Learning portal are from LMICs.

In 2022, IARC and the WHO Academy set up a collaboration within the development of the WHO Academy's Learning Experience Platform (LXP). Within the framework of this collaboration, LCB has provided training design expertise to support the development of the LXP, including through advice on key LXP functionalities and testing of demo versions. The WHO Academy team has created a dedicated Learning Space on the LXP, which will be managed by IARC autonomously. IARC self-paced and facilitated courses will progressively be migrated to the LXP, which will eventually replace the current IARC Learning infrastructure.

Key partnerships

Relationships between IARC and key stakeholders continued to be strengthened during the 2022–2023 biennium.

The Agency and the National Cancer Center of China (NCC China) signed a Memorandum of Understanding in May 2023 to set up a first regional learning centre, the IARC-NCC China Learning Centre (Figure 4); a first course (Introduction to Cancer Epidemiology) is planned for early 2024. Discussions are under way with the National Cancer Institute of Brazil (INCA) and the University of São Paulo to follow the same approach for Brazil and neighbouring and/or Portuguese-speaking LMICs.

As described above, IARC has been involved in the development of the WHO Academy at several levels. As well as contributing to governance and infrastructure aspects, two IARC learning programmes have been developed as part of the development of the first courses of the WHO Academy: the Comprehensive Learning Programme on Screening, Diagnosis, and Management of Cervical Precancer, and the Managing Infrastructure for Medical Research Learning Programme.

In addition, LCB pursued its partnership with ESMO on the *World Cancer Report* Updates learning platform, and with the International Federation of Cervical Pathology and Colposcopy (IFCPC) on the hosting of joint courses. Through European Union funding, LCB continued its collaboration with the Karolinska Institutet (Sweden) and other European institutions in the HEAP consortium, and started a new collaboration, together with EPR and CSU, with about 50 institutions within Europe to develop capacity of Comprehensive Cancer Infrastructures for Europe (CCI4EU).

Figure 4. Signature of the Memorandum of Understanding with the National Cancer Center of China in May 2023. © IARC.

IARC Summer School in Cancer Epidemiology 2023

The IARC Summer School in Cancer Epidemiology aims to improve the methodological and practical skills of cancer researchers and health professionals. In 2023, both modules – Introduction to Cancer Epidemiology, and Implementing Cancer Prevention and Early Detection – were held in a blended format, including 2–4 weeks of online self-paced activities (recorded lectures and assignments, punctuated by a few live sessions) followed by 1 week on site in Lyon, focused on practical and networking activities. A brand-new Public Events Series was part of the programme; 12 live public events were successfully organized throughout the period (https://www.youtube.com/@iarclearning5527/streams) and attracted 260–1100 viewers per event.

A total of 70 cancer researchers and health professionals from 41 countries (most of which were LMICs) participated in the two modules, representing a wide variety of disciplines and nationalities, which is what makes the IARC Summer School so unique. All the resources used to deliver the IARC Summer School 2023 are available on the IARC Learning portal (https://learning.iarc.who.int).

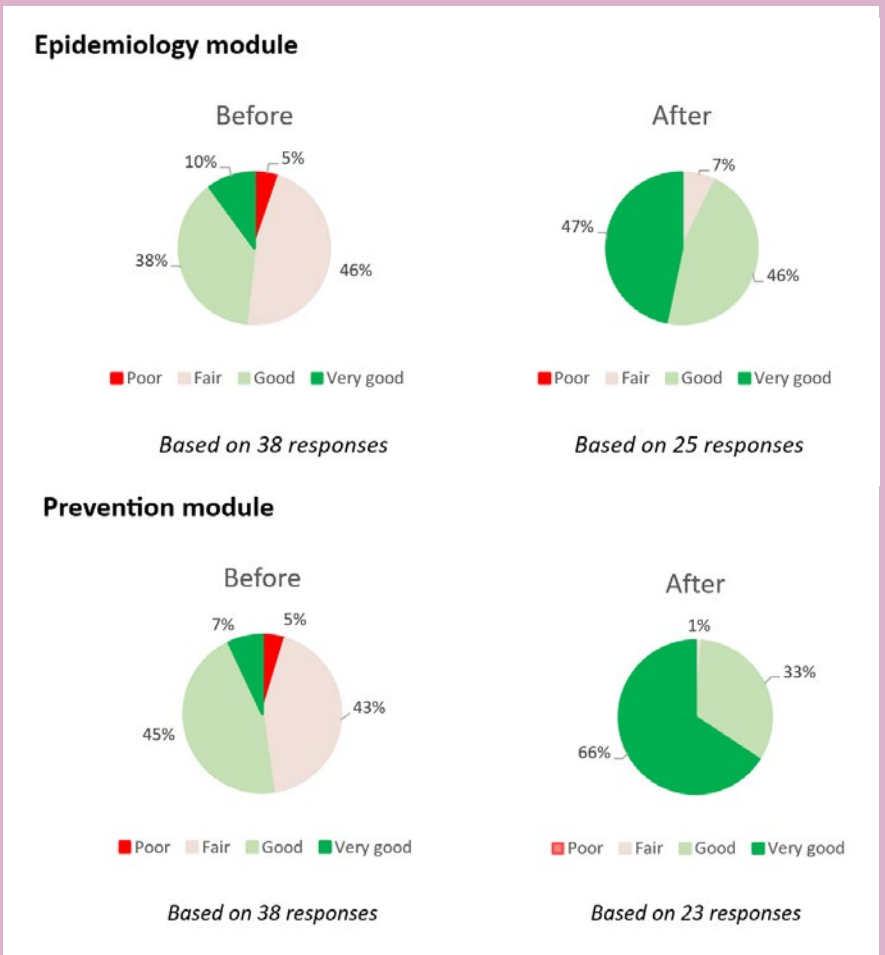
Pre-course and post-course surveys were administered to measure the impact of the course on participants' self-perceived level of confidence with regard to knowledge and skills covered in the modules. The results showed a substantial progression, which was also clearly expressed by the participants in their oral and written feedback and quotations.

The participants' testimonials perfectly illustrate the spirit of the IARC Summer School: the shared learning through the provision of multiple opportunities for interaction, the sharing of experiences, and the fostering of collaboration and networking for cancer prevention across countries.

"Being both a nurse and a PhD student, attending this Summer School will enable me to effectively execute my research project and suggest further studies that will aid in mitigating the risk of cancer among our population."
—Majid Omari, Morocco

"The IARC Summer School programme is one of the most wonderful role models in the world in service capacity-building. It involves a world without boundaries to combat the deadly disease cancer."
—Girma Mulisa Misgana, Ethiopia

Impact of participating in the IARC Summer School on participants' self-ratings about their confidence in the knowledge and skills covered in the two modules. Comparison of pre-course and post-course survey results. The numbers of responses "Poor", "Fair", "Good", and "Very good" across all learning objectives per module are expressed as percentages. © IARC.



Services to Science and Research Branch (SSR)

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Director of administration and finance
Dr Tamás Landesz (until October 2023)
Ms Charu Mehta (acting)

Administrative and legal officer
Ms Virginie Vocanson

Data protection and legal officer
Ms Jolien Jongerius

Senior assistant (Coordinator, governing bodies and meetings)
Ms Agnès Meneghel
(until December 2023)

Administrative assistant (DAF Office coordinator)
Ms Nathalie Lamandé

Administrative assistant
Ms Claudia Culierat

Administrative Services Office

Administrative services officer
Ms Elisabeth Françon (until May 2023)
Dr Tamás Landesz
(acting, until August 2023)
Mr Sylvain Lubiato (acting)

Project manager
Mr Sylvain Lubiato

Administrative assistant
Ms Sophie Servat

Principal assistant (Procurement)
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(Laboratory and administration)
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Mr Michel Javin (Reprography)
(until July 2022)
Mr Hafed Lamouchi
(Electronic maintenance)

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Administration and finance officer
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Mr Bent Jorgensen (acting)

Resource mobilization and grant officer
Ms Claire Salignat

Project management officer
Mr Corentin Chaboud

Budget officer
Ms Editta Odame

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Assistants (Resource mobilization)
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Trainees
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Ms Anna Schmutz
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Ms Juliette Pentecôte

HUMAN RESOURCES OFFICE

Human resources officer
Mr David Kavanagh

Associate human resources officer
Ms Catherine Bassompierre (until December 2022)
Mr Mohamed Atteya

Assistants (Human resources)
Ms Nur Iliyana Ishak
Ms Aurélie Rosado
Ms Julianna Soos (Training)
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Ms Sophie Sibert

Staff physician
Dr Berth Atik

Secretary to IARC Staff Association Committee and Staff physician
Ms Isabelle Poncet

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IT officers
Mr Philippe Boutarin
Mr Nicolas Tardy

Senior assistant (Service analyst and Development)
Ms Lucile Alteyrac

Assistant (Digital workplace)
Mr Sébastien Agathe
Mr Rémi Valette (until January 2023)

Assistant (Network and communications)
Mr Hafed Lamouchi

Assistant (Service desk)
Mr Benjamin Danet

PUBLISHING, LIBRARY, AND WEB SERVICES

Knowledge manager
Ms Teresa Lee

Managing editor
Dr Karen Müller

Institutional webmaster
Ms Maria de la Trinidad Valdivieso Gonzalez

Information assistants
Ms Latifa Bouanzi
Ms Sylvia Lesage
Mr Othman Yaqoubi

The Services to Science and Research Branch (SSR), led by the Director of Administration and Finance (DAF), is made up of six specialized operational units, which provide services intrinsic to the successful implementation of the Agency's scientific programmes: (i) Office of the Director of Administration and Finance, including legal support, data protection, and coordination of governing bodies; (ii) Budget and Finance Office, including supporting resource mobilization activities; (iii) Human Resources Office, including staff training and capacity-building; (iv) Administrative Services Office, including procurement, conference services, building management, and security; (v) Information Technology Services, including telecommunications; and (vi) Publishing, Library, and Web Services, including publications production and copyright management. SSR ensures that the Agency's activities meet the highest sector standards of resource management, operational efficiency, and accountability in the use of the resources made available by IARC's Participating States and donors.

SSR remains committed to the principle of continuous quality improvement, striving to further enhance the Agency's processes and support services by, among others, collecting feedback through regular service surveys. The following five impact areas were defined by SSR to enable the Agency to fulfil the IARC Medium-Term Strategy 2021–2025 and to transition towards a learning- and knowledge-driven organization fully fit for the 21st century: (i) faster delivery of results, (ii) pooling of resources, (iii) technological innovation and advancement, (iv) fit for Open Science, and (v) culture shift and personal growth. SSR holds monthly Administrative Town Hall meetings to communicate SSR objectives and planned activities and to explain new operational policies and administrative procedures of general interest. This enables SSR to maintain close proximity with IARC personnel, to address the needs of personnel promptly, and to prevent potentially problematic issues from becoming unmanageable.

To retain its focus and use IARC resources in the most efficient way, SSR defined the following three overarching priorities for the 2022–2023 biennium: (i) to complete the move to the new IARC building in the Gerland Biodistrict of Lyon; (ii) to expand and externally pilot the IARC Scientific IT Platform, supported by a strong data protection framework; and (iii) to join WHO in implementing a new state-of-the-art enterprise resource planning system, called the Business Management System.

The new IARC building is not only the Agency's new headquarters; it also symbolizes the main ambitions of the IARC Medium-Term Strategy 2021–2025. The architectural concept

of the new building aims to promote the concept of Open Science and to enhance collaboration with local and national partners. The physical structure reflects the IARC values of transparency and collaboration. The concept of Open Science is at the heart of the new building. It will enable IARC to ensure open access to research infrastructures and to scientific data and knowledge, and will open up new possibilities for dialogue and engagement with society. Located in the Gerland Biodistrict of Lyon, the new building will contribute to better synergies with numerous partners in research and health. The Gerland Biodistrict is home to Lyon's leading research institutes (e.g. INSERM, ENS, BIOASTER), health organizations (e.g. ANSM, ANSES, HCL), and possibly private health-care companies, within an attractive ecosystem. IARC already has interactions with many of these institutions. The proximity of the new building to the future premises of the WHO Academy and to the WHO Lyon Office establishes a public health hub on a global scale, the Lyon WHO Hub. This hub will enable IARC to share programmes, resources, and service providers, and offers a unique opportunity for IARC to increase collaborations and partnerships locally and around the world.

IARC continued to further solidify its data protection framework and data security measures during the 2022–2023 biennium, to ensure that the Agency's data protection framework remains in line with internationally recognized standards. IARC has developed solutions that enable the Agency to share data with its collaborators remotely via the IARC Scientific IT Platform. These solutions have been set up in accordance with internationally recognized data protection standards, and the initial pilot phase has been successful. IARC continues to collaborate with its collaborators, the European Commission, the European Data Protection Supervisor, several networks of international organizations, and data protection authorities to work on long-term solutions to simplify data sharing with IARC.

In the Agency's continued efforts to modernize its administrative management systems, IARC joined forces with WHO and embarked on the implementation of a new Business Management System (BMS). IARC's current enterprise resource planning system (ERP) is out of date, requiring time- and resource-intensive manual entry, which leads to inefficiencies, risk of errors, and demotivation of staff members. Because IARC's currently outdated system will be decommissioned by the supplier by the end of the biennium, IARC explored alternative ERP solutions to modernize its administrative management systems in support of the IARC Medium-Term Strategy 2021–2025. The best-value-for-money solution was identified by joining forces with WHO and together transitioning to a new ERP solution: the new BMS. This will enable IARC and WHO to jointly simplify processes and adapt rules by applying best-in-breed solutions. The new system will be seamless, more user-friendly and intuitive, and simpler to use. It will reduce the risk associated with manual entries, provide business intelligence and analytical tools for improved resource planning, and integrate all existing IT systems, enabling them to communicate with each other.

In the framework of the Quality of Work Life work plan and in light of the Respectful Workplace initiative, efforts were dedicated to supporting and promoting cultural transformation, to increase colleagues' engagement in driving and embedding cultural change. Individual coaching sessions were offered to provide further support to supervisors, managers, and their teams in strengthening interpersonal

relationships, effective communication, and teamwork. In addition, to contribute to the implementation of culture shift towards a project- and activity-based work environment, specific learning paths were designed. The Research Leadership Training Programme aims to reinforce a strategic leadership culture at IARC and to strengthen partnerships and collaborations with researchers outside the Agency. Participation rates in mandatory training courses were very high; these courses aim to, among others, increase awareness about abusive conduct, sexual abuse, and exploitation and equip IARC personnel with specific guidance, tools, and techniques on how to prevent and address various types of prohibited conduct.

SSR supported the Director in efforts to mobilize additional external financial resources to deliver the approved programme of work, in developing a new IARC Investment Case to help resource mobilization efforts, and in launching a new Informal Governing Council Working Group on Sustainable Financing.

SSR continued to ensure effective management of IARC accounts, retaining compliance with the International Public Sector Accounting Standards (IPSAS), validated by WHO external auditors on an annual basis. The Agency continued to receive unqualified (i.e. fully compliant) audit opinions from the external auditors throughout the biennium. IARC managed to close all prior year recommendations successfully during the biennium.

Finally, SSR continued to put in place measures aimed at maximizing the professional and personal potential of personnel and fostering a work environment that supports collaboration and excellence.

IARC Publications and Websites

During the 2022–2023 biennium, IARC published the following reference publications:

WHO Classification of Tumours

- WHO Classification of Central Nervous System Tumours, 5th edition (print)
- WHO Classification of Urinary and Male Genital Tumours, 5th edition (print)
- WHO Classification of Paediatric Tumours, 5th edition (print)
- WHO Classification of Head and Neck Tumours, 5th edition (print)

IAC-IARC-WHO Cytopathology Reporting Systems

- WHO Reporting System for Lung Cytopathology, 1st edition (print)
- WHO Reporting System for Pancreaticobiliary Cytopathology, 1st edition (print)

IARC Monographs

- Volume 126, Opium Consumption (print)
- Volume 127, Some Aromatic Amines and Related Compounds (print)
- Volume 128, Acrolein, Crotonaldehyde, and Arecoline (print)
- Volume 129, Gentian Violet, Leucogentian Violet, Malachite Green, Leucomalachite Green, and CI Direct Blue 218 (PDF)
- Volume 130, 1,1,1-Trichloroethane and Four Other Industrial Chemicals (PDF)
- Volume 131, Cobalt, Antimony Compounds, and Weapons-Grade Tungsten Alloy (PDF)
- Volume 132, Occupational Exposure as a Firefighter (PDF)

IARC Handbooks

- Volume 18, Cervical Cancer Screening (print and PDF)
- Volume 19, Oral Cancer Prevention (PDF)

IARC Working Group Reports

- Best Practices in Cervical Screening Programmes: Audit of Cancers, Legal and Ethical Frameworks, Communication, and Workforce Competencies, IARC Working Group Report No. 11 (PDF)

Biennial Report

- Rapport biennal 2020–2021 (PDF)

Non-series publications

- Cervical Cancer Elimination in Africa: Where Are We Now and Where Do We Need to Be? (PDF)
- Mise en œuvre d'un programme pilote de dépistage du cancer du col de l'utérus intégré dans les services courants de soins de santé primaires au Bénin, en Côte d'Ivoire et au Sénégal (PDF)
- Implementation of a Pilot Cervical Cancer Screening Programme Integrated in Routine Primary Health-Care Services in Benin, Côte d'Ivoire, and Senegal: Report of a Pilot Project (Care4Afrique) in Three African Countries (PDF)

Electronic resources

- Atlas of Breast Cancer Early Detection, IARC CancerBase No. 17
- Using HPV tests for cervical cancer screening and managing HPV-positive women – a practical online guide, IARC CancerBase No. 18
- Cancer Incidence in Five Continents, Volume XII, IARC CancerBase No. 19
- Atlas de l'inspection visuelle à l'acide acétique du col de l'utérus pour dépister, trier et déterminer l'éligibilité des lésions au traitement ablatif
- Tests VPH pour le dépistage du cancer du col de l'utérus et prise en charge des femmes positives au VPH – guide pratique
- Atlas de colposcopie – principes et pratique
- Atlas de la inspección visual del cuello uterino con ácido acético para tamizaje, triaje y evaluación para el tratamiento
- Uso de pruebas de VPH para el tamizaje del cáncer cervicouterino y el manejo de mujeres VPH positivas – una guía práctica en línea
- Atlas de colposcopia – principios y práctica

In addition, during the biennium the Web Services team developed or validated and launched the following websites:

- World Code Against Cancer Framework: https://cancer-code-world.iarc.who.int/
- Cancer Inequalities: https://cancer-inequalities.iarc.who.int/
- EpiDRIVERS: Identifying epigenetic driver genes (epidrivers) in cancer and their link to environmental carcinogens/exposures: https://epidrivers.iarc.who.int/
- ARISTOCANCERS: Investigating human cancers associated with exposure to aristolochic acids: https://aristocancers.iarc.who.int/
- EpiMARKS+: Identifying epigenetic biomarkers of breast cancer risk and their environmental/lifestyle determinants: https://epimarks.iarc.who.int/
- Mapping the Evidence for the World Health Organization Classification of Tumours: a Living Evidence Gap Map by Tumour Type (WCT EVI MAP): https://wct-evi-map.iarc.who.int/
- Bladder Cancer Epidemiology and Early Detection in Africa (BEED) Study: https://beed.iarc.who.int/
- DISCERN: Discovering the Causes of Three Poorly Understood Cancers in Europe: https://discern.iarc.who.int/
- Research on Potential Long-Term Health Effects of Tattooing: https://tattoo.iarc.who.int/
- CanScreen-ECIS: https://canscreen-ecis.iarc.who.int/
- VOYAGER: Human Papillomavirus, Oral and Oropharyngeal Cancer Genomic Research: https://voyager.iarc.who.int/
- Latin America and the Caribbean (LAC) Code Against Cancer: https://cancer-code-lac.iarc.who.int/
- Cancer Incidence in Five Continents (CI5): https://ci5.iarc.who.int/
- European Prospective Investigation into Cancer and Nutrition (EPIC): https://epic.iarc.who.int/

Office of the Director

Director
Dr Elisabete Weiderpass

Director's Office team

Programme officer
Dr Véronique Chajès

Ethics and compliance officer
Dr Chiara Scoccianti

Strategic Engagement and External Relations (SEE)

Strategic engagement and resource mobilization officer
Mr Clément Chauvet

Communications officer
Ms Véronique Terrasse

Information assistants
Mr Nicholas O'Connor
Ms Morena Sarzo

Executive assistant to the Director
Ms Nadia Akel (until February 2023)
Ms Sally Moldan

Secretaries
Ms Laurence Marnat
Ms Sylvie Nouveau

Consultants
Mr Olivier Exertier
Ms Manami Shoji

Trainees
Ms Houda Bouabdallah (until May 2022)
Ms Manami Shoji (until March 2023)

The Office of the Director provides strategic leadership to the Agency by setting scientific and managerial priorities and providing specialist knowledge in strategic engagement, resource mobilization, communications, and external relations, as well as expertise in bioethics, ethics, and compliance.

The Director's Office supports the Agency in the implementation of the *strategic scientific priorities*, as set out in the IARC Medium-Term Strategy 2021–2025. The Agency continues its work on cancer research priorities identified in the Medium-Term Strategy and has taken a step closer towards fulfilling its mission of "cancer research that matters". The Agency continues to address its *fundamental research priorities* and is gradually strengthening its engagement in three *emerging priorities*, notably *implementation research*. Progress in the implementation of the Medium-Term Strategy will be assessed within an evaluation framework composed of pertinent key performance indicators (KPIs), as approved by the IARC Governing Council in May 2022.

Ethics and compliance are an integral part of the Director's Office, to ensure ethical, evidence-based, and human rights-based research and research integrity, freedom from conflicts of interest, and accountability, and to protect the Agency's reputation. Thus, the major role of the Director's Office in ethical appraisal is based on ensuring rigorous science and promoting a clear ethical vision that reflects the trust placed in IARC by its Participating States, external stakeholders, and the public, and that encourages positive behaviours and conduct throughout the Agency. It supports and monitors IARC personnel's adherence to the highest principles of ethical and professional conduct, including research integrity, and to the IARC Accountability Framework. The Director's Office produced the 2021–2022 biennial report on research ethics for the IARC governing bodies.

The Director's Office continues to promote *strategic partnership* by *strengthening and expanding* the Agency's network of Participating States, governmental and nongovernmental partners, funding

agencies, and collaborators. After strategic discussions that were initiated in 2022–2023, at least two countries have shown a strong interest in becoming IARC Participating States in 2024: Saudi Arabia and Egypt.

The Agency signed nine *Memoranda of Understanding*, with the Sociedade Beneficente Israelita Brasileira Albert Einstein in Brazil, the National Center for Disease Control and Public Health in Georgia, the Trustees of Columbia University in the City of New York in the USA, the National Cancer Registry operated by the National Institute of Oncology in Hungary, the Programme National de Lutte contre le Cancer in Côte d'Ivoire, the National Centre for Disease Informatics and Research, Bengaluru in India, the Union for International Cancer Control (UICC) in Switzerland, Charles University in Czechia, and the National Central Cancer Registry and the National Cancer Center in China.

In addition, the Agency renewed four Memoranda of Understanding, with the Beijing Genomics Institute at Shenzhen/China National GeneBank in China, the National Cancer Center Japan, the National Cancer Center of the Republic of Korea, and the Danish Cancer Society in Denmark.

The Agency continues to strengthen its collaboration with local partners, both scientifically and through co-organized public events.

The Director's Office continues to promote coherent *resource mobilization*. Since 2020, IARC has been officially recognized by the Organisation for Economic Co-operation and Development (OECD) Development Assistance Committee as an international organization eligible to receive official development assistance (ODA) funding; this has offered more opportunities for resource mobilization. The Director's Office reached out to the current IARC Participating States for possible investment in some 100% ODA-compliant low- and middle-income countries, which could help them to fulfil their development objectives. For example, the IARC Secretariat has recently held discussions with the Ministry of Health, Welfare and Sport of the Netherlands for them to fund a large project on childhood cancer in Africa.

During the 2022–2023 biennium, the Director's Office developed a new *communication strategy*, which covers three different axes: (i) an "institutional communication" component, which aims to increase the visibility of the Agency; (ii) a "dissemination for impact" component, which aims to increase the dissemination of the Agency's specific scientific activities; and (iii) a "fundraising and resource mobilization" component, which aims to increase income generated by the fundraising campaigns, events, and other related activities.

During the biennium, the Director's Office had some *important achievements*. In May 2023, the IARC Governing Council re-elected Dr Elisabete Weiderpass as Director of IARC for a second five-year term. The Director is an expert member of the European Mission Board for Cancer, an integral part of the Europe's Beating Cancer Plan, to advise the European Commission on the implementation of the actions launched (e.g. the European Initiative to Understand Cancer; UNCAN.eu), and since 2023 she has been the "ambassador" for international organizations.

To improve the implementation of cancer prevention interventions globally, the Agency gave a strong endorsement to further intensifying the coordination and collaboration with WHO, to enable more effective links between science and policy. In 2022–2023, IARC and WHO finalized a joint strategic work plan for 2023–2025, which is now being implemented, and intensified the coordination of technical activities. This strategic plan will support the provision of relevant indicators to inform and evaluate progress in scaling up the three WHO global cancer initiatives (i.e. the Cervical Cancer Elimination Initiative, the Global Breast Cancer Initiative, and the Global Initiative for Childhood Cancer) and, more broadly, support the implementation of national cancer control plans.

After 50 years in the tower building in the Grange Blanche district, IARC moved into its new headquarters in the Gerland Biodistrict of Lyon at the end of 2022. On 12 May 2023, the Agency held an official inauguration ceremony for the new building, which was attended by the French Minister of Health and Prevention, local government officials, members of the IARC Governing Council, dignitaries from IARC Participating States, representatives of WHO, national and international collaborators, and the principal funders of the construction project.

IARC developed an innovative *mobilization strategy* to mobilize in-kind and financial resources for the new headquarters building. As a result, the Agency secured in-kind donations from more than 13 different companies. The most iconic and visible locations in the new building were furnished by these companies: the reception areas, the cafeteria, and the social areas. The Agency also obtained an in-kind donation of 93 new height-adjustable desks for its new offices.

With its iconic shape, the new building embodies the Agency's vision for Open Science and international collaboration in cancer research. It will become a beacon for cancer research and a catalyst to strengthen collaborations between scientists, health professionals, and the general public.

New IARC Initiatives

IARC Research Teams

The concept of IARC Research Teams was developed to tackle a perceived silo mentality within the existing IARC Research Branches and to facilitate scientific work across the Branches and introduce more flexible scientific collaboration and coordination on closely related research. The Research Teams are informal organizational units created across Branches. The added value of these Teams is to catalyse completion of projects through a cross-Agency research approach, by gathering people with complementary expertise in traditional and molecular epidemiology, exposure assessment, biostatistics and data science, database management, and project management. Teams are made up of staff scientists, early career scientists, and support personnel; their composition ensures capacity and flexibility, with a strong focus on mentorship and training.

During the 2022–2023 biennium, 19 IARC Research Teams were established (https://www.iarc.who.int/research-teams/), including the first international Team: the Population-Based Long-Term Surveillance Team, with Team members from IARC and the National Cancer Center Japan. The Research Teams explore a broad range of topics, with two overarching goals: (i) to inform primary prevention by advancing the understanding of cancer etiology, and (ii) to inform secondary prevention by optimizing early detection strategies. The main topics addressed by the Teams include nutritional, metabolic, lifestyle, infection, and occupational cancer epidemiology; molecular characteristics of rare cancers; discovery of biomarkers for early detection; cancer risk prediction; public health decision modelling; and dissemination and communication. IARC's emerging priorities, such as *cancer inequalities, health economics,* and *implementation research*, as defined in the IARC Medium-Term Strategy 2021–2025, are considered from the perspective of cross-Agency Teams. In addition, IARC Research Teams related to the WHO Global Initiatives on breast cancer, cervical cancer, and childhood cancer were established, with the objectives of improving information sharing and knowledge that relates to the WHO Global Initiatives and improving dialogue and coordination with the WHO Cancer Team.

IARC Equity and Diversity Advisory Group (EDAG)

The IARC Equity and Diversity Advisory Group (EDAG) actively promotes equity, diversity, and inclusion at IARC. This is achieved through initiatives to foster an inclusive culture, ensure fair treatment, enable development of all personnel, and promote equal access to opportunities for learning and career advancement.

In June 2022, the EDAG launched the IARC Equity, Diversity, and Inclusion (EDI) Strategy and Action Plan. The Strategy establishes a strong foundation for sustainable and transformative progress in the realm of EDI at IARC. The Action Plan complements the Strategy by detailing the current EDI policies and proposing concrete actions to address gaps in these policies. This dual approach ensures a comprehensive and systematic plan to promote a diverse, inclusive, and equitable work environment.

A significant achievement of the EDAG during the 2022–2023 biennium was the launch of the IARC Award for Women in Cancer Research during 2022. This award recognizes and honours outstanding contributions in the field of cancer prevention research globally by scientists who identify as women. The inaugural recipient of the award, Dr Cristina Stefan, presented her work during an online event on 19 May 2022. The 2023 awardee is Dr Neerja Bhatla, who presented her work during a ceremony in the new IARC headquarters building on 13 October 2023.

Other activities of the EDAG in 2022 included a survey on disability – the first ever in WHO – to gain insights into staff needs, knowledge about the issue, and perceptions of IARC services and resources related to this topic. As a result of this survey, a Working Group on Disability was formed and an IARC Open Forum on Disability was planned.

As part of the Pride Month celebrations in 2023, an LGBTQ+ After-Work Social event was held. It was a success, and future events are envisioned. Talks are under way with Interpol (another international organization with its headquarters in Lyon) about the possibility of hosting joint activities, and the EDAG has also met with UN-GLOBE (https://www.unglobe.org/).

Overall, the EDAG has demonstrated its commitment to fostering a diverse and inclusive culture at IARC, making significant strides in achieving its mission.

European Code Against Cancer, 5th edition (ECAC5)

First published in 1987, the European Code Against Cancer (ECAC) has become a cornerstone of cancer prevention actions across Europe. Under the World Code Against Cancer Framework established by IARC, the ECAC 5th edition (ECAC5) project aims to

build on previous editions by incorporating the latest scientific developments in cancer prevention and expanding the scope of the ECAC to include policy recommendations.

The ECAC5 project was initiated in 2022 and will last for 4 years. It is funded by the European Commission. The project aims to revise and update the existing ECAC using a rigorous scientific methodology that integrates insights from behavioural science and modern communication strategies to enhance health literacy. ECAC5 is structured into three distinct levels of information, or outputs. Level 1 provides evidence-based recommendations to the general public and is supported by complementary recommendations to policy-makers. Level 2 offers supplementary Knowledge Translation Outputs in the form of fact sheets and policy briefs to contextualize the ECAC5 recommendations, serving as a valuable resource for increasing awareness and education on cancer prevention. Level 3 targets the scientific community through a series of articles for publication, which delve into the scientific justification behind each of the recommendations in ECAC5.

As the coordinator of this project, IARC brings together several multidisciplinary working groups of 60 experts from 19 countries to scrutinize the evidence and propose draft recommendations for inclusion in ECAC5. A Scientific Committee consisting of representatives from leading cancer and public health institutions in 12 European Union Member States, plus a representative of WHO, will review and ultimately adopt the recommendations ahead of the anticipated launch of ECAC5 in 2025. Thereafter, a period of systematic monitoring and evaluation of the ECAC is foreseen.

IARC Cross-Cutting Working Group on Cancer Prevention Knowledge Translation and Transfer (KTT WG)

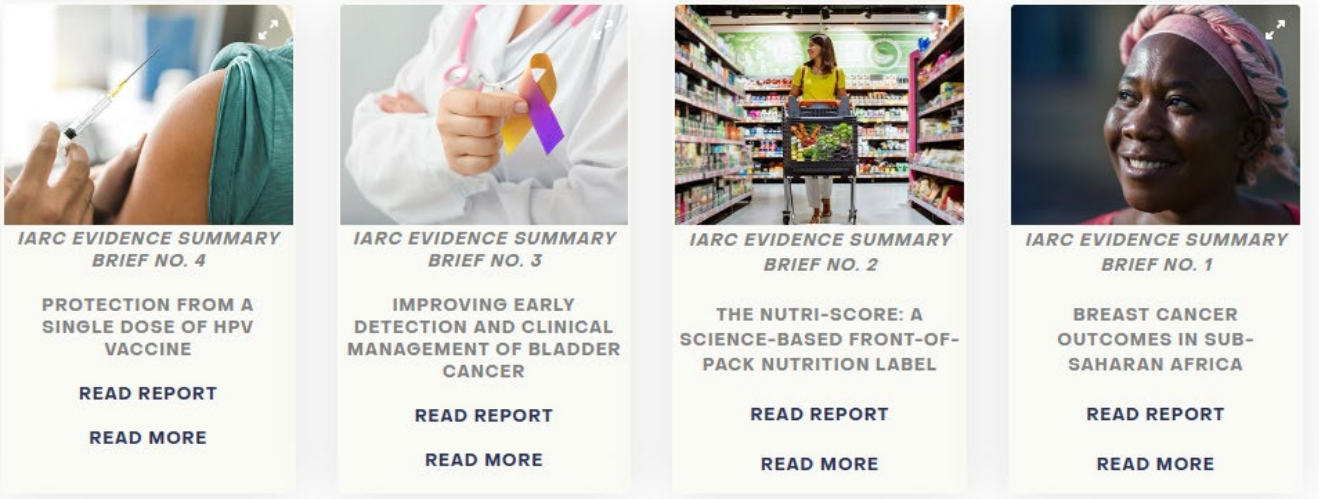
The IARC Cross-Cutting Working Group on Cancer Prevention Knowledge Translation and Transfer (KTT WG) was created in 2020 to translate the evidence on cancer prevention produced by IARC and its collaborators and disseminate it to specific audiences and stakeholders involved in decision-making (i.e. policy-making, implementation, advocacy, and also research).

So far, the KTT WG has published four IARC Evidence Summary Briefs: on breast cancer outcomes in Sub-Saharan Africa, the science behind the Nutri-Score nutrition label, early detection and clinical management of bladder cancer, and protection from a single dose of the human papillomavirus (HPV) vaccine. The fifth IARC Evidence Summary Brief is currently being developed and will be launched at the end of 2023. These Evidence Summary Briefs may assist in accelerating the adoption and implementation of evidence-based strategies, while creating new opportunities for capacity-building and research.

In early 2023, the IARC Scientific Council approved the constitution of an Editorial Board, composed of two members of the IARC Scientific Council, the WHO Noncommunicable Diseases (NCDs) Department focal point, and some IARC members. In addition, the KTT WG developed an internal survey for the identification and eligibility of new topics for future Evidence Summary Briefs. The submitted topics will be brought to the Editorial Board at the end of each year, in order to select the right scientific topics to be showcased in the Evidence Summary Briefs during the next year.

During the 2022–2023 biennium, the KTT WG organized two internal events, to increase the visibility of the initiative within the Agency and to encourage IARC personnel to participate by submitting their suggestions for research topics and/or by joining the KTT WG. The KTT WG is also working on a dissemination and evaluation strategy to maximize the impact of the Evidence Summary Briefs.

The dedicated webpage of the IARC Evidence Summary Briefs series (https://www.iarc.who.int/evidence-summary-briefs-series/) shows the four Briefs launched to date.



Committees

Laboratory Steering Committee (LSC)

Laboratory research plays an indispensable role in facilitating IARC's investigations into the causes and mechanisms of cancer, a cornerstone of the Agency's cancer prevention efforts. These research laboratories are intricately woven into five Branches: Genomic Epidemiology (GEM); Nutrition and Metabolism (NME); Epigenomics and Mechanisms (EGM); Early Detection, Prevention, and Infections (EPR); and Evidence Synthesis and Classification (ESC). The IARC Laboratory Steering Committee (LSC) serves as a vital body, overseeing the core laboratory facilities at IARC and providing guidance to the Director on their optimal use.

During the 2022–2023 biennium, the LSC, working closely with Laboratory Support, Biobanking, and Services (LSB) and the Administrative Services Office (ASO), assumed several pivotal responsibilities and conducted scheduled and ad hoc meetings. These responsibilities encompassed the smooth and efficient relocation of laboratory resources to the new IARC building with minimal disruption to ongoing scientific endeavours, the coordination of the procurement and installation of state-of-the-art laboratory equipment, diligent monitoring and reporting of technical challenges arising during the resumption of activities and/or in relation to the new building, active participation in devising safety protocols and corresponding standard operating procedures (SOPs), the orchestration of comprehensive maintenance for laboratory equipment, and the organization of technical and scientific seminars. These seminars served as a platform to explore emerging laboratory technologies and local scientific resources, fostering opportunities for potential partnerships and collaborations.

Biobank Steering Committee (BSC)

The role of the IARC Biobank Steering Committee (BSC) is to support biobanking activities at the Agency and advise the Director regarding the strategic development of the Biobank.

During the 2022–2023 biennium, many of the activities of the BSC were dedicated to supporting the transfer of the IARC Biobank to the new IARC premises in Gerland. This transfer required an intense logistic effort from Laboratory Support, Biobanking, and Services (LSB) and the Administrative Services Office (ASO), not only in the physical move of the samples but also in the setting up and compliance with strict standard operating procedures (SOPs) and national regulations. Furthermore, the BSC supported the inaugural implementation of the sample disposal policy, with the aim of identifying collections that needed to be disposed of before the move; this policy was successfully implemented and will be maintained.

In addition, the BSC supported the ongoing compliance with French regulations (Conservation d'éléments du corps humain; CODECOH), the organization of the logistics of the move, and the request for the certification of the IARC Biobank by Infrastructures de recherche en biologie, santé et agronomie (IBiSA). Importantly, the BSC has strongly encouraged and successfully obtained the outsourcing of the roster for the IARC Biobank to an external, highly specialized company.

Computational Biology, Bioinformatics, and Biostatistics Committee (C3B)

The IARC Computational Biology, Bioinformatics, and Biostatistics Committee (C3B) is composed of three working groups, which have continued to oversee the Agency's activities in these areas.

The Bioinformatics Working Group and the Biostatistics Working Group facilitate interaction and promote skills development and knowledge sharing in bioinformatics and biostatistics across Branches in the Agency, between collaborative partners, and, more generally, across the cancer research community. The move to the new IARC building has enabled the working groups to resume in-person meetings, and the new state-of-the-art conference rooms have facilitated the organization of hybrid seminars at a reduced cost and with a smaller carbon footprint.

During the 2022–2023 biennium, the main activity of the Informatics Working Group was the opening of the IARC Scientific IT Platform to external collaborators to facilitate data sharing and collaboration between research institutions, in line with internationally recognized data protection standards. This platform will enable external collaborators to remotely access and analyse data from epidemiological studies such as the European Prospective Investigation into Cancer and Nutrition (EPIC), the Lung Cancer Cohort Consortium (LC3), the International Lymphoma Epidemiology Consortium (InterLymph), and other consortia initiatives.

Ethics Committee (IEC)

The IARC Ethics Committee (IEC) ensures that research conducted or supported by IARC conforms to international ethical standards for research involving humans. The IEC ethical review is complementary to local and/or national ethical approval. During the 2022–2023 biennium, the IEC was composed of 11 senior individuals of diverse backgrounds and nationalities. The IEC is chaired by Professor Samar Al-Homoud, supported by the vice-chairperson Dr Angeliki Kerasidou and by Dr Chiara Scoccianti as the secretary. An external Ethics Advisory Group (EAG) provides guidance on an ad hoc basis on areas where specialist expertise is required.

During the biennium (up to June 2023), the IEC evaluated 73 new projects and 51 resubmissions of projects previously reviewed by the IEC. The IEC continued to support the IARC principal investigators with its procedure for expedited review, clearing an average of 50% of projects between official meetings. Given the recorded consistent rise in the number of projects cleared between official meetings, the IEC agreed to set the maximum number of expedited reviews to two every two weeks.

The IEC updated its standard operating procedures (SOPs) with clarifications of responsibilities by the IEC secretary and by the IARC principal investigators. IEC members received training on the United Nations data protection principles applicable to IARC/WHO and on WHO ethical guidance on artificial intelligence. Finally, the IEC continued to monitor progress on the Asbest Chrysotile Cohort Study, a large-scale retrospective research study of risk of oncological disease caused by occupational exposure to dust containing chrysotile asbestos, as per document GC/56/5.

Occupational Health and Safety Committee (OHSC)

The IARC Occupational Health and Safety Committee (OHSC) was restructured in 2023 to adapt its composition to the new IARC building. The OHSC consists of 10 members, who represent each floor of the building, the Staff Association Committee (SAC), the Administrative Services Office (ASO), the Laboratory Safety Officer, and the Staff Physician.

During the 2022–2023 biennium, the OHSC met seven times. The minutes of each meeting are posted on the IARC intranet.

Several major contributions of the OHSC during the biennium were linked to the move and the resumption of activities in the new IARC building, to help ensure optimal working conditions. They included the organization and implementation of a global risk assessment of the premises and all associated activities (in accordance with French law), the implementation of a communication and alarm system, and the contribution to the building manual and security guidelines. In addition, the guidelines for laboratory activities during pregnancy were revised in collaboration with the Staff Physician.

The mission of the IARC Staff Association is to foster the aims of the Agency in cooperation with management and to ensure that staff employment conditions conform with the principles established in the IARC Statute and in the Staff Rules and Regulations and, in particular, to ensure that these conditions permit the efficient discharge by the staff of their duties.

It is the remit of the IARC Staff Association Committee (SAC) to safeguard the collective and individual rights and interests of staff members, to promote staff welfare, to aid staff members who find themselves in difficulties, and to organize social, sporting, and recreational activities for its members.

The SAC is a group of staff members, elected by the staff, that meets regularly with management and with representatives from the other WHO Regional Staff Associations to carry out its various duties.

Governing and Scientific Councils

The International Agency for Research on Cancer (IARC) was established in May 1965, through a resolution of the Eighteenth World Health Assembly, as an extension of the World Health Organization, after a French initiative. It is governed by its own governing bodies: the IARC Governing Council and the IARC Scientific Council.

Governing Council

IARC's general policy is directed by a Governing Council, composed of the Representatives of Participating States and of the Director-General of the World Health Organization. It meets every year in ordinary session in Lyon, usually the week before the World Health Assembly. The Governing Council elects IARC's Director for a 5-year term. The Council re-elected Dr Elisabete Weiderpass in May 2023 to serve for a second 5-year term as from 1 January 2024. The chairperson of the Governing Council prepares the meetings together with the Secretariat and advises the Director throughout the year.

Scientific Council

The Scientific Council consists of highly qualified scientists selected on the basis of their technical competence in cancer research and allied fields. Members of the Scientific Council are appointed as experts and not as representatives of Participating States. When a vacancy arises on the Scientific Council, the Participating State that nominated the departing member may nominate up to two experts to replace that member. Scientific Council members are appointed for 4-year terms by the Governing Council. The Scientific Council reviews the scientific activities of the Agency and makes recommendations on its programme of permanent activities and priorities. The Scientific Council meets every year in ordinary session in late January/early February.

Budget

IARC activities are partially funded by the regular budget contributions paid by its Participating States. In addition, substantial funding comes from extra-budgetary sources, mainly grant awards, both national and international. The regular budget for the 2024–2025 biennium was approved in May 2023 at a level of €48 683 313.

Participating States and Representatives at IARC Governing Council's Sixty-Fourth Session, 12–13 May 2022 (Held Remotely)

Canada

Dr Stephen M. Robbins, Chairperson
Scientific Director, Institute of Cancer Research
Canadian Institutes of Health Research
Calgary, Alberta

Ms Madeleine Bird
Manager, Multilateral Relations Division
Office of International Affairs for the Health Portfolio
Montreal, Quebec

Ms Jennifer Izaguirre
Senior Policy Analyst, Multilateral Relations Division
Office of International Affairs for the Health Portfolio
Ottawa, Ontario

Ms Chantele Sitaram
Policy Analyst, Multilateral Relations Division
Office of International Affairs for the Health Portfolio
Ottawa, Ontario

Mr William Wang
Policy Analyst, Multilateral Relations Division
Office of International Affairs for the Health Portfolio
Ottawa, Ontario

Mr Michael Urgolo
Senior Partnership Lead, Canadian Institutes of Health Research
Ottawa, Ontario

Mr Kay Sadiq
Advisor, International Relations
Canadian Institutes of Health Research
Ottawa, Ontario

Norway

Professor Pål Richard Romundstad, Vice-Chairperson
Norwegian University of Science and Technology (NTNU)
Trondheim

Dr Karianne Solaas (unable to attend)
Special Adviser, The Research Council of Norway
Lysaker

Switzerland

Ms Diane Steber Buechli, Rapporteur
Senior Advisor, Federal Office of Public Health
Division of International Affairs
Bern

Australia

Professor Dorothy Keefe
Chief Executive Officer, Cancer Australia
Surry Hills, New South Wales

Ms Sarah McNeill
International Policy Advisor, Cancer Australia
Surry Hills, New South Wales

Mr Agastya Bharadwaj
Director, International Engagement on Healthier Populations and NSPF Representative
International Strategies Branch, Portfolio Strategies Division
Department of Health
Canberra

Austria

Ms Elisabeth Tischelmayer
Austrian Federal Ministry of Education, Science and Research
Vienna

Belgium

Ms Anne Swaluë
Attachée, SPF Santé publique, Sécurité de la Chaîne alimentaire et Environnement
Brussels

Mr Pieter Vermaerke
Conseiller, Mission permanente de la Belgique auprès de l'Office des Nations Unies et des institutions spécialisées
Geneva, Switzerland

Brazil

Dr Ana Cristina Pinho Mendes Pereira
Director-General, National Cancer Institute (INCA)
Rio de Janeiro

Dr João Ricardo Rodrigues Viegas
International Affairs Analyst, National Cancer Institute (INCA)
Rio de Janeiro

Dr Ronaldo Corrêa Ferreira da Silva
National Cancer Institute (INCA)
Rio de Janeiro

China

Professor Jie He
President, National Cancer Center of China
Beijing

Dr Lin Duan
Deputy Division Director, Bureau of Disease Prevention and Control
National Health Commission
Beijing

Dr Xiaochen Yang
Deputy Division Director, Department of International Cooperation
National Health Commission
Beijing

Dr Jing Wu
Chief, Chronic Diseases Center
Chinese Center for Disease Control and Prevention
Beijing

Dr Yang Ding
First Secretary, Permanent Mission of China to the United Nations and other international organizations
Geneva, Switzerland

Denmark

Professor Anders Hviid
Statens Serum Institut
Copenhagen

Finland

Dr Markku Tervahauta
Director-General, Finnish Institute for Health and Welfare (THL)
Helsinki

Ms Tuula Helander
Director, Ministry of Social Affairs and Health
Helsinki

France
Professor Norbert Ifrah
Président, Institut national du Cancer (INCa)
Boulogne-Billancourt

Mr Thomas Dubois
Responsable des affaires européennes et internationales
Institut national du Cancer (INCa)
Boulogne-Billancourt

Dr Jocelyne Bérille
Chargée de mission, Ministère de l'Enseignement supérieur, de la recherche et de l'innovation
Direction générale de la recherche et de l'innovation
Paris

Ms Christine Berling (unable to attend)
Cheffe, Mission des affaires européennes et internationales
Direction générale de la Santé (DGS/MAEI)
Ministère des Solidarités et de la Santé
Paris

Germany
Mr Thomas Ifland
Senior Adviser, Federal Ministry of Health
Berlin

Dr Chris Braun
Federal Ministry of Health
Berlin

Hungary
Professor Gabriella Liszkay
Head, Department of Dermatology
National Institute of Oncology
Budapest

Professor Péter Nagy
Scientific Director, National Institute of Oncology
Budapest

India
Dr Jayanta Chakrabarti (unable to attend)
Director, Chittaranjan National Cancer Institute (CNCI)
Kolkata

Dr Rupinder Singh Dhaliwal
Scientist, Indian Council of Medical Research (ICMR)
New Delhi

Dr Tanvir Kaur
Indian Council of Medical Research (ICMR)
New Delhi

Iran (Islamic Republic of)
No Representative

Ireland
No Representative

Italy
Professor Silvio Brusaferro
President, Italian National Institute of Health
Rome

Dr Sergio Iavicoli
Director General, Directorate for Communication and European and International Relations
Ministry of Health
Rome

Dr Mauro Biffoni
Italian National Institute of Health
Rome

Japan
Dr Naoki Akahane
Senior Coordinator for Global Health, International Affairs Division
Ministry of Health, Labour and Welfare
Tokyo

Dr Masako Horita
Deputy Director, International Affairs Division
Ministry of Health, Labour and Welfare
Tokyo

Dr Hitoshi Nakagama
President, National Cancer Center Japan
Tokyo

Dr Tatsuya Suzuki
Deputy Director, Strategic Planning Bureau
National Cancer Center Japan
Tokyo

Dr Tomohiro Matsuda
Head, Office of International Affairs
National Cancer Center Japan
Tokyo

Ms Kay Ohara
Manager, Office of International Affairs
National Cancer Center Japan
Tokyo

Morocco

Dr Rachid Bekkali (unable to attend)
Director-General, Lalla Salma Foundation for Cancer Prevention and Treatment
Rabat

Dr Latifa Belakhel
Head, Noncommunicable Diseases
Ministry of Health and Social Protection
Rabat

Dr Loubna Abousselham
Head, Cancer Prevention and Control
Ministry of Health and Social Protection
Rabat

Ms Loubna Olouy
Representative of the Cooperation Division
Ministry of Health and Social Protection
Rabat

Netherlands

Dr Susan Potting
Ministry of Health, Welfare and Sport
The Hague

Mr Pim ten Broeke
Ministry of Health, Welfare and Sport
The Hague

Qatar

Dr Al-Hareth M. Al-Khater
Senior Consultant Physician, Oncologist
Deputy Medical Director for Clinical Affairs
Hamad Medical Corporation
Doha

Dr Mohammed Ussama Al Homsi
Senior Consultant Physician, Oncologist
Deputy Medical Director of Education, Research and Quality
Hamad Medical Corporation
Doha

Dr Mohamed Yassin
Senior Consultant Physician, Haematologist
Fellowship Program Director – Haematology
Hamad Medical Corporation
Doha

Republic of Korea

Dr Sangkyun Han
Director, Division of Disease Control Policy
Bureau of Public Health Policy, Office for Healthcare Policy
Ministry of Health and Welfare
Sejong-si

Dr Taehwan Shin
Senior Deputy Director, Division of Disease Control Policy
Bureau of Public Health Policy, Office for Healthcare Policy
Ministry of Health and Welfare
Sejong-si

Dr Chongwoo Yoo
Director, Office of Public Relations and Collaboration
National Cancer Center of Korea
Goyang-si Gyeonggi-do

Dr Jaekwan Jun
Head, Cancer Knowledge and Information Center
National Cancer Control Institute
National Cancer Center of Korea
Goyang-si Gyeonggi-do

Russian Federation

Dr Igor Korobko
Director, Department of Science and Innovative Health Development
Ministry of Health
Moscow

Dr Oleg Sonin
Deputy Director, Department of International Cooperation and Public Relations
Ministry of Health
Moscow

Dr Elena Kirsanova
Deputy Head of the Division, Department of International Cooperation and Public Relations
Ministry of Health
Moscow

Dr Eduard Salakhov
Health Attaché, Permanent Mission of the Russian Federation to the United Nations Office
Geneva, Switzerland

Spain

Dr Elena Doménech Cruz
International Programmes Coordinator, Institute of Health Carlos III
Madrid

Dr Maria José González de Suso (unable to attend)
Programmes Director, Institute of Health Carlos III
Madrid

Sweden

Professor Madeleine Durbeej-Hjalt
Secretary-General, Medicine and Health
Swedish Research Council
Stockholm

Dr Karin Schmekel
Head, Unit for Research and Research Education
Karolinska Institutet
Stockholm

United Kingdom of Great Britain and Northern Ireland

Dr Mark Palmer
Director of International Relations
Medical Research Council
London

Dr Mariana Delfino-Machin
Programme Manager for Cancer
Medical Research Council
Swindon

United States of America

Dr Mara Burr
Director, Multilateral Relations Office
Office of Global Affairs
Department of Health and Human Services
Washington, DC

Dr Sarah Emami
Senior Global Health Officer, Multilateral Relations Office
Office of Global Affairs
Department of Health and Human Services
Washington, DC

Ms Adriana Gonzalez
Health Advisor, Office of Economic and Development Affairs
Bureau of International Organization Affairs, Department of State
Washington, DC

Dr Ann Chao
Health Science Administrator
National Cancer Institute, National Institutes of Health
Department of Health and Human Services
Bethesda, Maryland

Dr Krycia Cowling
Global Health Officer, Multilateral Relations
Office of Global Affairs
Department of Health and Human Services
Washington, DC

Dr Satish Gopal
Director, Center for Global Health
National Cancer Institute, National Institutes of Health
Department of Health and Human Services
Bethesda, Maryland

Ms Dalana Johnson
Advisor on Multilateral Partnerships
National Cancer Institute, National Institutes of Health
Department of Health and Human Services
Bethesda, Maryland

Dr Gregory McElwain
Senior Advisor, Office of Management, Policy, and Resources
Bureau of International Organization Affairs, Department of State
Washington, DC

Dr Marie Ricciardone
Program Director, Center for Global Health
National Cancer Institute, National Institutes of Health
Department of Health and Human Services
Bethesda, Maryland

World Health Organization

Dr Bente Mikkelsen
Director, Noncommunicable Diseases
WHO headquarters
Geneva, Switzerland

Ms Sigrid Kranawetter
Principal Legal Officer
WHO headquarters
Geneva, Switzerland

Observers

Scientific Council

Dr Manami Inoue
Incoming chairperson

Dr Janne Pitkäniemi
Outgoing chairperson

Union for International Cancer Control (UICC)

Dr Sonali Johnson
Head, Knowledge, Advocacy and Policy
Geneva, Switzerland

External Audit

Mr Krishnaraju Subramaniam
Director of External Audit (WHO)
Office of the Comptroller and Auditor General of India
Geneva, Switzerland

Participating States and Representatives at IARC Governing Council's Sixty-Fifth Session, 10–12 May 2023

France

Professor Norbert Ifrah, Chairperson
Président, Institut national du Cancer (INCa)
Boulogne-Billancourt

Dr Thomas Dubois
Responsable des affaires européennes et internationales
Institut national du Cancer (INCa)
Boulogne-Billancourt

Ms Christine Berling
Cheffe, Mission des affaires européennes et internationales
Direction générale de la Santé (DGS/MAEI)
Ministère de la Santé et de la Prévention
Paris

Mr Nicolas Albin
Ministère de l'Enseignement supérieur et de la Recherche
Paris

United States of America

Dr Mara Burr, Vice-Chairperson
Director, Multilateral Relations Office
Office of Global Affairs
Department of Health and Human Services
Washington, DC

Ms Christina Taylor
Global Health Officer
Department of Health and Human Services
Washington, DC

Dr Maya Levine (unable to attend)
Deputy Director, Multilateral Relations Office
Department of Health and Human Services
Washington, DC

Dr Tracy Carson (attended remotely)
Health Attaché, Permanent Mission of the United States to the United Nations and other international organizations in Geneva
Geneva, Switzerland

Dr Satish Gopal
Director, Center for Global Health
National Cancer Institute, National Institutes of Health
Department of Health and Human Services
Bethesda, Maryland

Ms Adriana Gonzalez
Health Advisor, Office of Economic and Development Affairs
Bureau of International Organization Affairs, Department of State
Washington, DC

Australia

Ms Sarah McNeill, Rapporteur
International Policy Advisor, Cancer Australia
Surry Hills, New South Wales

Professor Dorothy Keefe
Chief Executive Officer, Cancer Australia
Surry Hills, New South Wales

Austria

Ms Elisabeth Tischelmayer
Austrian Federal Ministry of Education, Science and Research
Vienna

Belgium

Dr Marc Van den Bulcke
Head of Service, Sciensano
Brussels

Ms Anne Swaluë (attended remotely)
Attachée, Relations internationales
SPF Santé publique, Sécurité de la Chaîne alimentaire et Environnement
Brussels

Ms Eloïse Delforge
Attachée, Relations internationales
SPF Santé publique, Sécurité de la Chaîne alimentaire et Environnement
Brussels

Brazil

Dr João Paulo de Biaso Viola
Deputy Director-General, National Cancer Institute (INCA)
Rio de Janeiro

Dr Luis Felipe Ribeiro Pinto (unable to attend)
Deputy Research Coordinator, National Cancer Institute (INCA)
Rio de Janeiro

Canada

Dr Fei-Fei Liu
Scientific Director, Institute of Cancer Research
Canadian Institutes of Health Research
Toronto, Ontario

Ms Jennifer Izaguirre
Senior Policy Analyst, Multilateral Relations Division
Office of International Affairs for the Health Portfolio
Ottawa, Ontario

China

Professor Jie He
Director, National Cancer Center of China
Beijing

Ms Qi Shi
Minister-Counsellor, Permanent Mission of China to the United Nations and other international organizations
Geneva, Switzerland

Ms Xin Huang
Division Director, National Health Commission
Beijing

Dr Wenqiang Wei
Consultant, National Cancer Center of China
Beijing

Mr Wanqing Chen
Consultant, National Cancer Center of China
Beijing

Ms Ni Li
Consultant, National Cancer Center of China
Beijing

Ms Jing Wu
Director, National Center for Chronic and Noncommunicable Disease Control and Prevention
Beijing

Denmark

Dr Morten Frisch
Statens Serum Institut
Copenhagen

Finland

Dr Markku Tervahauta
Director-General, Finnish Institute for Health and Welfare (THL)
Helsinki

Ms Tuula Helander
Deputy Director-General, Ministry of Social Affairs and Health
Helsinki

Germany

Mr Thomas Ifland
Senior Adviser, Federal Ministry of Health
Berlin

Hungary

Professor Péter Nagy
Scientific Director, National Institute of Oncology
Budapest

India

No Representative

Iran (Islamic Republic of)

Dr Yunes Panahi
Vice Chancellor for Research and Technology
Ministry of Health and Medical Education
Tehran

Dr Sajad Sahab Negah
Director, International Affairs, Research and Technology Deputy
Ministry of Health and Medical Education
Tehran

Ireland

Mr Eoin Dornan (unable to attend)
Department of Health
Dublin

Mr Andrew Kelly
Department of Health
Dublin

Italy

Dr Mauro Biffoni
Italian National Institute of Health
Rome

Japan

Dr Hitoshi Nakagama
President, National Cancer Center Japan
Tokyo

Dr Takashi Suzuki
Senior Coordinator for Global Health, International Affairs Division
Ministry of Health, Labour and Welfare
Tokyo

Dr Kanami Kobayashi
Deputy Director for Global Health, International Affairs Division
Ministry of Health, Labour and Welfare
Tokyo

Ms Kay Ohara
Manager, Office of International Affairs
National Cancer Center Japan
Tokyo

Morocco

Dr Latifa Belakhel
Head, Noncommunicable Diseases
Ministry of Health and Social Protection
Rabat

Dr Youssef Chami Khazraji
Lalla Salma Foundation for Cancer Prevention and Treatment
Rabat

Netherlands

Ms Susan Potting
Ministry of Health, Welfare and Sport
The Hague

Mr Pim ten Broeke
Ministry of Health, Welfare and Sport
The Hague

Norway

Professor Pål Richard Romundstad
Norwegian University of Science and Technology (NTNU)
Trondheim

Dr Karianne Solaas (attended remotely)
Special Adviser, The Research Council of Norway
Lysaker

Qatar

Dr Al-Hareth M. Al-Khater
Senior Consultant Physician
Deputy Medical Director for Clinical Affairs
Chairperson, Corporate Healthcare Ethics Committee
Hamad Medical Corporation
Doha

Mr Abdullatif Ali Al-Abdulla (unable to attend)
Manager, International Health Relations
International Health Relations Department
Ministry of Public Health
Doha

Republic of Korea

Dr Min Won Lee
Minister-Counsellor, Permanent Mission of the Republic of Korea to the United Nations and other international organizations
Geneva, Switzerland

Dr Hyeon Gyu Park
Assistant Director, Division of Disease Control Policy
Ministry of Health and Welfare
Sejong-si

Mr Yeol Kim
Head, Division of Public Health and Social Support
National Cancer Center of Korea
Goyang-si Gyeonggi-do

Russian Federation

Dr Eduard Salakhov
Advisor, Permanent Mission of the Russian Federation to the United Nations Office
Geneva, Switzerland

Mr Ivan Tarutin
Third Secretary, Permanent Mission of the Russian Federation to the United Nations Office
Geneva, Switzerland

Dr Anton Alekseevich Barchuk (unable to attend)
N.N. Petrov National Medical Research Center of Oncology
Ministry of Health
Moscow

Spain

No Representative

Sweden

Professor Madeleine Durbeej-Hjalt
Secretary-General, Medicine and Health
Swedish Research Council
Stockholm

Dr Karin Schmekel
Head, Unit for Research and Research Education
Karolinska Institutet
Stockholm

Switzerland

Mr Florian Dolder
Conseiller, Office fédéral de la santé publique (OFSP)
Division Affaires internationales
Bern

United Kingdom of Great Britain and Northern Ireland

Dr Mark Palmer
Director of International Relations
Medical Research Council
London

Dr Isobel Atkin
Programme Manager
Medical Research Council
London

World Health Organization

Dr Bente Mikkelsen
Director, Noncommunicable Diseases
WHO headquarters
Geneva, Switzerland

Ms Sigrid Kranawetter
Principal Legal Officer
WHO headquarters
Geneva, Switzerland

Observers

Scientific Council

Dr Manami Inoue
Chairperson

IARC Ethics Committee

Dr Samar Al-Homoud
Chairperson

Union for International Cancer Control (UICC)

Dr Cary Adams
Chief Executive Officer
Geneva, Switzerland

External Audit

Ms Ritu Dhillon (attended remotely)
Director of External Audit (WHO)
Office of the Comptroller and Auditor General of India
Geneva, Switzerland

Scientific Council Members (2022)

Professor Janne Pitkäniemi, Chairperson
Finnish Cancer Registry
Institute for Statistical and Epidemiological Cancer Research
Helsinki, Finland

Dr Manami Inoue, Vice-Chairperson
Chief, Division of Prevention
National Cancer Center Institute for Cancer Control
Tokyo, Japan

Professor William Gallagher, Rapporteur
University College Dublin School of Biomolecular and Biomedical Science
Dublin, Ireland

Dr Einas Abdulaziz Eid Al Kuwari
Chairperson, Department of Laboratory Medicine and Pathology
Hamad Medical Corporation
Doha, Qatar

Dr Marc Arbyn
Coordinator, Unit of Cancer Epidemiology
Belgian Cancer Centre
Brussels, Belgium

Dr Karima Bendahhou
Cancer Registry of Casablanca
Centre Mohammed VI pour le traitement des cancers, CHU Ibn Rochd
Casablanca, Morocco

Professor Walter Berger
Center for Cancer Research
Medical University of Vienna
Vienna, Austria

Professor Tone Bjørge
Epidemiology and Medical Statistics Section
Department of Global Public Health and Primary Care
University of Bergen
and
Cancer Registry of Norway
Bergen, Norway

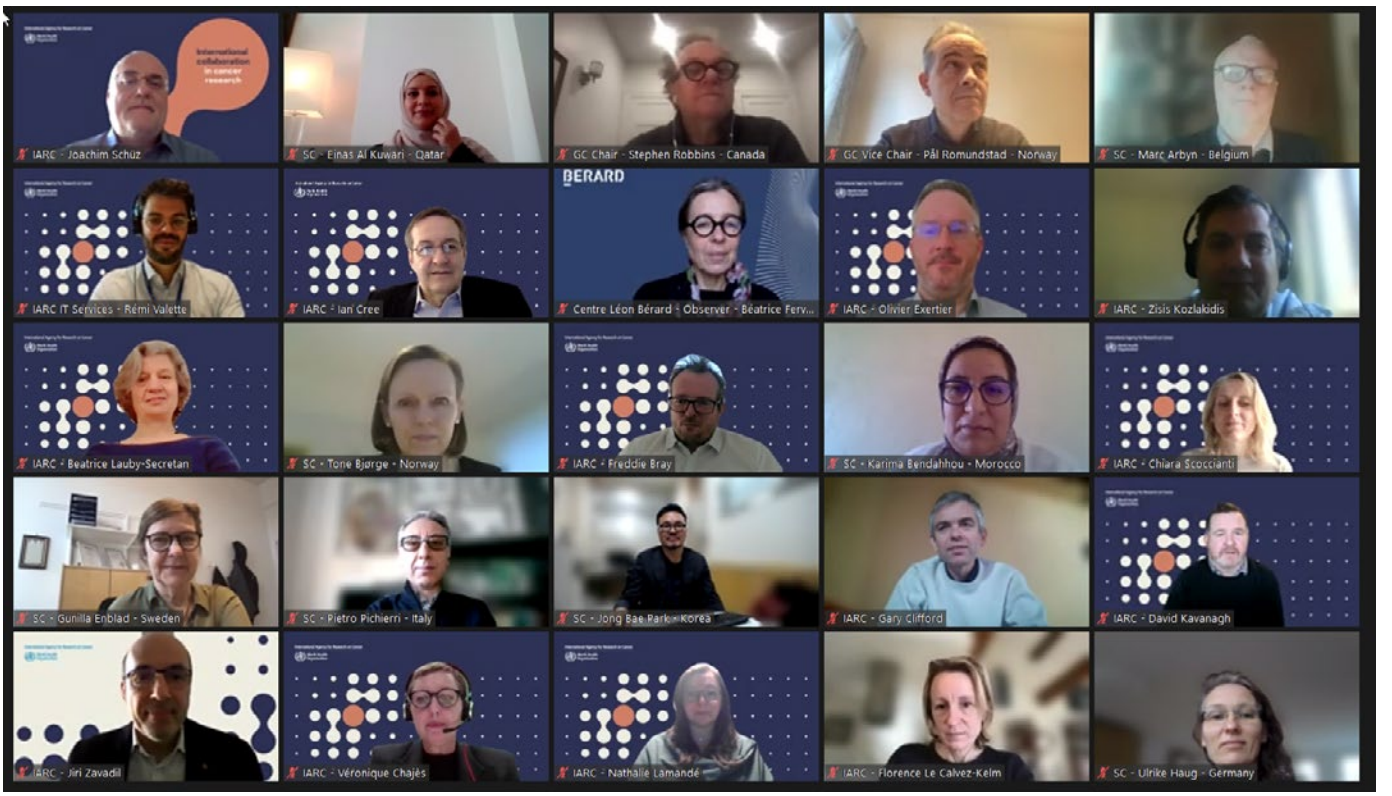
Dr Hendriek Boshuizen
Department Statistics, Informatics and Mathematical Modelling
National Institute for Public Health and the Environment (RIVM)
Bilthoven, The Netherlands

Dr Ferrán Catalá-López
Department of Health Planning and Economics
National School of Public Health
Institute of Health Carlos III
Madrid, Spain

Professor James Robert Cerhan
Chairperson, Department of Artificial Intelligence and Informatics
Mayo Clinic
Rochester, Minnesota, USA

Professor Kalipso Chalkidou
Visiting Professor, Imperial College London
London, United Kingdom
and
Head, Health Finance
The Global Fund to Fight AIDS, Tuberculosis and Malaria
Grand-Saconnex, Switzerland

Professor Gunilla Enblad
Department of Immunology, Genetics and Pathology
Uppsala University
Uppsala, Sweden



Professor Louisa Gordon
QIMR Berghofer Medical Research Institute
Royal Brisbane Hospital
Brisbane, Australia

Professor Ulrike Haug
Leibniz Institute for Prevention Research and Epidemiology (BIPS)
Bremen, Germany

Professor Jie He
President, National Cancer Center of China
Beijing, China

Professor Sergey Ivanov
A. Tsyb Medical Radiological Research Centre
National Medical Research Radiological Centre
Obninsk, Russian Federation

Professor Ravi Mehrotra
Director, National Institute of Cancer Prevention and Research
Indian Council of Medical Research (ICMR)
Uttar Pradesh, India

Professor Péter Nagy
Scientific Director, National Institute of Oncology
Budapest, Hungary

Professor Marie-Elise Parent
Epidemiology and Biostatistics Unit
Centre Armand-Frappier Santé Biotechnologie
Institut national de la recherche scientifique
Université du Québec
Laval, Canada

Professor Jong Bae Park
Dean, National Cancer Center Graduate School of Cancer Science and Policy
Goyang-si Gyeonggi-do, Republic of Korea

Dr Pietro Pichierri
Senior Researcher, Team Leader, Genome Stability Group
Mechanisms, Biomarkers and Models Unit
Department of Environment and Health
Istituto Superiore di Sanità
Rome, Italy

Dr Luis Felipe Ribeiro Pinto
Head, Molecular Carcinogenesis Program
National Cancer Institute (INCA)
Rio de Janeiro, Brazil

Dr Sabine Rohrmann
Epidemiology, Biostatistics and Prevention Institute (EBPI)
University of Zurich
Zurich, Switzerland

Dr Anne Tjønneland
Danish Cancer Society Research Center
Copenhagen, Denmark

Dr Mathilde Touvier
Sorbonne Paris Nord University, INSERM
Nutritional Epidemiology Research Team (EREN)
Bobigny, France

Dr Kazem Zendehdel (unable to attend)
Deputy of Research, Cancer Research Center
Cancer Institute of Iran
Tehran University of Medical Sciences
Tehran, Islamic Republic of Iran

Scientific Council Members (2023)

Dr Manami Inoue, Chairperson
Chief, Division of Prevention
National Cancer Center Institute for Cancer Control
Tokyo, Japan

Dr Luis Felipe Ribeiro Pinto, Vice-Chairperson
Head, Molecular Carcinogenesis Program
National Cancer Institute (INCA)
Rio de Janeiro, Brazil

Professor William Gallagher, Rapporteur
University College Dublin School of Biomolecular and Biomedical Science
Dublin, Ireland

Dr Einas Abdulaziz Eid Al Kuwari
Chairperson, Department of Laboratory Medicine and Pathology
Hamad Medical Corporation
Doha, Qatar

Dr Marc Arbyn (unable to attend)
Coordinator, Unit of Cancer Epidemiology
Belgian Cancer Centre
Brussels, Belgium

Dr Karima Bendahhou
Cancer Registry of Casablanca
Centre Mohammed VI pour le traitement des cancers, CHU Ibn Rochd
Casablanca, Morocco

Professor Walter Berger
Center for Cancer Research and Comprehensive Cancer Center
Medical University of Vienna
Vienna, Austria

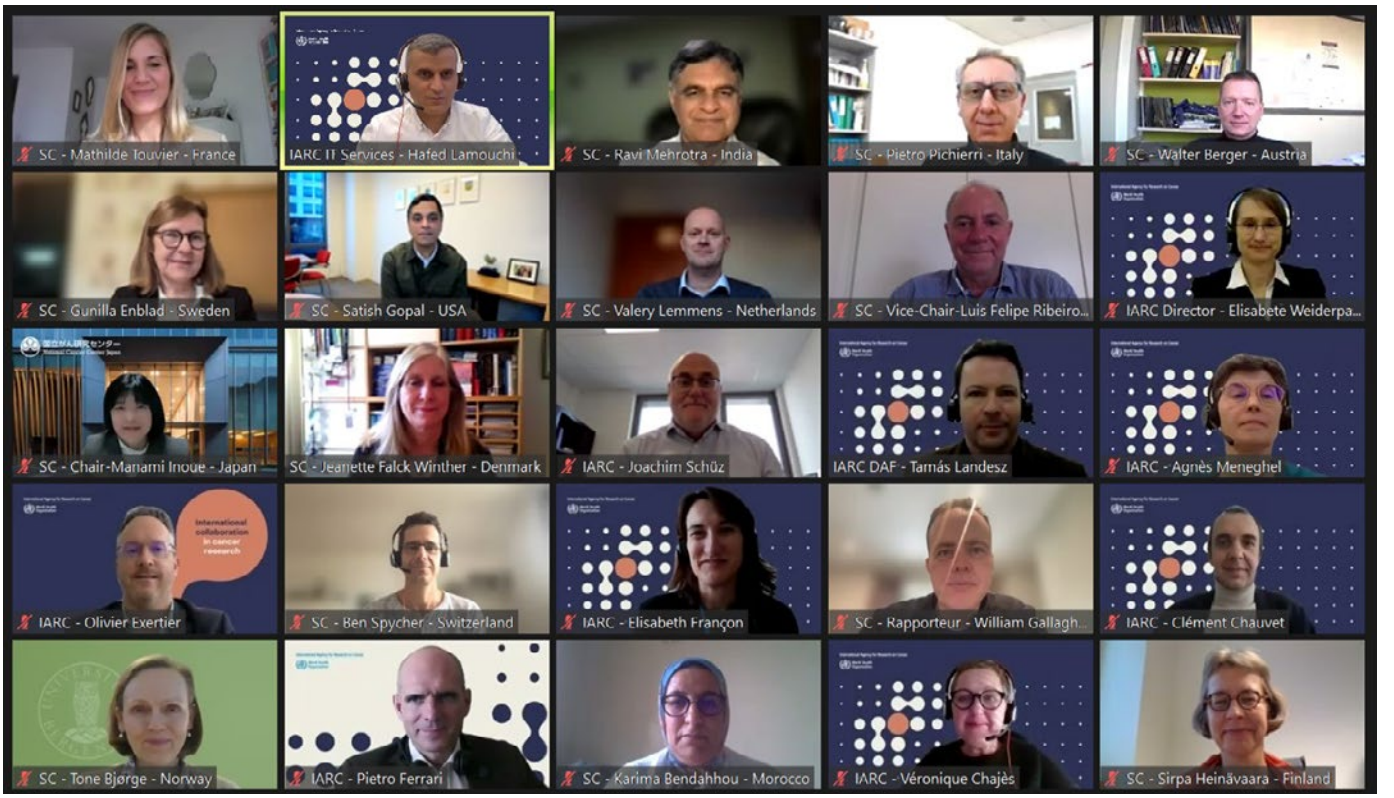
Professor Tone Bjørge
Epidemiology and Medical Statistics Section
Department of Global Public Health and Primary Care
University of Bergen
and
Cancer Registry of Norway
Bergen, Norway

Dr Ferrán Catalá-López
Department of Health Planning and Economics
National School of Public Health
Institute of Health Carlos III
Madrid, Spain

Professor Kalipso Chalkidou
Visiting Professor, Imperial College London
London, United Kingdom
and
Head, Health Finance
The Global Fund to Fight AIDS, Tuberculosis and Malaria
Grand-Saconnex, Switzerland

Professor Gunilla Enblad
Department of Immunology, Genetics and Pathology
Uppsala University
Uppsala, Sweden

Professor Jeanette Falck Winther
Head, Childhood Cancer Research Group
Danish Cancer Society Research Center (DCRC)
Copenhagen, Denmark
and
Department of Clinical Medicine, Faculty of Health
Aarhus University and University Hospital
Aarhus, Denmark



Dr Satish Gopal
Director, Center for Global Health
National Cancer Institute, National Institutes of Health
Department of Health and Human Services
Bethesda, Maryland, USA

Professor Louisa Gordon
QIMR Berghofer Medical Research Institute
Royal Brisbane Hospital
Brisbane, Australia

Professor Ulrike Haug
Leibniz Institute for Prevention Research and Epidemiology (BIPS)
Bremen, Germany

Professor Jie He (unable to attend)
President, National Cancer Center of China
Beijing, China

Dr Sirpa Heinävaara
Cancer Society of Finland
Finnish Cancer Registry
Helsinki, Finland

Professor Sergey Ivanov
A. Tsyb Medical Radiological Research Centre
National Medical Research Radiological Centre
Obninsk, Russian Federation

Professor Valery Lemmens
Integraal Kankercentrum Nederland (IKNL)
Utrecht, The Netherlands

Professor Ravi Mehrotra
Former Director, National Institute of Cancer Prevention and Research
Indian Council of Medical Research (ICMR)
Uttar Pradesh, India

Professor Péter Nagy
Scientific Director, National Institute of Oncology
Budapest, Hungary

Professor Marie-Elise Parent
Epidemiology and Biostatistics Unit
Centre Armand-Frappier Santé Biotechnologie
Institut national de la recherche scientifique
Université du Québec
Laval, Canada

Professor Jong Bae Park
National Cancer Center Graduate School of Cancer Science and Policy
Goyang-si Gyeonggi-do, Republic of Korea

Dr Pietro Pichierri
Senior Researcher, Team Leader, Genome Stability Group
Mechanisms, Biomarkers and Models Unit
Department of Environment and Health
Istituto Superiore di Sanità
Rome, Italy

Dr Ben Spycher
Senior Researcher, Head of Research Group
Institute of Social and Preventive Medicine
University of Bern
Bern, Switzerland

Dr Mathilde Touvier
Sorbonne Paris Nord University, INSERM, INRAE, CNAM
Nutritional Epidemiology Research Team (CRESS-EREN)
Bobigny, France

IARC Staff Publications 2022–2023

As at 30 November 2023

Abnet CC, Buckle GC, Chen Y, Dawsey SM, Kayamba V, Mwachiro MM, et al.; African Esophageal Cancer Consortium (2022). Expanding oesophageal cancer research and care in eastern Africa. Nat Rev Cancer. 22(5):253–4. https://doi.org/10.1038/s41568-022-00458-1 PMID:35246668

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Aisyah D, Lokopessy AF, Naman M, Diva H, Manikam L, Adisasmito W, et al. (2023). The use of digital technology for COVID-19 detection and response management in Indonesia: mixed methods study. Interact J Med Res. 12:e41308. https://doi.org/10.2196/41308 PMID:36623206

Aisyah DN, Kozlakidis Z, Diva H, Trimizi SN, Sianipar LR, Wijayanti E, et al. (2022c). The spatial-temporal distribution of chronic lymphatic filariasis in Indonesia: a 18-year registry-based analysis. Microbiol Res (Pavia). 13(4):681–90. https://doi.org/10.3390/microbiolres13040049

Aisyah DN, Manikam L, Kiasatina T, Naman M, Adisasmito W, Kozlakidis Z (2022a). The use of a health compliance monitoring system during the COVID-19 pandemic in Indonesia: evaluation Study. JMIR Public Health Surveill. 8(11):e40089. https://doi.org/10.2196/40089 PMID:36219836

Aisyah DN, Mayadewi CA, Budiharsana M, Solikha DA, Ali PB, Igusti G, et al. (2022b). Building on health security capacities in Indonesia: lessons learned from the COVID-19 pandemic responses and challenges. Zoonoses Public Health. 69(6):757–67. https://doi.org/10.1111/zph.12976 PMID:35618675

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Collaborators

Cancer Surveillance Branch (CSU)

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Sabiha Bouzbid, Marym Ramzia Mohammady, Fadhila Toudeft, Algeria; Gisel Fattore, Florencia Moreno, Graciela Nicolás, Carlos Vásquez, Argentina; Joanne F. 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