

International Agency for Research on Cancer



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IARC

The World Cancer Research Agency

Medium-Term Strategy 2021–2025

“A world where fewer people
develop cancer”



IARC
WHO

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Abbreviations

BCNet	LMICs Biobank and Cohort Building Network
CI5	Cancer Incidence in Five Continents
DALYs	disability-adjusted life years
EBV	Epstein–Barr virus
ECVS	Early Career and Visiting Scientists
EPIC	European Prospective Investigation into Cancer and Nutrition
FENSA	Framework of Engagement with Non-State Actors
GCO	Global Cancer Observatory
GICR	Global Initiative for Cancer Registry Development
<i>H. pylori</i>	<i>Helicobacter pylori</i>
HBV	hepatitis B virus
HCV	hepatitis C virus
HPV	human papillomavirus
IACR	International Association of Cancer Registries
IAEA	International Atomic Energy Agency
IARC	International Agency for Research on Cancer
IC³R	International Collaboration for Cancer Classification and Research
IICC	International Incidence of Childhood Cancer
ISO	International Organization for Standardization
LMICs	low- and middle-income countries
MTS	Medium-Term Strategy
NCDs	noncommunicable diseases
ODA	Official Development Assistance
OECD	Organisation for Economic Co-operation and Development
PBCRs	population-based cancer registries
SDG	Sustainable Development Goal
UN	United Nations
UNEP	United Nations Environment Programme
UNFPA	United Nations Population Fund
UNIATF	United Nations Interagency Task Force
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation
UV	ultraviolet
WHO	World Health Organization

Executive summary

The global cancer burden is growing, and there is an urgent need to address the disease more effectively, both as a public health issue and as an economic problem.

This document provides guidance on IARC's priorities over the next five years, with a view to ensuring that its activities have a significant and sustainable impact on the global burden of cancer and, ultimately, on the life and health of the world's citizens.

The **Medium-Term Strategy 2021–2025** of the International Agency for Research on Cancer (IARC) seeks to position IARC as the leading global cancer authority, promoting scientific excellence in and improved knowledge of cancer prevention. As the cancer research agency of the World Health Organization (WHO), IARC is focused on cancer prevention research.



“A world where fewer people develop cancer”

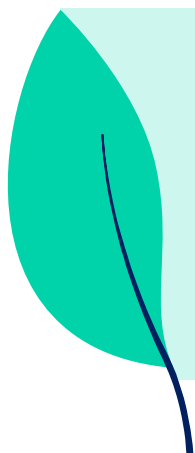
This vision will guide IARC's scientific work in the next five years and beyond. IARC will enhance global understanding of causes of cancer, their respective pathways, and potential prevention measures. Furthermore, IARC will intensify research that addresses the demand for effective and resource-sensitive interventions for cancer prevention.



“Cancer research that matters”

To realize its mission, IARC will channel its strengths and competencies towards a stronger public health impact. More specifically, IARC will generate scientific evidence and set standards that contribute to answering urgent questions about cancer prevention that have been raised by the global cancer control community.

IARC will continue to respond to four key questions on cancer prevention that represent its **fundamental scientific priorities**:



Who gets cancer, where and when?

Why do people get cancer?

How to prevent cancer effectively?

How to mobilize the knowledge gained and strengthen global capacity in cancer science?

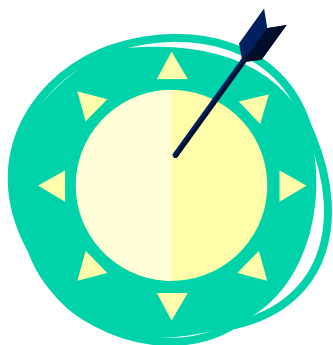
In addition, IARC identified emerging priorities through broad stakeholder consultations, including with key experts from the international cancer control community, WHO counterparts, and IARC's governing entities, who corroborated the importance of these issues for advancing cancer prevention research. Based on this guidance, IARC's emerging priorities will be:

Evolving cancer risk factors and populations in transition

Implementation research

Economic and societal impacts of cancer

IARC will seek to provide sustainable, enabling **operating conditions** that foster a strong and well-defined organizational identity based on IARC's vision, mission, values, and priorities, among both its personnel and its Participating States. In light of continuing resource constraints, IARC will further prioritize activities and ensure that the Agency remains fit for purpose and sufficiently agile to respond effectively to the evolving operational environment for cancer research. IARC will strengthen its capacity to work in an increasingly politicized health environment while maintaining its neutral and independent position.



To reduce the burden of and suffering from cancer – today and among future generations

IARC's overall goal reflects the Agency's ambition to contribute sustainably to the fight against cancer.

More specifically, from 2021 to 2025, IARC seeks:

1 To serve as a global reference for cancer surveillance data and indicators to the international cancer community by:



- supporting measurable improvements in the coverage, quality, and networking capacity of cancer registries in partner countries¹;
- providing global indicators of the disease burden across the continuum of cancer control, including those highlighting social disparities and economic impact; and
- quantifying the long-term public health and economic benefits of integrating preventive interventions into national cancer control plans.

These outcomes will be achieved in collaboration with population-based cancer registries worldwide and are expected to inform national health authorities and policy-makers and drive cancer control action at the national and global levels.

To enhance global understanding of known as well as of unidentified causes of cancer, their respective pathways, and potential prevention measures, by:

2

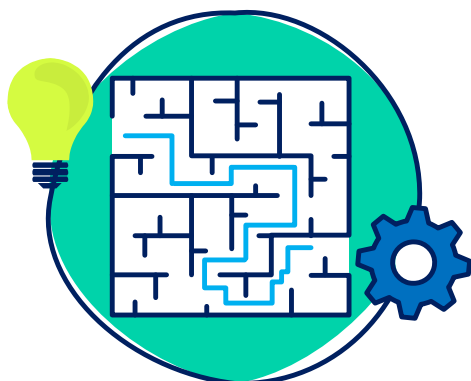
- identifying new environmental, nutrition, lifestyle, infectious, or genetic risk factors for cancer by conducting epidemiological studies in both high-income countries and low- and middle-income countries; and
- identifying mechanistic and causal pathways that underlie the associations of specific risk factors with cancer.



The results of this research are expected to initiate and inform the development of novel preventive strategies for cancer.

1. GICR partner countries are countries committed to working with IARC in addressing their needs through an implementation plan. <https://gicr.iarc.fr/gicr-partner-countries/>

3 To generate scientific evidence related to the effectiveness of implementing primary and secondary prevention interventions, including:



- the prevention or reduction of exposure to established modifiable risk factors;
- the screening of asymptomatic at-risk populations for selected cancer types; and
- the early diagnosis of common cancer types in symptomatic individuals.

The outcomes of this research are expected to inform and support preventive cancer control interventions that can be adapted to specific health system settings.

To enhance global knowledge of cancer classification, hazards, and potential preventive means...

4

This will be done through:

- improved and systematized definitive evidence-based classifications of all cancer types;
- definitive evaluations of the human carcinogenicity of specific agents – ranging from chemicals to viruses – based on the assessment of relevant scientific evidence; and
- definitive evaluations of the potential of specific agents and interventions to prevent cancer.



The outcomes of these activities are expected to enable national health authorities to better understand and manage cancer hazards and to support national decision-making on appropriate preventive interventions.

...To strengthen global and national capacities for cancer science by training and educating the next generation of cancer prevention researchers across the whole spectrum of relevant disciplines.

These activities are expected to support the participation of cancer scientists and their host institutes, including those from low- and middle-income countries, in international collaborative cancer research projects.

THE WORLD CANCER

RESEARCH AGENCY

OUR MISSION

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CANCER RESEARCH THAT MATTERS

PUBLIC HEALTH ISSUES

Cancer to become the **leading cause of premature death** in most countries in the 21st century

#1

Increased longevity = public health imperative to reduce cancer risk



inequities in cancer burden and access to interventions to widen

Evidence for **effective preventive interventions** urgently needed



Open and neutral research platform

Research and capacity-building in LMICs

Independent and impartial authority

Global scientific convening power

Large collaborative research network



UN family member

COMPARATIVE ADVANTAGES



BETTER HEALTH AND WELL-BEING
One billion more people enjoying

3 GOOD HEALTH AND WELL-BEING

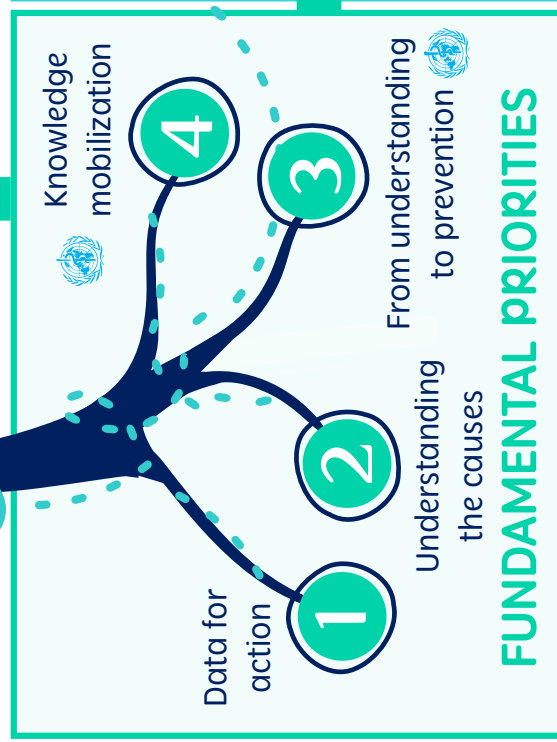
2

million lives saved

OUR VISION
A world where fewer people develop cancer

OUR GOAL

To reduce the burden of and suffering from cancer – today and among future generations



= Collaboration with the World Health Organization (WHO)

Introduction

The Medium-Term Strategy 2021–2025 (MTS) of the International Agency for Research on Cancer (IARC) seeks to position IARC firmly as a thought leader and global convener of scientific excellence in cancer prevention research, as well as a leading authority on global cancer prevention research and related information.

The MTS is based on the IARC Statute and an objective that has guided IARC's work since 1965: *to promote international collaboration in cancer research*. This aspiration remains relevant to all of IARC's activities today. Built on IARC's mandate, the MTS seeks to set a path of evolution that focuses on the Agency's comparative advantages over time. Furthermore, it provides robust guidance on IARC's priorities over the next five years and beyond, with a view to ensuring that its activities have a significant and sustainable impact on the global burden of cancer and, ultimately, on the life and health of the world's citizens.

This MTS document commences with a brief contextual overview of the global cancer control landscape, followed by information about IARC's vision, mission, and goals. Subsequently, IARC's strategic approach and priorities for the next five years are laid out in detail, followed by a chapter on the importance of IARC's cooperation with the World Health Organization (WHO). Next, a chapter provides more details on the implementation of the MTS, structured along IARC's main scientific and support pillars. A chapter on IARC's strategic partnership, outreach, and resource mobilization activities concludes the main document.

The MTS is accompanied by two Annexes, including detailed implementation plans for each scientific unit, as well as an overview of IARC's programme relevant for the MTS time frame.

Context

Strengthening IARC's position and impact in an evolving global cancer control landscape



During the 21st century, cancer will become the leading cause of premature death in most countries.

Throughout the next decade, the world will continue to transform at an ever-accelerating pace, driven by interdependent phenomena such as globalization, urbanization, population growth, technology advancement, climate change, and environmental degradation. The resulting developments will affect societies, health systems, communities, and individuals.

The cancer incidence and mortality burden will double by 2040, from an estimated 18.1 million new cases and 9.6 million deaths per year², exerting considerable strain on health systems. The greatest proportional increases in the cancer burden – ranging from 60% to more than 100% – will occur in low- and middle-income countries (LMICs), many of which are already facing a

2. These statements are based on IARC's cancer surveillance work that brings together cancer statistics globally. <https://gco.iarc.fr>

IARC generates the scientific evidence of the causes of cancer and of the impact of preventive interventions and communicates its findings through well-established channels to the global cancer control and public health community. IARC approaches cancer prevention research comprehensively. Its work spans all aspects of cancer prevention: cancer surveillance, research into causes of cancer, research into the implementation of interventions, mobilizing the evidence-based knowledge, and strengthening global capacities in cancer science. The discharge of IARC's mandate is greatly facilitated by its unique dual position as an international cancer research institute and as a specialized WHO agency within the United Nations (UN) system.

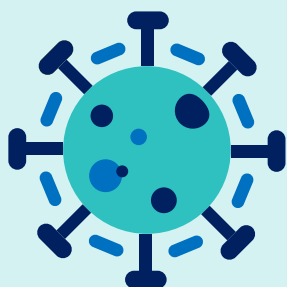
significant burden from infection-related diseases alongside a continuing rise in noncommunicable diseases (NCDs) including cancer. Indeed, NCDs currently account for almost three quarters of all premature deaths (i.e. at ages 30–69 years) worldwide³.

Changes in population structure, the environments in which people live, and the extent to which health systems deliver effective cancer control interventions will affect the incidence, mortality, and prevalence of cancer over the next decades as the underlying cancer risk profiles shift. IARC is operating in this rapidly evolving disease landscape.

This transition is not just a crisis for public health; every additional cancer case or cancer death represents an increasing economic and societal burden as well as a personal and societal loss. National

prosperity requires major domestic investments in effective and cost-effective cancer prevention strategies⁴. Such investments are expected to lead to economic and public health dividends in the longer term: a lower number of cancer patients in the future will reduce the spiralling costs of curative treatment, and curbing the number of premature cancer deaths will contribute to increasing national productivity.

Against the backdrop of a growing cancer burden, the global cancer control landscape continues to evolve. Awareness of the above-mentioned interconnectivity is mounting among governments and within the public health community. This recognition has prompted important global policy initiatives seeking to inform and advance the fight against cancer. IARC will contribute to the relevant initiatives from the perspective of a leader in cancer prevention research.



The global coronavirus disease 2019 (COVID-19) pandemic has greatly affected the social and economic situation as well as health-care systems of all countries. The resulting economic downturn is expected to continue to affect the availability of resources for: health systems and care, including preventive interventions; NCD-related research, including cancer research; and capacity-building for health in LMICs. IARC recognized and acted early on research opportunities at the intersection of cancer and COVID-19 in 2020 in close cooperation with WHO and will continue to do so in the next years as necessary.

Given that health-care systems are intrinsically fragile, they remain vulnerable to unforeseen developments. Overwhelmed health systems quickly affect the implementation of cancer control programmes (including vaccination, screening, and early detection), and the respective resources become rapidly depleted. With such scenarios in mind, IARC will emphasize operational research devised to develop and assess preventive interventions that are resilient to contextual threats and to share the respective results with pertinent stakeholders in the cancer control community.

3. WHO (2020). https://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html

4. WHO (2017). Updated Appendix 3 of the WHO Global NCD Action Plan 2013–2020. <https://www.who.int/ncds/governance/appendix3-update/en/>.

1 Vision and mission

Over the past half a century, IARC has established and fostered its role as the international authority on global data on the occurrence of cancer. IARC has initiated and conducted international research into the causes of cancer that has paved the way for a number of landmark preventive interventions worldwide. In the next years, IARC will seek a significant and sustainable impact of its activities on the global burden of cancer. A new vision will guide IARC's research and scientific work in the next five years and beyond:



IARC'S VISION

“ A world where fewer people develop cancer ”

IARC will enhance global knowledge and understanding of known as well as of important unidentified causes of cancer, their respective pathways, and potential prevention measures.

Primary and secondary prevention will become the chief response and a national priority for tackling the cancer epidemic in most countries this century. Therefore, and given that up to half of all cancer cases could be prevented⁵, IARC will intensify its research that addresses the demand for effective, relevant, and applicable interventions for cancer prevention.

With a growing number of cancer survivors, increasing the knowledge on second primary cancers and the late effects of treatment in real-world settings is paramount.

5. If the current scientific knowledge was effectively applied.

IARC'S MISSION

“ Cancer research that matters ”

IARC will channel its strengths and competencies towards a stronger and sustainable public health impact and emphasize cancer research that endeavours to make a difference in people's lives.

More specifically, IARC will focus on generating scientific evidence that contributes to answering some of the most urgent questions about cancer prevention raised by the international public health community. This ambition will be facilitated by IARC's exceptional competency in identifying and understanding cancer prevention priorities and in considering these when initiating and designing research projects



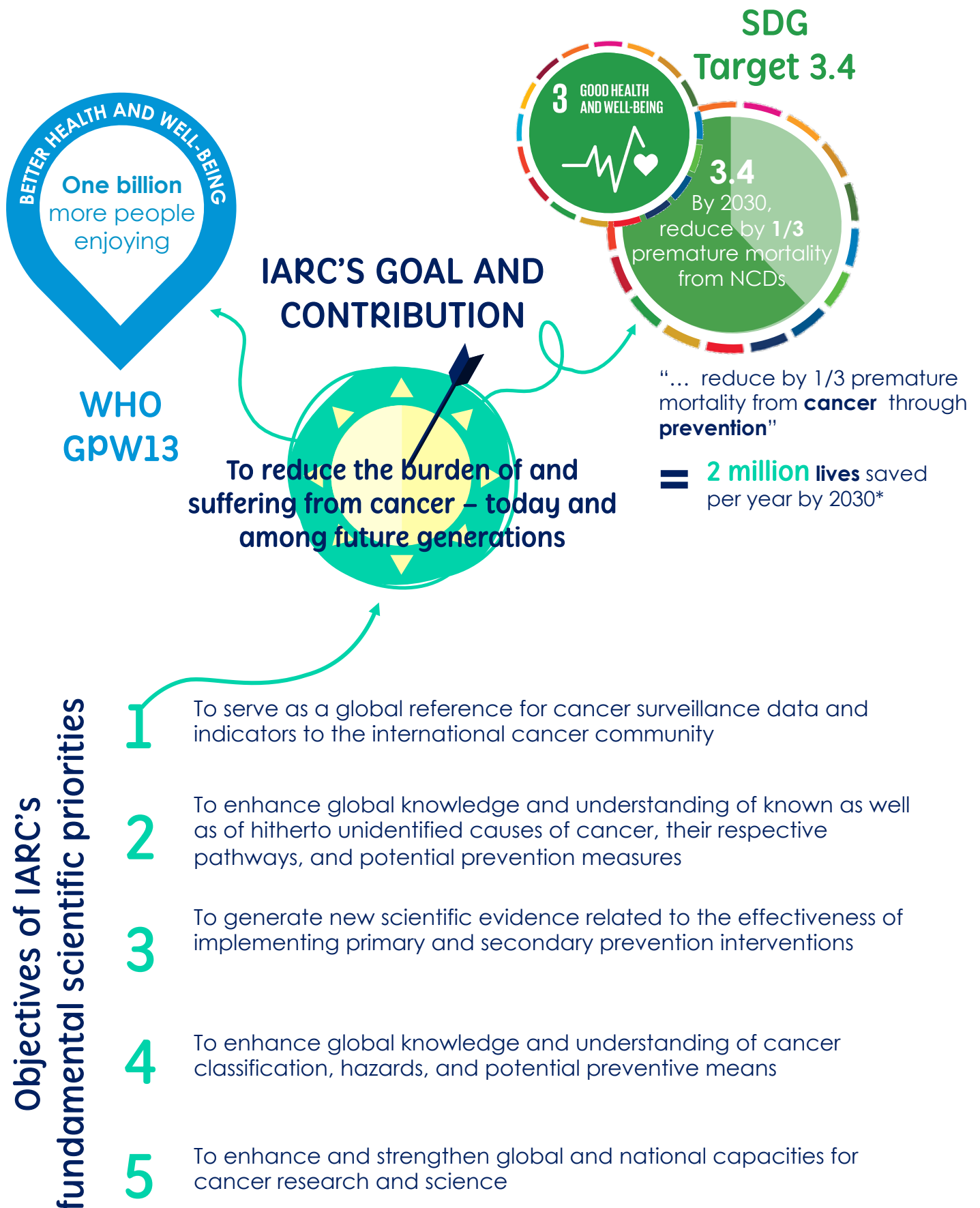
IARC'S GOAL

“ To reduce the burden of and suffering from cancer – today and among future generations ”

This goal reflects the Agency's crucial contribution to the fight against cancer. IARC is uniquely positioned – at the nexus of cancer prevention research, evidence generation for health system interventions, and contribution to relevant UN Sustainable Development Goals – to make a difference.



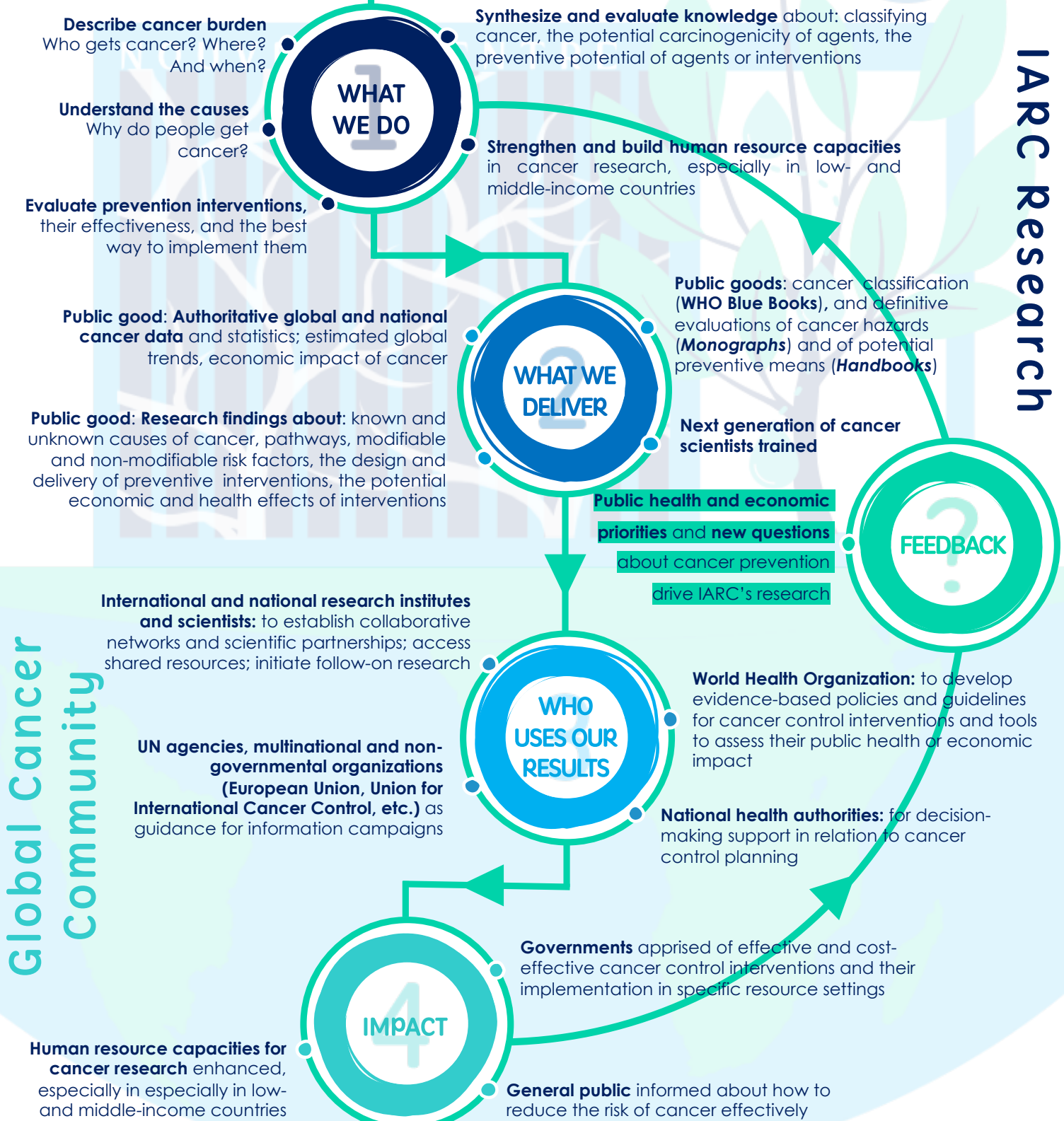
Specifically, IARC will provide high-quality evidence-based knowledge for effective cancer control interventions, geared towards contributing to the achievement of Target 3.4 of the UN Sustainable Development Goals (SDGs).



*Estimate based on IARC cancer surveillance data

IARC will further strengthen its **impact pathway**, shown below, by placing more emphasis on research driven by feedback from cancer control interventions, as well as global public health and economic priorities.

Pathway to address...



... The global cancer burden

Pursuant to its global mandate, IARC will ensure that relevant cooperation activities are conducted in a balanced manner across all continents and regions. Building on successful, ongoing regional cooperation, IARC will enhance research collaboration in regions that are currently not well covered, and study designs will consider regional characteristics where this is meaningful and feasible.



Building and strengthening global capacities in cancer science remains a key component of IARC's mandate. IARC will pursue the education and training of the new generation of cancer researchers and health professionals across the whole spectrum of cancer research disciplines, with a particular focus on LMICs.

2

IARC's prioritization approach

IARC will focus its scientific and research work on areas where it has the **greatest public health impact and matters the most to the ultimate beneficiaries**, i.e. individual human beings. This aspiration has driven the identification of IARC's priorities, along with considerations of IARC's mandate and comparative advantages.

The prioritization process included consultations with a broad set of stakeholders: IARC staff, key experts from the international cancer control community, WHO counterparts, and IARC's governing entities. As a result, two interlinked categories of priorities were identified: **fundamental scientific priorities** and **emerging priorities**, which are explained below.

IARC'S COMPARATIVE ADVANTAGES



Research and capacity-building in LMICs



IARC occupies a unique position in successfully coordinating research and for delivering sustainable capacity-building activities in LMICs. IARC's expertise in cancer prevention, its open and collaborative approach to research, and its status as a UN family member have facilitated its recognition as an enabler and supporter of cancer prevention research.

Furthermore, IARC facilitates capacity-building in cancer prevention-related science in LMICs. Through frequent and intensive interaction with research stakeholders in LMICs, IARC has developed a unique and broad network of collaborators and partners, and has acquired long-lasting expertise with regard to challenges, resource settings, and the situational context of cancer research in LMICs.

Because IARC is increasingly cognizant of specific gaps in knowledge and skills, it is well placed to develop appropriate and tailored capacity-building programmes and to identify the most relevant target audiences for training or mentoring activities.

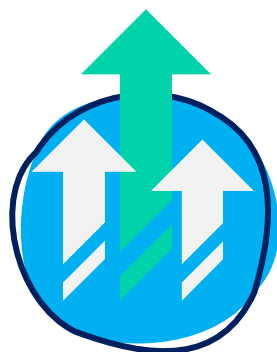
UN family member

IARC has a very close relationship with WHO. Given the complementary nature of IARC's and WHO's missions and their contributions to shared goals, the close collaboration and coordination of the respective work programmes and communication between both organizations is key. Being part of WHO is important for IARC, because WHO's NCD- and cancer-related work, including the translation of IARC's research findings and the synthesis of the scientific evidence about cancer causes and prevention, informs public health recommendations, guidelines, interventions, and policies.



As a member of the UN family, IARC cooperates seamlessly and effectively with many relevant UN agencies, benefiting, where suitable, from their presence in the field. The UN affiliation also facilitates IARC's work with health-focused nongovernmental organizations at the global or regional level.

Open and neutral research platform



IARC provides its scientific collaborators and partners with access to a research platform that is unique in its reach, impartiality, and neutrality. IARC's dual position as an international research institute and as an autonomous, specialized agency of WHO enables it to facilitate and advance cancer research across national borders and political fault lines. This position enables IARC to lead and significantly contribute to large-scale international research consortia on cancer prevention.

For example, population-based studies of rare cancers, rare exposures, or a combination of both benefit greatly from an international and coordinated research approach and access to relevant data across borders and health systems. Similarly, IARC is well suited to lead population-based research into the unique clustering of specific cancers, in particular where these occur in geographical regions with limited capacities or experience to initiate the respective research.

Independent and impartial authority on carcinogenicity and cancer burden

Since 1971, IARC has evaluated more than 1000 potential carcinogens and has shared the results with the global health community. When regulating the use of and exposure to relevant substances or conditions, global and national authorities rely on and refer to IARC's evaluations, because of the expertise and independence that underscore them. The *IARC Monographs* are used as practical guides and resource documents for the development of cancer control measures.



IARC's track record of consistently providing unbiased, state-of-the-art scientific knowledge about carcinogenicity is unique. It is grounded in IARC's ability to engage eminent, independent, and impartial subject matter experts from around the world. In addition, the procedures underlying the evaluations for the *IARC Monographs* are widely respected for their transparency and rigour and serve as a model for other carcinogenicity evaluations throughout the world.

IARC is the global authority and the definitive and independent reference source for global cancer indicators, providing policy-makers with a reliable evidence base for decision-making. IARC enables the global cancer community to understand the current magnitude and trends in cancer risk at the national, regional, and global levels.

Central to IARC's ability to disseminate these national cancer surveillance indicators freely is mutual support and collaboration with population-based cancer registries (PBCRs) worldwide. PBCRs are a unique and sustainable means to inform national cancer control planning and foster local cancer research. IARC's Global Initiative for Cancer Registry Development (GICR) brings together international and national agencies committed to improving cancer surveillance at the national level.

Global scientific convening power and large collaborative research networks



IARC is recognized for its global convening power across all research areas and scientific disciplines that revolve around cancer prevention. Since IARC's creation, its ability to assemble global expertise and scientific excellence in cancer prevention has steadily grown. This unique feature enables IARC to easily partner with outstanding individual experts and leading institutions through scientific consultations, expert assessments, or collaborative research. Moreover, IARC is at the centre of an unrivalled and vast collaborative research network, which effectively straddles five continents. This network enables and empowers IARC to launch, and lead with authority, collaborative scientific projects in cancer prevention that address questions of global public health relevance.

Over the next five years, IARC will further enhance its convening power and enlarge its collaborative network, with a renewed focus on LMICs.

FUNDAMENTAL AND EMERGING PRIORITIES

IARC will continue to address its **fundamental scientific priorities** and respond to the four key questions about cancer prevention:

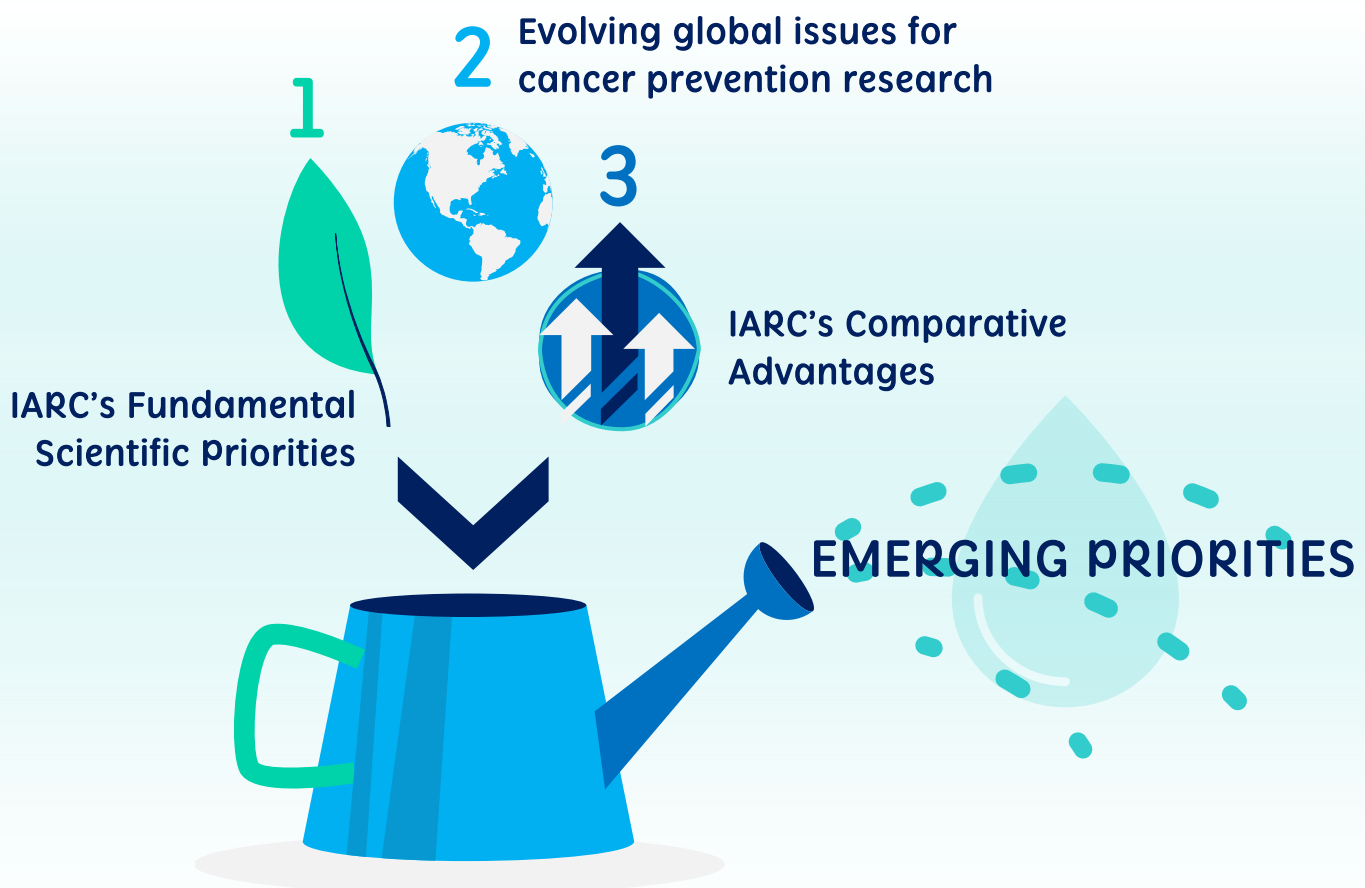
- **Who gets cancer, where and when?**
- **Why do people get cancer?**
- **How to prevent cancer effectively?**
- **How to mobilize the knowledge gained and strengthen global capacity in cancer science?**

In addition, three topics were identified as important and evolving global issues for cancer prevention research and labelled as IARC's emerging priorities for the next five years:

- ◆ **Evolving cancer risk factors and populations in transition,**
- ◆ **Implementation research, and**
- ◆ **Economic and societal impacts of cancer.**

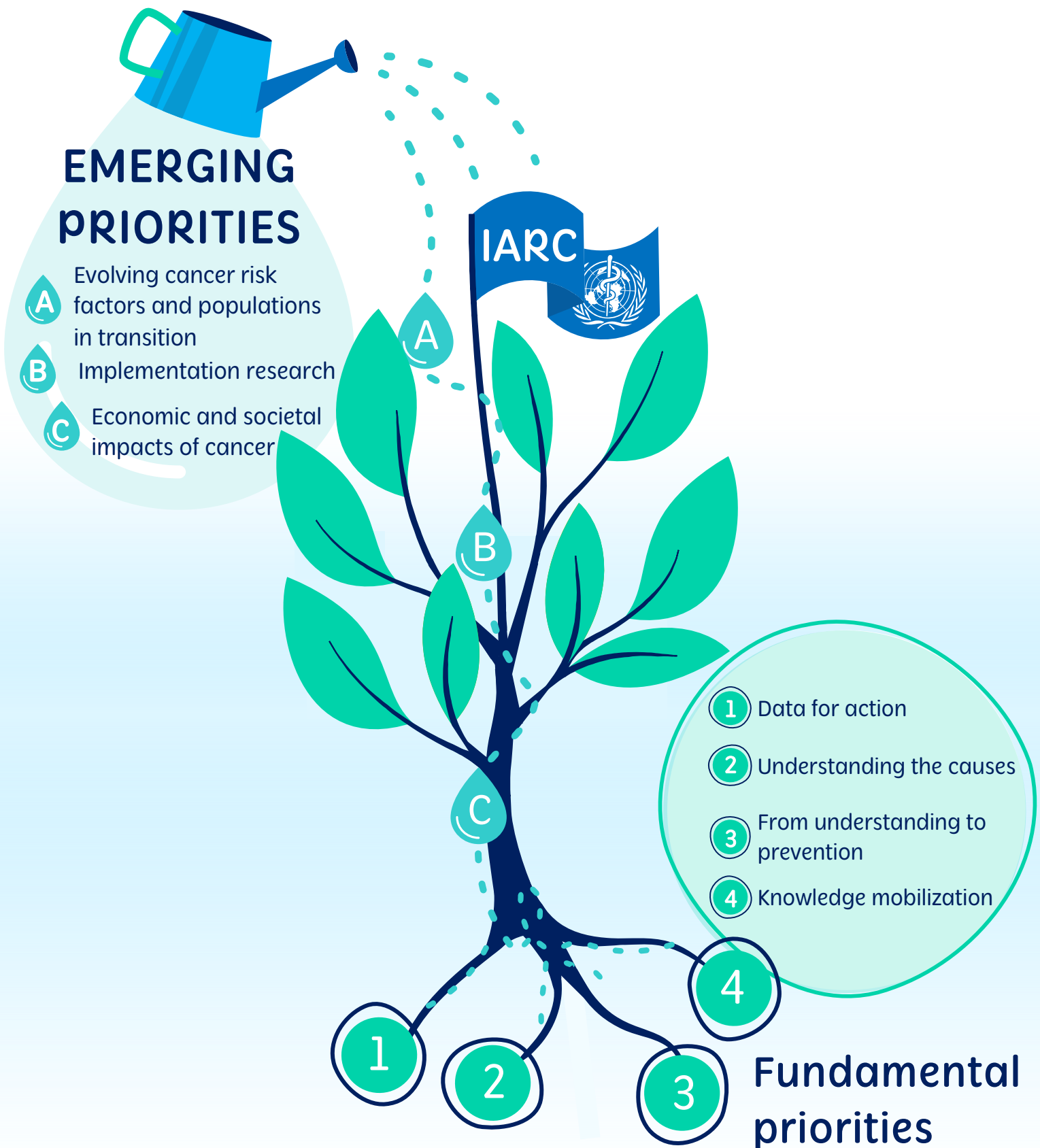
The relevance of these topics was established considering that they:

- 1** correspond best to and are relevant across IARC's fundamental scientific priorities,
- 2** allow IARC to capitalize on its comparative advantages, and
- 3** have major potential for advancing cancer prevention research and for affecting the global cancer burden over the next years.



The stakeholder consultations held in early 2020 underlined and corroborated the increasing importance of these issues for advancing cancer prevention research.

Fundamental and emerging priorities are clearly **interlinked**:



FUNDAMENTAL PRIORITIES

1. Data for action

Who gets cancer, where and when?

Describing the cancer burden by person, place, and time is essential in understanding the causes of cancer, in documenting the impact of preventive interventions, and in providing a means to channel knowledge synthesis, transfer, and mobilization towards the most relevant actors and beneficiaries.

In-depth assessments of the geographical and temporal variations in incidence and survival, the proportion of the cancer burden attributable to risk factors, and the long-term impact of preventive interventions at the population level will provide information about the public health and economic benefits of cancer prevention worldwide.



2. Understanding the causes

Why do people get cancer?

Understanding known and identifying important yet unknown causes of cancer, their respective pathways, and causal links between exposure to environmental, lifestyle, nutrition, genetic, infectious, and other risk factors and cancer is essential for enhancing the evidence base for cancer prevention and for developing effective interventions.

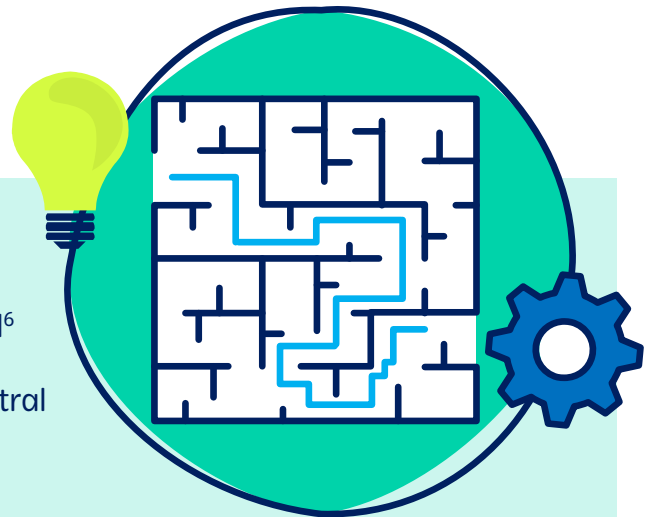
Biological determinants of cancer will be identified by applying state-of-the-art -omics profiling techniques, including metabolomics, proteomics, epigenomics, and next-generation sequencing to large-scale, population-based epidemiological cohorts.

3. From understanding to prevention

How to prevent cancer effectively?

Transforming the knowledge obtained during etiological⁶ cancer research into actionable information and an evidence base for cancer prevention interventions is central to having a public health impact, for example through vaccination.

The enhanced understanding of the causal pathways of cancer development will support the design of preventive interventions targeting cancer in early stages, for example through cancer screening. A thorough understanding of causes also facilitates evaluating how effectively relevant health-care interventions are implemented.



4. Knowledge mobilization

How to mobilize the knowledge gained ...

To advance the global understanding of cancer, pertinent research findings and scientific knowledge must be made available to the international cancer control and public health community in adequate formats, including through systematic evaluations and synthesis, and through well-established channels.

The timely dissemination of scientific evidence about cancer occurrence, causes, and effective interventions will support informed decision-making by cancer experts, national authorities, and policy-makers on relevant health-care interventions.

... and strengthen global capacity in cancer science?

The generation and application of scientific evidence and knowledge requires skilled researchers and health professionals. Adequate national capacities must be available to understand the evidence, to interpret it with respect to national settings, and to design and implement relevant interventions. Insufficient research infrastructure and qualified human resources remain a particular challenge in many countries, particularly in resource-limited settings. A new generation of cancer researchers and health professionals will be trained across the whole spectrum of cancer research disciplines, including through mentored training, which integrates research trainees into collaborative research projects and exposes them to field studies as well as to laboratory work. The use of e-learning tools and other remote means of training will be increased significantly over the next years.

6. Assigning or seeking to assign a cause.

EMERGING PRIORITIES

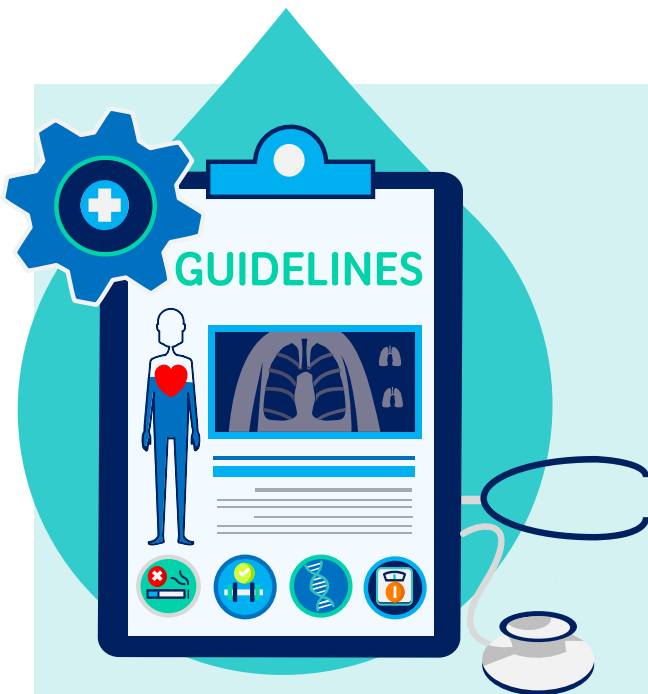
A. Evolving cancer risk factors and populations in transition



The ongoing epidemiological transitions⁷, which have, for example, laid the path for an increasing predominance of NCDs, a double burden of both communicable diseases⁸ and NCDs in many LMICs, and a resurgence of selected infectious diseases, are affecting the global cancer burden. The impact of such transitions on the causes and progression of cancer needs to be better understood, described, and investigated with regard to future impact and potential preventive interventions, especially in LMICs.

Concurrently, an environmental risk transition⁹ – linked to urbanization and globalization – affects cancer risks by the evolution of environmental and lifestyle factors such as changing diets, increasing levels of obesity, decreasing levels of physical activity, new occupational and lifestyle hazards, exposure to industrial pollutants, and changes in environmental pollutants in air, food, and water. IARC's pertinent competences are its descriptive epidemiological work, in particular the study of cancer incidence attributable to relevant risk factors; its etiological research with population-based and experimental studies; and its multidisciplinary, which facilitates studies into multidimensional exposures to risk factors and their interdependency.

B. Implementation research



Implementation research for cancer prevention is the scientific study of the processes, tools, and methods used to implement cancer prevention interventions as well as the relevant contextual factors. A major purpose is to support and guide the successful application of interventions that have been demonstrated to be effective. The successful adaptation and scaling up of such interventions depend on the local context and health system capacities, on the availability of adequate human, financial, and infrastructural resources, and on the availability of relevant and high-quality population-based data.

Relevant factors and health systems conditions, their interdependence, and how they affect interventions must be better understood.

IARC will build upon the relevant experience it has accumulated so far in evaluating population-based early diagnosis and screening programmes, and in conducting international multicentre studies and leading collaborative research networks. This work is expected to facilitate IARC's gradually increasing engagement in studying the implementation of evidence-based cancer prevention interventions in a variety of settings and involving various groups of populations, with a focus on LMICs.

7. Omran AR (2005) [1971]. The epidemiologic transition: a theory of the epidemiology of population change. *Milbank Q.* 83(4):731–57.

8. Mercer AJ (2018). Updating the epidemiological transition model. *Epidemiol Infect.* 146(6): 680–87.

9. Smith KR, Ezzati M (2005). How environmental health risks change with development: the epidemiologic and environmental risk transition revisited. *Annu Rev Environ Resour.* 30:291–333. [Note: Here, the term "environmental risk transition" includes cancer-relevant global transitions related to climate change, for example changes in the distribution of infectious risk factors.]

C. Economic and societal impacts of cancer

Economics of cancer

Countries at all income levels face significant challenges in responding to the growing burden of cancer, and inequities in cancer outcomes are widespread between and within countries, leading to avoidable and premature deaths and also threatening health budgets and economies and causing financial catastrophe and impoverishment for individuals and families.

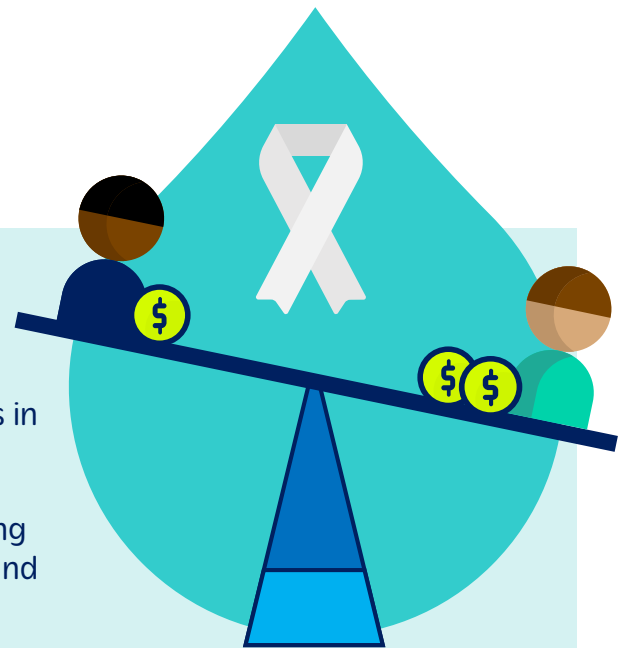
IARC has conducted research related to the economics of cancer since 2014, including the systematic description of the economic burden of cancer and the generation of evidence and tools to inform national policy-making and resource allocation related to cancer prevention.

Cancer inequalities

The cancer burden is not equally distributed across countries, within countries, and between different groups within societies. The structural determinants of health are the social and economic conditions in which people are born, live, work, and age.

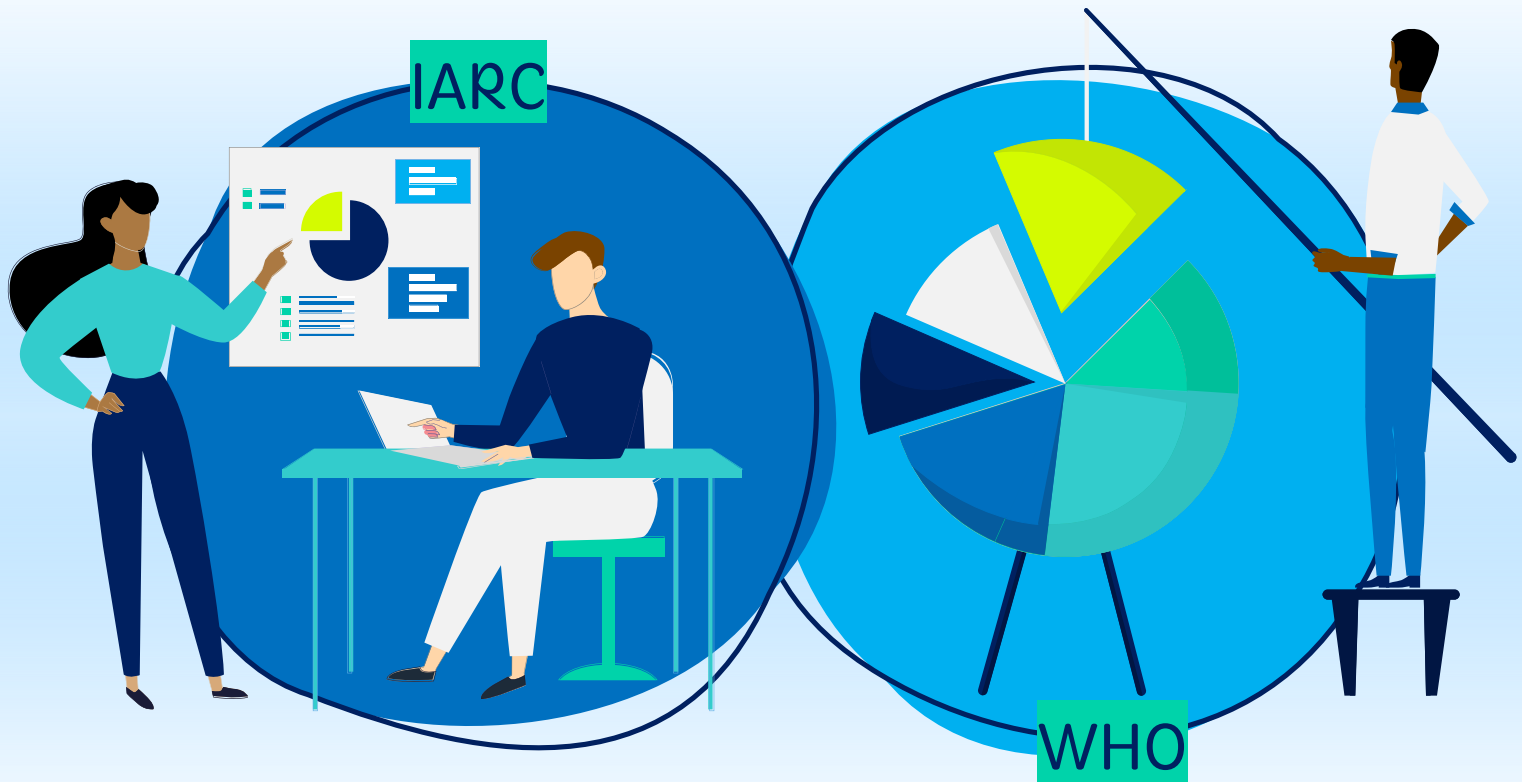
These produce well-documented social gradients in the incidence, survival, and mortality of many cancers. Inequalities in cancer and cancer risk factors disproportionately affect disadvantaged individuals and social groups.

IARC's ability to catalyse research partnerships to study phenomena that need to be understood at the local and global levels makes it well suited to undertake research in relation to cancer inequalities. Furthermore, IARC's experience and capacity in data collection, comparative assessment of international studies, and synthesis of scientific evidence will facilitate its gradually enhancing engagement in this area. Finally, IARC will be able to rely on its experience in conducting studies in different resource settings using human development indicators to examine specific cancer disparities.



3

Cooperation with the World Health Organization (WHO)



IARC is the specialized cancer agency of WHO. The relationship between the two organizations is marked by the complementarity of their mandates and by the close coordination of their respective cancer prevention activities.

The collaboration between WHO and IARC ranges from specific joint projects to supporting WHO's leadership in the implementation of the NCDs agenda. IARC will further strengthen this relationship and seek to establish stronger linkages between IARC's research in cancer prevention and WHO's normative work. More specifically, the establishment of a **formal engagement structure** between IARC, WHO headquarters, and WHO regional offices is envisioned. This new engagement framework will involve:

- a high-level oversight committee (comprising relevant senior leaders of WHO and IARC) that advises on the implementation of a joint WHO/IARC operational plan on cancer prevention, and
- an implementation committee/working group (comprising pertinent staff at operational level) that coordinates the implementation of this plan.

WHO Global Strategy to Accelerate the Elimination of Cervical Cancer

For example, IARC contributes to the implementation of the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem through: the re-evaluation of the effectiveness of cervical cancer screening; the monitoring and evaluation of cervical cancer elimination in sub-Saharan Africa; the evaluation of human papillomavirus (HPV) vaccination interventions in different countries; and the evaluation of the effectiveness of programmes for cervical cancer screening and treatment of precancerous lesions.

Over the next five years, IARC will evaluate the efficacy and effectiveness of, as well as model the impact of, HPV vaccination programmes (including, for example, reduced dosing schedules) in different implementation scenarios. The evidence generated will support health authorities in implementing mass HPV vaccination programmes.

Scientific evidence generated by IARC on cancer occurrence, causes, and effective interventions is integral to WHO's numerous cancer-related activities. Particular areas of cooperation between IARC and WHO are related to: cancer surveillance and monitoring; evaluation of possible environmental carcinogens; childhood cancer (registration and causes, economic impact); environmental and nutritional risk factors for cancer; cancer burden attributable to infection with hepatitis B virus (HBV) and hepatitis C virus (HCV); evaluating the implementation of evidence-based strategies and interventions for cancer prevention; economic consequences of cancer; cancer inequalities; and the World Code Against Cancer.

IARC will enhance the interaction with WHO in the above-mentioned areas, increase its engagement, and intensify the cooperation with all relevant WHO divisions and departments, including through the joint planning and implementation of specific activities, where this is feasible and meaningful.

IARC's participation in the UN Interagency Task Force (UNIATF) on the Prevention and Control of NCDs is a core element of the IARC mission. In this cooperative framework, IARC will contribute tools and expertise in cancer registration, nutritional surveillance, and early detection and screening to support WHO Member States in addressing the NCD Global Monitoring Framework.

4

Implementing the Medium-Term Strategy 2021–2025

STRATEGIC LEADERSHIP

IARC will provide sustainable enabling conditions for the implementation of this MTS, including a strong common vision and mission that is expected to foster a clear and well-defined IARC identity among its personnel and its Participating States.

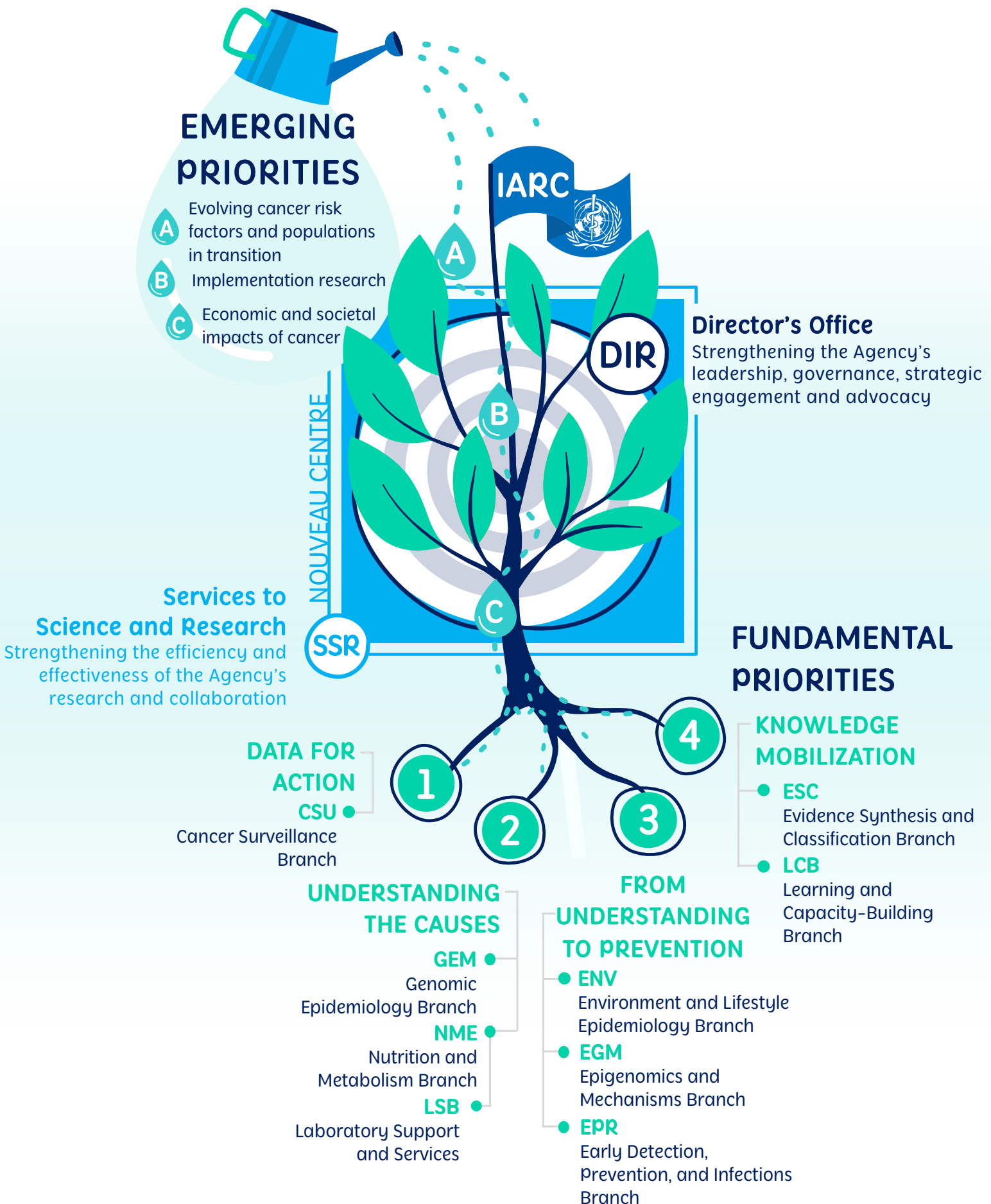
IARC remains ready to adapt to change, to further prioritize its activities, and to tackle upcoming challenges. In addition, IARC will strengthen its capacity to work in a politicized health environment while maintaining its neutral and independent position, including by forging strategic relationships with similarly independent and internationally operating partners.

IARC will intensify its interaction with national health policy-makers and experts in Participating States, in close consultation with WHO country offices, in order to identify interest in particular cancer prevention research priorities. In addition, IARC will strengthen its engagement with multinational and regional entities that play an increasingly important role in cancer control and prevention, such as the European Commission.



IARC will seek to remain fit for purpose and ensure that its organizational structure is sufficiently agile to respond to evolving challenges. IARC's organizational structure will reflect its fundamental scientific priorities, promote collaboration across scientific disciplines, and facilitate communication about IARC's contribution to tackling the global cancer burden.

IARC organizational structure



DATA FOR ACTION

In keeping with its vision of a world where fewer people develop cancer, IARC collates, analyses, evaluates, and disseminates cancer data for the benefit of the wider cancer community as a means of informing global cancer control and research.

Increasingly, the evidence provided to national health authorities, relevant international organizations, and WHO will include data on the public health and economic benefits of integrating specific preventive interventions into national cancer control plans.

IARC will disseminate flagship databases and publications such as GLOBOCAN¹⁰ and *Cancer Incidence in Five Continents (CI5)*, via the Global Cancer Observatory (GCO) in a timely manner. The cancer surveillance data collected by cancer registries will remain the basis for the national indicators, which will facilitate cancer planning and prioritization globally and help individual countries in determining changes in the scale and profile of cancer, the role of specific risk factors, and the impact of interventions.

CI5 will remain the reference source of data on the international incidence of cancer, based on IARC's direct collaboration with population-based cancer registries (PBCRs) worldwide, as the secretariat for the International Association of Cancer Registries (IACR). IARC will continue its support to PBCRs, especially in LMICs, focusing on improving their coverage, quality, and capacity.

The Global Initiative for Cancer Registry Development (GICR)¹¹ will be completed. Six GICR Regional Hubs and associated IARC-GICR Collaborating Centres will provide tailored assistance to a set of targeted LMICs, considering needs and national preparedness.

As cancer profiles in LMICs increasingly resemble those in high-income countries, IARC enables reporting on relevant changes in the magnitude and distribution of relevant global indicators. In addition, IARC will develop a systematic framework for quantifying the proportion of cancers attributable to major lifestyle and environmental risk factors – including tobacco use, alcohol consumption, infections, obesity, physical inactivity, unhealthy diet, and ultraviolet (UV) radiation – alongside the beneficial effects of breastfeeding on the risk of breast cancer and ovarian cancer.

Capturing and benchmarking cancer survival internationally, stratified where possible by stage at diagnosis, is of mounting importance. The growing number of cancer survivors worldwide is accompanied by increasing disease sequelae associated with diagnosis and treatment.



Disability-adjusted life years (DALYs) will be at the forefront in IARC's work on quantifying the quality of life of cancer patients. IARC will increasingly seek to empower registries in LMICs to estimate cancer survival statistics. To ensure the availability and comparability of cancer staging data internationally, IARC will enhance its collaboration with relevant international experts and organizations.

IARC will predict the number of future cases and deaths averted for major cancers and the **economic gains associated with interventions** that target, among others, tobacco use, alcohol consumption, obesity, and the major infectious agents. Such studies seek to enable countries to initiate policies that will lead to a reduction in the future cancer burden.

10. The GLOBOCAN database provides national estimates of the incidence, mortality, and prevalence in 185 countries or territories for 36 cancer types by sex and age group.

11. The GICR is a partnership to strengthen the quality of cancer data in LMICs and the use of the data for cancer control planning.

In addition, IARC will expand its activities in **health economics and cancer**, by measuring the economic burden and socioeconomic inequalities in cancer integrating economic data into the GCO, evaluating the impact, cost, and feasibility of country-specific priority interventions, and developing tools to estimate resources required to initiate, implement, and sustain cancer registration activities. Using the WHO/IARC costing tool, which is under development, a series of scenario-based research studies will seek to quantify the public health and economic impacts of implementing effective preventive measures in different settings.

Causal pathways from a social disadvantage to a **cancer/health disadvantage** are complex and not yet fully understood. To address that knowledge gap, IARC will conduct research on social inequalities and cancer in collaboration with international research and public health institutions. IARC will enhance support to countries in collecting data that will enable a better description and understanding of cancer disparities across countries. The provision of high-quality cancer data from PBCRs worldwide is critical, and continued efforts to foster international standards of registry data collection and reporting in collaboration with the IACR are key in this respect.

To understand the drivers of inequalities, IARC will study social determinants, their interaction with characteristics of health systems and other factors, and their potential effects on individuals' access to preventive and screening interventions. In addition, local and context-specific barriers to screening and



CHILDHOOD CANCER

International Incidence of Childhood Cancer (IICC)¹² is a flagship project of IARC that describes the incidence of cancer among children and adolescents, in collaboration with cancer registries worldwide. IARC has contributed to the WHO Global Initiative for Childhood Cancer¹³ since its launch in September 2018, by building capacity in cancer registries to collect and disseminate reliable data on childhood cancer worldwide sustainably. As of 2020, and in partnership with St. Jude Children's Research Hospital, IARC is providing assistance to national childhood cancer registration activities in targeted countries, developing tailored training programmes, and bringing International consensus to registry practices. IARC periodically reviews the classification of cancers in childhood and in young adults; the first edition of the *WHO Classification of Paediatric Tumours* will be published in 2021.

In the next years, IARC will collaborate with the International Initiative for Pediatrics and Nutrition at Columbia University Irving Medical Center to investigate the role of diet, obesity, and metabolic health in childhood cancer, with a focus on LMICs.

Furthermore, IARC will investigate potential links between power distribution lines – with extremely low-frequency magnetic fields – and an increased risk of childhood leukemia, and between parental exposures to pesticides – through agricultural work – and an increased risk of childhood cancer.

In addition, IARC will enhance the understanding of molecular causes of cancers in children and adolescents driven by risk factors specific for in utero and early life, such as maternal and paternal age, adiposity during pregnancy, smoking, and alcohol consumption. IARC will also examine risk factors for second cancers and produce guidelines for registries on reporting second primary tumours in young patients.

IARC will also assess the economic impact of childhood cancer through an evaluation of the respective familial financial hardships in LMICs.

12. International Incidence of Childhood Cancer (IICC) is a collaborative project of IARC and the International Association of Cancer Registries (IACR).
 13. WHO Global Initiative for Childhood Cancer. <https://www.who.int/cancer/childhood-cancer/en/>

early diagnosis and their effects on cancer mortality (survival) will be identified. Subsequent research results are expected to support policy-makers and health authorities in identifying and delivering appropriate and effective interventions.

UNDERSTANDING THE CAUSES

Understanding the causes of cancer is a fundamental prerequisite for identifying suitable prevention measures. More specifically, understanding the mechanisms and causal pathways of cancer development is critical for the conception and implementation of effective interventions, and to realize a world where fewer people develop cancer. Likewise, it is important to identify and evaluate key risk factors, in particular modifiable ones, and enhance the understanding of how these affect the cancer burden.

IARC will emphasize etiological cancer research in connection with risk factors and other determinants that are predominant during the respective transitions, including obesity, sedentary lifestyle, unhealthy dietary habits, alcohol consumption, tobacco use, exposure to environmental pollutants (or chemicals, in general), occupational hazards, and radiation-related cancer risks (from ionizing, optical, and non-ionizing radiation), as well as climate change-driven influences on cancer risks.

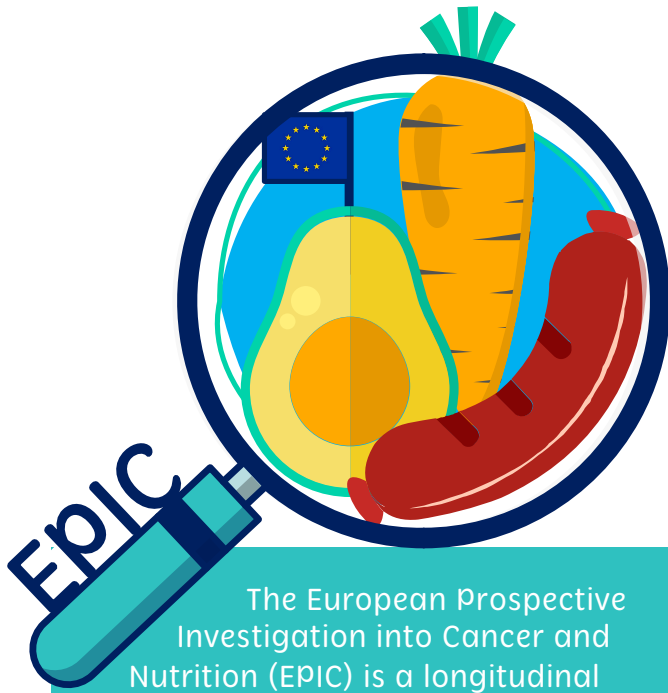
Research into the role of **lifestyle, nutrition, and metabolism** in cancer development and prevention will remain a major focus, aiming to inform the design of appropriate prevention measures. IARC will go beyond the traditional domains of nutrition in cancer research and exploit methodological advances in molecular profiling techniques, integrating -omics data within population-based cohorts and intervention studies. Molecular and genomic epidemiology studies are important for identifying biomarkers of cancer development and

highlighting potential causal pathways. These studies will be accompanied by experimental studies that help to confirm causality and deepen mechanistic understanding.

IARC will study the role of obesity and metabolic dysfunction in cancer development, identify biomarkers of diet and nutrition and their application to cancer etiology, and investigate multimorbidity and biological pathways common to cancer, diabetes, and cardiovascular diseases, by applying its laboratory and biostatistical expertise to large-scale, population-based cohorts, such as the EPIC cohort, as well as to cohorts and studies in South Africa, Morocco, and Latin America.

For example, IARC will perform metabolomic and proteomic profiling on pre-diagnostic, biobanked blood samples from thousands of cancer cases and healthy controls to identify metabolic signatures of cancer development. This research will uncover novel pathways of the cancer process and will improve the understanding of the mechanisms linking obesity, diet, and lifestyle with specific cancer types. Relevant studies will focus on cancer sites with clear links to nutrition and metabolic abnormalities, i.e. primarily colorectal, pancreatic, and liver cancers, as well as on hormone-related cancers such as breast, thyroid, and endometrial cancers.

IARC will support the accurate evaluation of relevant lifestyle factors and environmental exposures, and provide biobanking and pathology expertise. IARC will facilitate the work of international consortia to assemble the necessary sample sizes for these types of informative genetic and genomic studies and explore the usability of data sets available in regional databases.



The European Prospective Investigation into Cancer and Nutrition (EPIC) is a longitudinal cohort study with about 521 000 participants recruited across 10 European countries from 1992 to 1999.

EPIC was established to investigate the role of diet, lifestyle, and genetics in the etiology of cancer. The number of incident cancer cases has grown considerably, and the cohort now has the largest number of incident cancers with pre-diagnostic biospecimens and questionnaire data in the world. More than 62 000 EPIC participants have been diagnosed with cancer.

EPIC data and biospecimens are a key resource for IARC and numerous collaborators worldwide and are increasingly accessed for studies on the causes of cancer and other diseases. Major initiatives around proteomics, metabolomics, genomics, and tumour sequencing will be conducted in the next five years, and a new round of follow-up will be conducted in 2021.

obesity-related molecular changes will be investigated. These studies will consider links to specific cancer types, such as cancer of the breast, colorectum, prostate, and kidney, or to LMICs, such as oesophageal and oral cancers or non-Hodgkin lymphoma. IARC will characterize the biological properties of HPV and polyomaviruses, some of which are known to cause cancers in humans. These functional studies will be complemented by epidemiological studies to corroborate and further evaluate their contribution to causing human cancers. Furthermore, IARC will seek to identify new putative oncogenic viruses, with a focus on the polyomavirus family, some of which may have oncogenic properties relevant for humans.

IARC will continue to conduct **genetic studies** to further elucidate the causes of cancer in diverse populations, including relevant mechanisms of genetic susceptibility, the role of germline and somatic variation in cancer outcome, and effects of specific environmental exposures. Such studies will focus on populations that are at high risk of developing a specific type of cancer, and will involve fieldwork, including the collection of tumour specimens with linked blood and other body fluid samples and epidemiological and clinical data in collaboration with local partners.

IARC will expand on its earlier genetic susceptibility studies for lung cancer, head and neck cancers, renal cancer, and lymphomas and seek to identify additional susceptibility variants for these cancer types and extend these studies to cover underrepresented populations.

Genomic "mutational signature"-type studies of tumour tissue will be conducted to identify driver genes in distinct populations and cancer genes associated with particular clinical outcomes. IARC will lead some of the largest genomic sequencing studies globally; in particular, the whole-genome sequencing of 5000 cancers from diverse populations will continue and, where possible, be expanded.

IARC will investigate genetic and epigenetic patterns and interrelated molecular pathways deregulated by exposure to selected risk factors as well as their contribution to underlying mechanisms of carcinogenesis.

IARC will identify molecular changes associated with exposure to selected environmental or lifestyle factors, such as mycotoxins, heavy metals, dietary contaminants, and consumption of very hot food and beverages. In addition, exposure to suspected environmental carcinogens, such as endocrine disruptors and pesticides, as well as

IARC will validate a model of virus-driven carcinogenesis, in which the virus in cooperation with selected environmental factors, such as UV radiation, triggers the first event of cellular transformation and becomes dispensable afterwards. Subsequent epidemiological studies are expected to corroborate this model and inform the development of relevant prevention interventions, such as vaccination of high-risk populations.

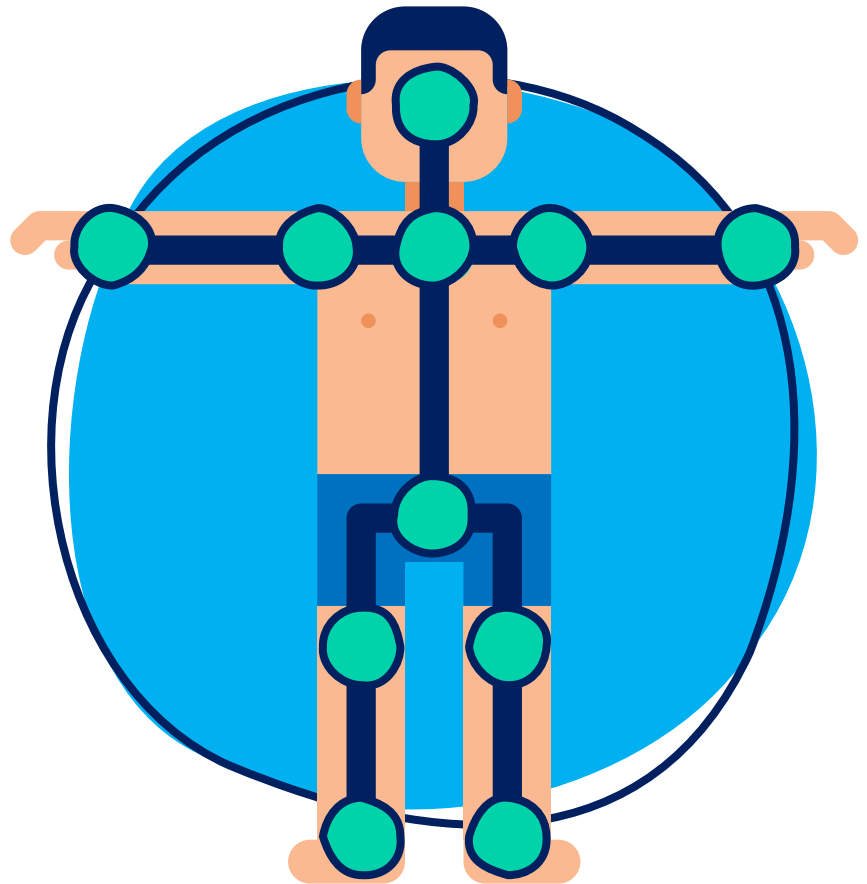
IARC will expand its research on cancer risk factors driven by the anthropogenic and natural environment. Notably, IARC will continue to study the ill-understood belt of high incidence of oesophageal cancer along the African Rift Valley, where initial studies suggest a major role of environmental pollution (from the water sources and indoor air pollutants) and certain lifestyle habits (special home brews, consumption of very hot beverages, khat use). IARC will engage in fieldwork studies involving environmental and biological sampling, to establish whether there is a link between these risk factors and this highly fatal cancer.

In addition, IARC will investigate the impact of heavy **environmental contamination**, particularly in LMICs, which often affects the most disadvantaged populations, with a focus on residential exposures to uranium and other chemicals in mine tailing areas, household air pollution from use of wood and solid fuels, contamination from electronic waste dumping, and radioactive contaminations. Alongside UNEP, IARC will study the effect of environmental oil contamination on cancer.

IARC will coordinate research on exposures of agricultural workers (mainly to pesticides) in relation to haematological malignancies and cancers of the breast, prostate, and testes, and on the interplay of known workplace lung carcinogens, seeking to disentangle the effects of different chemicals and smoking. IARC will investigate exposure levels and pathways, workers' protection measures, and age of exposure in emerging economies, where the population's features often differ from the reference population in high-income countries, on which similar studies were conducted and which form the basis of current protection guidelines. Relevant populations will include chrysotile workers, coal miners, drivers (exposure to traffic exhaust), and workers in the oil industry.

IARC will examine protracted **exposures to low-dose radiation** in environmental settings linked to the disposal of radioactive waste, nuclear testing, and nuclear accidents. Furthermore, IARC will study occupational radiation exposure of workers in the nuclear industry and in relation to medical radiation. Results from occupational exposure research will inform the relevant prevention interventions through the involvement of the respective authorities in these studies, such as workers' protection and radiation protection authorities.

IARC will also continue to perform research on the impact of exposures to wireless communications, seeking to establish whether heavy mobile phone use can cause brain tumours.



FROM UNDERSTANDING TO IMPLEMENTATION

Transforming knowledge about cancer causes and risk factors into evidence-based preventive interventions that can inform policies to save lives is central to IARC's mission.

IARC will intensify the development and evaluation of tools and interventions that have the potential to reduce the global cancer burden. The respective interventions are broadly categorized here into those relevant to:

- 1 primary prevention of established **modifiable risk factors** (e.g. preventing HPV infection through vaccination);
- 2 secondary prevention by **screening of asymptomatic at-risk populations** for selected cancer types (e.g. cervical, breast, and colorectal cancer); and
- 3 **early diagnosis** of common cancer types in symptomatic individuals, with a view to shifting the stage distribution of tumours detected towards a lower stage, and improving survival and quality of life after treatment.

IARC will increasingly generate evidence of the effectiveness of cancer prevention and early detection strategies delivered as integrated services through routine health care, particularly in LMICs. This research will focus on the translation of interventions with proven efficacy in controlled settings to real-world settings, considering the local context, health system challenges, and sustainability.

IARC's research on **primary prevention** will continue to focus on **infection-attributable cancers**, given their amenity to prevention (vaccines, diagnostic tools, and therapies) and their disproportionate burden in LMICs (up to 25% of all cancers in large parts of Asia and Africa). Specifically, IARC will continue its engagement in evaluating the efficacy and effectiveness of, as well as modelling the impact of, HPV vaccination programmes in different implementation scenarios. The evidence generated will support health authorities in implementing mass vaccination programmes (e.g. reduced dosing schedules), and thereby inform the WHO Cervical Cancer Elimination Initiative.

Furthermore, IARC will evaluate the **impact of preventive interventions** against HBV (vaccination) and HCV (diagnosis and treatment) on liver cancer burden, with a focus on high-burden countries in Africa and Asia, thereby contributing to the WHO target for the global elimination of viral hepatitis as a public health threat. In anticipation of results from ongoing IARC trials to establish the effectiveness of screening and treatment for *Helicobacter pylori* on the gastric cancer burden, IARC will study the implementation of *H. pylori* prevention programmes in LMICs. Regarding interventions that target other modifiable cancer risk factors, IARC will investigate the effectiveness of promoting evidence-based lifestyle recommendations for cancer prevention during screening programmes, in particular the effect on the quality of life and biological pathways linked to cancer development (e.g. physical activity, anthropometrics, gut microbiota, nutritional biomarkers).

In the domain of **secondary prevention**, IARC will evaluate innovative technologies (e.g. machine learning algorithms, application of mHealth in patient navigation, use of spectroscopy for detection of HPV) and identify novel biomarkers that support risk-stratified screening (e.g. for lung cancer, gastric cancer, bladder cancer, or anal cancer). Furthermore, IARC will evaluate means to address health system barriers to equitable and high-quality implementation of screening for cervical, breast, and colorectal cancer, in collaboration with national screening experts, in the framework of Cancer Screening in Five Continents (CanScreen5).

This collaborative work will generate evidence on **effectiveness of cancer screening** from real programmatic settings. In addition, this work will identify quality gaps and help reduce access barriers due to economic or social factors.

Aligned with the WHO recommendation to prioritize **clinical early diagnosis of common cancers** in symptomatic populations, IARC will strengthen research to design and evaluate multilevel strategies aimed at improving health-seeking behaviour of people with symptoms suspicious of cancer. IARC will evaluate the impact of such interventions on shifting the stage distribution of cancers detected towards a lower stage, reducing mortality, and improving survival and patients' quality of life, in different resource settings. Barriers to timely, accurate diagnosis and access to treatment will continue to be studied with regard to breast cancer in sub-Saharan African countries.

IARC will identify and validate novel biomarkers relevant for **early detection of cancer and/or cancer risk stratification**; biomarkers include virological, genetic, transcriptomic, and epigenetic changes, both in liquid biopsies (including tumour-derived nucleic acids from blood and other body fluids) and in other surrogate tissues, derived from IARC studies. The predictive value of biomarkers linked to obesity will be assessed as well. Furthermore, IARC will investigate whether obesity-related epigenetic and other molecular changes associated with cancer risk (breast and colorectal cancer) are reversible after weight loss or treatment targeting metabolic imbalance conditions.

Pertinent evidence generated through the above-mentioned research will inform the development and evaluation of region-specific Codes Against Cancer (**evidence-based cancer prevention recommendations** to the general public and health policy-makers on how to effectively reduce the risk of cancer), with a focus on updating the European Code Against Cancer and developing the first Code Against Cancer for Latin America and the Caribbean. Strong collaboration with WHO is essential in this area, with the acknowledgement of WHO's responsibility regarding the subsequent integration of pertinent interventions into national health systems and sustainable delivery at the national level. This close collaboration will ensure that the evidence generated through research led by IARC will continue to be translated into policies that can affect every individual in the world.

KNOWLEDGE MOBILIZATION

Scientific evidence and information generated through IARC's work, including about cancer occurrence, classification, causes, hazards, effective interventions, and potential preventive means, must be made available in a timely manner to relevant experts, authorities, and decision-makers. In addition, national capacities to implement the evidence-based intervention must be strengthened, to ensure that advanced global knowledge about cancer is translated into a public health impact.

Sharing knowledge and scientific evidence

IARC will focus on expanding the knowledge base about cancer science within the international and national cancer community by providing public goods based on impartiality, scientific excellence, and high public health relevance. IARC's public goods approach to disseminating and publishing its research findings will remain a unique and sustainable means to increase equity of knowledge in cancer science among the world's countries.

During the next five years, the work on the 5th edition of the *WHO Classification of Tumours* series, which commenced in 2018, will be completed (in 2023) by covering the remaining 9 out of 14 topics (volumes): Central Nervous System Tumours; Paediatric Tumours; Urinary and Male Genital

Tumours; Head and Neck Tumours; Endocrine and Neuroendocrine Tumours; Haematolymphoid Tumours; Skin Tumours; Eye and Orbit Tumours; and Hereditary Tumours. With the completion of the 5th edition of the series, work on the 6th edition will commence.

In addition, IARC will coordinate the generation of an associated series of publications, the *WHO Cytopathology Reporting System*, with volumes planned for lung, lymph node, pancreatobiliary, and soft tissue cytopathology over the next three years. This standardized terminology system will illustrate the key diagnostic cytopathological features of each particular lesion or neoplasm, discuss ancillary studies for diagnostic and prognostic evaluation, and touch on the

implications of the diagnosis for patient care and management, all of which will improve the quality of diagnosis and reporting of cytopathology.

The *WHO Classification of Tumours* (“WHO Blue Books”) series provides the international standards for cancer diagnosis, which underpin the diagnosis of all cancers, worldwide. The series comprises a unique synthesis of histopathological diagnosis with clinical features, epidemiology, radiology, cytology, and digital and molecular pathology. The classification of tumours underpins individual patient treatment, as well as research into all aspects of cancer causation, prevention, therapy, and education.

IARC Monographs

The *IARC Monographs* are an authoritative and trusted source of scientific information on a wide range of carcinogens, including chemicals, complex mixtures, occupational exposures, physical agents, biological agents, and other factors. They serve as guidance and reference for the development of cancer control measures, including actions to prevent avoidable exposures to or reduce exposures to known or suspected carcinogens. Their plain-language summaries inform interested individuals and policy-makers. Since 1971, more than 1000 environmental agents have been evaluated, of which more than 500 have been identified as carcinogenic, probably carcinogenic, or possibly carcinogenic to humans. *IARC Monographs* were influential in the setting of policies on tobacco control and played a key role in decisions to ban sunbeds in numerous countries.

IARC will increasingly partner with relevant regional organizations to further advance high-quality diagnostic practice for cancer pathology and research. The International Collaboration for Cancer Classification and Research (IC³R) initiative will enhance the collection and evaluation of diagnostic information for translation into clinical practice, harmonize practice worldwide by setting standards for analytical procedures and pathological diagnoses, including through computational pathology, and encourage external quality assurance.

IARC will continue to provide definitive unbiased assessments of carcinogenic hazards in the form of the *IARC Monographs* on the Identification of Carcinogenic Hazards to Humans. *IARC Monographs* evaluations will be conducted according to principles and procedures outlined in a recently modernized Preamble, which incorporates scientific innovations and increased rigour of systematic review methods. The results will be disseminated rapidly as published scientific summaries, followed by the timely publication of the full *Monographs*.

IARC will continue to assess the carcinogenic hazard posed by agents that are of high priority from the public health perspective.

Evaluations will focus on specific chemicals, biological and physical agents, and other environmental factors identified by leading, independent advisors as meriting a new evaluation or a re-assessment. To that end, IARC will continue to assemble independent global experts in cancer epidemiology, cancer bioassays, mechanistic evidence, and exposure characterization to examine the published and publicly available scientific evidence related to the human carcinogenicity of priority agents.

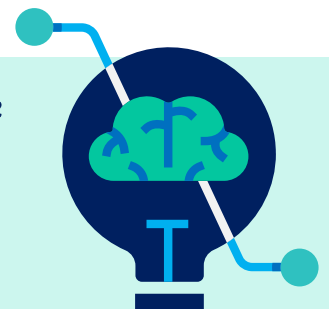
IARC will continue to assess the effectiveness of selected preventive interventions through comprehensive, systematic reviews and consensus evaluations of the relevant evidence. Results in the form of the *IARC Handbooks of Cancer Prevention* support national and international health authorities in developing relevant evidence-based interventions or policy recommendations. Interventions to be evaluated are selected based on their expected public health impact and may include, for example, the effects of chemopreventive agents; behavioural changes; screening programmes; or taxation policies.

Over the next five years, IARC will evaluate and publish a *Handbook* on oral cancer prevention, with a particular focus on populations in South Asia, where oral cancer is a major public health concern. Potential further topics for *Handbooks* on primary prevention include a re-evaluation of the preventive effects of aspirin and sunscreens, in light of new evidence on their cancer-preventive effects on colon cancer and skin cancer, respectively, and first-time evaluations of the potential preventive effects of vitamins B and D.

In addition, IARC plans to evaluate and publish *Handbooks* on screening for prostate cancer and lung cancer, both of which are among the most common cancer types worldwide; the latter will take into account new research findings and information from risk biomarkers and genetic susceptibility to identify individuals at high risk of lung cancer to be targeted for screening.

Strengthening global capacities in cancer science

Skilled and competent human resources in cancer science are one of the prerequisites to generate additional and complementary scientific knowledge and participate in global cancer research undertakings. Insufficient capacities remain a particular challenge for countries with resource-limited settings.



With this issue in mind, IARC will pursue the education and training of the new generation of cancer researchers and health professionals across the whole spectrum of cancer research disciplines. Mentored training will involve the integration of research trainees within collaborative research projects, and their exposure to field studies as well as laboratory work.

IARC will offer learning content and training events in IARC's priority areas, such as cancer surveillance, early detection, economic and societal impacts of cancer, implementation research, and cancer epidemiology, increasingly through e-learning, to support the lifelong learning of researchers and health professionals. For example, a new learning platform will provide complementary material and updates on *World Cancer Report*, such as webinars, specific learning modules, infographics, interviews, and case studies.

A partnership with the new WHO Academy¹⁴ in Lyon is expected to result in additional cutting-edge e-learning modules and training events as of 2023.

14. WHO Academy, www.who.int/about/who-academy



The WHO Academy seeks to accelerate the development and adoption of evidence-based policy, practice, and research for better health, using the latest technologies in digital and remote learning and capacity-building. As an example of the envisioned cooperation, the Comprehensive Learning Programme on Screening, Diagnosis, and Management of Cervical Precancer, developed by a WHO-wide consortium and led by IARC, will be developed and launched by the WHO Academy during 2021–2022.

Gradually, IARC will enhance the focus of its **capacity-building** activities to beneficiaries **in LMICs**. This capacity-building includes awarding up to 10 two-year IARC Postdoctoral Fellowships per year to early career scientists from relevant countries, provided that sufficient extrabudgetary resources can be mobilized.

Furthermore, IARC will offer hands-on training in the field to strengthen national capacities in LMICs for delivering prevention and early detection interventions, as well as for monitoring the impact of HPV vaccination protocols. All these activities will be supported through the generation and dissemination of appropriate learning content, involving increasingly more use of electronic and virtual tools.

IARC will continue to offer training, through customized workshops and online, to laboratory staff engaged in clinical cancer research and population studies in LMICs. This training is expected to advance the establishment of population cohorts for research purposes in LMICs, and to increase the local research capacity, resulting in an enhanced representation of LMICs' populations, including their biological samples and associated information, in cancer research studies.

IARC will pursue research collaborations involving the LMICs Biobank and Cohort Building Network (BCNet), with an emphasis on web-based components to allow entirely virtual collaborations. Moreover, BCNet members will increasingly use regional groups for peer-to-peer staff exchanges and training, thereby strengthening BCNet's regional impact on capacity-building.



LMICs Biobank and Cohort Building Network (BCNet)

IARC created BCNet in 2013 as an opportunity for LMICs to cooperate effectively, and to jointly mobilize knowledge and address challenges in research infrastructure and biobanking. The latter include the collection of biological samples under standardized protocols, and the development of appropriate governance frameworks for biobanking, addressing operational, ethical, legal, and social issues.

BCNet now comprises 36 institutions from 23 countries around the world, which are supported through harmonized protocols, best practices, and standards. Beyond providing educational support and a forum for the exchange of experiences and expertise, BCNet facilitates the joint participation of LMIC-based infrastructures in international collaborative research on cancer.

ENABLING OPERATING ENVIRONMENT

Implementing the MTS in an effective and efficient manner will depend on several factors, including suitable operational conditions and prerequisites as well as scientific capacities that enable the pursuit of the strategic direction set out above.

Nouveau Centre – Open Science

The move of IARC to its new headquarters building, the Nouveau Centre – expected to occur in 2022 – will enable IARC to transition smoothly to a state-of-the-art, eco-friendly Agency, embracing and living the concept of Open Science. The smart building will provide an inspiring environment for scientific collaboration and for advancing global cancer research. Its physical structure will emphasize transparency and echo an Open Science concept.

The Nouveau Centre will host cutting-edge technologies for meeting management, digital and flexible workplaces, collaborative workspaces, cloud-based scientific data management, and a modern biobank and laboratories.

Efficiency measures through innovation and digital transformation

Emphasis will be placed on digital transformation, with a focus on transforming business processes – including administration and data management – as well as on redefining organizational processes, and capabilities for the digital world. Administrative processes and policies will be reviewed for their continued added value and streamlined as necessary.

In the Nouveau Centre, conference services and laboratory services will be provided centrally to research teams. The Nouveau Centre's proximity to the future WHO Academy may result in further synergies and opportunities to share resources.



Open Access as a cornerstone of Open Science

IARC will increasingly engage in open research data sharing, aimed at facilitating and maximizing data reuse. A new data sharing policy will facilitate sharing IARC's research data widely, while protecting the interests of IARC, its Participating States, and partners as well as the rights of individuals, including ethical and legal considerations.

IARC is developing increasingly complex data analysis tools and will share these resources as open-source code, thereby supporting capacity-building for cancer research, as well as transparency and reproducibility.

Precision research is based on the analysis of well-characterized, research-ready samples combined with data and/or on the biological validation of data-driven observations. The concept of Open Access to scientific resources will extend to IARC's biobank, i.e. its collections of biological samples under a transparent governance and accessibility framework. To ensure the sustainability of the biobank's operations, selected samples may be made available on a cost-recovery basis.

“Green” research and measures to reduce IARC’s ecological footprint

IARC will seek to reduce its ecological footprint and the environmental impact of its work. Several effective measures that are already in place will be continued, such as flexible teleworking arrangements, reductions in air travel for meetings and training events, and an increased use of e-learning tools. The new provisions include the shift to paperless offices, along with corresponding sustainable capacity enhancements of information technology infrastructure and business solutions.

Scientific data and data security

Traditionally, IARC houses data from international cancer research projects. IARC intends to enhance and facilitate the access of research communities around consortia to data and relevant analytical resources, including high-performance computing. These resources will be subject to responsible data management across the entire Agency's IT system, while ensuring compliance with applicable personal data security and data protection policies. Concurrently, IARC will foster a culture of enhanced cyber security while moving gradually to open data and cloud solutions.

IARC’s laboratory platforms and biobanking services

Laboratory platforms and biobanking services will continue to constitute a crucial part of IARC's overall support matrix for its scientific activities, in close coordination with other support services, and to ensure that laboratories meet necessary standards and enable state-of-the-art laboratory-based research work.



Furthermore, IARC's laboratory services will continue to generate global standards and best practices in laboratory activities and biobanking. For example, in collaboration with the International Organization for Standardization (ISO), IARC will disseminate relevant information to the research community about these best practices, thereby strengthening global laboratory practice. IARC's biobank, aligned with the Open Science principle, will continue to be responsible for one of the largest and most varied international collections of clinical samples in the world, with a focus on gene–environment interactions and disease-based collections.

Whenever appropriate and cost-effective, IARC will continue to undertake laboratory analysis externally by using resources available through its vast collaborative network. Internally, IARC will strengthen laboratory applications and techniques that respond to IARC-specific needs and are not accessible through collaborative partners. Thus, internal services and efforts will complement national efforts and services rather than duplicating or competing with them.

Attracting, retaining, and building talent

IARC's most important asset will remain its personnel, with high levels of expertise, knowledge, skills, and qualifications, which are matched by motivation and dedication to IARC's mandate. To realize its new mission, IARC will need to attract and retain appropriate talent and skills, both at the scientific level and at the research support and management level. IARC will identify and seek to address potential future gaps regarding human resources capacities and will continue to recruit the most suitable and best skilled talent, while ensuring geographical balance and diversity among its staff. As an international agency, IARC is fully aware of the need to ensure a well-balanced geographical representation among its scientific staff, and in the years to come will actively seek to enhance the representation of Participating States that are currently underrepresented.

Respect for equality and diversity are essential to the success of IARC's work, because these principles promote an environment of inclusiveness, where innovation and scientific creativity can thrive and where differences are recognized, respected, and valued. These important core values will be promoted, and equal treatment of all personnel will be ensured regardless of race, gender, disability, religion or belief, sexual orientation, and age.



Furthermore, IARC will expand the profile of its scientific staff and – in addition to scientific excellence – give more prominence to skills related to flexibility, teamwork, and communication, as well as integrative and holistic systems thinking. Concurrently, IARC will continue to strengthen its human resources capacities by encouraging continuous education. IARC intends to further improve the work–life balance of its personnel, for instance by providing even more flexible working arrangements including remote working, where possible.

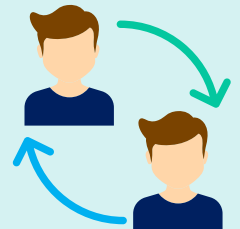
Continuing on a course initiated in early 2019, IARC staff will be increasingly empowered to participate in debates that inform scientific decision-making. This approach will be accompanied by enhancing the accountability of staff for results within their area of responsibility.

Managerial accountability, risk management, and evaluation

The allocation of resources will be strongly aligned with IARC's priorities. Likewise, IARC will report on its results achieved and the impact of its work in connection with the priorities set. This approach will strengthen IARC's accountability for delivering on its overall goal and on the underlying scientific results. IARC aims to introduce an output assessment system that is transparent, meaningful, accountable, and holistic.

Accountability mechanisms will help to ensure that transactions are conducted effectively and in keeping with the highest standards of professional and ethical conduct. IARC's risk management approach will be adapted to the evolving operational environment as needed, supported by an enhanced enterprise risk management system.

IARC's scientific units will remain subject to peer reviews by the Scientific Council on a five-year cycle. In line with advice from the IARC governing bodies, this external peer review remains the primary mechanism of evaluating activities in relation to the MTS, including informing decisions to cease certain activities or programmes and reinforce others.



5

Partnerships, Outreach, and Resource Mobilization

Currently, numerous actors are actively engaged in the fight against cancer at the community, national, and international levels, including patient organizations, nongovernmental organizations, research institutes, national cancer centres, UN agencies, private sector companies, and national health authorities.

Effective outreach and communication activities, which inform key audiences about IARC's work, its contribution to public health, and its global impact, are crucial for strengthening IARC's position within the global cancer research community and for ensuring IARC's continued relevance.

IARC will seek to further strengthen its engagement with UN agencies, building upon well-established cooperation models such as with UN Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the UN Environment Programme (UNEP), the UN Population Fund (UNFPA), and the International Atomic Energy Agency (IAEA), and will also initiate new partnerships and means of collaboration.

IARC will increasingly adapt its social media presence and content to attract the interest and address the information needs of the lay public, health authorities, and pertinent policy-makers. IARC's enhanced emphasis on its public health impact will be accompanied by corresponding messages, which will be developed in close coordination with WHO and relevant partners. Whenever feasible and meaningful, IARC will make use of partnerships to communicate relevant content broadly and effectively.

Equally important are high-quality **publications** and the **broad dissemination** of both IARC's research findings and its authoritative information among stakeholders in academia, government, and research institutes. IARC will further professionalize its publishing activities, while keeping up to date with publishing industry standards. IARC publications are a public good and will continue to be devised with specific target audiences in mind and to be promoted as living resources. The close coordination with WHO on joint technical documents and relevant accompanying messages will be maintained and intensified as needed.

IARC will intensify its collaboration with other UN agencies, especially with WHO, towards jointly engaging with potential donors through a coordinated and comprehensive approach. The relevant activities will be supported by and aligned with targeted outreach and communication activities.



To fulfil its strategic goals and achieve its mission, IARC needs **to mobilize** a substantial amount of **financial resources**. The overall target is an increase of 25% of IARC's revenue over the next 10 years, mostly deriving from an expected steep increase in direct funding and in successful innovative resource mobilization.

With a focus on four strategic areas, IARC will implement its resource mobilization action plan (2020–2030):

1 IARC will increase its promotional activities to encourage additional countries to join the Agency and become Participating States.

2 Competitive grant awards are currently the main source of extrabudgetary funds. IARC will at least maintain its current level of funding from competitive grant awards, recognizing the increasing competition internationally and the limited number of such funding sources that are accessible. Collaborations with international and national partners will be key to attract new extrabudgetary resources.

3 IARC will further broaden its portfolio of attractive projects and will continue to identify potential funders, both existing and new ones, whose strategic priorities match with IARC's. IARC will use its new status as an Official Development Assistance (ODA)-eligible recipient international organization¹⁵ to attract funding from non-traditional sources, including development agencies.

4 In line with the Framework of Engagement with Non-State Actors (FENSA), IARC will create strategic partnerships with private sector entities, especially with a view to covering the funding gap of the Nouveau Centre project.

15. This means that 51% of Participating States' assessed contributions to IARC can be reported by them to the OECD as ODA. In addition, IARC projects that focus on LMICs could be considered 100% ODA-compliant; this is often an advantage when seeking funding from development agencies.

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Annex 1:

Detailed implementation plans

Cancer Surveillance (CSU) Branch

The Cancer Surveillance Branch systematically collects, analyses, interprets, and disseminates cancer data and statistics to inform global, regional, and national priorities for cancer control action. CSU documents the continuing cancer transitions while advocating for local data collection through: support to cancer registries, provision of international compendiums of high-quality registry data and national estimates of incidence, mortality, and prevalence, respectively, and in-depth assessments of the international variations in cancer and quantification of the extent to which key risk factors contribute to the burden.

Specific aims

- To consolidate IARC's role as the definitive reference source in describing the global cancer burden in adults, children, and adolescents.
- To support the development of population-based cancer registries (PBCRs) worldwide by providing standards and building capacity, including the provision of measurable improvements in registry coverage, quality, and use, particularly in low- and middle-income countries (LMICs).
- To conduct descriptive epidemiological research that directly responds to the noncommunicable diseases (NCDs) and sustainable development agenda and maximizes IARC's public health and economic impacts.

Major approaches/areas of activity in the next five years

1 The Global Cancer Observatory (GCO) will be reconfigured as a centralized resource for cancer indicators that informs global, regional, and national cancer control policies and research:

- The GLOBOCAN estimates will be published biennially via the Cancer Today subsite of the GCO, and the findings will be published in peer-reviewed high-impact journals.
- Based on registry data compiled in the *International Incidence of Childhood Cancer* (IICC) series, national estimates of childhood cancer will be developed based on the key diagnostic subgroups included in IICC.
- Extended indicators, including those with social and economic dimensions, will be integrated into the GCO platform, to cater for a wide range of end users, accompanied by infographics and narratives that explain key findings.

2 The *Cancer Incidence in Five Continents* project permeates the work of the Cancer Surveillance Branch. The collaboration with the International Association of Cancer Registries (IACR) ensures a direct line of communication with every PBCR worldwide, and the incidence data form the basis of indicators and research activities. As a key partner of the Global Initiative for Cancer Registry Development (GICR), coordination with the IACR is important to expand high-quality PBCRs in a sustainable manner.

Key activities include:

- Joint IACR-GICR work plans developed according to best practice and international standards.
- A redesigned IACR website to serve as a resource for and on registries worldwide, including dedicated tools to analyse registry-specific data through the GCO.
- Regular calls for data will allow registries to showcase their timeliness as well as their high-quality data, enabling investigations of contemporary patterns and trends of cancer risk among diverse populations worldwide.

3

The GICR model will be fully implemented, with resource mobilization efforts intensified under a global fund that allows for a continuing expansion of global and regional partners. Support to LMICs will be enhanced by scaling up the GICR Regional Hubs and associated IARC-GICR Collaborating Centres. Specifically:

- Tailored assistance will be provided to 30 partner countries based on identified requirements, national readiness, and an alignment with the overall GICR goals.
- Training will be provided by local experts via standardized educational material through the GICRNet and the launch of a Mentorship Programme. E-learning components will be developed to complement in-person activities.
- New electronic tools and reference works (*Cancer Registration: Principles and Methods*, 3rd edition; *International Classification of Diseases for Oncology*, 4th edition [ICD-O-4], e-TNM, CanReg5+) will be produced in several languages, including online learning modules, with links to the IACR and WHO.
- A WHO-IARC Toolkit will assist governments in meeting reporting requirements for cancer.
- An open access tool will be developed to estimate the costs and resources required for cancer registration in different settings.

4

Support to the WHO Global Initiative for Childhood Cancer, through a bilateral agreement with St. Jude Children's Research Hospital, will focus on:

- The development of childhood cancer registration in partner countries;
- An educational programme, including the provision of standard training materials based on the principles of the GICRNet;
- Descriptive economics research on (i) the costs of childhood cancer registry implementation, and (ii) an evaluation of familial financial hardship associated with childhood cancer in LMICs.

5

The provision of a global evidence base for cancer prevention will include:

- A systematic framework of indicators that support the planning and evaluation of programmes across the cancer control spectrum. These include:
 - The proportion of cancers attributable to major risk factors by country and world region. Studies will quantify the proportion of cases attributable to high body mass index, smoking, alcohol consumption, infections, and UV radiation.

- Prevalence by phase of care. A global update of methods and estimates to identify the needs of cancer patients and related economic costs, including estimates of cancer in children and adolescents.
- Extended indicators such as disability-adjusted life years (DALYs) and healthy life expectancy that respond to the rising number of cancer survivors and the increasing disease sequelae associated with diagnosis and treatment, and provide an assessment of gains in life expectancy.
- A quantification of the public health and economic benefits of integrating preventive interventions into national cancer control plans. Activities include:
 - Prediction of the number of future cases and deaths that could be averted, including economic gains associated with specific interventions. Models will predict the future burden to 2070 under specific scenarios, for example screening/vaccine roll-out, and tobacco or alcohol taxation.
 - Mortality trends will be used to predict future premature deaths from cancer and other NCDs, as well as the contribution of risk factors and prevention strategies in achieving SDG and other targets.

6 The capturing and benchmarking of cancer outcomes internationally will continue, stratified where possible by prognostic factors such as stage at diagnosis. Activities include:

- Provision of high-quality survival indicators through systematic approaches to understanding how registry processes and stage affect survival (SURVMARK), emphasis on bilateral collaboration to increase local capacity and ensure complete follow-up (SURVCAN), and assessment of the impact of major risk factors (SURVPOOL) and new emerging factors such as the COVID-19 pandemic (in collaboration with the COVID-19 and Cancer Global Modelling Consortium).
- To evaluate the impact of early detection and awareness programmes and provide relevant information on determinants of outcome, the availability of comparable cancer staging data internationally will be supported (including data on long-term recurrence or metastases), collaborating with staging experts and clinical experts, including the UICC-TNM Core Group, through:
 - An easily accessible automated tool to calculate tumour–node–metastasis (TNM) and stage groups, entitled CanStaging, is being developed to facilitate accurate staging of cancer by registries worldwide.
 - Essential TNM, a simplified staging system for registries when information on full TNM is absent, aims at staging cancer in its most advanced disease form by summarizing the extent of disease.
 - Assessment of data availability and processes within the registry to estimate long-term outcomes linked to stage, such as recurrence and metastases.

7 CSU will expand its research on the societal and economic impacts of cancer, including:

- Collaboration with WHO to assist national policy-makers in identifying cost-effective priority interventions as part of national cancer plans.

- The descriptive epidemiology of social inequalities in cancer, including temporal and geographical variations, the specific associations between social factors and different cancer types, and the impact of overdiagnosis and overtreatment.
- Populations-within-populations approaches: studies that use more granular data to identify inequities in subpopulations, such as ongoing collaborations with the World Cancer and Indigenous Populations Consortium.

Expected outcomes

- A step change in the global depth, utility, and use of the cancer databases held at IARC, via a complete integration of descriptive research findings into the GCO platform, including a major emphasis on documenting social disparities and economic impact.
- The GICR will have attained a global fund that ensures Regional Hubs are fully operational, and through global partnerships, a network of trainers, and online courses, there are measurable improvements in the coverage, quality, and networking capacity of registries in 30 partner countries.
- The global evidence base for cancer prevention – including the long-term public health and economic benefits – will have progressed so that governments integrate such interventions into their cancer control plans.
- The emerging priorities are increasingly emphasized and integrated into the work of CSU.

Genomic Epidemiology (GEM) Branch

Identifying specific genes and gene variants that contribute to the development of cancer is important for several reasons, including to identify individuals who are at a high risk of developing cancer and to reveal new causes of cancer. These studies can involve a focus on germline variation (i.e. the DNA variation we inherit from our parents) as well as the somatic variation that occurs within tumours. The basis of these studies is usually extensive fieldwork with partners throughout the world, with a particular focus on populations that are at a high risk of developing a specific type of cancer. These studies involve accurate evaluation of lifestyle factors and environmental exposures and require extensive biobanking and pathology expertise.

Specific aims

- To identify cancer predisposition genes through large-scale case–control studies of specific cancers, including whole-genome scans comprising millions of genetic variants.
- To identify how germline and somatic DNA variation contribute to cancer risk by conducting genome sequencing studies of tumour DNA.
- To identify lifestyle-related and environmental causes of cancer through interrogation of both germline and somatic genetic variation, using Mendelian randomization and mutational signature-type studies.
- To estimate how genetic and other biomarkers can contribute to improved early detection of cancer.
- To facilitate large international genetic and genomic studies by building capacity in biobanking, pathology, laboratory sciences, and bioinformatics.

Major approaches/areas of activity in the next five years

- 1 The large Mutographs of Cancer project will continue, with the aim of identifying new causes of cancer through whole-genome sequencing and linking mutational signatures to possible novel cancer causes.
- 2 The development of large-scale international consortia of case–control and cohort studies, specifically for three cancer sites (lung, head and neck, and kidney) will continue, and comprehensive genome-wide association studies for these cancers will be conducted, coupled with large-scale analyses of germline genetic variation using a Mendelian randomization approach.
- 3 Lung cancer research activities will focus on identifying susceptibility genes that influence risk along with other, non-genetic biomarkers of risk. This research, conducted within the Lung Cancer Cohort Consortium, seeks to improve risk prediction models for lung cancer, which may have direct relevance for screening of lung cancer. Studies of head and neck cancer will include identifying genes involved in susceptibility and how these genes interact with other risk factors, in particular alcohol consumption, tobacco use, and HPV infection. Extensive fieldwork activities will continue, including recruitment and follow-up of case–control studies for lung, head and neck, and renal cancers, particularly in high-risk regions of central Europe and South America, as well as coordinating large cohort studies, including those in the Russian Federation, the Islamic Republic of Iran, and Europe.
- 4 Testing the utility of circulating tumour DNA (ctDNA) as a biomarker for detecting cancer at early stages will continue. Using and further expanding the genomic tools that were developed for detecting low-abundance ctDNA mutations, GEM will assess the potential of tumour-derived alterations as an early biomarker in various cancer types, including bladder cancer and head and neck cancers.
- 5 Multi-omics characterization of rare tumours, with a current focus on molecular characterization of malignant pleural mesothelioma, and also unveiling the molecular pathways underlying the development of pulmonary carcinoids.
- 6 Capacity in biobanking, pathology, laboratory sciences, genomics, and bioinformatics will be built, adapted to the multicentre genetic and genomic studies through knowledge sharing and training activities, as well as through the provision of access to data and samples.

Expected outcomes

GEM will focus on conducting 20 priority projects across 6 outcome areas, the successful delivery of which will depend on the acquisition of the necessary external funding¹⁶.

- Understanding genetic susceptibility of multiple cancers (1 project)
 - Expanding genetic susceptibility studies for multiple cancers, including lung cancer, head and neck cancers, renal cancer, and lymphomas, via coordination and publication of large genome-wide studies
- Identifying causes of cancer through genomic techniques (3 projects)
 - Mutographs study – Conducting the largest genomic epidemiology studies of 5 cancers across 5 continents and involving 5000 cancer cases

16. Typically, the majority of GEM funding comes from external sources through competitive grant applications. When both staff and non-staff costs are included, about 75% of GEM funding over the past 10 years has been via external competitive grants.

- Identifying mutational signatures for specific exposure, including opium, alcohol, and aristolochic acid
- Understanding the role of obesity and metabolic factors for multiple cancer types – Mendelian randomization and direct exposure measurements in large cohorts
- Reduced mortality and morbidity through early detection of selected cancers (4 projects)
 - Identifying proteomic markers for early detection of lung cancer
 - Cross-agency collaborations on lung cancer screening
 - Biomarkers for early detection of head and neck cancer
 - Towards the clinical validation of urinary *TERT* promoter mutations (alone or combined) as non-invasive biomarkers for the early detection of bladder cancer (URITERT+)
- Building global capacity in cancer science (1 project)
 - Data coordinating centre for the international consortia projects
- Molecular characterization of cancer through somatic cancer genomics (6 projects)
 - Integrative studies on germline, somatic, and molecular biomarkers in renal cancer incidence and survival
 - Building the largest genomics resource of somatic and viral genetic changes involved in head and neck cancer onset and outcome in diverse populations
 - Multidisciplinary and multi-omics molecular characterization of neurocrine neoplasms
 - Multi-omics characterization of malignant pleural mesothelioma (MESOMICS)
 - Investigating the heterogeneity of rare cancers through molecular maps
 - Unveiling the molecular pathways underlying tumour evolution through mechanistic and computational models (LungNENomics)
- Understanding variations in cancer incidence and survival (5 projects)
 - Genomic basis of hereditary breast and ovarian cancer in admixed populations
 - Understanding the causes of late diagnosis of head and neck cancer
 - Genomic characterization of oral pre-neoplasia
 - Towards clinical implementation of urinary *TERT* promoter mutations as biomarkers for monitoring minimal residual disease or recurrence of urothelial cancer (CLINITERT)
 - Understanding the role of opium and opioids in cancer onset (OPICO)

Nutrition and Metabolism (NME) Branch

Going beyond what may be considered the traditional domains of nutrition in cancer research, NME seeks to fully exploit methodological advances in nutritional epidemiology as well as molecular profiling techniques to implement an integrated, multidisciplinary programme of research, with important contributions from epidemiology, biostatistics, bioinformatics, and laboratory sciences.

Specific aims

- To provide robust causal evidence on the link between nutrition and cancer.
- To understand the role of obesity and metabolic dysfunction in cancer development.
- To investigate the determinants of cancer comorbidity and identify biological pathways common to cancer, diabetes, and cardiovascular diseases.

Major approaches/areas of activity in the next five years

NME research will focus on cancers that have clear links to nutrition and metabolic abnormalities, for which the etiology remains to be discovered, that have a high or rapidly rising incidence, and for which preventive strategies may be most effective. These include gastrointestinal cancers (colorectum, pancreas, stomach, and liver) as well as hormone-sensitive cancers (breast, endometrium, and thyroid). Major areas of activity will entail:

- 1 Nutrition, diet, and cancer** NME will continue to pursue research on identifying nutritional factors and dietary patterns that are associated with cancer development. This will include the application of innovative new methods for capturing aspects of the diet newly hypothesized to affect cancer risk, including consumption of ultra-processed foods, food additives, and contaminants, as well as diet biodiversity.
- 2 Measurement of nutritional and metabolic biomarkers** in biospecimens from cohort and intervention studies using metabolomics approaches and targeted assays. Biomarkers of diet and nutrition are needed to complement questionnaire-based data and can help infer causality. The established metabolomics platform in NME will be used to discover novel markers of diet where there is currently a lack of definitive evidence regarding links with cancer or where knowledge on biological mechanism is needed (e.g. red and processed meat, fibre, fruits and vegetables, coffee, alcohol, fat, industrially processed foods). Untargeted approaches will first be used to identify metabolic signals associated with diet, and then based on these discoveries targeted, quantifiable assays will be developed for application in epidemiological studies of cancer. In addition to metabolomic discovery, targeted assays including steroid hormones, immune markers, growth factors, and other protein-based markers will be applied to epidemiological studies using immunoassays or by mass spectrometry. They will also be used to discover novel biomarkers of exposure to cancer risk factors such as diet, microbiota, fat distribution, or mammographic density and to identify their main determinants in cross-sectional and intervention studies.
- 3 Coordination and enhancement of epidemiological resources** including the European Prospective Investigation into Cancer and Nutrition (EPIC) and breast cancer case-control studies in Africa (South Africa Breast Cancer [SABC] study, Determinants of Breast Cancer in Morocco [EDSMAR] study) and Latin America (Molecular Subtypes of Premenopausal Breast Cancer in Latin American Women [PRECAMA] study). Although EPIC will continue to be an invaluable resource for IARC, research will increasingly consider LMICs where secular changes in diet and lifestyle patterns contribute to increasing rates of certain cancers.

This will include the development of large-scale case–control studies and biorepositories for the studies of breast and colorectal cancers in Africa and in Latin America. Progressively, work will be intensified with international partners and in large cohort consortia where NME is leading major research initiatives (e.g. alcohol and cancer, diabetes and cancer, early-onset colorectal cancer). In addition, international epidemiological resources for research on the microbiome and cancer will be developed, with a particular emphasis on using ongoing colorectal cancer screening programmes as a platform for collecting faecal specimens, epidemiological data, and end-point data.

4 Development of statistical methods that optimize the handling and analysis of epidemiological and molecular data within prospective cohorts, case–control studies, and interventions, with a specific focus on the role of nutrition in cancer. NME will capitalize on its preliminary work on the identification of molecular signatures of diet and lifestyle to develop statistical frameworks to thoroughly investigate the complex intersection of nutritional and molecular factors in cancer etiology.

Methodological investment is planned to comprehensively elucidate the robustness of evidence produced by causal inference applied to observational data (e.g. mediation analysis and Mendelian randomization studies), in contexts characterized by networks of interrelated factors, residual confounding, and potential reverse causality. Multivariate statistical techniques will be customized and further developed to capture this complexity, together with methodology for longitudinal data. Risk prediction models will be developed along with corresponding applications of biomarker data. Methodological work will also embrace activities related to biomarker discovery, as well as cross-linking -omics data to further develop the exposome concept in cancer research. Furthermore, NME will apply multistate modelling and competing risks analysis to evaluate the transitions between multiple morbid conditions in the context of cancer comorbidity and multimorbidity.

Expected outcomes

NME actively pursues extrabudgetary funding, and the expected deliverables are largely based on secured funding for 2021–2025.

- Enhancement of the EPIC central database and biorepository at IARC
 - Centralization of diet and lifestyle data collected during the follow-up period (post-baseline assessment) and completion of a new round of cancer and mortality end-point follow-up.
 - Completion of sample replenishment for cancer cases where the biosample has been depleted.
- Availability of population-based breast cancer research resources in South Africa, Morocco, and Latin America (Mexico, Colombia, Brazil, Chile, and Costa Rica) through the conduct of specific studies, including:
 - Nutrition, dietary factors, and body fat distribution
 - Metabolic health and reproductive factors
 - Molecular studies of breast tumour subtypes
 - Impact of social inequalities on the link between nutrition and cancer

- Feasibility studies of establishing prospective cohorts with pre-diagnostic stool samples nested within colorectal cancer screening programmes for advancement of microbiome research in population-based settings.
- Annotation of the circulating metabolome and significant advancement of understanding of the metabolic perturbations that contribute to cancer development. Specific projects include:
 - Metabolome-wide association study of colorectal, pancreatic, and endometrial cancer in EPIC, and follow-up validation of signals within external cohorts and consortia
 - Identification of novel biomarkers of dietary factors and investigation in relation to cancer
 - Analysis of microbial metabolites in relation to colorectal, pancreatic, and liver cancer.
- Novel insights into the role of obesity and metabolic health in cancer development, specifically:
 - Genetic (Mendelian randomization) studies of adiposity subtypes and metabolites with cancer
 - Annotation of the obesity metabolome and association with cancer
 - Identification of circulating biomarkers (metabolites and proteins) of adipose tissue distribution and application to studies of cancer
 - Investigation of mediating pathways linking obesity and metabolic health with cancer through the application of advanced causal inference methods.
- Intervention studies of lifestyle change and their impact on cancer biomarkers and intermediate outcomes, including lifestyle intervention (adherence to cancer prevention recommendations) among individuals within the French colorectal cancer screening programme.
- Improved understanding of the causes of cancer comorbidity and shared biological pathways between cancer, type 2 diabetes, and cardiovascular disease.
- Completion of large-scale studies within international consortia (e.g. NCI Cohort Consortium), including alcohol and cancer (with a focus on cancers for which there is uncertainty regarding links with alcohol consumption) and diabetes and cancer. In addition, establishment of a new pooled resource on early-onset colorectal cancer, to identify epidemiological and molecular risk factors.

Epigenomics and Mechanisms (EGM) Branch

The Epigenomics and Mechanisms Branch (EGM) seeks to advance understanding of cancer causes by investigating genetic and epigenetic patterns and interrelated molecular pathways deregulated by exposure to risk factors and the underlying mechanisms of carcinogenesis, thus enhancing the evidence base for implementing interventions and cancer prevention.

Specific aims

- To understand molecular causes of cancers in children and adults by investigating epigenetic and other molecular changes driven by risk factors during in utero and early life and identifying biomarkers for cancer risk stratification and early detection.
- To understand the impact of established and emerging environmental risk factors for cancer on genome/epigenome integrity and function and provide mechanistic evidence for their contribution ("driver roles") to disease risk, for their inclusion in human carcinogen evaluation and classification, and in molecular epidemiology study designs.
- To identify specific molecular changes associated with and/or caused by specific dietary/lifestyle factors and assessing whether these changes can serve as sensitive biomarkers in monitoring the impact of interventions aimed at reducing cancer risk.

Major approaches/areas of activity in the next five years

EGM will apply (epi)genomic and profiling methodologies and bioinformatics/biostatistics tools to experimental models and biobank samples associated with population-based and case-control studies. EGM will emphasize potential contributions to translational studies through the expected discovery of biomarkers of exposure, early detection, and risk stratification. This will include:

- enhancing the wet-lab pipelines for next-generation sequencing (NGS)-based (epi)genome analysis, focusing on a rapid and cost-effective replication/validation of hits identified by large-scale genome-wide sequencing,
- applying genome-wide functional screens to identify "driver" genes and or (epi)genetic changes in human cultured cells and organoids in combination with genome-editing tools,
- developing rapid models for mutational signature analysis through single-cell sequencing of the genome and transcriptome, and
- developing and advancing bioinformatics and biostatistics tools with application to molecular biology and molecular epidemiology.

1 Research on cancer causes and biomarkers will capitalize on unique prospective cohorts (which enable the measurement of (epi)genetic and other molecular events at different time points before diagnosis, typically in surrogate tissues, including blood cells and cfDNA, or on tumours), and case-control studies (covering high-incidence regions or high-exposure scenarios and enabling the detection of (epi)genetic aberrations directly in the "tumour target" tissues).

The focus will be on, for example, integrating (epi)genomics and metabolomics (breast and colorectal cancers from EPIC), exposure adductomics and mutational signature analysis in renal cancer (NLCS tumour collection), and mutational signatures and epigenomics (oesophageal cancer, ESCCAPE study). For childhood cancer studies, cord blood samples from a consortium of international birth cohorts (I4C, CLIC, PACE) linked to childhood cancer will be used. These data will be combined with the use of cutting-edge methodologies for genome-wide profiling of (epi)genomic and transcriptomic alterations and robust bioinformatics and biostatistics pipelines that incorporate other -omics layers (adductomics, metabolomics), enabling integrated analyses aimed at evaluating the potential functional impact of changes and causal relationships with cancer risk (e.g. through the use of genetic proxies by the Mendelian randomization approach).

2 For **the identification of functionally important (“driver”) genes in cancer and their link to environmental carcinogens/exposures**, pan-cancer analyses integrating genome, epigenome, and transcriptome alterations across cancer types will be conducted by building on the most recent knowledge of the cancer genome and epigenome, new concepts, and genomic databases.

This research will include the application of novel bioinformatics approaches, integrating the strengths of various “driver” prediction and multi-omics algorithms followed by state-of-the-art orthogonal in vitro validation of functionally important epigenetic “driver” genes (“epidrivers”) and molecular pathways (using the CRISPR-Cas9 system) altered by specific cancer risk agents. Mechanistic evidence generated through experimental studies in vitro will be included in the hazard assessment of cancer risk factors and in the design as well as the interpretation of molecular epidemiology studies, through the established MutSpec2.0 research programme. Novel experimental exposure models, based on mutation spectra analysis in single-cell genomic DNA and RNA, will be combined with established screening approaches. Selected experimentally identified molecular changes and markers will be investigated in samples from animal bioassays and in available epidemiological collections.

3 The investigations of the **impact of interventions on epigenetic and other molecular biomarkers associated with cancer risk** will capitalize on randomized trials in metabolically unbalanced breast cancer survivors at higher risk of recurrence. The study will take advantage of: (i) a population of monozygotic twins discordant for body mass index (BMI) (with obese co-twins being subjected to diet-induced weight loss) and (ii) a population of massively obese patients after bariatric surgery, and (iii) an intervention study, The Impact of Diet-Induced Weight Loss on Biomarkers for Colorectal Cancer (INTERCEPT), that provides epigenetic profiles in colorectal tissue.

Expected outcomes

The successful delivery of these outcomes will depend on the acquisition of the necessary external funding.

- Understanding of mechanistic evidence and biological plausibility for cancer causation by emerging risk factors or suspected human carcinogens, such as dietary acrylamide (with a potential mode of action/role established), chemicals present in cooked meat, environmental tobacco smoke, and dietary factors and their metabolites affecting breast cancer risk, which will contribute important information to carcinogen evaluation and help improve prevention strategies.
- Provision of new epigenetics-based biomarkers of exposures and cancer risk. Potential users of epigenetics-based pre-diagnostic markers and risk models are many, including scientists and centres involved in screening and developing risk models for breast cancer and colorectal cancer.
- The results from the childhood cancer study will promote knowledge sharing and accelerate translational research for the benefit of patients.
- Intervention studies related to obesity and cancer outcomes are expected to answer whether the epigenome integrates the influence of both genetic and environmental/lifestyle factors on a phenotype (e.g. obesity) and potentially reveal epigenetic alterations that exert downstream functional outcomes (including metabolic disorder, comorbidity, cancer risk, and response to intervention). They should also result in provision of epigenetic markers that predict future cancer recurrence and prevention of recurrence (and other comorbidities). Identifying epigenetic biomarkers associated with metformin and/or weight loss may prove instrumental in clinical trials with a clinical end-point (cancer incidence) in larger populations at high risk of developing breast cancer or colorectal cancer, or their recurrence in cancer survivors.

Environment and Lifestyle Epidemiology (ENV) Branch

The overall objectives of ENV are to investigate environmental, lifestyle, occupational, and radiation-related causes of cancer in human populations, to identify major barriers to improving survival of curable cancers contributing to premature mortality, and to promote cancer prevention through synthesis and translation of research evidence. Although primary prevention is the ultimate aim of cancer prevention, tertiary prevention is an essential component of every cancer control plan, especially for less-preventable but curable cancers; therefore, ENV also assesses multifactorial determinants of cancer prognosis and cancer outcomes. These objectives are achieved through the conduct of collaborative international epidemiological studies including coordination of international consortia or through the initiation of specific analytical epidemiological and field studies.

Specific aims

- To investigate environmental and lifestyle causes of cancers.
- To study the epidemiology of cancers associated with known and suspected carcinogens in the occupational setting.
- To study the carcinogenic effects of protracted exposure to low doses of ionizing radiation and of exposure to non-ionizing radiation (electromagnetic fields).
- To identify barriers to improving survival of common curable cancers in LMICs.
- To enable cancer prevention and control through translation of research evidence into cancer plans and codes.

Major approaches/areas of activity in the next five years

1 Environmental and lifestyle causes of cancer: The study of environmental and lifestyle causes of cancer will continue through the investigation of cancers suspected to be influenced by such factors and through further characterization of dose–response curves and effect modifiers of cancer risks due to known carcinogens.

- Etiological epidemiological studies of the East African oesophageal cancer belt, which has distinct geographical, age, and sex patterns suggestive of strong environmental or behavioural risk factors, will be pursued. These research activities will be continued on a collaborative platform across Kenya, Malawi, and the United Republic of Tanzania in the form of the Oesophageal Squamous Cell Carcinoma African Prevention Research (ESCAPE) study. The role of several agents will be evaluated, including household air pollution, micronutrient deficiencies, geophagia, consumption of very hot beverages, and poor water quality. In addition, the role of oral health and hygiene will be evaluated, and, in collaboration with the African Esophageal Cancer Consortium, the oral microbiome in this cancer.
- Carcinogenic exposures and cancer risks linked to populations living around the uraniferous gold mine tailings in Gauteng, South Africa, where earlier investigations pointed to elevated exposure to uranium, will continue to be studied. Also in sub-Saharan Africa, cancers and carcinogenic exposures associated with widespread oil spills and oil contamination will be investigated alongside a UNEP-led investigation of the negative environmental and health impacts associated with the oil industry in Ogoniland, Nigeria.

- Investigations into tattooing will be initiated; tattoo inks contain several known and suspected carcinogens but have not yet been well studied.
- Childhood cancer research will continue, mainly via the Childhood Cancer and Leukemia International Consortium (CLIC, established in 2007), of which IARC hosts the central Data Coordination Center. Research activities on pesticide exposures will be conducted. In the framework of the Global Acute Leukaemia network (GALnet), a global network of paediatric oncology units that includes 3–5 representative paediatric units per continent, the extent to which major geographical incidence differences are driven by risk factors will be explored, compared with referral patterns and resources in health-care systems.

2 **Occupation and cancer:** Investigations of known and suspected carcinogens in the occupational setting will continue, including those linked to current and historical industries.

- Cancer risks associated with pesticides, herbicides, and fungicides used in the agricultural sector are relevant to the global cancer burden, given that agricultural workers are among the largest workforces globally, and that exposures to these agents may pose a risk to workers, people living close to farms, and consumers. Relevant investigations will continue through the coordination of an international consortium of agricultural studies, including of pesticide applicators and farmers (AGRICOH).
- Collaboration in studies investigating the role of occupational exposures, especially in relation to pesticide exposures, for testicular cancer will continue, because exposures appear to explain distinct geographical patterns. The same hypothesis applies to several types of childhood cancer for which the CLIC data (see under 1. above) will be used.
- Investigations of occupational lung cancer risks will continue and be expanded to occupational cancer studies in emerging or developing economies, including the Russian Federation and the Islamic Republic of Iran. The focus of research in new settings will be on context-specific exposure levels, pathways, and co-exposures, which may differ greatly from those in high-income countries. IARC will disseminate findings to the global occupational cancer research community and the respective worker protection initiatives.
- Based on the world's largest cohort study of miners and millers exposed to chrysotile asbestos, cancer mortality in the cohort in Asbest town, Russian Federation, will be reported in 2021. This data resource will be complemented and expanded by additional information that considers co-exposures of workers.

3 **Radiation and cancer:** Research to characterize cancer risks associated with environmental exposures after nuclear accidents, nuclear waste dumping, or nuclear weapons testing will continue, including the coordination of or collaboration on cancer studies at major nuclear sites, including Chernobyl (Ukraine), the Southern Urals (Russian Federation), Semipalatinsk (Kazakhstan), and Fukushima (Japan).

4 Research will focus on direct quantification of cancer risks from protracted exposure to low-dose ionizing radiation during different stages of life (from preconceptional to fetal, early life until adulthood) and include development of innovative methodological approaches to estimate individual radiation doses and related uncertainties, integration – where possible – of biological approaches to understand mechanisms contributing to and modulating radiation carcinogenesis, and addressing public health concerns in the population.

- 5 Whether exposure to electromagnetic fields (EMF) is associated with an increased risk of certain cancers will continue to be investigated. In view of IARC's expertise and capacity in this area, research will continue through involvement in long-term prospective studies of users of mobile phones and other wireless technologies. Research work on exposure to power-frequency magnetic fields and its relation to childhood leukemia will continue as well.
- 6 Research to **improve survival of common curable cancers in LMICs** will focus on the epidemiology of breast cancer in sub-Saharan Africa, including studies of barriers, within a social and cultural context, to early presentation/diagnosis, treatment, and ultimately survival. For example, studies will include whether early diagnosis leads to a greater proportion of cured cancers, quality of life of breast cancer survivors in this LMIC setting, and modelling scenarios of how to improve breast cancer survival, looking at different combinations of downstaging (i.e. shifting the stage distribution of tumours detected towards a lower stage) and treatment improvements, and at reducing social inequalities in survival.
- 7 Under the overall umbrella of a World Code Against Cancer, regional Codes Against Cancer will be developed jointly with regional health policy-makers, based on synthesized scientific evidence. A framework will be developed to implement and measure the impact of region-specific Codes Against Cancer, building on relevant pilot studies. For each regional code, regional cancer experts and stakeholders will be brought together for the formulation of education, training, dissemination, and evaluation activities. The implementation of a future Code Against Cancer for Latin America and the Caribbean will be assessed in a multicentre study in Colombia and Argentina. Several dissemination strategies on the acceptability of mobile phone messages (mHealth) for cancer prevention will be also investigated.

Expected outcomes

The successful delivery of these outcomes will depend on the acquisition of the necessary external funding.

- Identification of risk factors for peculiar cancer patterns, including oesophageal cancer in Africa, lung cancer in workplaces with carcinogenic co-exposures, paediatric cancer, and haematological malignancies, mainly in LMICs, with hypothesized environmental and lifestyle contributions to the clustering.
- Identification of cancer risks associated with low-dose exposures affecting large populations. This research includes: (i) specific pre-selected active ingredients in pesticides and haematological malignancies, breast cancer, prostate cancer, testicular cancer, and paediatric cancer; (ii) selected main industries (agriculture, petroleum, mining); (iii) anthropogenic radiation (lifetime cancer risk after nuclear accidents, nuclear testing, and nuclear waste dumping; non-ionizing (radiofrequency)), and (iv) locally contaminated environments (household air pollution, heavy metals, radionuclides).
- Recommendations on transforming knowledge on risk factors into individual-level and population-level prevention measures, through: (i) regional Codes Against Cancer (updating for Europe, first development for Latin America and the Caribbean, preparatory work for other regions); (ii) informing on preventing premature breast cancer deaths in Africa; and (iii) input on updating of radiation protection guidelines, as well as occupational cancer prevention and compensation schemes.

Early Detection, Prevention, and Infections (EPR) Branch

From 2021 onwards, the former research sections “Infections” and “Early Detection and Prevention” will be merged and cooperate under the Early Detection, Prevention, and Infections (EPR) Branch.

Given the particular amenity of carcinogenic infectious agents to cancer prevention (e.g. vaccines, diagnostic tools, and therapies) and the disproportionate burden of infection-attributable cancers in LMICs (>25% of all cancers in certain global regions), a significant proportion of IARC’s prevention research focuses on infection-related cancers. The activities include a wide portfolio of study designs, from etiology/natural history, through global burden assessment, to evaluation and modelling the impact of interventions.

Specific aims

- To transform knowledge about established cancer causes and mechanisms, with a special focus on carcinogenic infections, into evidence-based preventive interventions that can prevent cancer suffering and death.
- To evaluate tests and strategies for cancer early detection, with a view to reducing the disease burden and improving survival and quality of life of patients after treatment.

Major approaches/areas of activity in the next five years

The evaluation of interventions that have the potential to reduce the global cancer burden will be further intensified. These interventions can be broadly categorized into those relevant to: (i) primary prevention of established modifiable risk factors (e.g. preventing HPV and HBV infection through vaccination; testing and treatment of *H. pylori* and HCV); (ii) screening of asymptomatic at-risk populations for selected cancer types (e.g. cervical, gastric, anal, breast, colorectal, and lung cancer); and (iii) early diagnosis of cancer in symptomatic individuals, with a view to shifting the stage distribution of tumours detected towards a lower stage, and improving survival and quality of life after treatment. Importantly, the evaluation of prevention, screening, and early diagnosis will focus on their effectiveness in real health-care settings and also on understanding the related implementation challenges.

1 Primary prevention of carcinogenic infections: Priorities include establishing the population attributable burden of HIV to cancer (e.g. cervical, Kaposi sarcoma, non-Hodgkin lymphoma, anal) and of Epstein–Barr virus (EBV) to non-Hodgkin lymphoma and gastric carcinoma. This programme serves to raise awareness, inform recommendations for preventive action, prioritize resources, and monitor the long-term impact of cancer prevention policies that target infectious agents, at both local and global scales.

HPV vaccination is the main component of the WHO goal to eliminate cervical cancer, but has had only limited roll-out in LMICs to date. The engagement in evaluating the efficacy and effectiveness of, as well as modelling the impact of, HPV vaccination in different implementation scenarios will therefore continue, most notably that of a single HPV vaccine dose. The evidence will guide health policies and support national authorities in implementing HPV vaccination programmes, particularly in LMICs, in order to reduce global cervical cancer disparities.

H. pylori is the most important infectious cause of cancer worldwide. In anticipation of results from ongoing research (the HELPER trial), which is expected to establish the efficacy of testing and treatment of *H. pylori* on gastric cancer incidence, research into the implementation of such programmes in LMICs will be expanded, both by undertaking

expertise in modelling the natural history of carcinogenic infections, to predict the evolution of gastric cancer burden according to the absence or presence of different implementation scenarios.

2 Screening of asymptomatic at-risk populations: A range of studies will be conducted that evaluate new technological inventions in cancer screening and management of premalignant conditions and assess their suitability and applicability for implementation, in particular in limited-resource settings.

To accelerate the introduction of HPV-based screening in alignment with the WHO Cervical Cancer Elimination Initiative, the IARC portfolio on cervical cancer screening includes: evaluation of novel HPV detection tests (detection of high-risk HPV E6/E7 oncoproteins, detection in urine using infrared spectroscopy); techniques for triage of HPV-positive women (e.g. the ESTAMPA study in Latin America); artificial intelligence for pattern recognition to detect cervical precancer; HPV screen-and-treat programmes in Africa, with a particular focus on women living with HIV; and a randomized controlled trial in Zambia on the efficacy, safety, and cost-effectiveness of cervical thermal ablation.

Continued follow-up of a randomized controlled trial to evaluate clinical breast examination for breast cancer screening in India will generate valuable evidence on the efficacy of this test. Collaboration is foreseen in a study that combines *H. pylori* eradication with endoscopic assessment to treat gastric cancer precursors and investigates detection of hTERT mutation in urinary samples for bladder cancer screening (GISTAR).

A range of studies will be conducted to understand the major barriers to accessing quality-assured cancer screening in LMICs, and to evaluate interventions directed at women and health-care workers to increase participation. An ongoing study, Cancer Screening in Five Continents (CanScreen5), will evaluate the coverage and quality of cancer screening programmes globally. Implementation research studies aim to document the challenges that countries face while introducing major changes in their existing screening programmes (e.g. transitioning from cytology-based to HPV-based cervical cancer screening).

Furthermore, collaboration with ministries of health in several countries (priorities for LMICs) will continue to assist them in planning and implementing quality-assured cancer control programmes.

3 Early diagnosis of common cancers: Clinical early diagnosis of symptomatic patients followed by stage-appropriate treatment can improve the survival and quality of life for cancer patients. To better understand the challenges in implementing cancer early diagnosis and the means to improve it, in particular in LMICs, barriers to accessing timely diagnosis and treatment for symptomatic individuals will be evaluated, including measuring delays (access, systems, and treatment) across the cancer care pathway, and identifying setting-appropriate solutions to minimize such barriers and delays.

Studies will be conducted that identify relevant gaps in the health systems across the cancer care continuum and suggest contextualized and sustainable solutions. Keeping pace with advancement of technology, the applicability of new technology will be assessed: mobile technology to educate the community, the use of mobile phone-based applications to navigate patients, and the web-based promotion of telepathology and distance learning for service providers.

Expected outcomes

The successful delivery of these outcomes will depend on the acquisition of the necessary external funding.

- Robust evidence on the efficacy of single-dose HPV vaccination, which is expected to accelerate the implementation (feasibility, cost) of HPV vaccination programmes in LMICs.
- Results of effectiveness of HPV-based cervical cancer screening algorithms in programmatic settings across Latin America, which will inform implementation of HPV-based screening in LMICs.
- Interim findings are expected to establish the efficacy of testing and treatment of *H. pylori* on gastric cancer incidence in the Republic of Korea, an important step for implementation of prevention programmes in high-risk populations, particularly in Asia.

Evidence Synthesis and Classification (ESC) Branch

WHO Classification of Tumours Programme

The *WHO Classification of Tumours* ("WHO Blue Books") series underpins the diagnosis of cancer, precancerous conditions, and benign tumours. In line with the IARC Statute (2014), the series is an international collaboration of more than 2000 clinicians and scientists who evaluate and synthesize diagnostic evidence to produce the classification, on which all cancer reporting and coding systems are based.

The IARC International Collaboration for Cancer Classification and Research (IC³R) operates alongside the WHO Blue Books, and aims to harmonize cancer diagnosis-related data, set standards for analytical procedures, and identify critical gaps in research, data registration, and classification.

Specific aims

- To provide timely, definitive synthesis and evaluation for tumour classification based on expert consensus review of reproducible peer-reviewed published evidence. The *WHO Classification of Tumours* will continue to be available in multiple formats to meet the needs of users in low-, middle-, and high-income countries.
- To provide the ICD-O coding system and support to cancer registries in its use, as well as continuous improvement of the ICD-11 coding system.
- To advance the practice of high-quality cancer pathology diagnostic practice and research globally, through IC³R and other initiatives.

Major approaches/areas of activity in the next five years

- 1 The 5th edition of the *WHO Classification of Tumours* series provides an evidence-based approach to cancer classification, and hence diagnosis. Evidence is gathered from scientific peer-reviewed publications, in-house and external systematic reviews, IC³R, and expert consensus review. The 6th edition will commence in 2023 and will make greater use of the database, allowing integrated diagnosis across specialties and further improving its consistency.

- 2 The *WHO Classification of Tumours* will adhere to international standards such as SI units, HGVS genetic nomenclature, and others as required. Levels of evidence will be incorporated where and when feasible. This integration will include diagnostic evidence criteria (i.e. how good is the evidence for a feature in diagnosis and grading?). These will be developed with IC³R, approved by the *WHO Classification of Tumours* Editorial Board. Evidence may be linked to statements by kitemarks. Up to three Editorial Board meetings will be held each year to review current volumes and commence new ones. Although most meetings will continue to be held in Lyon, some may be held elsewhere to encourage collaboration. Collaborations with other international organizations are important and will be strengthened.
- 3 In partnership with the International Academy of Cytology (IAC), the *WHO Cytopathology Reporting System* series will be produced, linked to the WHO Blue Books, harmonizing cytological diagnosis with the classification, and strongly linked to the International Collaboration on Cancer Reporting (ICCR). Work on cancer staging will continue, based on the *WHO Classification of Tumours*, in partnership with the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) and with major pathology organizations through the International Liaison of Pathology Presidents (ILPP), and directly with the College of American Pathologists (CAP).
- 4 The production of the *WHO Classification of Tumours* is paperless and automated at all stages as far as possible. This process can be accessed using the WHO Blue Books Online Submission System (BBOSS2) database. This online system enables automation of some checks and ensures compliance with WHO/IARC requirements.

Expected outcomes

The successful delivery of these outcomes will depend on the acquisition of the necessary external funding.

- The 5th edition of the *WHO Classification of Tumours* series comprises 14 volumes (<https://whobluebooks.iarc.fr/>). During 2021–2025, ESC will publish in print and online the remaining 9 volumes in the current (5th) edition and will commence the 6th edition. Publication of four volumes of the *WHO Cytopathology Reporting System* series (for lung, pancreatobiliary, lymph node, and soft tissue cytological diagnosis) is expected during 2022, and these publications will be followed by two volumes each year.
- IC³R is expected to produce ISO standards for research laboratory accreditation similar to ISO 15189 for clinical diagnostic laboratories. The project on evidence-based pathology and a number of other projects under discussion at present are likely to produce publications during the next five years, but the proof of its success will be in the translation of research results into practice within the *WHO Classification of Tumours*.
- Collaborative links with IC³R, with ICD-O programmes, and with pathology organizations are expected to continue to grow internationally.

IARC Monographs Programme

For nearly 50 years, the *IARC Monographs* series has been the world's premier reference work for the identification of the preventable causes of human cancer. The availability of an international consensus from an independent, specialized agency provides an authoritative basis for national decision-making, and facilitates national recommendations. National and international health agencies use the *IARC Monographs* to guide and support their actions to prevent exposure to known, probable, and possible carcinogens. In this way, the *IARC Monographs* contribute substantially to cancer prevention and the improvement of public health.

Specific aims

- To generate robust evaluations of the human carcinogenicity of specific agents by assembling, rigorously reviewing, and synthesizing the publicly available scientific evidence on carcinogenic hazards to which humans are exposed, including chemicals, complex mixtures, physical agents, biological agents, occupational exposures, and other factors.
- To serve as a focal point for developing and applying methods for systematic review of observational epidemiology, animal bioassay, and mechanistic evidence for purposes of cancer hazard identification.

Major approaches/areas of activity in the next five years

- 1 The Preamble to the *IARC Monographs*, which was substantively amended in 2019¹⁷, details the methods by which the *Monographs* evaluations are undertaken by expert Working Groups. Over the next five years, the Preamble's updated methodology will be applied in convening independent Working Groups of global experts to evaluate a diversity of agents of public health importance. This approach will allow the *IARC Monographs* to take advantage of scientific and procedural advancements in providing state-of-the-art expert evaluations with global impact.
- 2 The priorities for future *Monographs* evaluations, recommended by an independent Advisory Group in 2019, encompass nominations from the general public, the scientific community, national health agencies, and other organizations. Some have recognized and/or widespread exposures, including in LMICs.
- 3 Other future *Monographs* evaluations may address emerging public health concerns, such as those identified by Participating States. Agents are selected for evaluation based on: (i) evidence of human exposure, and (ii) some evidence or suspicion of carcinogenicity. Agents and exposures can be re-evaluated if significant new data become available. Agents for evaluation are selected in consultation with WHO partners and relevant programmes elsewhere. The topics for each meeting are publicly announced approximately one year before the meeting.
- 4 IARC convenes an international, interdisciplinary Working Group of expert scientists to develop each volume of *IARC Monographs*. IARC selects experts for the Working Group based on their knowledge and experience and absence of conflicting interests, with consideration given to gender and geographical balance. These independent experts assemble and critically review the scientific evidence according to strict criteria.
- 5 Each Monograph consists of a comprehensive, rigorous review and summary of publicly available scientific evidence (published peer-reviewed research articles, and publicly available data from government agencies). The principles of systematic review are applied in the identification, screening, synthesis, and evaluation of evidence for *Monographs*. The evaluations are finalized during a meeting of approximately 8 days, whose objectives are peer review and consensus.
- 6 IARC publishes the names and affiliations of all meeting participants two months before each meeting. During the meeting, four subgroups (related to exposure characterization, cancer in humans, cancer in experimental animals, and mechanistic evidence) review pre-meeting drafts, and develop consensus subgroup drafts and summaries. The Working Group then meets in plenary session to review the subgroup drafts and develop a consensus evaluation. In all, the process for developing *Monographs* extends over a two-year period (from announcement of topics on the *Monographs* website to publication of the full-text *Monographs*), during which IARC engages with the public in the interest of transparency.

17. The amended Preamble increased the emphasis on mechanistic evidence, on the critical evaluation of epidemiological studies including of the exposure assessment methods, and on the strengthening of the systematic review methodology.

7 The *IARC Monographs* have enhanced methods for timely dissemination of the results of the evaluation meetings. Shortly after each meeting, an open access scientific summary of the results will be published in *The Lancet Oncology* and translated into French.

The resulting *Monographs* will be published within a year of the meeting in electronic form and will also be made available in printed books. Electronic copies can be obtained at no cost from the *Monographs* website or as e-books on the United States National Library of Medicine Bookshelf. In addition, all evaluation results are available online, as an embedded [spreadsheet](#), as well as in a [list of classifications by cancer site](#) (also available in [French](#)). The dissemination of *Monographs* evaluations will be further enhanced with the development of a user-friendly and searchable Internet database of *Monographs* results. Together with the stronger focus on online publication and e-books, and coupled with new print-on-demand options, the print run will be further reduced. In collaboration with national and international public health institutions, efficient means of translation into other major languages will be made available.

To further increase transparency and efficiency in the *Monographs*, new tools will be implemented and existing tools for systematic review will be refined, standardizing literature searches, and creating databases of information on study designs and results, as well as for communicating these search methods transparently to *Monographs* readers.

8 Building on [IARC Scientific Publication No. 165](#), global experts will be engaged in future international consensus workshops to refine these methods, and develop a database of end-points and assays to measure the key characteristics of carcinogens in epidemiological as well as experimental studies. Liaising with the occupational and environmental epidemiology communities will enable discussions on how study design and end-point measurement can influence the utility of studies of exposed humans in mechanistic evidence synthesis. These efforts will aid interpretation and evaluation of mechanistic data in forthcoming *Monographs* evaluations.

To stay at the forefront in identification of cancer hazards, additional scientific workshops will be organized on topics related to cancer hazard identification and communication (e.g. best practices for cancer hazard communication; methods for bias impact assessment in systematic reviews of epidemiological studies).

The *Monographs* summarize data that are key to informing prevention-focused policies and research needs, such as on global exposure prevalence and levels. Some of IARC's important collaborative projects involving the *Monographs* include the European Code Against Cancer, the French burden of cancer project, and analytical epidemiology research projects (e.g. the International Nuclear Workers Study, INWORKS).

Expected outcomes

The successful delivery of these outcomes will depend on the acquisition of the necessary external funding.

- In 2021–2025, two to three *Monographs* meetings per year will be held on agents accorded high, medium, or low priority by an independent Advisory Group convened in 2019 to recommend priorities for the *IARC Monographs* programme during 2020–2024 (see https://monographs.iarc.fr/wp-content/uploads/2019/10/IARCMonographs-AGReport-Priorities_2020-2024.pdf).

- Agents publicly announced for evaluation in 2021 include the dyes gentian violet and its metabolite leucogentian violet, malachite green and its metabolite leucomalachite green, and C.I. Direct Blue 218, which will be evaluated in Meeting 129. Other high-priority agents that may be evaluated during the next five years include endocrine-disrupting chemicals, particles and fibres, and complex exposures such as firefighting. As noted above, topics are publicly announced approximately one year in advance on the *Monographs* website.
- In 2021, publication of *Monographs* volumes 126 (Opium Consumption), 127 (Some Aromatic Amines and Related Compounds), and 128 (Acrolein, Crotonaldehyde, and Arecoline) is foreseen, within one year of the respective meetings. In 2022, volumes 129 and 130 will be published, and in subsequent years, the volumes corresponding to meetings held in the previous year.
- Organization of scientific workshops and other collaborations on topics related to cancer hazard identification, and presentation of the findings in scientific journals or IARC publications: in 2021, a workshop on “Key Characteristics of Carcinogens”, and in 2022, a workshop on “Tools for Bias Impact Assessment in Epidemiological Studies used in Cancer Hazard Identification”.

IARC Handbooks of Cancer Prevention Programme

The mission of IARC is the global control of cancer through primary or secondary prevention. Prevention is the most effective response to the rising burden of cancer, particularly in LMICs, where health services are least able to meet the impending challenge.

Important steps in cancer prevention are the identification of the causes of human cancer and the assessment of what works for cancer prevention. The *IARC Handbooks of Cancer Prevention* provide reliable information about which interventions can prevent cancer or detect cancer at an early stage, reduce the cancer burden worldwide, and save lives.

National and international health agencies use the *IARC Handbooks* to plan interventions aimed at cancer prevention. In this way, the *IARC Handbooks of Cancer Prevention* contribute to reducing the cancer burden worldwide.

Specific aims

- To critically review and evaluate the published scientific evidence on the effectiveness of interventions and strategies in preventing cancer, which could be used in cancer control.

Major approaches/areas of activity in the next five years

- 1** The *IARC Handbooks of Cancer Prevention* follow a rigorous review and evaluation process, established in the recently updated Preamble, which describes the general principles and procedures for the development of an IARC Handbook.
- 2** The *Handbooks* follow the principles of a systematic review: development of an analytical framework, development of review questions, systematic literature search with well-defined search strings, selection of studies according to pre-set criteria, assessment of study quality, assessment of the body of evidence, and expert evaluation.
- 3** The review and evaluation are performed by a Working Group comprising international experts, who are selected based on their knowledge and expertise in the field, and geographical and gender balance. The Working Group ensures the completeness of the body of evidence, summarizes the studies, reviews and evaluates each stream of evidence, and formulates the final evaluation.

Expected outcomes

The successful delivery of these outcomes will depend on the acquisition of the necessary external funding.

- A series of *IARC Handbooks of Cancer Prevention* will be produced. This includes: publication of one *Handbooks* volume every 15–18 months; publication of a short summary of the evaluations in a peer-reviewed journal (e.g. the *New England Journal of Medicine*); dissemination of outcomes through various social media; a dedicated website; and all volumes made freely available in PDF format.
- IARC will evaluate relevant evidence and publish a *Handbook* on oral cancer prevention, with a particular focus on populations in South Asia, where oral cancer is a major public health concern.
- Topics for evaluation of interventions for primary prevention include re-evaluations of aspirin (Vol. 1) and of sunscreens (Vol. 5); potential topics for first-time evaluations include vitamin D and vitamin B. For secondary prevention (screening), first-time evaluations of screening for cancers of the prostate and the lung are potential future topics.

Learning and Capacity-Building (LCB) Branch

IARC's capacity-building activities have made a substantial contribution to the development of human resources for cancer research in many countries. The two main areas of activity are capacity-building through:

- fellowships and through young scientists' participation in collaborative research projects;
- the provision of training courses, increasingly through remote and e-learning means.

Learning and capacity-building activities are expected to continue to inspire and shape IARC's research portfolio, to further broaden the Agency's network of collaborators, and to promote IARC as an international cancer research organization.

Specific aims

- To strengthen global knowledge as well as global and national capacities for cancer research and science,
- To strengthen professional skills of cancer scientists and researchers in: surveillance of cancer, understanding of the evidence of causes, interpreting evidence with regard to national settings, and the design and implementation of effective, quality-assured, and affordable interventions.

Major approaches/areas of activity in the next five years

1 Provision of mentored training to researchers at different levels of their career, through collaborative research projects, exposure to field studies, and laboratory work – IARC Research Training and Fellowship Programme

Beneficiaries of the IARC Research Training and Fellowship Programme, collectively referred to as Early Career and Visiting Scientists (ECVS), are financially supported either by IARC Fellowships or through project funds from relevant scientific units at IARC. IARC Postdoctoral Fellowships will be maintained, with a stronger focus on candidates from LMICs.

Funding sources will be identified and partnerships set up to complement the Regular Budget funding. The aim is to maximize the number of fellowships that can be offered, seeking to award up to 10 two-year IARC Postdoctoral Fellowships per year to early career scientists.

Complementary models of postdoctoral fellowships will be explored, such as bilateral “sandwich” fellowships, with alternating stays at national/home institutes and IARC. Shorter fellowships of 1–3 months’ duration will be maintained for selected fellows, subsequent to their participation in the IARC Summer School. It is foreseen to convert IARC’s Senior Visiting Scientist Award into several shorter Visiting Scientists Awards targeting mid-career scientists from LMICs and/or Participating States.

All ECVS benefiting from the IARC Research Training and Fellowship Programme will be administratively managed and accompanied in close collaboration with IARC’s scientific “host” entities; this involves about 100 new ECVS per year and involves: training contracts, visa/residence permit, travel, health insurance, day-to-day liaison, and support. Additional activities supporting career growth of ECVS, such as the IARC mentoring programme, will be launched. Ongoing successful initiatives will be continued, such as courses on career management for scientists.

With the aims of (a) strengthening IARC’s recognition as a unique and renowned host institute for PhD students and (b) facilitating the placement of ECVS at IARC, the interaction with relevant universities and research institutions will be intensified.

2 Supporting the lifelong learning of researchers and health professionals – IARC Courses Programme

IARC will further contribute to lifelong learning of researchers and health professionals through the delivery of learning content/events on priority areas of the Agency, such as cancer surveillance, early detection of cancer, economic and societal impacts of cancer, implementation research, or cancer epidemiology.

The IARC Learning Portal – launched in 2019 – will be further developed as a freely accessible single entry point to IARC learning and training resources and opportunities (e.g. webinar recordings, learning modules, infographics, interviews, case studies, upcoming courses and webinars), including e-learning material and courses. Content will be developed in English and other languages and made available through the IARC Learning Portal and its topical platforms (e.g. *World Cancer Report Updates*).

Most courses will be provided as (i) blended online/on-site courses, with in-person sessions dedicated to highly interactive, technical, and/or networking learning activities, or (ii) fully online events, through web conferencing and training tools.

The IARC Summer School consists of a series of training modules, including on cancer registration, on descriptive and analytical epidemiology, and on implementing cancer prevention and early detection strategies. Participants can take combinations of modules. The IARC Summer School in 2023, marking the move of IARC to the Nouveau Centre, will be designed as a blended event. In addition, lecture sessions will be broadcast on the web to allow a maximum number of researchers and health professionals to attend.

3 Coordination of IARC training in scientific units

While overseeing the portfolio of IARC Learning and Capacity-Building, training courses initiated by the scientific units will be monitored and documented; if needed, support for the design, development, organization, and/or evaluation of relevant courses/material may be available. Joint funding proposals will be developed with relevant scientific units. In addition, IARC will lead the education and dissemination work package for the Human Exposome Assessment Platform (funded by the European Union until 2024).

Partnerships will be developed for the production of learning material and the organization of training events, mostly with institutions from Participating States, LMICs, as well as UN agencies. For example, the IARC-led Comprehensive Learning Programme on Screening, Diagnosis, and Management of Cervical Precancer was selected as among the first 20 course proposals to be developed and become part of the WHO Academy's initial course offerings. Other partnerships, such as through the LMICs Biobank and Cohort Building Network (BCNet), will allow the development and/or strengthening of research infrastructure.

Expected outcomes

The successful delivery of these outcomes will depend on the acquisition of the necessary external funding.

- By 2025, 500 additional PhD students and early career scientists will have been trained at IARC's scientific units, most of them from Participating States and LMICs.
- Currently, six to seven Postdoctoral Fellowships are awarded per biennium. By 2025, sustained fundraising and partnership efforts are expected to allow the resumption of annual calls and the awarding of up to 10 Postdoctoral Fellowships per year to early career scientists from LMICs.
- The IARC Learning Portal will have developed into a key resource for research in cancer prevention, in particular through the intensive use of the *World Cancer Report Updates* learning platform, launched in November 2020, and the IARC Summer School, redesigned from 2021 onwards.
- By 2025, more than 3000 cancer researchers and health professionals, the majority from LMICs, will have been trained through relevant IARC capacity-building mechanisms and, as a result, will have become competent in IARC's areas of expertise.

Annex 2: The IARC Project Tree

Level 1 Objective: To reduce the burden of and suffering from cancer – today and among future generations		Contribution to fundamental (F) and emerging ¹⁸ (E) priorities			
Level 2 Objective	Level 3 Objective	F	E1	E2	E3
1. Describing the occurrence of cancer	1.1 Improve and expand reporting of cancer data and statistics to inform global, regional, and national priorities for cancer prevention and cancer control	X	X	X	X
	1.2 Improve coverage, quality, and utility of cancer registration data worldwide, with an emphasis on low- and middle-income countries (LMICs)	X		X	
	1.3 Enhance understanding of global, regional, national, and subnational changes in cancer risk, including in relation to ongoing socioeconomic transitions and social inequalities	X	X	X	X
	1.4 Enhance understanding of economic consequences of cancer and cancer disparities – descriptive economics	X			X
2. Understanding the causes of cancer	2.1 Enhance understanding of new and known causes/risk factors for human cancer, including those that accompany key cancer transitions, and those related to cancer disparities, through the conduct of epidemiological studies	X	X	X	X
	2.2 Enhance understanding of and elucidate biological mechanisms of carcinogenesis relevant to environmental/lifestyle factors, including those that accompany key cancer transitions, and those related to cancer disparities, through the conduct of laboratory studies	X	X		X
	2.3 Enhance understanding of exposure sources, including those related to key cancer transitions, and those related to cancer disparities, and related pathways	X	X		X
	2.4 Enhance understanding of potential risk factors, including those that accompany key cancer transitions, and those related to cancer disparities, in underresearched populations and/or in LMICs and their interplay with the observed cancer patterns	X	X		X
3. Evaluating cancer prevention interventions	3.1 Enhance understanding of evidence-based interventions for cancer prevention and control to support their practical application, including those related to cancer disparities	X		X	X
	3.2 Enhance understanding of the efficacy and effectiveness of population-based interventions and cancer prevention programmes			X	
	3.3 Enhance understanding about the development and application of biomarkers for early detection and outcome through translational studies	X			
4. Synthesizing and mobilizing knowledge and strengthening global capacities in cancer science	4.1 Strengthen global knowledge and global and national capacities in cancer research and science	X			
	4.2 Strengthen the understanding and use of tumour classification to underpin cancer diagnosis, management, and research	X			
	4.3 Strengthen global knowledge and global and national capacities to implement effective, quality-assured, affordable interventions	X			
	4.4 Enhance understanding of the causes of human cancer, including emerging cancer hazards, through cancer hazard evaluations of the available evidence base by leading independent experts	X			
5. Strengthening the Agency's leadership, governance, strategic engagement, and advocacy	5.1 Define the vision and implement the scientific strategy of the Agency, enabling an empowering culture, providing the framework for the fulfilment of its objectives	X			
	5.2 Oversee the strategic direction of the Agency and the implementation of its programme with full respect of the Agency's values, ethical standards, and code of conduct	X			
	5.3 Create and maintain key strategic engagement with stakeholders at national, regional, and international organizations, and scale up resource mobilization activities	X			
	5.4 Strengthen the Agency's global image, communication and outreach to stakeholders	X			
6. Strengthening the efficiency and effectiveness of the Agency's research and collaboration	6.1 Ensure the availability of adequate laboratory and computing/statistical infrastructure to support and enhance research	X			
	6.2 Enable strategic vision and implementation, including management of financial, human, information, and infrastructure resources, to enable and support the effective delivery of the Agency's mandate	X			