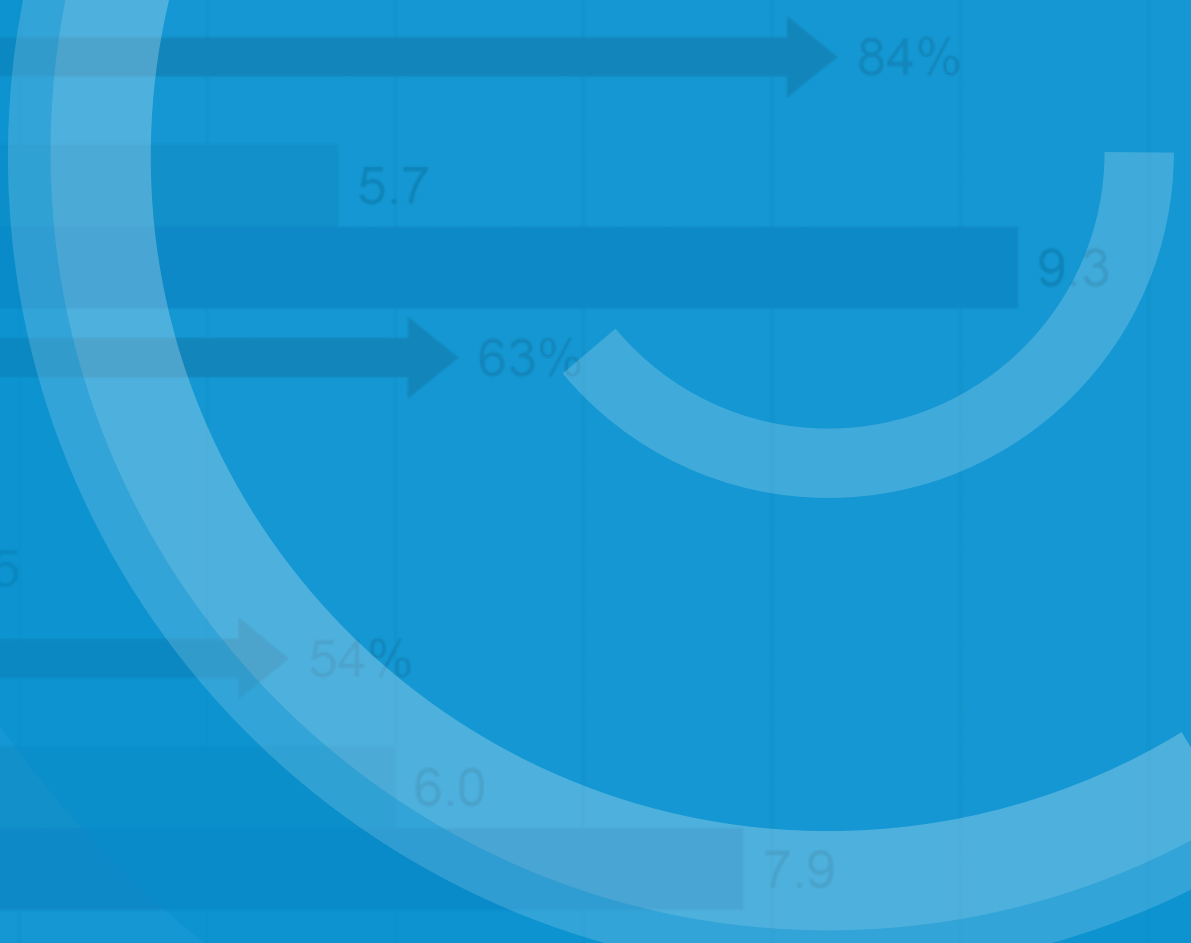


increase 2015-2035

40 50 60 70 80 90 100

IARC: THE SECOND 50 YEARS



4 5 6 7 8 9 10

IARC: THE SECOND 50 YEARS

*Advances will be accelerated by “collective intelligence”.
I not only use all of the brains I have, but all I can borrow.*
– Woodrow Wilson

BIG IDEAS AND SMALL BEGINNINGS

IARC was born of a big idea: to redirect some of the vast sums of money that countries were investing in their military might, and to use these funds not to fight each other but to fight together against a common enemy: cancer. Cooperation, not conflict.

The protagonists set a challenge. Take a tiny fraction of the money spent on defence, just 0.5%, from the greatest military powers on both sides of the Second World War, and see what good could be achieved – leaving 99.5% of the resources intact and the balance of military might unaltered. If the impact of this symbolic shift could be visualized in terms of reduced human suffering, then perhaps questions would be asked about what other benefits might be reaped from further redistribution of resources. There was certainly more than a whiff of twin objectives in the air, given the involvement in nuclear disarmament of several of those promoting the project. Nevertheless, the starting point was the singular experience of human suffering by Yves Poggioli's wife as a result of her cancer. Poggioli urged Emmanuel d'Astier de La Vigerie to use his influence to fight this disease, rather than using it only to fight for peace.

Of course, the dreamed-of financial model for IARC was never realized. The levy of 0.5% on defence budgets would have yielded an annual sum of US\$ 396 million, equivalent in 2014 to about US\$ 3 billion. For comparison, in 2014 the budget of the United States National Cancer Institute was US\$ 5.1 billion, that of the German Cancer Research Center was about US\$ 240 million, and IARC received US\$ 24 million. For Poggioli, the comparatively tiny 1965 budget for IARC, of less than US\$ 1 million, was a betrayal of the original vision. There is no record of whether d'Astier shared Poggioli's disappointment, but the constant arguments of the French delegates for higher financial contributions indicate their undimmed enthusiasm for an organization big enough to make a difference. The tenacity with which Eugène Aujaleu applied himself up to and beyond the crucial resolution at the World Health Assembly in 1965 implies a pragmatic acceptance that the most important point was to see the Agency created. This was accompanied by a belief that money would follow as other countries shared the vision and joined forces as Participating States.

One can argue that the outcome in 1965 was not a bad one. IARC was a new creation. It had no staff, no building, and no scientific programme. It was required to write its own history. A new agency born into an inheritance of several hundred million dollars annually would have faced unprecedented expectation and perhaps aroused not a little envy from the cancer research community. Without doubt it would have

been a very different organization. One can conjecture that, unable to spend such a budget on its own research, the Agency would have taken on a much greater role as a funder of existing national research institutes and projects, rather than serving as a nucleus and catalyst for international cooperation.

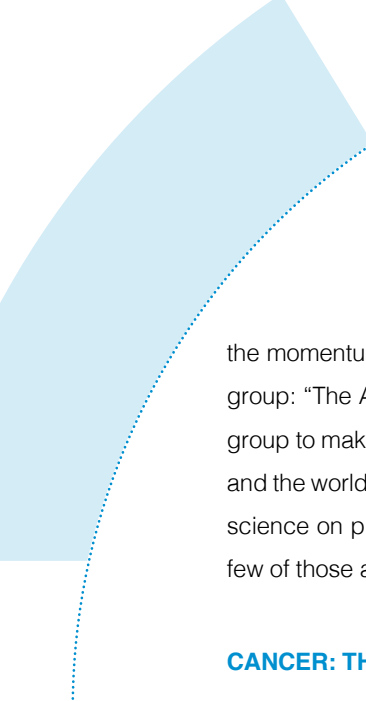
As it was, IARC was allowed a childhood. The newly recruited scientists had time and freedom to decide where they could make the biggest difference. Notably, from the outset, the international cancer research community expressed enormous goodwill and respect towards this new agency. In turn, IARC started to establish its collaborations, working on projects that were local or regional in conduct but global in significance. Research projects were accompanied by training for national scientists – often their first opportunity to become familiar with epidemiological and other research methods. This engagement emphasized a partnership of equals, built on reciprocal benefits and trust. To conduct its work, IARC relied not on gigantic wealth but on a giant wave of cooperation.

It also became evident that the collaborative model, adopted both by design and of necessity, catalysed research far in excess of what could be achieved by IARC's budget alone. In effect, the in-kind contributions through the participation of scientists in joint research with IARC led to activities immeasurably greater than the investment made; this is still the case today, when this model is further amplified by grant funding won jointly by IARC and its partners. In addition, it was evident that a little money could go a long way in the developing countries. IARC Regional Centres, for example, were sustained by just US\$ 5000 per annum, and many an IARC-initiated project has sprung to life with smaller sums than this.

Thus, although the financial model of a 0.5% levy never materialized, its absence perhaps helped ensure that the second component of the big idea – a spirit of cooperation, a fight against a common enemy – was realized, and flourished. There was strength in partnership.

IARC's status as part of the World Health Organization (WHO) was no doubt part of the attraction for its new collaborators. Increasingly, however, this feature was bolstered by recognition that IARC was being shaped by some of the leading lights in cancer research in the late 1960s. Excellent scientists with an exciting vision started to draw together others of like mind from across the world, and

“
Equal credit and more goes to our colleagues in the countries because they have been working in the field. It is very gratifying to work in this large network and to know these people who, working under difficult circumstances, helped us.
– Rengaswamy Sankaranarayanan, IARC scientist



the momentum built. Nick Day, who joined IARC in late 1969, recalls the excitement among that pioneering group: “The Agency was only just beginning to get up steam, and I think we all felt that it was up to us as a group to make a success of this imaginative new venture. With the range of scientific disciplines represented and the worldwide contacts the Agency could call on, we felt we could make a difference by focusing modern science on problems of totally absorbing interest.” The short history contained in this book has illustrated a few of those areas where IARC has done just that over the first five decades of its existence.

CANCER: THE RIGHT PLACE AT THE RIGHT TIME

IARC has evolved markedly over 50 years to fulfil its mission to reduce the burden of cancer worldwide. Knowledge about the patterns of the disease, its causes, and its underlying biology, as well as advances in scientific methodology and technology and changes in the scale and make-up of the cancer research community have all shaped IARC’s progression. In contrast to these changes in activity, key principles continue to underpin the unique contribution of the Agency to international cancer research. Principled adaptability is the basis for a successful future.

The landscape of human disease is changing. IARC was born into a world where unique and extraordinary cancer patterns were found in developing countries, and much was learned about the causes of cancer from investigating these patterns. Nevertheless, at that time the major cause of premature death in these

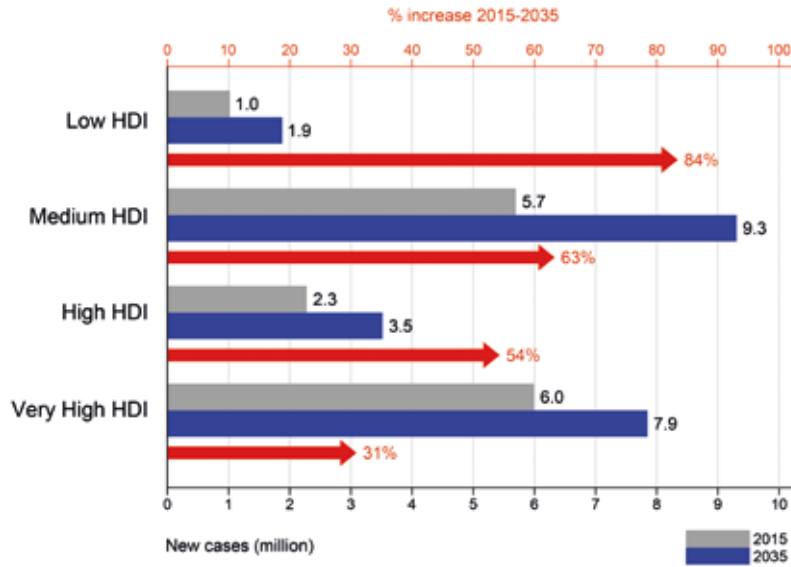
Principled adaptability is the basis for a successful future.

countries was not cancer but infectious diseases, malnutrition, maternal and infant mortality, and other consequences of poverty. All too often the research findings from developing countries only found their practical application in terms of cancer prevention in developed countries; an example is the slow uptake of hepatitis B virus vaccine in the regions where infection with this virus is endemic. However, the beginning of the 21st

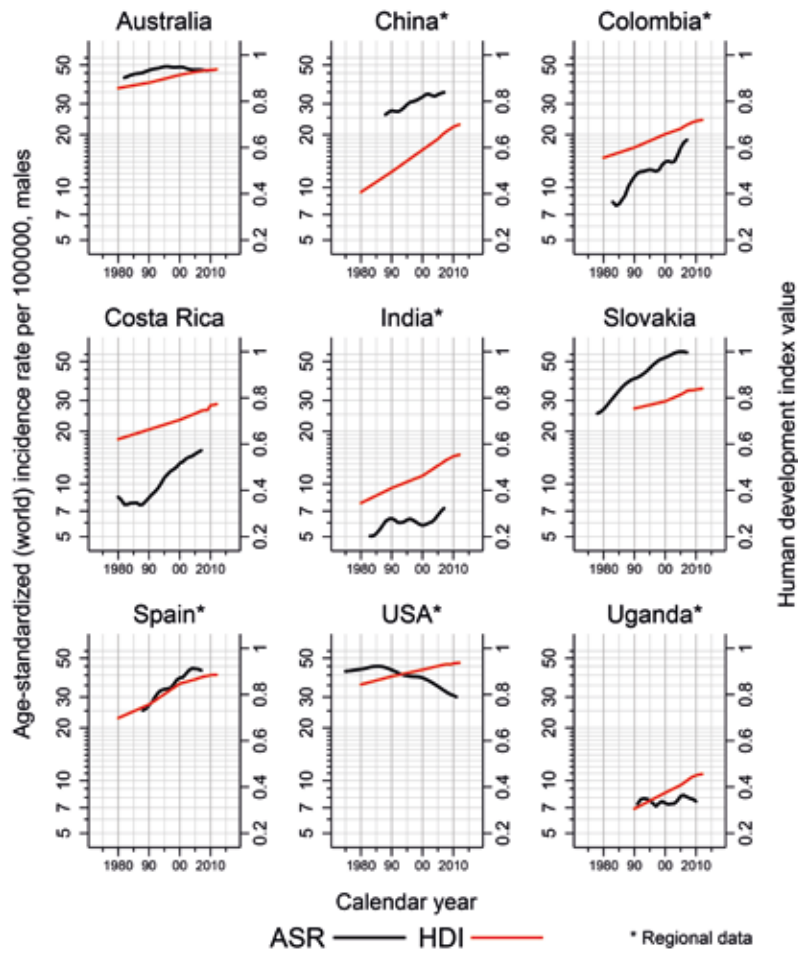
century is witness to a transition in developing countries, driven by population growth and ageing overlaid with evolving risk factor profiles, which are combining to cause rapid rises in the burden of noncommunicable diseases, including cancer.

Politicians are catching up with these trends in disease. Through the leadership of WHO and its partners, noncommunicable diseases are increasingly recognized by governments of low- and middle-income countries as a leading burden on health and the economy, presenting a barrier to sustainable human development. While this realization has not yet translated into a significant shift in health development assistance being directed to these chronic conditions, it surely will as the donors join the scientists and politicians in recognizing the transition.

These changes are significant for IARC: research results are less and less likely to be obtained in developing countries only to find application in developed countries. Increasingly, scientists and



The estimated number of new cancer cases according to four levels of the Human Development Index (HDI): global projections for 2015 and 2035, assuming that rates remain constant, and the percentage increase over the 20-year period.



Trends in age-standardized (world) incidence rates (ASR) of colorectal cancer in men in 1978–2010 and in the Human Development Index (HDI) in 1980–2012 in selected countries.

health ministries in low- and middle-income countries will propose research directly relevant to cancer control in their own countries or regions. At the same time, scientific evidence for cancer control can be transferred from high-income countries to low- and middle-income countries, and vice versa, as countries face related challenges. In this context the collaborative model of the Agency is ideal, allowing IARC the freedom to conduct research wherever important questions can be best addressed and to make that information available to the widest audience possible.

Furthermore, among the noncommunicable diseases, cancer presents a particularly complex case in its diverse patterns, etiology, and underlying biology. It is fortunate, therefore, that there is a specialized cancer agency within WHO. IARC is ideally placed to assume a leadership role in shaping the cancer research agenda and providing the evidence base for cancer control in the decades ahead. However, such a response will require innovative approaches and new resources if the potential to make a difference is to be fully realized.

This future opportunity for IARC has arisen neither by chance nor by good luck. Rather, it is based on a relevant mission and vision, a strong research programme, and a 50-year track record of high-quality research conducted through partnership with colleagues throughout the world. Mutual trust and respect in time bear their fruit.



My best memory is of working with a group of very good scientists who were also very good people. For a young scientist to be able to work in that environment and gain from that experience was fantastic.

– Manolis Kogevinas, former IARC scientist

PREVENTION: THE RIGHT TOPIC AT THE RIGHT TIME

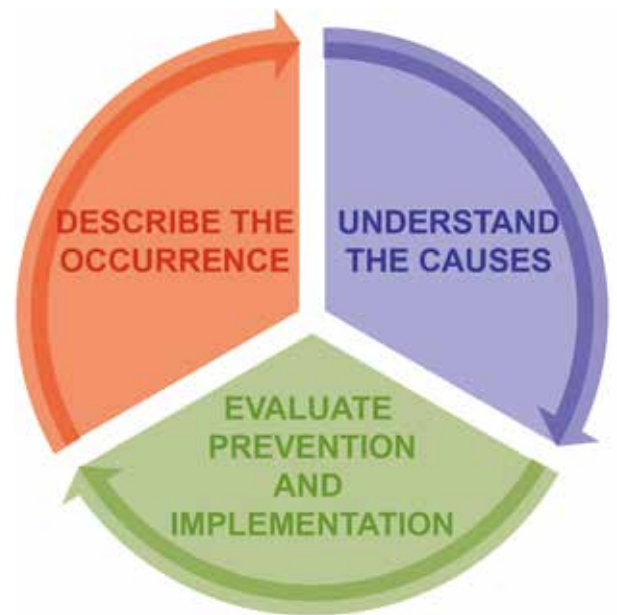
Cancer research is a broad endeavour, and IARC has to decide on priorities. The result is a concentration on “cancer research for cancer prevention”. Such research is essential but has been chronically under-resourced. For example, in 2014 Cancer Australia reported that in Australia, Canada, and the United Kingdom, only 2–3% of cancer research funding was assigned to prevention, with perhaps 10% to studies of etiology. This is despite the fact that the rapidly increasing burden of cancer and the spiralling costs of treatment and care mean that no country can treat its way out of the cancer problem.

The priority given in the high-income countries to investment in research into new therapies is driven by a complex mix of philosophy, emotion, advocacy, economics, and politics, far beyond the scope of this book. Over time, however, the contrast between the cost-effectiveness of treatment and that of prevention and early detection will be writ too large for policy-makers to ignore. At that point, a better balance across the

cancer research spectrum will be struck, at least for investment of public resources. The understandable desire to do better for patients will have to be complemented by efforts to avoid the development of cancer in the first place. The universal appreciation of this wisdom was represented in IARC's *World Cancer Report 2014* by a proverb from the Kalenjin tribe in Kenya: "It is better to put out the fire while it is still small." This provides an idiom for cancer prevention.

Prevention means different things to different people. For IARC, the emphasis is on describing the burden, understanding the causes, and evaluating interventions and their implementation. In turn, this cycle is completed by a visible reduction in burden, ultimately measured in cancer registries. This focus is best served by an interdisciplinary approach: from one end, bringing to bear the knowledge and technology derived from laboratory-based advances in understanding cancer biology, and from the other, the disciplines of behavioural and social sciences addressing important cancer risk factors operating all the way through from individuals to communities or whole societies. IARC will pursue its integration of the full spectrum of disciplines, drawing as it always has on the specialized expertise of national scientists through collaborative partnerships.

The past decade has seen a determined search for the causes of cancer in the molecular details of genetic variation between individuals in ever-bigger genome-wide association studies. One goal was to identify genetically susceptible subgroups of people and tailor preventive interventions, in an analogous fashion to the clinical treatments targeted to a genetically susceptible subgroup of tumours. However, cancer does not result from a simple individual attribute, genetic or otherwise. There is a need to come to a fresh understanding of health being affected by numerous complex individual characteristics and the wider societal context, requiring epidemiological studies that embrace the social determinants of cancer in a broad sense. An overarching factor will be the impact of climate change on health, something for which the scale and nature cannot be predicted at present. Each of these considerations will need to embrace the effects of exposures experienced at different stages of life, with the attendant clues as to critical windows for effective timing of interventions.



Cancer prevention is addressed by the Agency in three major areas of activity, as illustrated in this diagram.

Cancer prevention will one day become a fundamental question, and one with which IARC will be able to help France, which is lagging behind in that area.

– Thierry Philip, long-term IARC collaborator

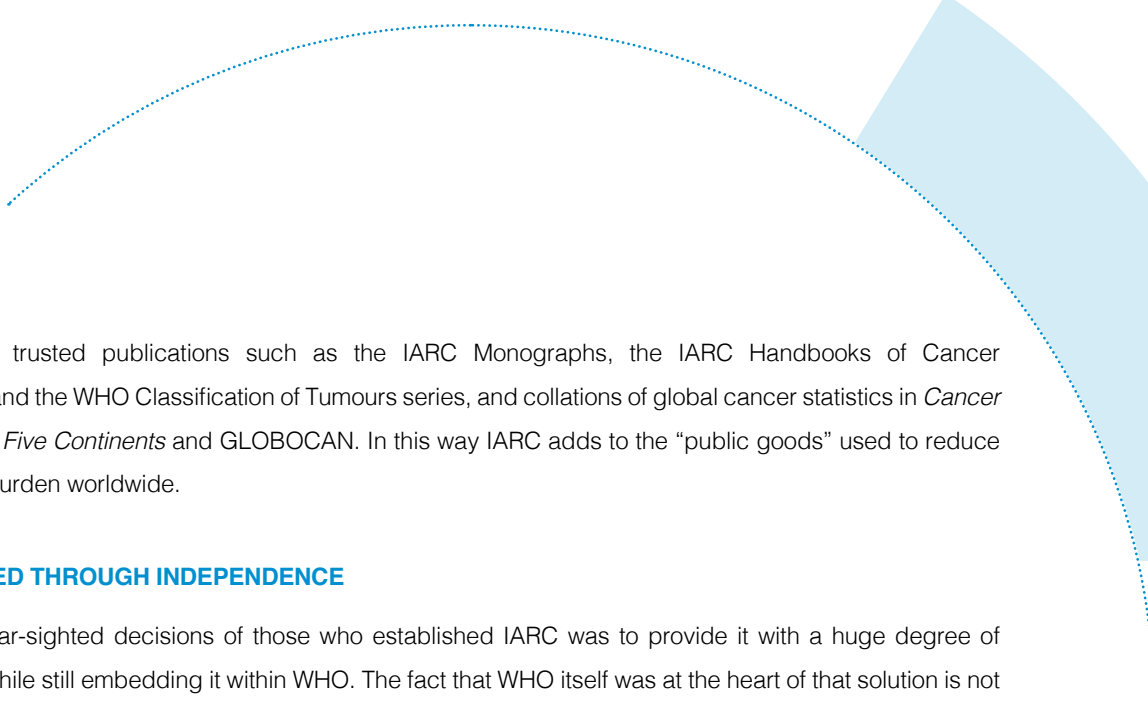


IARC is conducting research with the government of Thailand to evaluate how best to implement a colorectal cancer screening programme and to enable effective scaling up of the programme across the country (see the chapter “Cancer screening and early diagnosis”). Shown here are some of the educational materials used to inform the population about the programme, as well as the tests used to detect blood in the faeces.

Notwithstanding the progress that has been made in cancer prevention to date, there remains a gap between the demonstrated efficacy of an intervention within the confines of an experimental trial and the effectiveness once that intervention is implemented at the health services level. There is a stark need to study the factors that either enable or block successful implementation. Such elements will likely differ between and within societies in relation to the widening inequities due to free-market economics. Implementation research is therefore an important but understudied area, and one that IARC is well placed to address, not only through its expertise but also through the opportunities that its international status brings to work with scientists and governments in evaluating and improving national programmes. Undoubtedly this research, with direct relevance to public health, will feature greatly in the future of the Agency.

Research will be further oriented to inform policy in moving to the next phase of the life of the Agency, but this eye towards application must never compromise scientific quality. Accurate data on the occurrence of cancer, on risk factors, and on preventive interventions all provide a portion of the evidence base for informed cancer control measures, but only if the data are reliable. For this to be the case, the research must make use of cutting-edge methods and knowledge. Therefore, IARC will continue not only to contribute original research findings but also to provide its authoritative stamp to collections of

“
The Monographs Programme is a reference: governments worldwide use these books and their assessments for setting policy in cancer control.
 – David Zaridze, former IARC scientist




evidence in trusted publications such as the IARC Monographs, the IARC Handbooks of Cancer Prevention, and the WHO Classification of Tumours series, and collations of global cancer statistics in *Cancer Incidence in Five Continents* and GLOBOCAN. In this way IARC adds to the “public goods” used to reduce the cancer burden worldwide.

EMPOWERED THROUGH INDEPENDENCE


One of the far-sighted decisions of those who established IARC was to provide it with a huge degree of autonomy, while still embedding it within WHO. The fact that WHO itself was at the heart of that solution is not without significance. As John Higginson put it in 1971, IARC was “established within the framework of WHO, but empowered to develop its own research programmes.” It is a model that works well, akin to the healthy separation of powers, well established in political philosophy and practice.

The governance structure of IARC has allowed it to conduct its research free of political pressures. This independence also helps countries in the face of internal pressures, because the scientific conclusions from IARC are accepted as free from national interests. On occasion IARC’s voice will be heard where national scientific authorities may be censured to one degree or another. Second-hand tobacco smoke, diesel exhaust, mobile phones, shiftwork, nuclear radiation, and breast cancer screening are just some of the topics in recent years where the Agency has been able to consider the science free from outside influence. The IARC Governing Council deserves immense credit for maintaining this freedom and independence, which have underpinned the authority of the Agency’s work. Looking to the future, the constant vigilance on issues of conflict of interest must be maintained, just as much as the scientific vision and research programmes.

The quality, integrity, and independence of IARC are valued, but they increasingly stand out as exceptional. Therefore, these values should not be taken for granted. IARC works amid a maelstrom of lobbying, advocacy, and vested interests, often indirect and difficult to uncover. The push from many governments of developed countries during the past two decades to see academic researchers partner with the private sector has undoubtedly blurred the lines between the two domains. While bringing benefits in translating science into technology and economic growth, the reliance of researchers on private-sector funding erodes independence. This is problematic when independent evidence is needed. For example, if most research into nutrition and cancer were to be funded by the food industry, then maintaining freedom from real or perceived conflicts of interest would be fraught with difficulty.



“ IARC is quite different from the other entities in WHO, and it was refreshing to come to work here as the Agency is really oriented towards research.
– Keiji Saita, former Director of Administration and Finance at IARC



IARC will continue to guard its independence from vested interests, and must welcome outside scrutiny as a further check on adherence to its own values. A reputation is easily lost and is regained with difficulty. However, in keeping a distance from the private sector, IARC faces a challenge to fund its work, especially as countries tend to reduce in real terms their budget support to international organizations. Recent years have seen a split of about two thirds of IARC's overall expenditure from contributions by Participating States and one third from extrabudgetary sources, mainly from competitive grants and always in line with the approved IARC strategy. This balance would appear an important one to maintain. Donors and foundations offer an alternative to contributions from Participating States but have their own agendas, and the attendant risk of mission creep must be monitored. Therefore, the restriction on private-sector involvement goes hand in hand with the need to maintain an adequate regular budget from IARC Participating States. The original vision for IARC of a core regular budget supplemented by voluntary contributions from Participating States to support specific projects must be revisited as the economic recession of the past seven years lifts.

The possibility of linking the cancer agenda into the challenge of sustainable human development goals offers a creative way forward in relation to development assistance funding. The recognition of this link between cancer and human development also highlights again the link between cancer and the broader societal context in terms of the social determinants of the disease. In addition, as the cancer transition occurs, so too must a transition in the make-up of the governing body of the Agency, with more Participating States from the southern hemisphere stepping forward to add their insights, expertise, and financial contribution to this global cancer research effort.

ANOTHER WAY TO BE

IARC is a research agency, focused on cancer. It is founded on science. However, its modus operandi, in pursuing cooperation that cuts across human and infrastructure barriers, surely provides a beacon pointing to a different way of being in the 21st century, at a time when fractures within and across societies are all too evident. Under the one roof in Lyon, at any one time there are people of about 50 different nationalities and countless cultures working together in an atmosphere of friendship and towards common goals. This energy is fed by the constant stream of early career scientists arriving with their motivation and ambitions to make a positive contribution. The atmosphere is further magnified by the wider IARC "family" of collaborators from every part of the world. It is this spirit of cooperation that can carry the day even in the face of sensitive subjects. Certainly misunderstandings and disagreements arise in such settings, but the shared experience of meeting with like minds to address a humanitarian cause proves again and again to have the power to surmount differences.

An example of this theory in practice was evident at a meeting convened by IARC in 2013 that addressed the above-ground nuclear testing by the Soviet Union from 1949 to 1962 at Semipalatinsk in Kazakhstan and

the consequent exposure to radiation. Around the table were scientists from Germany, Japan, Kazakhstan, Norway, the United Kingdom, and the USA, trying to bring the best science to bear on a project that may provide important insights on low-dose radiation but that also touches on a difficult period in history. There are few organizations other than IARC that could have brought such a meeting together and created the space for fruitful scientific collaboration. In some ways this and other IARC-coordinated studies of

nuclear exposures – around the Techa River, after the accidents of Chernobyl and Fukushima, as well as international studies of nuclear industry workers – bring us full circle to the twin concerns of those early proponents of a new cancer agency: nuclear power and cancer. It is perhaps timely to revisit the moral arguments still to be made in favour of the redistribution of public expenditure from defence to health. Certainly one senses a degree of passivity and resignation in the face of constant demands for proof of cost-effectiveness of health care interventions, whereas such scrutiny seems remarkably absent from interventions of a military nature. This is not a position that the wider health care community should leave unchallenged.

In conclusion, one might well point to IARC as something more than a cancer research agency; it is a model where suspicion and self-interest are overcome by openness and cooperation, where national priorities are subsumed for the wider good. It is impossible, and probably undesirable, to try and measure the impact of such a positive experience on those passing through the Agency, and it will certainly never be the reason why IARC is funded. But it is nonetheless a benefit that comes from the “IARC way” of doing research, and one not without value in its own right. It is an example of what can be.

General Charles de Gaulle, in his first references to the new cancer agency, pointed to three features he hoped it would embody: cooperation between peoples, improvement of the human condition, and advancement of science. Although this is a statement drawn from an era that was quite different, one cannot but concur with the aspirations expressed. Let each of those who have responsibility for the future of the International Agency for Research on Cancer, an international inheritance, be guided by this vision.



At the IARC Staff Day in 2010, people joined together to represent the activities and values of the Agency in a painting.