

# SUCCESS IN FIGHTING THE TOUGHEST CANCERS DEMANDS INNOVATION

Over the last half-century, cancer survival rates have increased. But for the toughest cancers today, successful treatment remains elusive. The toughest cancers have seen minimal therapeutic advances, limited improvement in prognosis, and pose the most difficult challenges for patients and clinicians.<sup>1</sup> Researchers at Amgen are invested in gaining a better understanding of the underlying characteristics of tumor cells that historically have been difficult to treat. These efforts have inspired new thinking in our research labs to address the lack of successful treatment options for some of these cancers.

## THERAPEUTIC CHALLENGES AND NEW OPPORTUNITIES

The toughest cancers are commonly characterized as being refractory and resistant, rapidly progressing, diagnosed in advanced stages, invasive and metastatic, limited in therapeutic options, and heterogeneous with multiple subtypes.<sup>1-7</sup> These cancers present many barriers to treatment and are the focus of the most robust and exciting research today.

CANCER TYPE	CHALLENGES/BARRIERS	THERAPEUTIC OPPORTUNITY
<b>Refractory and resistant<sup>1</sup></b>	<ul style="list-style-type: none"> <li>• Intrinsically unresponsive to therapy</li> <li>• Acquired resistance</li> </ul>	<ul style="list-style-type: none"> <li>• Identifying mechanisms or mutations of resistance</li> <li>• Mutations include: KRAS, BRAF, MDR1</li> </ul>
<b>Rapidly progressing<sup>1,8,9</sup></b>	<ul style="list-style-type: none"> <li>• Rapid growth</li> <li>• Adaptive therapy</li> <li>• Infiltrative nature</li> </ul>	<ul style="list-style-type: none"> <li>• Identifying targets for molecular therapy</li> <li>• Research into microRNA and cancer stem cells</li> </ul>
<b>Commonly diagnosed in advanced stages<sup>4</sup></b>	<ul style="list-style-type: none"> <li>• Regional/distant metastasis</li> <li>• Can seem to suddenly appear</li> </ul>	<ul style="list-style-type: none"> <li>• Increased screening</li> <li>• Detection in earlier stages</li> <li>• More effective therapies at advanced stages of disease</li> </ul>
<b>Invasive and metastatic<sup>6</sup></b>	<ul style="list-style-type: none"> <li>• Spread from primary tumor to regional and distant organs</li> </ul>	<ul style="list-style-type: none"> <li>• Improve understanding of metastatic process at cellular and molecular level</li> <li>• Interrupting interactions of metastatic cells and host homeostatic mechanisms</li> </ul>
<b>Limited lines of therapy<sup>1-7</sup></b>	<ul style="list-style-type: none"> <li>• Cancers have escaped effectiveness of surgery or radiation therapy</li> </ul>	<ul style="list-style-type: none"> <li>• Discovering new signaling pathways using microarray testing for intervention</li> </ul>
<b>Heterogeneity with multiple subtypes<sup>6</sup></b>	<ul style="list-style-type: none"> <li>• Tumors with subpopulation of cancer cells that are drug resistant and highly metastatic</li> <li>• Cancer cells differ from primary tumor cells in terms of treatment and prognosis</li> </ul>	<ul style="list-style-type: none"> <li>• Development of innovative strategies to control these subtypes</li> <li>• Stimulating human immune system to destroy cancer cells</li> </ul>

Attempts to treat these advanced and difficult cancers can often exceed the capabilities of traditional cornerstones of cancer therapy. Conventional therapeutic options such as surgery, hormonal and radiation therapy, and chemotherapy have the most impact during early stages of the disease or in tumors highly unresponsive to drug therapy. Once cancer cells adapt and mutate in late stages of the disease, traditional treatment options lack effectiveness and patients experience relapse and require re-treatment.

## LOOKING FORWARD TO THE FUTURE

As the toughest cancers adapt and evolve, our approach in turn must be innovative and agile in the fight against cancer. Amgen continues to take on some of the toughest cancers, and this effort requires a greater understanding of the pathophysiology of cancer cells and the identification of new targets and signaling pathways so that novel oncologic therapies may be developed.

*Our researchers are investigating a number of targeted agents to take on the toughest cancers.*

The last two decades have seen remarkable progress, with scientific breakthroughs in genetics, molecular biology, and biotechnology. These advances have led to the emergence of biologic therapies and immunotherapies, which have now become important components of cancer therapy.<sup>10</sup> More recently, a greater appreciation of the human immune system has inspired the development of therapies that use the body's immune response. In fact, immuno-oncology may herald the beginning of an era that holds great promise for the long-term control of many cancer types.

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Look for more in this series at [AmgenOncology.com](http://AmgenOncology.com)  
as we continue to take on the toughest cancers.

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TAKING ON THE TOUGHEST CANCERS.

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Oncology

# THE INTERNATIONAL CANCER CONTROL PARTNERSHIP: BUILDING CAPACITY IN CANCER CONTROL PLANNING



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National cancer planning that supports a robust health system in order to effectively prevent and control cancer is a critical investment for both developed and developing countries alike. Cancer surveillance data are vital for formulating targeted and effective national cancer control plans (NCCPs) as well monitoring and evaluating their impact. Yet despite the compelling evidence that NCCPs can be effective in improving the coverage and quality of cancer services and patient outcomes, many countries struggle to develop and implement NCCPs with adequate funding and coordination support. The International Cancer Control Partnership (ICCP) is a key collaborative initiative to pool resources and bridge the gaps that currently exist in cancer control planning. The goal of the ICCP is to encourage and support the development, financing and implementation of comprehensive NCCPs in order to drive achievement of the overarching goal of the WHO Global Action Plan on NCDs, namely a 25% reduction in premature mortality from NCDs by 2025 (1).

In 2012, there were roughly 14.1 million new cancer cases, 8.2 million cancer deaths and 32.6 million people living with cancer worldwide (2). Cancer cases are estimated to dramatically rise to 19.3 million worldwide in 2025 as a consequence of a growing and ageing global population (3), with a disproportionate burden falling on low- and middle-income countries (LMICs). Globally, 57% (8 million) of new cancer cases, 65% (5.3 million) of cancer deaths and 48% (15.6 million) of 5-year prevalent cancer cases occurred in less developed regions and are predicted to further increase by 2025 (4).

Cancer places an economic burden not only on social welfare and health systems but also on national economies. Disabilities and prolonged absences from the workforce lead to a fall in labour force participation, and consequently in GDP (5). In 2010, the estimated total annual economic cost of cancer worldwide was roughly US\$ 1.16 trillion taking

into account the costs of prevention and treatment plus the annual economic value of disability-adjusted life years (DALYs) lost to cancer (6).

There is a growing body of empirical evidence confirming that investing in cancer prevention and control now far outweighs the costs of doing nothing and dealing with the consequences. Investment in appropriate strategies for prevention, early detection and treatment estimates to save between 2.4 and 3.7 million lives; 80% of them in LMICs (7). In economic terms, the value of the healthy years of productive life that could be saved totals between US\$ 331 and US\$ 451 billion, yielding an estimated return on investment in prevention and treatment ranging from US\$ 10 billion to US\$ 230 billion (8). Investing just US\$ 11.4 billion on a set of core prevention strategies in LMICs can yield a saving of up to US\$ 100 billion in cancer treatment costs (9).

Now more than ever, it is important for countries to direct resources more efficiently to cancer control efforts by developing comprehensive national cancer control plans (NCCPs). NCCPs provide all countries with a blueprint to deliver cost-effective cancer control programmes that can reduce cancer incidence and mortality, improve the quality of life of cancer patients and their communities and reduce the impact of cancer on national economies.

### What makes a good NCCP?

The World Health Organization (WHO) defines NCCPs as “public health programmes designed to reduce cancer incidence and mortality and improve the quality of life of cancer patients, through the systematic and equitable implementation of evidence-based strategies for prevention, early detection, diagnosis, treatment and palliation, making the best use of available resources” (10).

A number of elements are central to developing a comprehensive NCCP that meets the current and future health needs of a country’s cancer burden. In particular, many countries struggle to produce NCCPs that consider the whole continuum of care: prevention, early detection, diagnosis, treatment, rehabilitation, palliation and research (11). Moreover, many NCCPs fail to adopt a health systems approach that sets out governance arrangements, resource allocation and financing around measurable goals to support a country’s cancer control efforts.

An NCCP should provide a sustainable strategic plan for cancer control, based on the country’s cancer burden, cancer risk factor prevalence and the resources available to implement the plan. It should also take into account the socioeconomic environment and healthcare system in that country (12). The most effective NCCPs are developed with the involvement of multisector stakeholders to set realistic objectives that respond to the population’s cancer needs (13).

The availability of reliable cancer surveillance data, including cancer incidence, stage at diagnosis and mortality, generated by population-based cancer registries is vital for developing targeted and effective NCCPs and for evaluating the impact of national programmes. Yet, good-quality data are often unavailable; in Africa, Asia, and Latin America, coverage of high-quality data from registries is well below 10%. There is an urgent need to build this capacity in these regions (14).

Importantly, the cost of establishing a robust cancer registry in most countries is comparatively low when considered against the cost of the cancer burden in that country. In the United States alone, the annual burden of

cancer is more than US\$ 216 billion, whilst less than US\$ 75 million (0.03%) is spent annually to fund the Centers for Disease Control and Prevention’s (CDC) National Program of Cancer Registries (NPCR) (15).

### The current status of NCCPs: The global picture

Despite compelling evidence that NCCPs effectively improve cancer services and outcomes, many countries, particularly LMICs, have yet to develop or implement NCCPs. A major source of concern is that many countries implement NCCPs with significant gaps. A recent WHO Assessment Report highlights that as many as 81% of countries have cancer plans, policies or strategies in place, but when looking at those that have an operational plan, this percentage dropped to 59% and dropped again to 48% for operational plans with dedicated funding (see Table 1 and Fig. 1) (16). The Assessment Report defines “an operational ... plan as one that is currently being implemented in the country” while “a non-operational plan is one that exists on paper but is not being implemented” (17). The African Region has the lowest percentage of countries with cancer policies, plans or strategies, while the Region of the Americas, European Region and Western Pacific Region report the highest percentage (see Fig. 2) (18). The Eastern Mediterranean Region and South-East Asia Region also report a high percentage of countries with cancer policies, plans or strategies (see Fig. 2) (19).

Despite a high percentage of LMICs reporting plans, policies or strategies for leading NCDs, this highlights the widening gap between HICs and LMICs in capacity to develop, implement and fund NCD-related plans, policies or strategies (20). Although 83% of LMICs have an NCD policy, only 59% of them are operational and 51% are operational with dedicated funding compared to HICs where 96% have a policy and 87% have an operational policy with funding (see Fig. 3) (21).

### The evolving NCD agenda: An opportunity for accountability and action

As the incidence of cancer and other NCDs escalates to epidemic levels, there is a clear need to promote a sense of urgency among countries to develop and implement national cancer plans and to reassess existing plans. In doing so, the challenge incumbent upon the cancer community is to promote evidence-based policy-making while also advocating for an increase in resources to fund national cancer plan implementation and sustainable scale up.

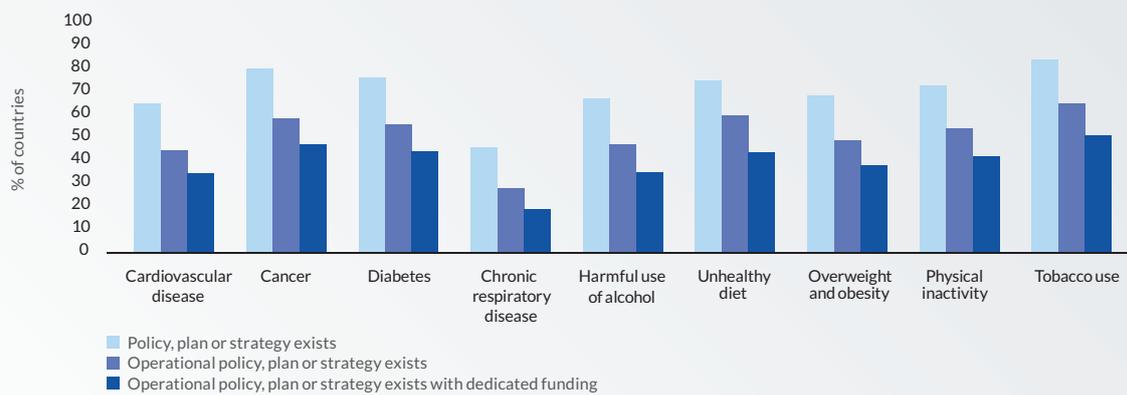
The UN Political Declaration on NCDs adopted in September 2011 laid out actions addressed to all

Table 1: Percentage of countries with a policy, plan or strategy addressing the major NCDs and/or their risk factors

	% of countries
Tobacco use	84
Cancer	81
Diabetes	77
Unhealthy diet	76
Physical inactivity	73
Overweight and obesity	69
Harmful use of alcohol	68
Cardiovascular disease	65
Chronic respiratory disease	46

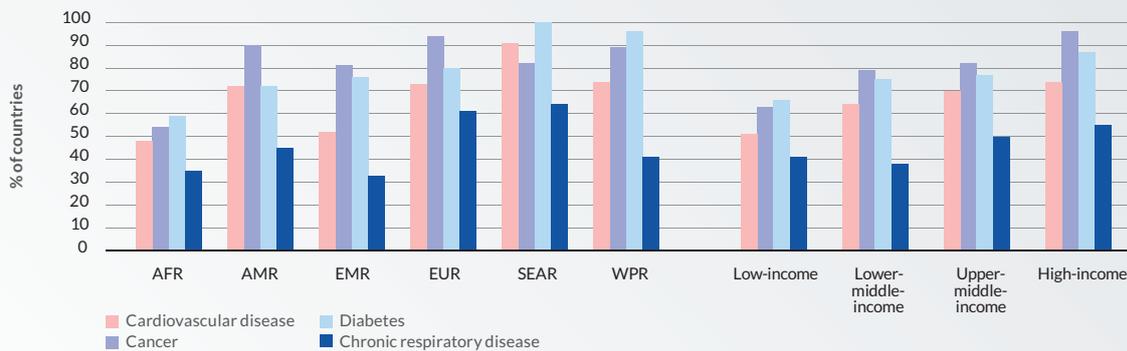
(World Health Organisation, Assessing national capacity for the prevention and control of non-communicable diseases: report of the 2010 global survey, Geneva, WHO Press: 2012)

Figure 1: Percentage of countries with policies, plans or strategies and whether or not these are operational or funded



(World Health Organisation, Assessing national capacity for the prevention and control of non-communicable diseases: report of the 2010 global survey, Geneva, WHO Press: 2012)

Figure 2: Countries with plans, policies or strategies for the leading NCDs and risk factors, by WHO region and World Bank income group

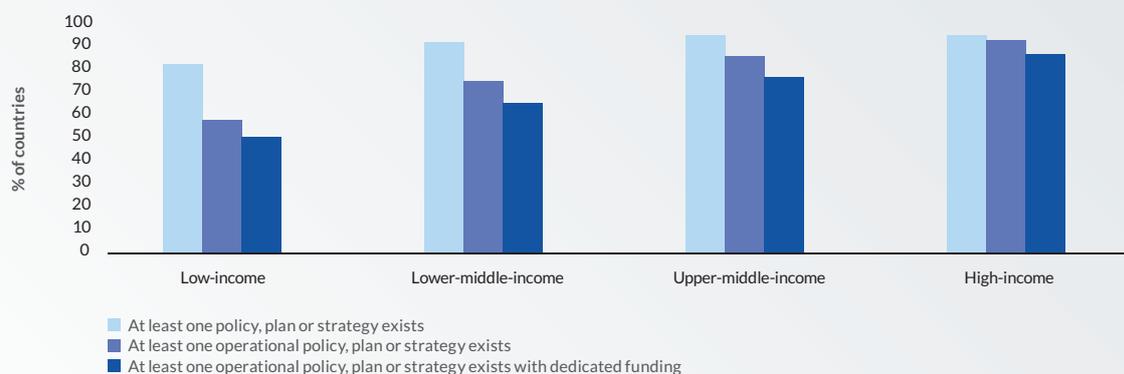


(World Health Organisation, Assessing national capacity for the prevention and control of non-communicable diseases: report of the 2010 global survey, Geneva, WHO Press: 2012)

stakeholders, in particular governments, and is reflected in the six objectives of the WHO Global NCD Action Plan 2013–2020 (GAP), which has been recognized by WHO Member States and UN agencies as a common roadmap in the fight against cancer and NCDs (22). The development of national capacity governance and multisectoral actions into

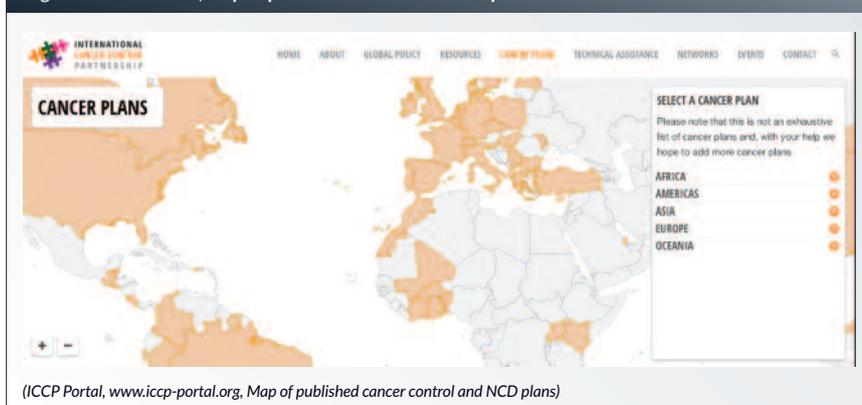
national plans (GAP objective 2) and implementing NCD prevention strategies (GAP objective 3) are central elements of the NCD framework (23). These commitments were reaffirmed at the 2014 NCD review and assessment in New York (24). Building on this increasing global momentum to address NCDs, countries have also committed to develop

Figure 3: Percentage of countries with policies, plans or strategies, operational or funded across all major NCDs and risk factors, by World Bank income group



(World Health Organisation, *Assessing national capacity for the prevention and control of non-communicable diseases: report of the 2010 global survey*, Geneva, WHO Press: 2012)

Figure 4: ICCP Portal, map of published cancer and NCD plans



(ICCP Portal, [www.iccp-portal.org](http://www.iccp-portal.org), Map of published cancer control and NCD plans)

cancer control plans recognizing their role and responsibility in responding to the rising NCD and cancer burden.

### Building capacity through the ICCP: The role of international cooperation to support national efforts

Until recently, the cancer community lacked an effective forum to coordinate cancer control planning efforts at both the national and global level. Formed in 2012 following discussions at the World Cancer Congress in Montreal, the International Cancer Control Partnership (ICCP) is one of the key measures being taken to bridge the gaps in cancer control planning. The ICCP is a collective of key international organizations united in their efforts to promote and support cancer control. ICCP partners currently include the African Organisation for Research and Training in Cancer (AORTIC), American Cancer Society (ACS), American Society of Clinical Oncology (ASCO), Breast Health Global Initiative (BHGI), Cancer Council of the Pacific Islands, Centers for Disease Control and Prevention, USA (CDC), International Atomic Energy Agency – Program of Action for Cancer Therapy (IAEA – PACT), International Cancer Control Congress Association (ICCCA), Latin American and Caribbean Society

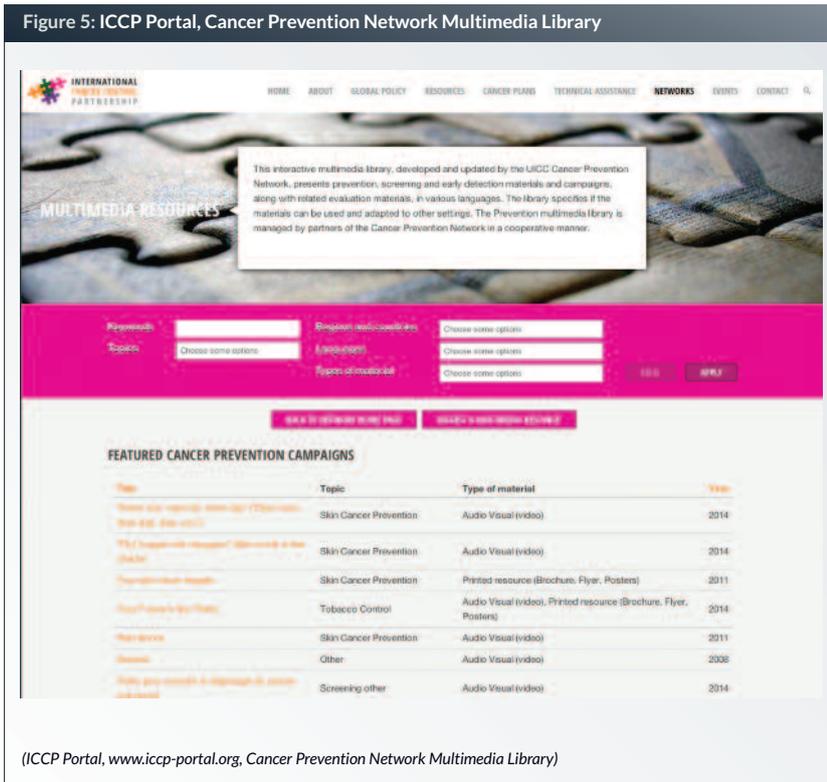
of Medical Oncology (SLACOM), Livestrong Foundation (LIVESTRONG), London School of Hygiene and Tropical Medicine, National Cancer Institute, USA (NCI), *Red de Institutos Nacionales de Cáncer* (RINC), Union for International Cancer Control (UICC), University of Hawaii, World Health Organization – AFRO, EMRO, EURO, Pan American Health Organization/World Health Organization, World Health Organization – HQ –

Department of Chronic Disease, IARC (International Agency for Research on Cancer), Two Worlds Cancer Collaboration, National Comprehensive Cancer Network (NCCN) and Health Promotion (CHP).

The ICCP builds on the opportunity afforded by the NCD movement to open a dialogue directly with national cancer planners and decision-makers and stimulate national-level advocacy on key cancer components of NCD plans. Long-term, the ICCP's primary objective is to help reach the voluntary goal within the Global Monitoring Framework of NCDs of a 25% reduction in premature mortality from NCDs by 2025. To achieve this, the ICCP aims to support cancer planners and decision-makers at global, regional and country level providing expertise across the cycle of planning, development, implementation, monitoring and evaluation. On World Cancer Day 2015, NCI and UICC organized a training webinar, *The Role of National Cancer Control Plans in the Global Fight against Cancer*, which takes an in-depth look at the ICCP and the ICCP Portal (25).

Launched in November 2013 at the World Cancer Leaders' Summit, the ICCP Portal ([www.iccp-portal.org](http://www.iccp-portal.org)) is the Partnership's first key output. The Portal is a web-based tool that brings the experience and best practice knowledge

Figure 5: ICCP Portal, Cancer Prevention Network Multimedia Library



through building topic-specific Networks across the cancer care continuum that identify best practices, key resources and gaps in those fields. The UICC Cancer Prevention Network (CPN) is the first Network to bring this concept to life. The CPN is a joint initiative between UICC and Cancer Council Victoria (CCV). The CPN builds on the expertise across the UICC membership to equip policy-makers and cancer advocates in the field of health promotion and social marketing with state-of-the-art knowledge exchange and best practices on cancer prevention, early detection and screening. The Network’s interactive multimedia library (see Fig. 5) showcases the latest effective prevention campaigns and social media marketing interventions worldwide (28). Moreover, cancer planning and capacity-building tools such as the *Cancer Country Profiles*, *Cancer Atlas* and CPN underscore

of leading cancer organizations and experts and offers policy-makers and cancer planners an online platform dedicated to providing selected resources and tools on cancer control all conveniently in one place. A key feature is the map of published national cancer and NCD plans, a fantastic resource for those setting out to develop plans (see Fig. 4). In addition, the portal aims to share best practices and experiences, technical assistance opportunities and updates on global cancer control initiatives and policy.

Since its launch, the ICCP Portal has served as an instrumental platform to share over 300 key UICC and ICCP members’ resources on cancer control planning and capacity-building. Recently published at the end of 2014, the *WHO Cancer Country Profiles 2014* and *The Cancer Atlas, Second Edition* produced by American Cancer Society, IARC and UICC, are two vital tools for the cancer community that are featured on the ICCP Portal. The *WHO Cancer Country Profiles 2014* is an essential tool for informing NCD and cancer control planning that analyses the global status of cancer prevention and control (26). Each profile features the individual country’s cancer burden, top cancer trends, cancer-specific risk factors, capacity for interventions, and monitoring. *The Cancer Atlas* reports on the latest available data and trends on the cancer burden from 184 countries worldwide providing statistics on the economic and social burden of cancer as well as steps to take action against it (27).

The ICCP invites expert groups to extend the portal offer,

the continuing necessity to monitor and assess gaps in the global response to addressing the rising cancer epidemic.

### The way forward to globally accelerate NCCP efforts and commitments

Bridging the gaps that currently exist in cancer control planning is essential to achieving the target of a 25% reduction in premature mortality from NCDs by 2025. Yet despite increased awareness of the accelerating global cancer burden and the staggering economic costs of cancer, many countries are struggling to take effective action. Successful cancer control strategies invariably depend on government support. The failure of NCCPs can generally be attributed to two factors: lack of funding and the absence of comprehensive coordination support. Initiatives such as the recent launch of the ICCP represent an important milestone in the efforts to redress these long-standing deficiencies in cancer control planning. By building capacity through international cooperation, the ICCP significantly increases the bandwidth that is available to support national cancer control efforts. The need remains, however, for greater high-level political commitments coupled with multi-stakeholder collaboration. Ultimately, the rising NCD and global cancer burden underlines the need for coordinated global initiatives that address cancer control funding, planning and execution at a national level. ●

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