

REVIEW

Developing evidence-based cancer prevention recommendations: Methodology of the World Code Against Cancer Framework to create region-specific codes

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Abstract

Prevention offers the greatest public health potential and the most cost-effective long-term cancer control strategy. Authoritative, clear, evidence-based, and region-specific recommendations to actively contribute to cancer prevention are extremely valuable for the public, health professionals, advocates, and policymakers worldwide. The World Code Against Cancer Framework offers a two-level hierarchy mechanism to systematically review and synthesize the latest scientific insights, while assessing the epidemiological, socioeconomic, cultural conditions, and health systems context of a given region of the world, to inform decision-making at the individual and system levels, implemented through Regional Codes Against Cancer. In this manuscript, we describe the rigorous methodology established by the International Agency for Research on Cancer, consisting of a step-by-step decision-making algorithm to develop region-specific Codes Against Cancer. These comprehensive evidence-based tools on cancer prevention aim to transfer the latest evidence from etiological research and preventive interventions into actionable information for the population and for policymakers.

Abbreviations: BMI, body mass index; EC, European Commission; ECAC, European Code Against Cancer; ECAC4, fourth edition of the European Code Against Cancer; ECAC5, fifth edition of the European Code Against Cancer; EU, European Union; FAQ, Frequently Asked Questions; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IARC/WHO, International Agency for Research on Cancer, World Health Organization; LAC Code, Latin America and the Caribbean Code Against Cancer; NCDs, Non-Communicable Diseases; OHAT, Office of Health Assessment and Translation (from the US National Institute of Environmental Health Sciences); PAHO, Pan-American Health Organization; WG, working group.

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KEYWORDS

cancer prevention, Code Against Cancer, evidence-based recommendations, evidence-informed decision-making, framework development

1 | INTRODUCTION

In 2022, close to 20 million new cancer cases occurred worldwide and around 10 million of deaths were due to cancer.¹ The most frequently diagnosed cancers were lung, breast, colorectum, prostate, and stomach; and the leading causes of cancer death were lung, colorectal, liver, breast, and stomach.² Global economic costs from 2020 to 2050 have been estimated at \$25.2 trillion (international dollars), unevenly distributed across cancer types, countries, and socioeconomic groups.^{3,4} A substantial proportion of the cancer burden has a potential for primary prevention through reduction of known cancer risk factors, such as tobacco and alcohol use, or high body mass index (BMI), that would result in healthier societies and longer life expectancy.^{5,6}

The availability of accurate health information is crucial in health promotion and disease prevention. Understanding health information and improving health literacy^{7,8} can lead to changes in individual behaviors, especially in populations most at risk of health inequalities.⁹ In a recent multi-country cancer awareness survey, participants were aware of some cancer risk factors such as tobacco, but were less aware of others like lack of physical activity or exposure to certain viruses.¹⁰ Moreover, individuals from lower-income as compared to higher-income households across all countries were less likely to recognize cancer risk factors.¹⁰ Since behavioral risk factors are strongly influenced by the environment in which people live, notably the social and commercial determinants of health,¹¹ equitable population-level health approaches that go beyond individual behavior-oriented prevention may be more effective long-term strategies to modify exposures to prevent cancer.¹² Policies, understood as coordinated packages of measures like legislative or regulatory actions issued by governments or organizations, can influence health-related behaviors.¹³ However, despite the availability of comprehensive policy instruments,¹⁴ adoption and implementation of policies such as increasing excise taxes and prices on tobacco and alcohol purchases, reformulating food products, or front-of-package labeling remain underutilized.¹⁵ For example, only 14% of countries have endorsed the World Health Organization (WHO) Framework Convention on Tobacco Control tax guidelines.¹⁶ Thus, the reduction of this implementation gap calls for concerted research to investigate interventions in real-world settings, to better understand the context in which programs, policies, or practices are implemented.¹⁷

Identifying leading modifiable risk factors for cancer around the world, ideally through robust local data, and targeting context-specific interventions for cancer prevention are key to informing national cancer control planning. A combination of individual- and system-level approaches aiming at improving knowledge on cancer risk factors and

effective interventions may provide an equitable cancer control strategy. Considering this, the International Agency for Research on Cancer from the World Health Organization (IARC/WHO) set out to develop a comprehensive methodology to develop cancer prevention recommendations in different world regions through the World Code Against Cancer Framework.^{18,19} The framework is a strategic two-level hierarchy mechanism to develop or update and expand region-specific Codes Against Cancer (Regional Codes) through common methods explained below. Its aim is to transfer the latest evidence from etiological cancer research and preventive interventions into actionable information on cancer prevention, to inform decision-making at the individual and system levels, and adapted to the needs of different regions of the world. The Regional Codes are expected to be comprehensive evidence-based instruments on primary and secondary prevention of cancer that provide simultaneously educational guidance for the public, a policy instrument, and knowledge dissemination resources via a layered structure. With the ambition of achieving global coverage, region-specific Codes Against Cancer have been developed for the European Union (EU)^{20,21} and Latin America and the Caribbean,^{22,23} and Codes for Asia, the Gulf region and Arabic countries, and sub-Saharan Africa are in the planning or exploration phase.²⁴ The current paper provides an in-depth description and rationale of the methodological basis for this framework to develop Regional Codes Against Cancer.

2 | PRINCIPLES OF THE WORLD CODE AGAINST CANCER FRAMEWORK

2.1 | Regional Codes Against Cancer within the World Code Against Cancer Framework

The World Code Against Cancer Framework is a multi-stakeholder initiative to promote cancer prevention globally, by serving as an umbrella strategy to develop or update independent Regional Codes Against Cancer. The target audiences are the public and policymakers, as well as health professionals and advocacy groups. Through a two-level hierarchy mechanism, the framework establishes at one level the common principles, governance, rigorous methodology, and work processes to develop any region-specific code,^{18,19} while the second level implements the framework through independent Regional Codes, considering and assessing the epidemiological, socioeconomic, and cultural conditions, as well as the health system context of a given region, to provide the cancer prevention priorities. Regional Codes articulate evidence-based and contextualized recommendations to empower individuals of the region to act on reducing their risk of

cancer, while informing policy formulation and programs that are feasible to implement.

The World Code Against Cancer Framework was conceptualized both inspired and learning from the experience of the European Code Against Cancer (ECAC).²⁰ ECAC is a long-lasting initiative of the European Commission (EC), with its first edition published in 1987.²⁵ Each edition has built on the previous ones, maintaining consistency in addressing the empirically established causes of cancer and effective interventions, while reflecting the developments in the body of evidence as they occur between revisions. Nevertheless, the scope and especially the provision of supporting material of the recommendations have changed with each edition with the aim to support implementation. As the ECAC addresses the public in the EU, the recommendations are developed with this broad target group in mind, and not specific sub-populations whose distinctive characteristics require tailored preventive approaches. In 2012, IARC was commissioned and funded by the EC to produce the current fourth edition of the ECAC (ECAC4) (Supporting Information S1),^{20,21} introducing a systematic methodology described elsewhere²⁶ to assess the scientific evidence and formulate recommendations in clear, actionable language to be understood without requiring specialist skills, knowledge, or training. In 2021, the EC's Europe's Beating Cancer Plan reaffirmed IARC's role to update the ECAC with the target of producing the fifth edition (ECAC5) by 2025.²⁷ In 2023, the first edition of the Latin America and the Caribbean Code Against Cancer (LAC Code) (Supporting Information S1) was coordinated and published by IARC in collaboration with the Pan-American Health Organization (PAHO), as the first Regional Code developed outside of Europe under the World Code Against Cancer Framework. The LAC Code is tailored to the context and needs of Latin America and the Caribbean, considering the specific risk factors, cancer burden, social inequalities, economic barriers, and health care systems' portfolio of services. It includes for the first time explicit recommendations for policymakers.^{22,23} Specific recommendations for Latin America and the Caribbean not included in ECAC4 (e.g., limiting consumption of very hot beverages, avoiding indoor air pollution, screening and treatment of infections) are summarized elsewhere.²⁸ Recently, the Asian National Cancer Centers Alliance recognized the importance of developing a set of cancer prevention recommendations for Asia and established contact with IARC to plan a future Asian Code Against Cancer.²⁴ Less advanced but under negotiation are the discussions with the Gulf Centre for Disease Prevention and Control, starting with defining the appropriate geographical scope for an independent Regional Code.

The development of each Regional Code progresses along three main phases: (1) preparation, (2) development, and (3) dissemination, monitoring, and evaluation. To ensure and sustain the scientific integrity of the final product (the Regional Code) the PRECEDE-PROCEED model of health promotion used in implementation research²⁹ has been proposed as a planning, monitoring, and evaluation framework to logically organize all activities and mixed methods utilized. The model has been successfully used for the development of the LAC Code,²² from formative implementation research conducted in the region³⁰ to studies currently being designed for the evaluation of the

impact of the LAC Code. It is also being used in the development of ECAC5. In our adaptation of the PRECEDE-PROCEED model, the "Health programme" corresponds to the Regional Code (Figure 1) with its multi-layered levels of information described elsewhere,^{22,26} allowing integration of individual-level recommendations and system-level recommendations (Education strategies-Level 1 and Policy regulation organization-Level 1, respectively, in Figure 1). For each Regional Code, specific knowledge translation outputs will be proposed by the regional stakeholders at the planning phase and developed according to the needs and priorities of the region. These serve to provide additional information and explanations on each of the recommendations to foster proper dissemination across the region (Figure 2). Notably, the rigorous assessment of the scientific evidence applies equally to all outputs of the Regional Codes' development, including the recommendations to the individuals and to policymakers, as well as the supporting material (i.e., Frequently Asked Questions [FAQs] for the public in ECAC4²¹ and training for health professionals in the LAC Code²³).

2.2 | Main principles and planning phase

Evidence-based public health is an approach to improving population health outcomes through the use of the best available evidence to inform decision-making in developing, implementing, and evaluating public health policy, programs, and interventions.^{31–33} Through the systematic review and synthesis of the evidence of epidemiological studies, intervention trials, and other types of studies, it identifies public health priorities and evaluates the impact of interventions, while engaging communities and stakeholders in the process. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology is one of the most widely used systematic approaches to assess evidence quality and support evidence-based decision-making in a structured and transparent way.³⁴ GRADE evaluates the quality of the evidence based on factors such as study design, risk of bias, consistency of results, and other considerations that are applied to the body of the evidence. Additionally, it uses Evidence to Decision frameworks to support the process of moving from evidence to decisions in the context of clinical, health system, or public health recommendations.³⁵

To develop recommendations under the World Code Against Cancer Framework, the body of evidence on a risk factor and preventive intervention should be classified as "sufficient" by authoritative sources. On this basis, adopting a recommendation would lead to reducing an individual's risk of developing or dying from cancer. The main authoritative sources used in the process, described elsewhere²⁶ and in Figure 4, are the IARC Monographs,³⁶ the IARC Handbooks of Cancer Prevention,³⁷ the Global Cancer Update Programme of the World Cancer Research Fund International,³⁸ and WHO Guidelines.³⁹ If an authoritative source of evidence on a particular topic is not yet available not sufficiently recent, new systematic literature reviews may be performed using GRADE as the methodological basis of the framework, as detailed below. In addition, the World Code Against

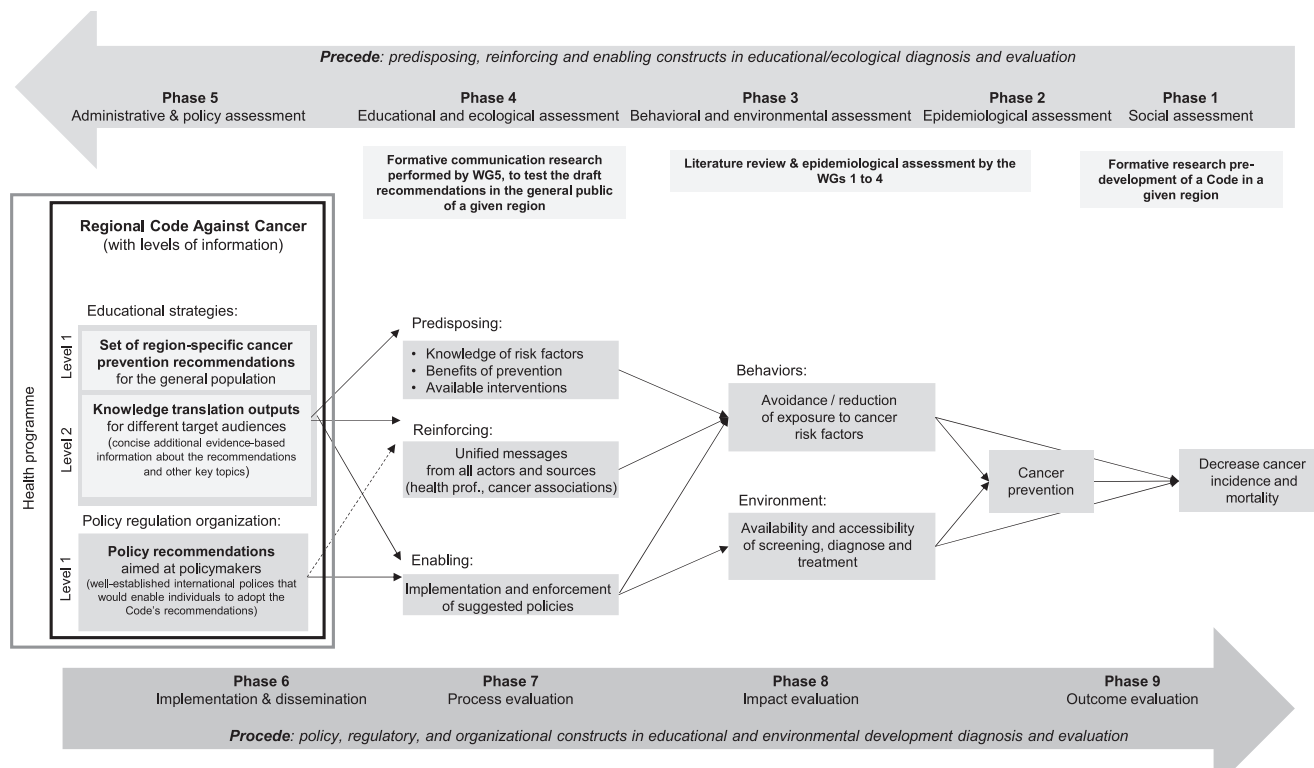


FIGURE 1 Adaptation of the PRECEDE-PROCEED model to the World Code Against Cancer Framework. WGs, working groups.

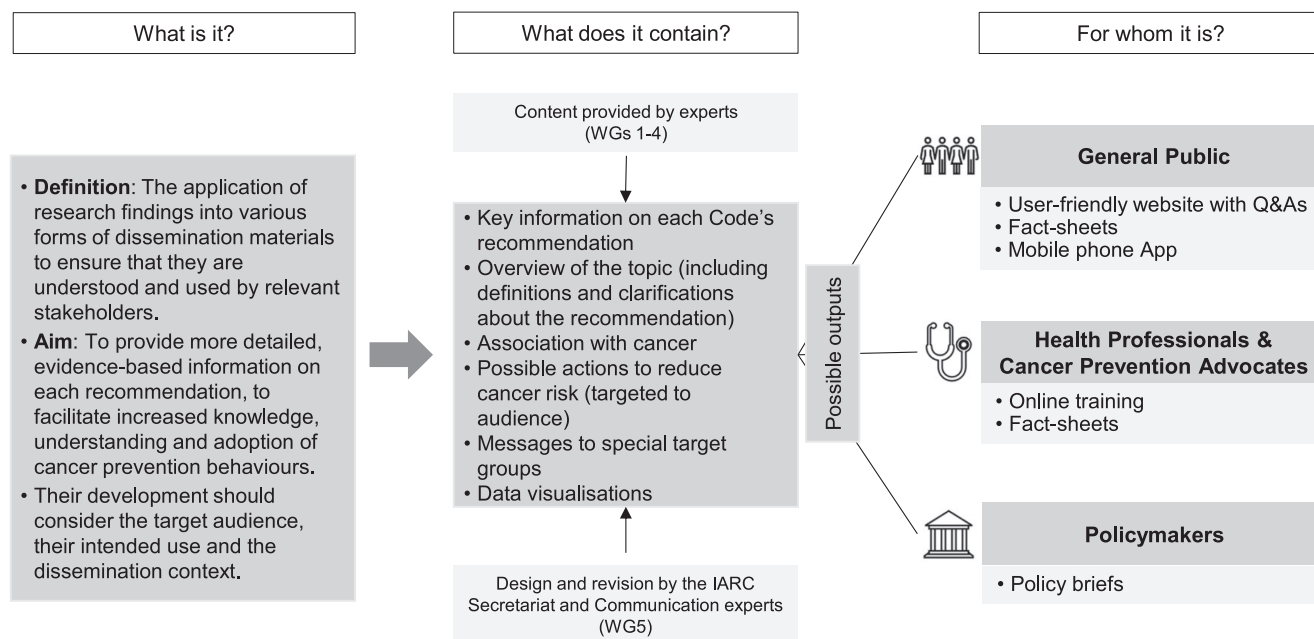


FIGURE 2 Knowledge translation outputs have been developed for each Regional Code to provide additional information to several target audiences. WGs, working groups.

Cancer Framework now includes complementary guidance to policy-makers based on international sources of policy evidence such as the “WHO Best Buys”¹⁴ or existing legislative instruments such as EU Directives.

In the planning phase of a Regional Code, a so-called “Scoping meeting” is organized to define the scope of the region of interest through a thorough scientific and contextual assessment done by IARC in partnership with key stakeholders in each region.

Epidemiological features such as the cancer burden, the prevalence of exposures, the breadth and diversity of populations, and health system context are the main criteria to consider. Socioeconomic and political aspects are also discussed and taken into account but do not drive the decisions. In the case of the EU, dynamics of countries joining or leaving the EU are incorporated into the scientific assessments. During these “Scoping meeting,” joint resource mobilization strategies, identification of regional experts, and implementation plans are also discussed.

3 | METHODOLOGY FOR THE DEVELOPMENT OF A REGIONAL CODE AGAINST CANCER WITHIN THE WORLD CODE AGAINST CANCER FRAMEWORK

3.1 | Structure, governance, and process

The process to develop any Regional Code entails a complex governance to produce all outputs and coordinate the work of many region-specific experts (Figure 3).

For the development phase of each Regional Code, senior scientific experts from the target region are identified by the IARC Secretariat based on publication records, experience in synthesizing scientific information, and advisory roles. Importantly, experts are

selected in their individual capacity and do not formally represent their affiliated institution. Conflicts of interest are diligently assessed using the rigorous IARC procedures. Experts are organized into several Working Groups (WGs) divided into Lifestyle Determinants (WG1), Environmental and Occupational Determinants (WG2), Infections (WG3), Medical Interventions (WG4), and Communication and Health Literacy (WG5). Each technical WG 1 to 4 reviews the literature, assisted by a dedicated Literature Group. With advice on communication from WG5, they propose cancer prevention recommendations following the rigorous methodological process described below. A Coordination Group, led by the IARC Secretariat, is established to ensure that each Regional Code remains consistent with the World Code Against Cancer Framework.¹⁹ The Coordination includes a Key Regional Partner, a public health institution with an authoritative mandate (e.g. the EC in the EU, PAHO in Latin America, or the Asian National Cancer Centers Alliance in Asia), a representative of the World Cancer Research Fund International, and the Chair of each of the WGs. A Scientific Committee, composed of senior experts in cancer control from the target region, with public health and scientific credibility and a leadership role, oversees the process, evaluates, and eventually approves the corresponding regional-specific recommendations, and endorses the Regional Code on behalf of the institution they represent. The final decision on the inclusion of recommendations in a Regional Code rests with the Scientific Committee. Each recommendation should be approved ideally by consensus

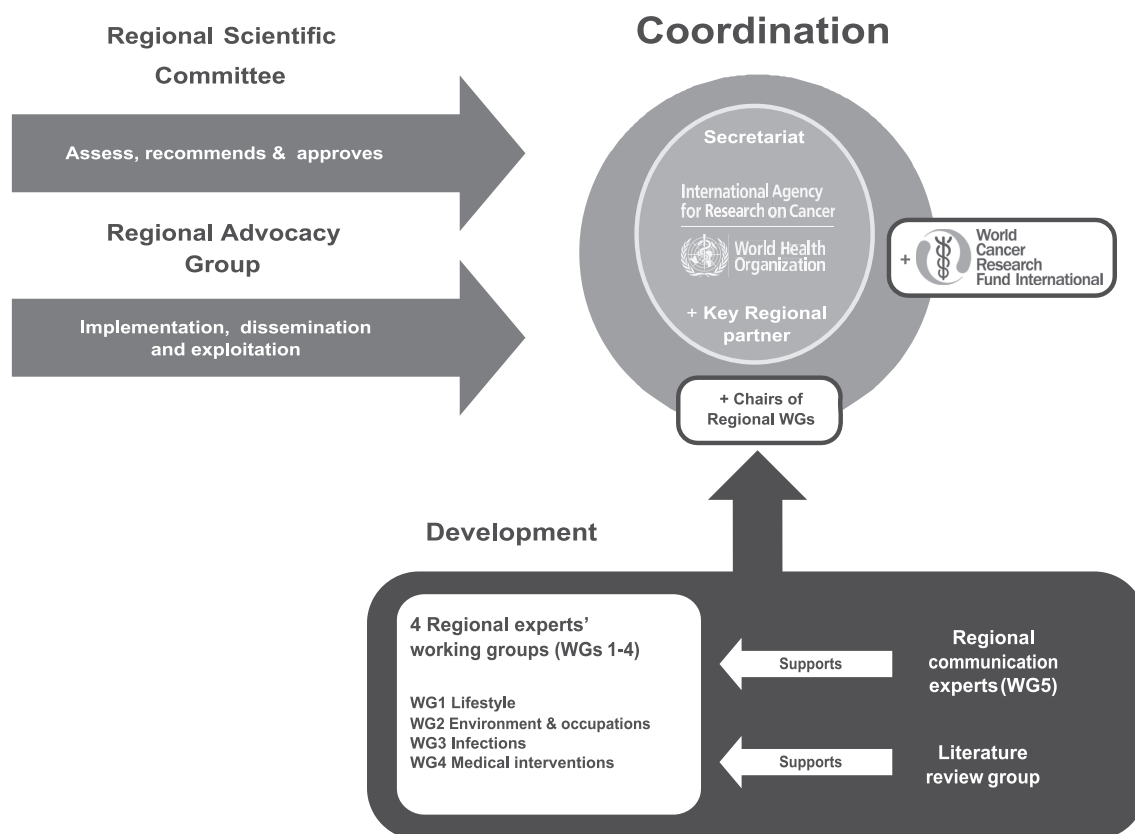


FIGURE 3 Illustration of the interactions between the five working groups (WGs) who revise the evidence (WGs 1–4) and propose recommendations, advise on the communication (WG 5), other committees, and the coordination.

in the Scientific Committee; otherwise, by absolute majority vote of the Scientific Committee members. In addition, a procedure for solving conflicts or disagreements within and across WGs has been established. Finally, an Advocacy Group formed of representatives of influential institutions in the region promotes and disseminates the corresponding Regional Code to the respective regional and national health decision-makers.

3.2 | Criteria and decision-making algorithm to review the scientific evidence, assess the communication, and formulate recommendations

To guide the WGs' experts, IARC has developed a thorough methodology that has optimized the transparency of the development process over time, while inevitably becoming more complex.^{22,26} Guided by stakeholders' advice,⁴⁰ we have now revisited and redefined the criteria that a recommendation needs to fulfill to be eligible for inclusion in a Regional Code. This has been summarized in the step-by-step decision-making algorithm presented here, containing

the four main criteria of the World Code Against Cancer Framework (Figures 4–6). Certain features inspired by the GRADE methodology have also been incorporated (Figures 4),⁴² as well as a new policy assessment process (Figure 6): (i) An adaptation of the GRADE Evidence to Decision frameworks is used to organize and make explicit the criteria underpinning the assessment of the evidence, the judgments made by the WGs, and additional considerations used to inform each judgment.³⁵ (ii) The Office of Health Assessment and Translation (from the US National Institute of Environmental Health Sciences) (OHAT) methodology,⁴³ also adapted from GRADE, has been utilized for assessing the certainty of the evidence coming from the targeted reviews of the literature commissioned by the WGs, in particular, the requirements of observational studies (namely, by grouping studies by key design features such as appropriateness of exposure assessment, timing of exposure prior to outcome, individual outcome assessment and appropriateness of comparison group). The process begins with a consideration of the most recently developed Regional Code, used as the basis to adapt, update, or newly create a set of recommendations following a sequential algorithm:

Criterion 1 - Confidence in the evidence to keep, modify or add a recommendation that is relevant for the entire region or a large sub-region

Step 1 : Certainty of the current scientific body of evidence

Assessment of the sufficiency of the strength of the evidence falls into two broad categories:

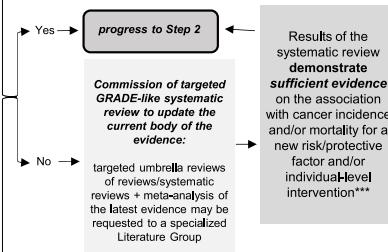
(1) **Risk factors and preventive actions to reduce the exposure** (chemical/physical/biological agents or a behaviour). Recommendations (e.g., having a healthy diet) should include established causes of cancer that can be avoided or reduced, or protective factors

(2) **Effective interventions at individual level**.*. Recommendations should include interventions proven effective to avert specific precancerous lesions, cancers or their consequences.

For infections-related individual-level interventions (e.g., vaccines and treatments), those approved by the authoritative bodies such as the EU European Medicines Agency or the US Food and Drug Administration, to be efficacious to take away or control the infection among individuals which stage has not progressed to precancerous disease, will be also considered as demonstrating sufficient evidence on effectiveness.

Categorised by the following authoritative sources of evidence as:

- "Group 1" by the IARC Monographs Programme on the Identification of Carcinogenic Hazards to Humans
- "Strong evidence" for causal relationship by the WCRF reports and the Global Cancer Update Programme (CUP Global)
- "Sufficient evidence" by the IARC Working Group Reports
- "Group A/Sufficient" by the IARC Handbooks of Cancer Prevention
- "Strong recommendation" by WHO Guidelines and related scientific position papers on cancer and/or NCDs control, and/or by landmark publications from a specific region, e.g. the European Commission Initiatives to update the EU Guidelines for Quality Assurance in Cancer Screening, scientific evidence reviews commissioned by the European Commission for the European Union
- "Sufficient evidence" by the IARC Working Group Reports



Step 2 : Relevance to the region or a large sub-region

Criteria adapted from the GRADE Evidence to Decision frameworks

a) **Epidemiological situation** in the region (e.g., prevalence of exposures), considering the current and future cancer burden:

→ Is it a priority for the whole region?

b) Potential impact of the recommendation on **equity** within the region, minimising social inequalities as much as possible:

→ Would the recommendation reduce social inequalities?

c) **Feasibility and accessibility** for the individual to uptake the intervention in the regional health systems context:

→ Is the intervention implemented/implementable in the regional context, and accessible and feasible to individuals?

d) **Affordability** for the individual to uptake the intervention in the regional health systems context:

→ Is the intervention implemented/implementable in the regional context, and affordable to individuals?

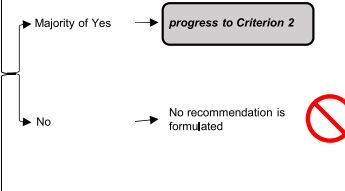
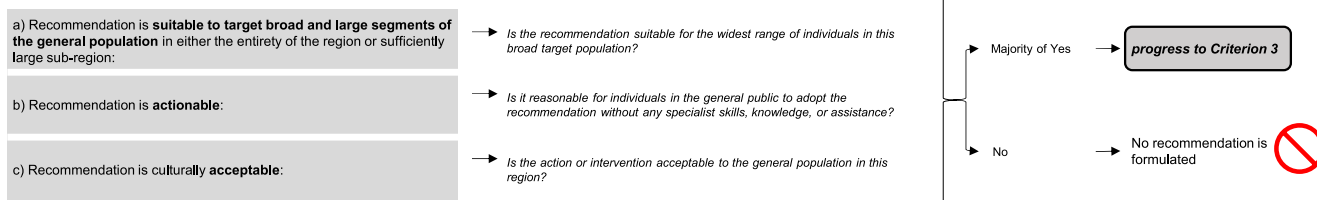


FIGURE 4 Methodological basis for the World Code Against Cancer Framework: step-by-step decision-making algorithm for Criterion 1. *For the World Code Against Cancer Framework, we define “effectiveness” as “the extent to which a specific intervention, procedure, regimen, or service, when deployed in the usual circumstances of living and practice, does what it is intended to do for a specified population. A measure of the extent to which an intervention or policy fulfills its objectives in practice. If possible, the determination of effectiveness should be based on pragmatic randomized controlled trials.”⁴¹ **“Individual-level interventions” are defined as those that seek to change individual behaviors (e.g., tobacco cessation advice or personal protective equipment at work) or uptake of a screening test or preventive therapy, versus population-level interventions that describe policies or programs (e.g., food labeling, air quality policies, organized cancer screening programs, or large-scale health information campaigns) delivered to the whole population. Population-level interventions will be assessed in Criterion 4. ***For individual-level interventions, other relevant outcomes such as downstaging of cancer in screening, the benefits/harms balance, or infection's control by confirmation that the precancerous disease has not progressed may be considered. ⁴²The decision tree process stops at that end if the criteria are not fulfilled. EU, European Union; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IARC, International Agency for Research on Cancer; WHO, World Health Organization; CUP, Cancer Update Programme.

Criterion 2 - Suitability, actionability, and acceptability for a broad target population of the general public

Criteria adapted from the GRADE Evidence to Decision frameworks



Criterion 3 - Intelligibility of the formulation of the recommendation for a lay audience

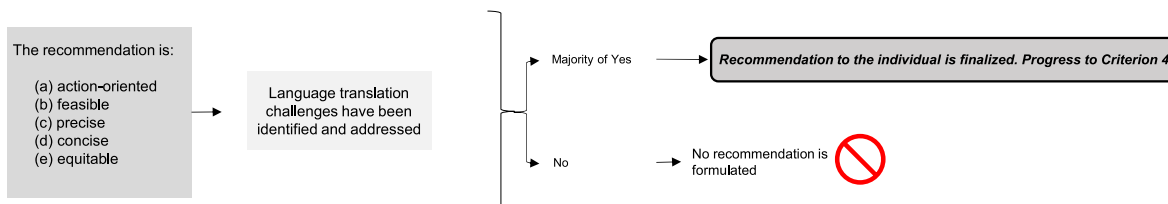


FIGURE 5 Methodological basis for the World Code Against Cancer Framework: step-by-step decision-making algorithm for Criteria 2 and 3. GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

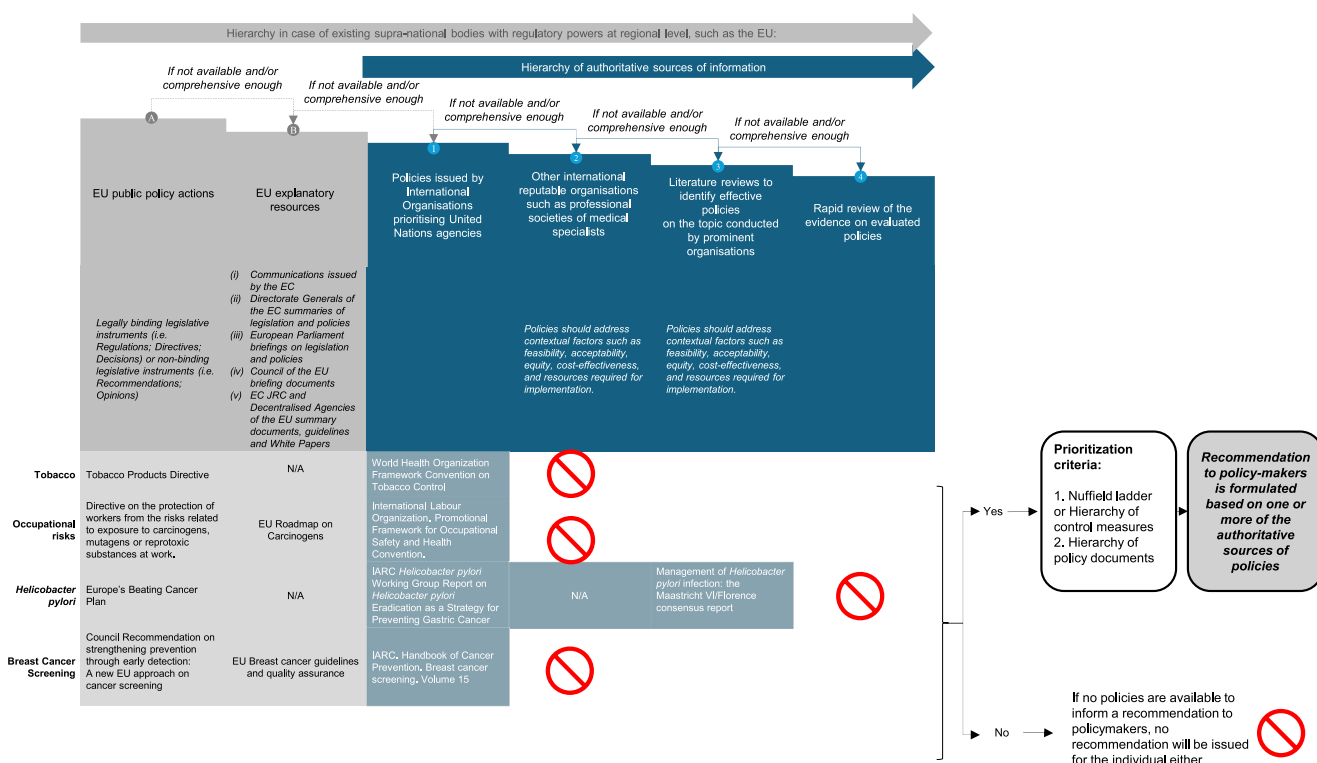


FIGURE 6 Methodological basis for the World Code Against Cancer Framework: step-by-step decision-making algorithm for Criterion 4 with examples. EC, European Commission; EU, European Union; EC JRC, European Commission Joint Research Centre; N/A, not applicable. ☒ indicates that the process has finalized, and the policy recommendation can be formulated based on the sources identified and using the Nuffield ladder or the hierarchy of control measures for occupational exposures as prioritization instruments.

- Criterion 1: Confidence in the evidence to keep, modify, or add a recommendation that is relevant for the entire region or a large sub-region.

The certainty of the evidence is addressed to maintain a recommendation that already exists in a Regional Code, modify it, adapt it, or introduce a new recommendation (Figure 4):

- Step 1-The current body of evidence should be classified as “sufficient” to demonstrate that adopting the recommendation would lead to reducing the risk of developing or dying from cancer, and that the benefits of adopting the recommendation outweigh the potential harms.
- Step 2-Key contextual factors should also be assessed for a recommendation to be relevant to the region, prioritizing local evidence.

Additionally, experts should identify potential synergies with other Non-Communicable Diseases (NCDs).⁴⁰ An evidence-based statement will be produced to provide brief information describing the association between the cancer recommendation and other NCDs.

- Criterion 2: Suitability, actionability, and acceptability for a broad target population of the public.

This criterion ensures that the proposed recommendation will target the public and not specific sub-populations that would benefit more from tailored preventive efforts (Figure 5).

To inform this criterion, it is recommended to perform region-specific formative research on the barriers of the public toward the adoption of cancer prevention messages. The results of such a study can support the experts' deliberations on this criterion (e.g., in Argentina³⁰ and Colombia⁴⁴) has informed the LAC Code^{22,23}; and in the EU⁴⁵ is informing ECAC's development (Phase 1 in Figure 1).

- Criterion 3: Intelligibility of the formulation of the recommendation.

It addresses whether the recommendation is intelligible for a lay audience, communicating the message in an understandable and unambiguous way. Recommendations requiring individuals to make benefit/risk assessments on their own are to be avoided, except for specific circumstances such as cancer screening (Figure 5). This criterion also considers the diversity of languages in each region and the importance of keeping the original scientific meaning in the translation process. For a Regional Code to be implemented effectively, words that may affect the meaning of the recommendations should not be replaced, deleted, or added, except for appropriate synonyms accepted by the public of each specific country to avoid misinterpretation. Region-specific communication expertise is essential to fulfill this criterion.

It is recommended to perform evaluation research to test the draft recommendations in the public of the target region (e.g., a mixed method study was conducted in five Latin American countries,⁴⁶ and an awareness experimental study is currently being conducted in nine EU countries [Phase 1 in Figure 1]).

- Criterion 4: Availability of international policies to enable environments to adopt the recommendations.

This criterion ensures that policies from authoritative organizations are included in the process. Consequently, each recommendation for the individual must be accompanied by a counterpart recommendation

at the system level for policymakers. The purpose of the recommendation to policymakers, as recommended in Espina et al.,⁴⁰ is to provide specific messages informing about policies that should be implemented to enable environments in which individuals can adopt the recommendations of the Regional Code. This criterion does not aim to propose new policies but rather focuses on the existing international policies that may reinforce the recommendation for individuals. The identification and assessment of the most relevant and suitable supra-national policies should follow the hierarchy of authoritative sources of information (Figure 6).

4 | FUTURE OUTLOOK OF THE WORLD CODE AGAINST CANCER FRAMEWORK TO REDUCE THE GLOBAL CANCER BURDEN

Cancer incidence and mortality have substantially increased globally.⁴⁷ A double approach tackling simultaneously individual-level^{48,49} and system-level prevention^{12,15} in primary prevention, cancer screening, and control could help bridge the gap between evidence and practice, averting millions of future cancer diagnoses and saving lives worldwide.

The World Code Against Cancer Framework offers a global mechanism to systematically translate the latest scientific insights into action, while the regional implementation (Regional Codes) optimally captures and tailors the local aspects of cancer prevention into the global framework, offering a multi-purpose powerful tool to help reduce the numbers of people developing and dying from cancer. First, it offers cancer prevention in concise messages for the public, while providing targeted guidance to policymakers on the corresponding structural aspects and international policies. Second, it describes the priority actions for a region, considering its socioeconomic and cultural context, and empowers regional stakeholders to speak with one voice. Third, it is a specific tool for cancer prevention that creates synergies in the global efforts to reduce the ever-growing NCD burden by promoting healthy environments. Fourth, it takes account of inequalities through its comprehensiveness, understandability, and by assigning responsibility to society and decision-makers. Finally, it offers an authoritative, systematic, and adaptable system resting on the most recent high-quality evidence and strong stakeholder involvement. Currently, the EU and Latin America are covered by a Regional Code. The ECAC has been updated repeatedly and incorporated into policymaking at national and sub-national levels.⁵⁰

Despite these strengths, some limitations are also hampering the further development of Regional Codes. Most importantly, a sustained programmatic mechanism to produce and periodically update the Regional Codes is lacking to maintain its high-quality process with a centralized governance via a permanent inter-institutional infrastructure.⁴⁰ Also, an agile process to incorporate newly classified carcinogens and effective interventions into the Regional Codes needs to be developed. The lay communication of the recommendations in the primary language of a Regional Code and the subsequent accurate translation into several regional languages remain challenging. And finally, a

systematic impact evaluation of each Regional Code and effective transfer of the lessons learned from one region to another are needed.

Regardless of the challenges, evidence-based and adequately implemented Regional Codes will assist all stakeholders in strengthening cancer prevention worldwide. The methodological guidance developed by IARC is expected to facilitate the development of additional Regional Codes so that eventually all world regions can benefit from appropriate cancer prevention information at both the individual and policy levels. At present, the EU region is setting the pace by launching the fifth edition of the ECAC in the coming months, the Latin American and Caribbean region is currently implementing the first edition of the LAC Code, and resource mobilization efforts are being pursued in other regions of the world to initiate the respective Regional Code in the near future.

AUTHOR CONTRIBUTIONS

Carolina Espina: Conceptualization; writing – original draft; methodology. **David Ritchie:** Writing – review and editing; visualization. **Ariadna Feliu:** Writing – review and editing; visualization. **Carlos Canelo-Aybar:** Writing – review and editing. **Erica D'Souza:** Writing – review and editing; visualization. **Panagiota N Mitrou:** Writing – review and editing. **Andre L. Carvalho:** Writing – review and editing. **Joachim Schüz:** Writing – review and editing. **Hajo Zeeb:** Writing – review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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