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Latin America and the Caribbean Code Against cancer 1st edition: Environment, occupation, and cancer☆

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ABSTRACT

Within the framework of the Latin America and Caribbean region (LAC) Code Against Cancer 1st edition, the current work presents recommendations to reduce exposure to environmental and occupational carcinogenic agents relevant for LAC. Using the methodology established by the International Agency for Research on Cancer (IARC) in the World Code Against Cancer Framework and experience from developing the European Code Against Cancer 4th edition, a working group of LAC cancer-prevention experts reviewed the list of Group I IARC carcinogenic agents, identified prevalent environmental and occupational exposures in the region, and proposed evidence-based cancer prevention recommendations suited to the epidemiological, socioeconomic, and cultural conditions of LAC countries. Two sets of recommendations were drafted: those targeting the general public and a second set for policymakers. Outdoor and indoor air pollution, ultra-violet radiation and occupational exposures to silica dust, asbestos, benzene, diesel, and welding fumes were identified as prevalent carcinogens in LAC and as agents that could be reduced or eliminated to prevent cancers. Recommendations for additional risk factors were not included due to insufficient data of their attributable burden in LAC (sunbeds, radon, aflatoxin), or lack of a clear preventive action to be taken by the individual (arsenic in drinking water, medical radiation), or lack of

Abbreviations: LAC, Latin America and the Caribbean; DALYs, disability adjusted life years; IARC, International Agency for Research on Cancer; WHO, World Health Organization; PAHO/WHO, Pan-American Health Organization; UV, ultraviolet; PM, particulate matter; $PM_{2.5}$, fine particulate matter; PAH, polycyclic aromatic hydrocarbons; BPA, bisphenol A; PELs, Permissible Exposure Limit Values; CO, carbon monoxide; PDAs, Environmental Decontamination Plans (PDAs for initials in Spanish *Plan de Descontaminación Atmosférica)*; CT, computed tomography.

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evidence of carcinogenicity effect (bisphenol A, phthalates, and pesticides). A broad consensus was reached on environmental and occupational carcinogenic exposures present throughout the LAC region and on individual-level and public policy-level recommendations to reduce or eliminate these exposures. Key educational content for the dissemination of these recommendations was also developed as part of LAC Code Against Cancer 1st Edition.

1. Introduction

The Latin America and the Caribbean (LAC) region comprises a total population of 648 million inhabitants [1] distributed in 33 countries and territories, with a large heterogeneity in terms of demographics, economics, geography, and climate [1]. Large disparities between rich and poor are, unfortunately, characteristic of the region. While income inequality has declined in recent decades, the amount of national income concentrated among the wealthiest 1% is the highest in the world [2]. Economic disparities are closely linked to disparities in environmental and occupational exposures and health outcomes [3,4]. For example, in some cities of LAC, a marked disparities in exposure to outdoor air pollution among lower socioeconomic communities have been found [5,6].

Globally, a large portion of cancer deaths (44%) and disability adjusted life years (DALYs) (42%) are attributable to modifiable risk factors and behavioral risks, including smoking and alcohol consumption [7]. Environmental and occupational risks represent the 6th and 7th leading risk factors [7] and, in contrast with other risk factors, are often beyond individual control. In 2019, the DALY age-standardized rate per 100,000 inhabitants associated with occupational and environmental factors in the LAC region was 98.3; notably, there was a large heterogeneity in rates across LAC countries [7], which may be in part due to differences in life expectancy in the region.

Under the overall umbrella of the World Code Against Cancer Framework [8], using the methodology established by the International Agency for Research on Cancer (IARC, cancer research agency of the World Health Organization, WHO) and the experience of developing and promoting the European Code Against Cancer 4th edition [9], the 1st edition of the LAC Code Against Cancer has been developed by cancer-prevention experts of LAC, in collaboration with the Pan-American Health Organization (PAHO/WHO). The LAC Code Against Cancer consists of two complimentary parts. Part 1 is a set of evidence-based individual-level cancer prevention recommendations targeted to the general population, suited to the epidemiological, socioeconomic, and cultural conditions of the region, and tailored to the availability and accessibility of health-care systems [10] (Fig. 1). Part 2 is a supplementary set of recommendations for policymakers (Supplementary material). Policy recommendations were only drafted if a corresponding individual-level recommendation was first agreed upon. Having regional Codes Against Cancer is important because, while a carcinogen causes cancer regardless of geography, exposures are not ubiquitous in all world regions and an individual's ability to modify his/her personal exposure may vary between regions.

While all recommendations from the LAC Code Against Cancer for the individual (Fig. 1) and policymakers (Supplementary material) can be reviewed, the current work focus on environmental and occupational exposures (Fig. 1: Recommendations 8–11 for the individual; Fig. 2: Recommendation for policymakers on "sun exposure", "indoor air pollution", "air pollution" and "occupational hazards"). Scientific justification for other recommendations can be found in other articles in the current issue. The LAC Code Against Cancer 1st edition also includes an online competency-based microlearning program on cancer prevention. The curriculum of this e-learning program builds capacity and competencies on how primary healthcare professionals can help their community reduce their risk of cancer [11].

In the current work, we describe our conclusions related to established (Group I IARC carcinogens) environmental and occupational carcinogens for which an individual could implement feasible actions to significantly decrease his/her exposure and, therefore, his/her risk of cancer. These recommendations were tested in the general public of LAC [12]. In addition, we systematically reviewed the most recent evidence of carcinogenetic effects of the burning of biomass for cooking and heating, an agent classified as a probable (Group 2 A) environmental carcinogen. Lastly, we provide justification for why other potential cancer-causing exposures are not included in the LAC Code Against Cancer 1st edition and briefly summarize other areas of interest evaluated for potential inclusion in future editions.

2. Environmental and occupational exposures in Latin America and the Caribbean

2.1. Environmental exposures and cancer risk

2.1.1. Solar radiation

Solar radiation is essential for life, but excessive exposure, particularly to its ultraviolet (UV) fraction, can cause different types of damage to the skin, including cancer. The amount and composition of solar radiation is greater in areas that have higher altitudes and are close to the equator, particularly in the summer months between 9 am to 3 pm and on surfaces that reflect it more effectively [13]. The amount of solar radiation reaching the earth's surface varies significantly in the LAC region and is the greatest in some areas in the west coast of Mexico and Central America, in the South American highlands, and the Caribbean islands [14]. Two groups particularly vulnerable to exposure to excessive solar radiation are children [15] and those who work mostly outdoors like farmers, construction workers or informal sector workers [16] (discussed in detail in Section 2.2). Skin cancer, both non-melanoma and melanoma, due to occupational exposure to solar radiation, is increasing worldwide and will continue to do so given climate change [17,18]. In the LAC region, the proportion of all cancer attributable to UV radiation has been estimated to be less than 1%, however 90% of melanoma cases were attributable to UV radiation [19]. A recent study conducted in Colombia noted high fatality rates for non-melanoma skin cancer, which may be indicative of late diagnosis or treatment barriers [20].

2.1.2. Indoor air pollution

Indoor air pollution is responsible for nearly 4 million premature deaths from respiratory, cardiovascular diseases and cancer worldwide and 8% of these deaths are attributable to lung cancer [21]. There are no updated estimates of the number of deaths from lung cancer attributable to indoor air pollution in the LAC region, however there are estimates of the percentage of total deaths attributable to indoor air pollution in each country of the region. Percentages vary widely from $< 1\%$ for Chile and Argentina and up to 14% for Haiti [22]. The risk of developing lung cancer associated with indoor coal burning is two times the risk of the general population and is even higher among women, due to their role in food preparation [23]. The composition of indoor pollution from burning fuels varies according to the type of fuel and, therefore, the evidence of its association with cancer should be evaluated separately. IARC classifies coal, a fossil fuel, as carcinogenic (Group 1) for lung cancer [23]. The indoor burning of biomass fuel was classified as probably carcinogenic to humans [23]. Biological mechanisms explaining the relationship between both coal and chemical subproducts of inefficient combustion of biomass fuel (polycyclic aromatic hydrocarbons, PAHs) and lung cancer are well established [23–25].

Latin America and the Caribbean Code against Cancer

Learn how to help prevent cancer in yourself and your family

Specialists on the subject and civil society representatives from Latin America and the Caribbean, convened by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) and the Pan American Health Organization (PAHO), have reviewed the scientific evidence and recommend the following 17 actions people can take to help prevent cancer:

1. Don't smoke or use any type of tobacco. If you do, quitting is possible, with professional help if needed. Don't use e-cigarettes either, as they lead to tobacco use.
2. Make your home a smoke-free place. Respect and promote laws that ensure smoke-free spaces to protect our health.
3. Achieve or maintain a healthy weight throughout your life to help prevent several types of cancer.
4. Get daily physical activity throughout your life and limit the time you spend sitting. Being a physically active person helps prevent several types of cancer.
5. Eat a healthy diet:
   - Eat as many fruits and vegetables as possible at each meal, and regularly include legumes such as beans and lentils.
   - Eat whole grains, such as whole-grain bread, corn tortillas, and brown rice, rather than refined grains such as white bread or rice.
   - Avoid sugar-sweetened beverages, drink water instead.
   - Limit your consumption of ultra-processed foods, such as sweets, sweetened breakfast cereals, salty snacks, pastries, and cookies, among others. Instead, eat natural foods or foods prepared at home.
   - Avoid processed meats, such as deli meats, sausages, or cured meats, and limit your consumption of red meat.
   - Limit your consumption of very hot beverages, such as tea, coffee, and *mate*. Wait a few minutes until the liquid no longer feels hot enough to burn your lips or tongue.
6. Avoid drinking alcoholic beverages. This helps prevent several types of cancer.
7. Breastfeed your baby—the more months the better—to help prevent breast cancer and excess weight in your baby.
8. Protect yourself from direct sun exposure during peak sunlight hours to help prevent skin cancer.
9. If you cook or heat your home with coal or firewood, make sure smoke doesn't build up inside your home.
10. If air pollution is high where you are, limit your time outdoors.
11. Find out if your job exposes you to substances that can cause cancer, and request and adopt the recommended protective measures.
12. Infection from *Helicobacter pylori* bacteria can cause stomach cancer. Check with health professionals to find out if you might benefit from screening and treatment for this bacterial infection.
13. Infection with viruses such as hepatitis B and C, human papillomavirus (HPV), and human immunodeficiency virus (HIV) can also cause cancer. Therefore:
    - Vaccinate children for hepatitis B virus in their first 24 hours of life. Vaccinate yourself and your family at any age if you have not yet done so.
    - Vaccinate girls and teens against the human papillomavirus (HPV), primarily to help prevent cervical cancer, as well as other types of cancer. Take this preventive measure at the ages recommended in your country. If available, vaccinate boys as well.
    - Talk to health professionals to see if you might benefit from screening and treatment for hepatitis B and C viruses to help prevent liver cancer.
    - Get tested for human immunodeficiency virus (HIV), and ask about the prevention and treatment programs available in your country.
    - Make sure to use condoms consistently and correctly, especially with new or casual partners.
14. Do not use hormone replacement for menopause unless directed to do so by your healthcare provider. Hormone replacement can cause breast cancer.

Cancer can be controlled and cured if it is detected and treated early:

15. If you are between the ages of 50 and 74, visit a health care provider and ask for an early detection test for colon and rectal cancer (fecal occult blood test or colonoscopy). Based on the results, follow your health professional's recommendations promptly.
16. If you are 40 years of age or older, visit a health care provider every two years for a clinical breast exam. From age 50 to 74, get a mammogram every two years. Based on the results, follow your health professional's recommendations promptly.
17. If you are between the ages of 30 and 64, visit a health care provider and ask for a molecular human papillomavirus (HPV) test at least every 5–10 years for early detection of cervical cancer. Ask if you can collect the sample yourself. If you don't have access to the HPV test, ask for the exam that is available in your country. Based on the results, follow your health professional's recommendations promptly.

Fig. 1. Latin America and the Caribbean Code Against Cancer 1st Edition: Recommendations for the general public.

The burning of solid fuels (coal and biomass) to produce energy occurs in all regions of the world; however, it is extremely prevalent in low- and middle-income countries [26]. Coal is a solid fossil fuel and not considered biomass. Biomass is all organic matter that can be converted into energy, such as wood, charcoal, animal manure, and solid waste. A recent publication has estimated that 2.8 billion people used solid fuels (wood, dung, garbage, charcoal, and coal, among others) for cooking and heating their homes in 2020 [27], very little difference since the most recent WHO estimate for 2014 [21]. The use of solid fuels, mainly biomass, is very common in the LAC region, although the type of fuel used differs by country. The proportion of the population dependent on solid fuels for cooking has been estimated to be as high as 51–70% in Guatemala and as low as $< 5\%$ in Argentina [26]. In 2019, it was estimated that 27% of the total energy supply for Central and South America came from biomass and coal [26]. The prevalence is lower in the Caribbean, with $< 15\%$ of energy from solid fuels in most countries,

although estimates are not as up-to-date [28]. In addition, the use of solid fuel for cooking is more common in rural than in urban areas [26]. The burning of solid fuels can lead to high levels of indoor air pollution, which in turn contributes to outdoor air pollution, deforestation, and negative health outcomes due to the inhalation of contaminated air. Exposure to indoor air pollution among women and young children in various countries around the world has been estimated to be between 20 and 100 times higher than maximum levels recommended by the WHO [21].

Following the IARC methodology applied for the European Code Against Cancer 4th edition [29] when evaluating agents classified as Group 2 A, we conducted a systematic review in April 2022 to evaluate the effect of household exposure to biomass smoke on risk of lung, esophageal, gastric and colorectal. The review consisted of two separate phases: a) an overview of systematic reviews on this field and b) a systematic review of individual studies (comparative cohorts or case control studies) to update the evidence identified from previous reviews. Results from systematic reviews [24,30–37] and individual studies [38–40] suggested that biomass burning increased risk of lung and esophageal cancer. One systematic review and meta-analysis evaluating risk of lung cancer, found an overall OR of 1.17 (95% CI: 1.01–1.37) associated with biomass for cooking or heating, with a higher magnitude of effect for women (OR=1.95, 95% CI: 1.16–3.27) [24]. Information was sparse for gastric [35,40] and colorectal cancer [40], with evidence of increased risk. An article published since the last IARC monograph meeting on indoor burning of biomass fuel, evaluated incidence of esophageal, colon, gastric and colorectal cancer among 50,045 participants with high prevalence of exposure to biomass for cooking and/or heating and found the strongest and most consistent effects for exposure to heating stoves without chimneys (HR: 1.19; 95% CI: 1.08–1.30 (esophageal); HR 1.26; 95% CI: 1.03–1.54 (colon), 1.11; 95% CI: 1.00–1.23 (gastric)) [40].

2.1.3. Outdoor air pollution

Outdoor air pollution is a threat to the public health of populations of LAC, where industrial sources, vehicular traffic of an aging fleet, and the lack or ineffectiveness of air quality regulatory measures converge [41, 42]. Residents of urban areas are at particular risk, as multiple sources of air pollution come together [43]. LAC is one of the most urbanized areas in the world, with more than 80% of the population living in cities larger than 20,000 inhabitants, yet only 5% of the cities in the region meet WHO air quality guidelines for particulate matter (PM) [42]. A recent study found that larger cities, cities with higher GDP and congestion had higher levels of fine PM ($PM_{2.5}$) [43]. Within countries of the region, different sub-groups of the population may be differently exposed to air pollution, as higher exposure often corresponds to proximity to main sources of pollution, namely primary roads/highways and industry [6, 43]. For example, in Santiago, Chile, a city of nearly 6 million inhabitants, ambient air pollution has improved in the last decades, but still routinely exceeds recommended national air quality standards and international recommendations and has a notable socioeconomic gradient [44].

Sun exposure[9]

- Promote public programs to reduce sun exposure, including the design of public spaces that protect the population.
- Regulate occupational exposure to the sun and monitor the implementation of programs to reduce sun exposure.

Indoor air pollution[10]

- Implement actions and programs to progressively reduce the indoor use of coal and firewood, such as using updated stoves or switching to cleaner energies.

Outdoor air pollution[11]

- Establish environmental air quality standards consistent with WHO guidelines or interim targets and implement strategies to meet them in the short term.
- Increase the coverage of the air quality monitoring network in heavily populated areas.
- Establish communication and information systems to keep the community informed of air quality.

Occupational hazards[12]

- Report, regulate, and monitor economic activities that expose workers—whether formal or informal—to type 1 carcinogens in the workplace.
- Ensure that both public and private companies eliminate or at least control the use of carcinogenic substances to reduce employees' exposure.

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[11] World Health Organization. WHO global air quality guidelines. Particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Geneva: WHO; 2021. Available from: https://apps.who.int/iris/bitstream/handle/10665/345329/9789240034228-eng.pdf?sequence=1&isAllowed=y.

[12] International Labour Organization. Promotional Framework for Occupational Safety and Health Convention. Geneva: ILO; 2006. Available from: https://www.ilo.org/dyn/normlex/es/f?p=1000:12100:0::NO::P12100_INSTRUMENT_ID,P12100_LANG_CODE:312332,en:NO.

Fig. 2. Latin America and the Caribbean Code Against Cancer 1st Edition: Recommendations for policymakers on environment and occupation.

There is solid evidence, including well described biological mechanisms, that both outdoor air pollution per se and PM from outdoor air pollution are carcinogenic to humans [45]. Exposure to $PM_{2.5}$ is estimated to be associated with more than 250,000 lung cancer deaths annually or 14% of all lung cancers worldwide and the global proportion of lung cancer deaths attributable to $PM_{2.5}$ exposure was exceeded only by smoking (14% versus 63%) [46]. Unfortunately, there are no exact figures on the burden of lung cancer associated with outdoor air pollution in the LAC region. It has been estimated that the number of cases and deaths from lung cancer will increase in the region in the coming years [47] and it has been suggested that the differences in outdoor air pollution levels could, in part, explain the differences in lung cancer incidence and mortality across LAC countries [47].

2.2. Occupational exposures and cancer risk

Chemical and physical agents are often present in the work environment and many of these agents can cause cancer [48,49]. Exposure to solar radiation is a major occupational health problem in LAC countries, since both agriculture and construction are relevant sectors of the regional economy and employ many workers [50–52]. In addition, exposure to respirable crystalline silica, asbestos fibers, diesel exhaust fumes, benzene, tobacco smoke, and welding fumes are common among millions of workers in LAC [53]. The 2017 Global Burden of Disease Study estimated that the risk of occupational lung cancer for LAC ranged from 8.9% (Caribbean) to 16.2% (South Latin America) [7]. Carcinogenic agents can and should be promptly identified to be controlled, eliminated, or replaced through engineering solutions, occupational hygiene procedures, and personal protection equipment. Notably, unlike lifestyle-related behavioral factors such as smoking and diet that can be controlled by the individual, workplace exposures are often beyond the understanding and control of workers. For this reason, the responsibility for exposure control lies primarily on the employer, who must try to control the exposure and inform workers what they are exposed to and provide means of protection from undesirable harm.

Many IARC Group I carcinogenic agents are found in the work environment in the form of gases, fumes, and dusts and the main routes of exposure are the skin and the respiratory systems [48]. It has been estimated that lung cancer accounts for 23% of cancers related to occupational agents [48] and about half of cases may be due to asbestos [54]. Exposure to crystalline silica, diesel exhaust, welding fumes, arsenic, coke oven emissions, and coal combustion are among other Group I agents that cause lung cancer [23,48,55–57]. In the last decade, benzene exposure was estimated to affect 0.9% of the Brazilian working population [58]. Estimated lifetime cancer risk of both occupational and environmental benzene and other volatile organic compounds exposure was greater than 1/106 in La Plata, Argentina [59]. Exposure to wood and leather dust in addition to exposure to formaldehyde, textile dusts, and nickel and chromium compounds, have a strong association with sinonasal cancers [60]. Common occupational and environmental carcinogens found in LAC countries and main target organs have been summarized in Table 1.

3. Interactions between risk factors

Lung and skin cancer are the leading cancer sites related to environmental and occupational exposures [61]. The main risk factors for lung cancer are smoking and environmental tobacco smoke [62,63], followed by radon exposure [64]. Burning household solid fuel can generate cancer-causing chemicals that add to the risk of lung cancer from smoking [25]. In the LAC region there is great heterogeneity in the prevalence of smoking, from 5% in Panama and up to 29% in Chile [65]. In most LAC countries, lung cancer mortality has decreased for men only, reflecting the increased prevalence of women who smoke. There is also evidence showing that the risk of death from outdoor air pollution-associated lung cancer is slightly higher among people who smoke, compared to those who do not smoke [66]. The interaction of both factors, smoking and air pollution, is synergistic, that is, their combined effect is greater than expected considering the sum of individual risks [66]. This interaction implies that interventions designed to reduce smoking and air pollution would result in a greater reduction in risk of lung cancer than a single-agent intervention. Exposure to asbestos [67], radon [68], silica dust [69], and PAHs [70] have also shown synergistic effects with smoking on the pathogenesis of lung cancer. Several studies have shown synergistic effects of the exposure to solar radiation and arsenic in drinking water on the risk of basal cell carcinoma [71–74]. Interactions may imply that the safety level for some regulated pollutants should be lowered in the presence of another exposure with a known synergistic effect. Interactions were considered when formulating recommendations for the individual and policy and also in the framework of providing advice for health professionals [11] to raise awareness to their patients and families.

4. The LAC Code Against Cancer 1st edition: recommendations on environmental and occupational exposures, individual interventions, and possible impact in public policies

Below we present recommendations to reduce the risk of cancer associated with exposure to indoor and outdoor air pollution, solar radiation, and occupational carcinogenic agents among LAC populations. Each recommendation is accompanied by a short justification.

4.1. Recommendations for individuals

4.1.1. Recommendation #8 of the LAC Code Against Cancer 1st edition

"*Protect yourself from direct sun exposure during peak sun hours to help prevent skin cancer*" (Fig. 1). Individual actions to reduce exposure include reducing the amount of time spent in direct sunlight particularly during hours of highest sunlight intensity, wearing protective clothing and accessories (e.g., long-sleeve shirts and hats), and using sunscreen [75]. Skin cancer is one of the most common types of cancer worldwide, including the LAC region [76]. Exposure to excessive solar radiation is a

Table 1
Common occupational and environmental carcinogens in Latin American and Caribbean countries and main target organs*.

Carcinogen	Target organ
Aflatoxins	Liver
Air Pollution	Lung
Arsenic	Lung, skin
Asbestos	Lung, pleura, peritoneum, pericardium, tunica vaginalis, larynx, ovary
Benzene	Hematopoietic system
Benzidine	Bladder
Beryllium	Lung
Cadmium	Lung
Chromium VI	Lung
Coal-tar pitches	Skin, lung, bladder
Engine exhaust, diesel	Lung
Formaldehyde	Nasopharynx, leukemia
Leather dust	Nasal cavity, paranasal sinuses
Lindane	Non-Hodgkin's lymphoma
Mineral oils	Skin
Nickel compounds	Nasal cavity, lung, paranasal sinuses
Radon	Lung
Silica	Lung
Solar radiation	Skin
Soot	Skin, lung
2,3,7,8-Tetrachloro-dibenzo-p-dioxin	All cancers combined
Tobacco smoke	Lung, bladder, oral cavity pharynx, larynx, esophagus
Vinyl chloride	Liver, lung, blood vessels
Welding fumes	Lung
Wood dusts	Nasal cavity, paranasal sinuses, nasopharynx

* Adapted from Clapp et al. [121] and Loomis et al. [122].

modifiable risk factor for the development of skin cancer and, therefore, its prevention is a key element to minimize its harmful effects.

4.1.2. Recommendation #9 of the LAC Code Against Cancer 1st edition

"*If you cook or heat your home with coal or firewood, make sure smoke doesn't build up inside your home*" (Fig. 1). Coal burning is an established carcinogen [23] and our systematic review indicated that exposure to biomass burning, especially with inadequate ventilation, is associated with cancer (particularly lung and esophageal cancer) [24,30–40]. Exposure to pollutants in indoor air can be reduced by controlling their sources and using efficient exhaust ventilation systems for cooking and heating. For example, individuals should be encouraged to use energy efficient cookstoves, change from the use of open devices, and/or change to lower emission sources of fuel (e.g., from firewood to natural gas or from natural gas to electricity) [21,77]. In the absence of exhaust or ventilation equipment, individuals can ventilate directly (e.g., opening a window or door) and, if that is not possible, as in the case of cooking, individuals may consider cooking outdoors.

4.1.3. Recommendation #10 of the LAC Code Against Cancer 1st edition

"*If air pollution is high where you are, limit your time outdoors*." (Fig. 1). Outdoor air pollution is a cause of lung cancer [45], thus reducing individual exposure may decrease risk. Individual-level interventions to reduce exposure to harmful levels of outdoor air pollution, either as part of chronic exposure or acute episodes, have begun to be evaluated. Harmful or high levels of air pollution is defined as levels that surpass local air quality regulation or WHO recommendations. The simplest and most frequent intervention is to stay indoors [78,79], ideally in a place that uses high-efficiency air filters. Staying indoors should be considered in combination with the physical and mental benefits of spending time outdoors and also infiltration of outdoor air pollution to indoor air spaces in contexts of poor insulation [80,81], common in the LAC region. We acknowledge that the ability to reduce time spent outdoors is likely not possible for many informal workers or traffic police workers for example, in the LAC region. Recent evidence also points to the effectiveness of face mask use in reducing individual exposure to outdoor air pollution [79,82]. Individuals who choose to exercise outdoors should consider the potential for exposure to air pollution from traffic sources and ideally select a location far away from major roads during traffic spikes or high-pollution episodes [78,79]. In addition, vulnerable groups of the population (e.g., the elderly, pregnant women, and those with asthma and other underlying health conditions) should take special care and may need to implement individual avoidance actions even sooner.

4.1.4. Recommendation #11 of the LAC Code Against Cancer 1st edition

"*Find out if your job exposes you to substances that can cause cancer, and request and adopt the recommended protective measures*." (Fig. 1). Millions of workers in LAC are exposed to harmful agents that can cause cancer (most notably lung cancer) in their place of work (see Table 1) [53]. Employers' recognition of ongoing exposure to carcinogenic agents in the workplace provides the opportunity to advise workers of their potential risks, but also to implement control mechanisms to reduce their exposure. In turn, workers must comply with the appropriate and necessary control measures for their own protection. Workers' participation by expressing opinions on ways to avoid harmful exposures is also fundamental.

4.2. Public policies recommendations

4.2.1. Solar radiation

The LAC Code Against Cancer 1st edition recommends public policies to: "*Promote public programs to reduce sun exposure, including the design of public spaces that protect the population*" and "*Regulate occupational exposure to the sun and monitor the implementation of programs to reduce sun exposure*" (Fig. 2). Exposure to solar radiation is ubiquitous, underscoring the importance of continued surveillance and support for prevention through public policies aimed at reducing the incidence and prevalence of skin cancer. Collective measures for sun exposure protection are, for example, shelters at bus stops, construction sites, schools, and at farms during sowing and harvesting periods, and increasing green areas in cities.

4.2.2. Indoor air pollution

The LAC Code Against Cancer 1st edition recommends public policies to: "*Implement actions and programs to progressively reduce the indoor use of coal and firewood, such as using updated stoves or switching to cleaner energies*" (Fig. 2). Adequate and equitable access to affordable clean energy sources or ventilation solutions for households that use solid fuels for cooking or heating should be available. In low-income contexts, households rely primarily on traditional solid fuel sources, such as crop residues, manure, and firewood. Only at the highest income levels do households switch from harmful solid fuels to cleaner non-solid fuels such as ethanol and natural gas. It is of utmost importance that public policies ensure equitable access to cleaner energy sources to reduce the number of individuals exposed to indoor air pollution. In addition, implementing smoke-free laws to protect bystanders of environmental exposure to tobacco second hand smoke and implementation of other proven cost-effective measures for tobacco control (e.g., smoking cessation, taxation, media campaigns, etc.) are key measures to reduce the risk of other carcinogens [83].

4.2.3. Outdoor air pollution

The LAC Code Against Cancer 1st edition recommends public policies to: "*Establish environmental air quality standards consistent with WHO guidelines or interim targets, and implement strategies to meet them in the short term*"; "*Increase the coverage of the air quality monitoring network in heavily populated areas*"; and "*Establish communication and information systems to keep the community informed of air quality*" (Fig. 2). National and international regulations and guidelines established in the last 50 years help to quantify and visualize the problem of air pollution. In most areas of the world, air quality measurement is the responsibility of governments that maintain monitoring stations, analyze and, ideally, make data available to the population. In a study published in 2016, it was reported that only 17 of 33 LAC countries actively measured air quality, with most stations located in capital and major cities and the best coverage in Brazil, Chile, Colombia and Mexico [42]. Investment in air pollution monitoring, including creating new monitoring networks and expanding existing ones, is necessary to raise awareness of the levels of harmful pollutants in the air. Once monitoring networks are in place, air quality information could be tailored to include additional information for groups particularly sensitive to the effects of air pollution. For example, there may be a level noted as "unhealthy for sensitive groups", separated from "unhealthy for the general population". Monitoring will also allow the evaluation of changes as a result of urban-planning programs to improve air quality (e.g., 15-minute cities and low emission zones) [84,85].

4.2.4. Occupational exposures

The LAC Code Against Cancer 1st edition recommends public policies to: "*Report, regulate, and monitor economic activities that expose workers—whether formal or informal—to type 1 carcinogens in the workplace*" and "*Ensure that both public and private companies eliminate or at least control the use of carcinogenic substances to reduce employees' exposure*" (Fig. 2). Occupational risks that cause cancer are being increasingly recognized and much of the cancer burden related to work exposures can be prevented. To identify and control carcinogens at work it is necessary to understand work processes and be able to identify and inform the in-place agents or processes that generate cancer risks with a multi-professional team including occupational hygienists and workers. Despite the mounting description of occupational carcinogens, there is still a need to advance knowledge of the prevalent causes of

occupational cancer in the LAC region, ideally with updated lists of the most prevalent carcinogens or processes by country to propose control mechanisms. Asbestos, the agent responsible for more than 30% of all occupational cancers, is banned in six LAC countries [86]. Even in the absence of local knowledge of exposed groups or reported of cancer cases, asbestos bans, and measures to protect workers and populations from in-place asbestos products should be pursued in the region.

In the absence of Permissible Exposure Limit Values (PELs) for carcinogens, exposures must be eliminated or avoided, and if this cannot be done, a way to control the risk, using occupational hygiene measures, must be found. Control mechanisms can be grouped into the following categories: regulation; elimination; substitution; and reduction. Federal authorities have a fundamental role in controlling exposures and compliance to these mechanisms must be under the jurisdiction of the competent health and labor authorities in each country. Additionally, authorities should include regulations requesting employers to inform their workers about the substances in their workplace that are associated with health risks, in particular cancer risk.

5. Cost-effectiveness and expected impact of recommended policies and experiences from LAC

There is a paucity of information about the effectiveness for cancer prevention of modifying individual environmental or occupational exposures. Since effectiveness refers to the impact of an intervention in real-life situations, it becomes especially problematic to extrapolate results of one environment, with its unique combination of pollutants, climate, geography, urbanism, living conditions, and genetics of the population. Similarly, there are no controlled studies of cancer incidence related to an intervention aimed at reducing indoor or outdoor air pollution, sun exposure or occupational exposures in the LAC region.

There are a few experiences in public policies to decrease indoor and outdoor air pollution in LAC. For example, many household stove programs have been implemented in Central America where it is estimated that 20 million people use biomass burning for cooking. One report that summarized the findings of several improved stoves concluded that carbon monoxide (CO) and PM was reduced on average by 59% and 95%, respectively [87], with individual studies reporting higher reductions [88]. In terms of outdoor air pollution, in Chile, where levels of outdoor air pollution are extremely high especially in cities in Southern Chile in which the population uses wood for heating and, to a lesser extent, cooking, public policies have been implemented via Environmental Decontamination Plans (PDAs for initials in Spanish *Plan de Descontaminación Atmosférica*) [89,90]. PDAs are specific to urban areas and contain a mix of policies aimed at reducing levels of specific pollutants. For example, the PDA for a particular city may include gradual prohibition of less efficient wood-burning stoves, banning of certain types of wood, as well as programs to improve home insulation and purchase more efficient heaters. PDAs have been evaluated, with one study showing a decrease in 8 $\mu g/m^3$ associated with the policy [91].

6. Risk factors discussed but not included in the LAC Code Against Cancer 1st edition

The importance of potentially including recommendations related to exposure to sunbeds, pesticides, bisphenol A, phthalates, aflatoxin, arsenic, radon, and medical radiation were also discussed, but were ultimately not included.

6.1. Sunbeds

In the European Code Against Cancer 4th edition [9], sunbeds were specifically mentioned ("*Do not use sunbeds*"). While discussed, this recommendation was not included in the LAC Code Against Cancer 1st edition, due to the lack of information on the use of sunbeds in the region. For example a systematic review and meta-analysis of prevalence of indoor tanning published in 2014, reviewed all records starting as far back as 1898 until 2013 reporting a prevalence of indoor tanning and did not include a single study from the LAC region [92].

6.2. Pesticides

Agricultural pesticide use is common in the LAC region and represents 20% of the world consumption [93]. This high use has resulted in widespread human exposure and, while much evidence exists relating exposure to pesticides to a variety of negative health outcomes, data on the association of exposure to current use pesticides and risk of cancer among LAC populations are limited [94]. Within the framework of the LAC Code Against Cancer 1st edition, we undertook a mapping of the literature on the association of current use pesticides with risk of cancer published between 2015 and 2022 and identified 60 published systematic reviews. Considering the variety of pesticides and cancer types represented in these reviews and that lack of strong evidence for a specific pesticide and/or cancer type, we decided to not conduct a formal systematic review. In addition, the working group discussed glyphosate (Group 2 A, probably carcinogenic to humans) [95]. Glyphosate is widely used in the region [96] and the subject of major debate; however, the IARC Advisory Group in 2019 indicated that there were no new studies of cancer in humans to conduct a new review of this pesticide [97]. Moving forward, it is essential to establish surveillance and monitoring systems for diseases associated with pesticide exposure in order to identify the magnitude of the problem and define evidence-based prevention policies and interventions [94].

6.3. Bisphenol A (BPA) and phthalates

There is growing interest in human exposures to synthetic chemical compounds in consumer products such as bisphenol A (BPA) and phthalates and risk of breast cancer [98–100]. BPA is an additive to increase durability of products and is found in food and water containers, baby bottles and pacifiers, among others [101]. Phthalates are additives found in many plastics (toys, medications, medical equipment, and diet supplements), and are considered endocrine disruptors [102]. It is estimated that almost the entire U.S. population has been exposed to BPA [103] and phthalates, [104] and we expect similarly high exposure levels in LAC populations. Few studies have found higher levels of BPA and phthalates among Mexican women with breast cancer [98,99]; however, to date there is not sufficient evidence to determine whether these synthetic compounds are carcinogenic or not [100].

6.4. Radon

Radon is an inert, radioactive, colorless, and odorless gas that is present in nature, in soil and rocks, as an element derived from uranium [105]. Exposure to radon gas is the second leading cause of lung cancer in the world and, in the U.S., is estimated to cause approximately 21,000 deaths each year [64]. This risk factor is included in the European Code Against Cancer 4th Edition [106,107], but not in the LAC Code. Despite the large number of mineral-rich areas in the LAC region, most countries have not implemented surveillance systems to identify areas and homes with elevated radon exposures [108]. Additionally, only nine countries in Central and South America have defined maximum permissible concentrations of radon [108]. Thus, the prevalence of radon exposure in occupational and residential settings is poorly documented or unknown in most LAC countries, making it impossible to suggest individual-level recommendations to reduce or eliminate this exposure. Surveillance of radon in the LAC region is necessary and should be a priority of local authorities.

6.5. Aflatoxin

Aflatoxin is a protein from a common fungus that can contaminate

foods such as corn, rice, peanuts, and tree nuts, and is a known Group I carcinogen [109,110]. Like with radon, suggesting individual-level recommendations for avoiding exposure to aflatoxin for the population of region is difficult because of the lack of evidence on the scale of the problem in the LAC region. Not a single LAC country has a surveillance system in place that would allow consumers to learn about their potential exposure. LAC countries need to measure, regulate and monitor aflatoxin exposure in food and also as an occupational exposure.

As new surveillance data becomes available for both radon gas and aflatoxin in the region, future editions of the LAC Code Against Cancer may consider their inclusion.

6.6. Arsenic

Arsenic is a natural metalloid, present in the earth's crust, and, in its inorganic form, is extremely toxic. As a result of natural (volcanic eruptions and rock erosion) or artificial processes (mining, use of arsenical pesticides, exploitation of aquifers), it is found in the high levels of soil, air, water, and food in certain LAC countries (e.g., Chile, Argentina, and Mexico) [111–113]. Arsenic is a known cause of skin, lung, and bladder cancer [114]. In 1993, the WHO recommended that the exposure level in drinking water be less than 10 μg/L and most countries of the region have adopted this recommendation [115]. However, not all countries have established a surveillance system on arsenic levels in water in urban and rural areas. Users of well water are often unaware that arsenic is present in water since it does not provide odor, color, or flavor. Likewise, users of private or municipal water services are unaware of arsenic content and, therefore, do not have the ability to protect themselves when levels are above safe limits. In this scenario, it is not possible to include an individual-level recommendation to reduce exposure to arsenic; nevertheless, we stress the necessity of health authorities to implement surveillance of arsenic levels in drinking water and adequately inform the population regarding the concentration of arsenic in the drinking water they consume and their protection alternatives [116].

6.7. Medical radiation

Medical radiation exposure remains by far the largest artificial source of exposure to ionizing radiation and continues to grow at a substantial rate [117]. Most of this increase was attributed to the markedly increased use of computed tomography (CT) scans and nuclear medicine procedures [118]. Although most increases have been reported in developed countries where populations have more access to healthcare, the increasing urbanization of the world population, including LAC, along with the gradual improvement in living standards will result in more individuals having access to healthcare systems. Consequently, population dose due to medical radiation exposures will continue to increase over time across all countries. While the benefits of using ionizing radiation in medicine is unquestionable, it is necessary to protect patients from potential harm caused by stochastic and deterministic effects of radiation exposure. Because ionizing radiation can cause damage to DNA, exposure may increase a person's lifetime risk of developing cancer [118]. Although the individual risk is very small, millions of exams are performed each year, making radiation exposure from medical imaging an important public health issue [119]. Several national and regional campaigns have been launched to reduce unnecessary use of diagnostic imaging exams [117,120], including the LatinSafe for LAC countries (http://latinsafe.org/). An individual-level recommendation for medical radiation was not included in the LAC Code Against Cancer because this exposure is generally outside the ability of the individual to decide since the benefit of the exposure might outweigh its potential risk [119].

7. Messages for primary health care professionals

Health promotion is key to ensure individuals are informed about evidence-based actions they should undertake to prevent and reduce their cancer risk. Primary healthcare professionals play an important role in cancer prevention since they are population's first contact with the healthcare system; thus, health promotion should be embedded in the daily practice of these professionals.

(1) **UV radiation**: Excessive sun exposure can cause skin cancer, especially in people with lighter skin. Health professionals should educate the public about this risk and how a person could protect him/herself and his/her family.
(2) **Indoor air pollution**: Burning of biomass (e.g., wood) and coal indoors for cooking or heating generates dangerous levels of indoor air pollution; women and young children are most at risk. Health professionals should recommend the use of appropriate exhaust ventilation methods to reduce exposure to harmful pollutants. Controlling exposure to smoke from indoor coal or biomass burning reduces the risk of lung cancer, other morbidities, and mortality.
(3) **Outdoor air pollution**: Air pollution and exposure to particles are causes of lung cancer with a clear dose-response relationship. Decreasing exposure to environmental pollutants in the air, especially when levels are high, lowers cumulative exposure and therefore reduces the risk of cancer associated with this source. Health professionals should recommend the population to avoid being outdoors during peaks of air pollution or wearing high efficiency masks if they cannot avoid being outdoors.
(4) **Occupational exposures**: exposures vary broadly in the LAC region; thus, health care professionals should learn about the occupational exposures of the population under their care, learn how to limit exposures, and how to protect workers. The population should also be advised how to protect themselves at work or avoid co-carcinogens like tobacco and sun exposure. Health professionals should look for early symptoms and signs of cancer in their patients.

8. Conclusions

We selected four risk factors to be included in the environmental and occupational exposures section of the LAC Code Against Cancer (Figs. 1 and 2). These were selected after a rigorous process, which included a systematic review for some of the agents that had not been recently evaluated by the IARC Monographs Program. Besides carcinogenicity and relevance for the region, we evaluated if there were feasible and easy to communicate actions an individual from the LAC region could carry out [12]. Arsenic, aflatoxins, radon, benzene, and asbestos are established Group I IARC carcinogens. However, we did not specifically include recommendations for each for different reasons. In the case of arsenic, we could not identify a clear preventive action that could be taken by the individual. For aflatoxins and radon, there was insufficient evidence of population exposure in LAC. Benzene and asbestos were included as part of occupational exposures. This first LAC Cancer code will be reviewed periodically as knowledge of exposures distribution and their regulation in the LAC region advance and clear actions for the individual are identified.

Thus, we describe here the most stringent set of measures that will decrease exposures to carcinogens present in the everyday lives of the LAC population. We propose public health measures that are realistic and could potentially have a large impact in the reduction of these selected exposures. We understand that, to generate an impact, our recommendations need to be broadly disseminated throughout the LAC region and that tailored health promotion and educational programs for local health professionals and the public should be developed. Our environmental and occupational exposures working group has also

developed educational modules for each of the recommendations described above to ensure primary healthcare professionals in the region are ready to advise patients and motivate them to adopt recommendations [11].

We are hopeful that this 1st edition of the LAC Code Against Cancer will be accompanied by follow-up studies that evaluate the adoption of recommendations and continued cancer surveillance in the LAC region to evaluate potential changes. Regional studies on the implementation of the LAC Code Against Cancer could be carried out by governments in collaboration with academic institutions and results shared to facilitate the exchange of experiences and summarizing of results. This will be a key source of information to improve future editions of the LAC Code Against Cancer.

CRediT authorship contribution statement

Estela Blanco: Conceptualization, writing-original draft preparation. Eduardo Algranti, Luis Abdon Cifuentes; Lizbeth López-Carrillo; Ana M. Mora; Julietta Rodríguez-Guzmán; Laura Andrea Rodríguez-Villamizar; Lene H.S. Veiga; Carlos Canelo-Aybar; Wendy Nieto-Gutierrez: Writing-Reviewing and Editing. Carolina Espina; Ariadna Feliu: Methodology, Conceptualization, Writing- Reviewing and Editing, Project administration, Funding acquisition. Catterina Ferreccio: Conceptualization, Writing- Reviewing and Editing, Supervision.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2023.102381.

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