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Latin America and the Caribbean Code Against Cancer 1st edition: Tobacco and nicotine-related products, secondhand smoke, and alcohol and cancer☆

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ABSTRACT

Tobacco, secondhand smoke (SHS), and alcohol, all carcinogens, are leading preventable cancer risk factors in Latin America and the Caribbean (LAC). Since 2000, smoking and SHS exposure have significantly decreased in the region. Yet alcohol consumption remains high. The entry of nicotine-related products such as electronic cigarettes (e-cigs) threatens achievements made in tobacco control and chronic diseases prevention, including cancer. E-cigs use is likely associated with smoking initiation among adolescents who had never smoked and dual use with combustible tobacco products. Therefore, the LAC Code Against Cancer recommends to the public actions they can take to reduce their risk of 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. and 3. Avoid drinking alcoholic beverages. This helps prevent several types of cancer. The Code recommends to policymakers a package of cost-effective policies based on the MPOWER and SAFER to prevent cancer at the population level. It also recommends that primary care health professionals: 1. Ask all their patients and their families whether they smoke or vape, inform them about the harms of smoking and vaping, and promote tobacco and nicotine related products cessation strategies among users. 2. Inform about the harms of exposure to SHS, especially among children, and promote smoke-free environments, and 3. Prevent alcohol use by their patients and their families, use tools to assess use, intensity, and frequency, and apply brief counseling intervention to support alcohol abstinence in primary care.

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1. Introduction

Tobacco and alcohol use are leading modifiable cancer risk factors worldwide and for both, there is no safe level of consumption [1,2]. Even though evidence-based interventions and policy strategies to reduce consumption exist for both, and some have been successfully implemented in Latin America and the Caribbean (LAC), they remain a public health threat in the region [3,4].

Under the umbrella of the World Code Against Cancer Framework [5,6], 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 [7], the 1st edition of the Latin America and the Caribbean Code Against Cancer (LAC Code Against Cancer) was developed in collaboration with the Pan-American Health Organization (PAHO). The LAC Code Against Cancer includes 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 [8] (Fig. 1). The Code also includes a set of recommendations for policymakers (Supplementary material I) and an online competency-based microlearning program on the topics covered by the recommendations. The aim of this learning program is to build primary healthcare professionals' capacity to advice patients and families on evidence-based actions on primary and secondary cancer prevention [9].

1.1. Prevalence of smoking, e-cigarettes use, exposure to secondhand smoke and alcohol in LAC

Current tobacco use prevalence has declined worldwide, including in the Americas (28 % in 2000 to 16.3 % in 2020). The region has the second-lowest smoking prevalence globally [4]. However, wide variation remains across subregions and countries. In 2020, adult tobacco use was the highest in Chile (29.2 %) and the lowest in Panama (5.0 %) and is higher among males compared to females. Regarding adolescents, 11.3 % currently consume tobacco in the region, with Dominica having the highest prevalence (25.3 %, 2009 data) [4,10]. As opposed to adults, there is no difference by gender. However, in Argentina, Brazil, Chile, and Uruguay prevalence is higher among females [4]. The LAC region's most widely consumed tobacco product is combustible cigarettes. Consumption of other combustible tobacco products is less common in the region. For example, in Argentina, Brazil, Costa Rica, Mexico, and Uruguay, only between 0.1 % and 0.3 % consume products such as waterpipes, pipes, or cigars [4,11]. Use of smokeless tobacco is generally low, ranging from 0.1 % in Costa Rica to 3.5 % in Venezuela [4,11].

Novel and emerging tobacco and nicotine-related products regulation remains a challenge worldwide and in LAC. Electronic cigarettes (e-cigs) are the most commonly consumed product among adolescents in the region [4]. Like smoking, e-cig use is higher among males compared to females, except in Colombia and Venezuela where use is almost the same between genders (9 % and 9.5 % in each country, respectively) [4]. Regarding flavored capsule cigarettes, which contain a crushable flavor capsule in the filter, LAC is the region where consumption is the highest worldwide (in Chile and Guatemala exceeds that of non-flavored cigarettes) [12].

Exposure to secondhand tobacco smoke (SHS), also known as involuntary or passive smoking, causes significant morbidity and mortality. Worldwide, SHS leads to an additional 1.2 million deaths to those caused from active smoking per year (15 % of the total deaths from smoking) [4]. Most of this burden is among women and children [13]. According to the Global Adult Tobacco Survey (GATS), the proportion of adults working in closed or semi-enclosed areas exposed to SHS varies widely in LAC. Ranging from 31.6% in Argentina to 5.3 % in Panama. Regarding exposure at home ranges from 33% in Argentina to 7.9 % in Brazil [11]. In Argentina, Colombia, Cuba, and Uruguay more than 40 % of adolescents are exposed at home [11].

Alcohol consumption in the Americas is one of the highest worldwide. Consumption results from a combination of individual (e.g., gender, income) and social (e.g., policies, marketing) factors. From 2010–2016, the percentage of the Americas' (including the US and Canada) adult population that drink alcohol decreased from 57.8 % to 46.1 %. Furthermore, *per capita* consumption of pure alcohol has decreased since 2012 from 8.2 to 8.0 liters [3]. However, the modest decrease is unlikely to yield any public health benefits *as* drinkers' consumption increased from 14.7 to 15.1 liters of pure alcohol [3]. High-income countries in the Americas have higher (9.0 liters) consumption compared to those in the upper-middle (6.8) and low- and lower-middle income (4.4). In 2019, Uruguay (10.9) had the highest per capita consumption while Guatemala the lowest (2.5). (Table 1). There are also differences within countries when analyzed by gender. While males in Uruguay drink 17.1 liters per capita, females drink 5.3 [3]. Regarding adolescents, the amount consumed is lower compared to adults, yet the Americas rank second worldwide (38.2 %). Heavy episodic drinking is highest among adolescents in Trinidad and Tobago, Saint Kitts and Nevis, Barbados, Saint Lucia, Grenada, Peru, and Brazil [14].

Beer remains the beverage of choice in the Americas (54 % of all drinks). Spirits are also common, particularly in Central America and the Caribbean [3]. Regarding drinking patterns, of all adults, 56.7 % are current drinkers, 23 % are current heavy episodic drinkers and 9 % have an alcohol use disorder [3].

1.2. Cancer burden in LAC attributable to tobacco, secondhand smoke, and alcohol

Every year 1.5. new cancer cases are diagnosed, and 700,000 deaths occur in the LAC region [15] (Fig. 2). The five most common cancers in 2020 were prostate (15 %), breast (14 %), colorectal (9 %), lung (7 %) and stomach (5 %) [15]. Among the modifiable risk factors for non-communicable diseases (NCDs), including cancer, tobacco and alcohol are the leading ones [2]. In 2019, smoking was responsible for 96,816 cancer deaths in LAC [2]. Lung cancer was the leading cause of cancer death (42,467 deaths attributable to smoking) [16]. The highest lung cancer incidence rates were in countries with high smoking prevalence (Uruguay, Cuba, and Argentina) [17]. Moreover, there were 3922 cancer death and 3109 lung cancer deaths attributed to exposure to SHS on its own [2].

Whereas lung cancer remained the leading cause of cancer death in South America and the Caribbean, liver cancer was in Central America [15,17].

In LAC, 39,300 new cases of cancer were attributed to alcohol in 2020 (5.3 % of total worldwide). The overall age-standardized incidence rate was 5.4 alcohol-attributable cancer cases per 100,000 persons [18]. In 2019, alcohol was responsible for 24,168 cancer deaths. Colorectal, liver, and esophageal cancer were the largest contributor to the alcohol-attributable cancer deaths in LAC [2,19].

Given the burden from tobacco (including SHS) and alcohol in LAC, we sought to describe the scientific evidence and the interaction effect of both cancer risk factors, as well as the prevention and control strategies. Therefore, we aim to provide evidence to support recommendations for the public and policymakers to decrease consumption of tobacco and alcohol.

2. Tobacco and nicotine-related products, secondhand smoke, and alcohol drinking association with cancer

2.1. Tobacco and nicotine-related products

Tobacco, a group 1 carcinogen [20,21], has 62 chemicals classified by IARC as carcinogenic to laboratory animals or humans (16 are carcinogenic to humans) [20,21]. Tobacco use is causally linked to 15

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.

Table 1
Tobacco and alcohol consumption, population 15 + years of age. Latin America and Caribbean (LAC) region and in its countries in 2015, 2010 and 2018.

	Tobacco smoking Prevalence (%)[a]	Total alcohol consumption per capita (liters of pure alcohol, projected estimates)[b]	
Year	2015	2010	2018
World		6.3	6.2
LAC region	17.1	7.0	6.3
LAC countries:			
1. Antiqua e Barbuda	NA	5.6	6.4
2. Argentina	22.5	9.1	9.7
3. Bahamas	11.3	4.1	4.8
4. Barbados	7.9	8.0	9.7
5. Belize	NA	7,1	6.2
6. Bolivia	NA	5,6	4.4
7. Brazil	14.3	8.5	7.4
8. Chile	38.7	9,3	9.1
9. Colombia	9.5	5.0	5.7
10. Costa Rica	12.1	4.8	4.9
11. Cuba	35.9	5.0	5.8
12. Dominica	NA	9.7	11.2
13. Dominican Republic	13.9	6.1	6.7
14. Ecuador	7.4	6.2	4.2
15. El Salvador	10.1	3.3	3.9
16. Grenada	NA	8.3	9.5
17. Guatemala	NA	3.5	2.5
18. Guyana	NA	6.8	6.9
19. Haiti	12.7	3.0	2.7
20. Honduras	NA	3.6	3.8
21. Jamaica	16.8	4.4	4.2
22. Mexico	14.5	5.2	5.0
23. Nicaragua	NA	4.8	5.2
24. Panamá	6.5	6.8	8.0
25. Paraguay	14.1	7.6	7.6
26. Peru	NA	7.7	6.4
27. St Lucia	NA	9.7	10.6
28. St. Kitts and Nevis	NA	9.4	8.9
29. St. Vincent and the Grenadines	NA	7.0	9.1
30. Suriname	26.2	6.2	5.3
31. Trinidad and Tobago	NA	6.2	6.7
32. Uruguay	18.1	7.1	6.9
33. Venezuela, RB	NA	8.7	4.1

[a] Source: PAHO [4] The prevalence of current tobacco smoking refers to the percentage of the adult population (persons aged 15 and over) who smoked any tobacco product in the last 30 days before the survey; it includes daily and occasional smokers. Data are available standardized for the year 2015. These data should be used strictly for comparison and not to calculate the absolute number of smokers in each country. There is no data available, or the necessary information was not obtained to carry out the standardization in the cases of Antigua and Barbuda, Belize, Bolivia, Dominica, Grenada, Guatemala, Guyana, Honduras, Nicaragua, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Trinidad and Tobago, and Venezuela.

[b] Source: World Bank Data https://data.worldbank.org/indicator/SH.ALC.PCAP.LI Accessed online in September 6 2022

cancer types: lung, larynx, esophagus, oral cavity, nasopharynx, pharynx, bladder, pancreas, kidney, liver, stomach, bowel, cervix, leukemia, and ovarian cancers [22]. Individuals who smoke are 15–30 times more likely to develop or die from lung cancer compared to nonsmokers [23]. In addition to causing cancer, tobacco consumption also stimulates cancer progression and decreases treatment response [23].

Smoking increases the risk of lung cancer in a dose-response manner, the longer and more cigarettes smoked, the higher the risk. This increase is also seen in those who consume low tar cigarettes, which are claimed to pose lower cancer risk. Of the lung cancer types, smoking increases the risk of squamous cell carcinoma more than that of adenocarcinoma [23].

Tobacco smoke causes genetic alterations and mutations leading to lung cancer initiation and progression. Of the agents classified as carcinogens in tobacco, polycyclic aromatic hydrocarbons (PAHs), volatile nitrosamines (e.g., 1,3-butadiene and ethylene oxide), and heavy metals (e.g., cadmium, Polonium 210) act directly on lung cells [20,21]. Five-year survival is low (13 %) and is lower in small and large cell carcinomas due to late diagnosis [24].

Smoking is also a cause of head and neck, and oral cancers and the risk is further increased with alcohol consumption. In active smokers, the relative risk ranges from 4.9 for oral cavity to 8.5 for pharynx (esophagus and larynx have risks in-between). Smoking also leads to (dose-dependent) lip, tongue, and salivary glands cancers. Cigar and pipe use are also leading causes of oral cavity cancers. Laryngeal cancer has one of the strongest associations with smoking. An estimated 83% of laryngeal cancer is due to tobacco use [20,21].

The effect of tobacco goes beyond the respiratory system. Breast cancer risk is also increased in women who smoke compared to those that do not. Digestive system cancers are also caused by tobacco consumption. The causal association with squamous cell esophageal cancer is clearly proven. Gastric cancer is also caused by smoking (50 % higher risk than non-smokers). The risk is higher for tumors in the distal stomach and is related to gastric ulcers (dose-dependent). Colon and rectal cancers risks are also increased in smokers compared to non-smokers (even higher risk alcohol consumption). The risk exists for both adenomatous and hyperplastic polyps (particularly after 10 years of smoking). Pancreatic cancer risk is nearly doubled in smokers compared to non-smokers (dose-dependent). Smoking is also causally associated with liver cancer (cellular hepatocarcinoma) [20]. In addition, urinary and reproductive systems cancers are also caused by smoking. Current and former smokers have a greater risk for renal-cell cancer (kidney cancer). The risk of bladder cancer can be up to 3 times higher in female and 4 times higher in male smokers compared to non-smokers. Cervical cancer, one of the most common in LAC, is also caused by tobacco. Regarding ovarian cancer (mucinous histological type), despite being rare, it is one of the most lethal and caused by smoking. Finally, tobacco has also been classified as a causative agent of leukemia, mainly myeloid [20,21].

As of June 2023, (e-cigs) have been related to sympathetic activation, arterial stiffness, and endothelial dysfunction and lung inflammation (including increased risk of asthma and chronic obstructive pulmonary disease) [25,26]. But in spite of most e-cigs aerosol include carcinogenic chemicals, their consumption has not been associated to cancer development. This might be due to different consumption patterns, product types and the long time it takes between the onset of population consumption and cancer development. However, as e-cigs use increase there is a need for a systematic and continuous assessment of the evidence on whether they are a gateway to cigarette or other tobacco products use among adolescents and cancer risk.

Following the IARC methodology [27], we conducted a systematic review to determine if e-cigs are a gateway to the use of combustible cigarettes or other tobacco products among adolescents. The review consisted of two separate phases: (a) an overview of systematic reviews that included observational studies or randomized clinical trials providing information on the possible association between e-cigs use with and without nicotine (including menthol and flavored cigarettes) and smoking initiation, and (b) a systematic review of individual studies (observational studies or randomized clinical trials) based on the most recent search among the systematic reviews selected. The results are shown in the "Recommednations to the individuals" section below.

2.2. *Secondhand smoke (SHS)*

SHS, is a human carcinogen (IARC Monographs Programs classification group 1), and exposure is causally linked to lung cancer among non-smokers [20,21]. SHS has higher carcinogen concentrations and therefore more toxic than the smoke inhaled by active smokers. It

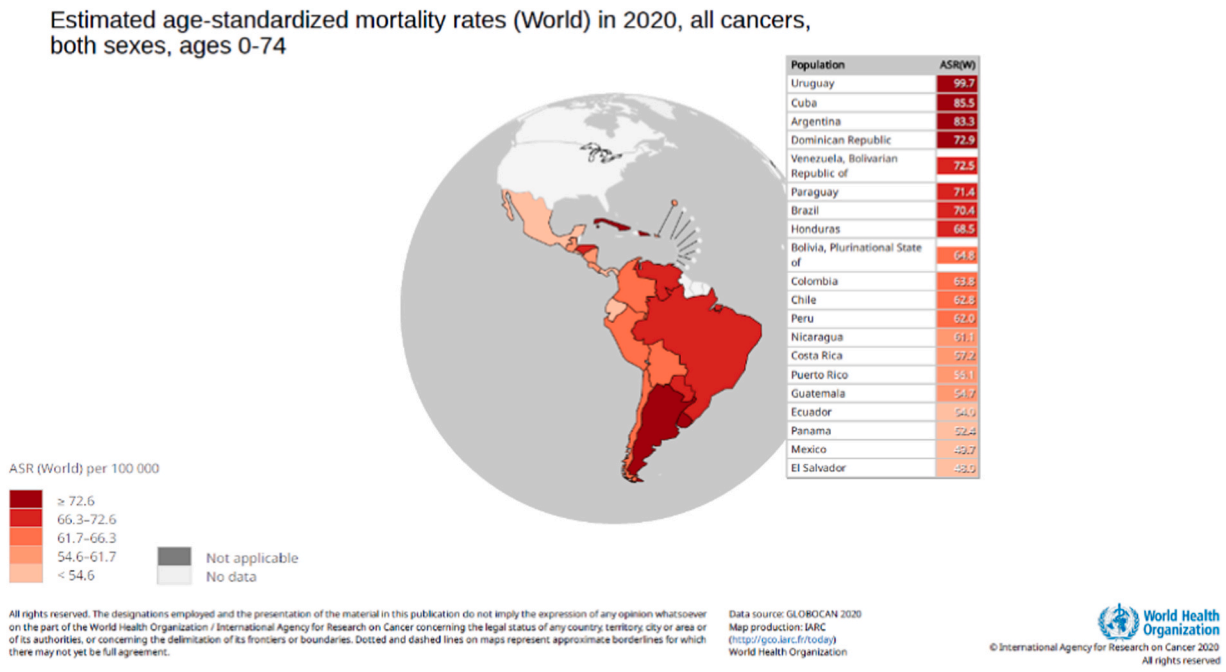

Fig. 2. Estimated age-standardized mortality rates world and LAC in 2020, both sexes.

contains more than 5000 toxic components (69 classified by IARC as Group 1 carcinogens) including benzopyrene and N-nitro dimethyl alanine [28]. Consequently, IARC concluded that SHS is a human carcinogen and there is no safe level of exposure. Even brief exposure can be harmful to one's health [20].

Adults exposed to SHS have higher (30 %) risk of developing lung cancer compared to non-exposed non-smokers [28]. The genotoxic potential of SHS and the mechanisms by which these modifications are expressed are well-established and increase lung cancer risk. However, this increase risk differs by histological type: adenocarcinoma (OR = 1.35, 95 % CI: 1.23–1.48), squamous cell (1.36, 1.17–1.58) and large cell (1.36, 1.04–1.79) are lower compared to that of small cell (1.63, 1.31–2.04) lung cancer [29]. In addition, SHS is likely to increase the risk of breast cancer in never-smoking women, particularly among pre-menopausal women [30]. Cancers of the larynx, pharynx, and nasopharynx are also increased by SHS [31]. It is also associated (evidence not yet sufficient to infer causality) with higher risk of leukemia, lymphoma, and brain tumors in children [28,32].

2.3. Alcohol

Alcohol, a group 1 carcinogen classified by IARC [33], consumption is causally linked to cancers of the upper aerodigestive tract (oral cavity, pharynx, larynx, and esophagus) and colon, rectum, liver, and female breast [18,33]. Yet the mechanisms of alcohol-mediated carcinogenesis are not completely understood one is through acetaldehyde metabolism. After alcohol intake, acetaldehyde, a genotoxic chemical, is formed in the oral mucosal and then metabolized by aldehyde dehydrogenases (ALDH*1) to acetate, a harmless chemical. As acetaldehyde is highly reactive within the cell, the more this process delays, the more acetaldehyde accumulates and blocks DNA synthesis and repair altering protein activity and/or function [34]. Therefore, up to 30% of East-Asian descendants with an inactive ALDH* 2 enzyme form (ALDH2 *2) have higher risk of head and neck cancers compared to those with the active form [35]. In LAC, Brazil for example, 1 % of the population (more than 2 million people) is from an Asian origin and therefore may be more susceptible to the carcinogenic effect of alcohol. [36,37].

Nutritional deficiencies resulting from chronic alcohol consumption (e.g., folate deficiency that affect DNA processing pathways) have also been identified in the casual pathway between alcohol and cancer. In addition, alcohol consumption is also thought to increase estrogen levels, thus increasing the risk of breast cancer in females [38]. Moreover, the alcohol-related immunodeficiency and immunosuppression may facilitate carcinogenesis in [34].

Alcohol drinking is associated with cancer of the oral cavity and pharynx, and esophagus (squamous cell) [39–41]. Therefore, it can be concluded that there is no safe level of alcohol consumption.

2.4. Interactions between alcohol and tobacco

Smoking and alcohol drinking are major risk factors for upper aerodigestive tract cancers and the simultaneous exposure has a multiplicative effect on carcinogenesis [42]. Acetaldehyde, the most abundant carcinogen in tobacco smoke, is likely to be the intermediary in the interaction between these two risk factors [43]. It is likely that the upper digestive tract mucosa of smokers who drink is chronically exposed to higher level of salivary acetaldehyde compared to those that do not. This, in part, explains the synergistic and multiplicative risk effect of smoking and drinking on the digestive cancer's carcinogenesis [44]. In addition, there may be synergistic interaction between tobacco and alcohol consumption related to increased risk of breast cancer [45,46].

Alcohol drinking is also considered a mediator of the association between smoking and SHS exposure in workplaces [47]. Furthermore, individuals who smoke consume more cigarettes while under the influence of alcohol. Adolescents and young adults who smoke are more likely than non-smokers to consume alcohol and binge drink [48].

3. Justification for the recommendations on tobacco and nicotine-related products, secondhand smoke, and alcohol of the LAC Code Against Cancer

Nearly half (44 %) of cancers are preventable by implementing policies at different levels (individual and population) to create a social and economic environment supportive of healthy choices [2].

Following the methodology described in this supplement (Espina et al., [8]) and after reviewing the evidence aforementioned for the LAC context, we provide the cancer prevention recommendations (Fig. 1), including some for policymakers (Supplementary Material I).

3.1. Recommendations to the individuals

3.1.1. Tobacco and nicotine-related products

The first recommendation "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". Smoking tobacco is a recognized carcinogen causally linked to 15 cancer types. There is no safe level of exposure to tobacco smoke, either active or passive, and therefore, everyone is advised to not starting and quitting if they smoke. The risk of cancer decreases among those who quit smoking compared with those who do not [49–51]. Quitting smoking reduces the risk of 12 cancers, including lung, laryngeal, oral, pharynx, esophageal, pancreatic, bladder, stomach, colorectal, cervical, kidney, and acute myeloid leukemia [20,52]. Regarding lung cancer, the risk decreases to half approximately 10–15 years after quitting compared to those who continue smoking. In addition, the earlier the age of quitting, the lower the risk of lung cancer [52].

Even though cancer data is not yet available, the systematic review yields that e-cigs are a gateway to combustible cigarette consumption among adolescents not consuming tobacco products and, hence, cancer-causing agents such as combustible cigarettes [53–57]. Therefore, we also recommend not using e-cigs.

We included ten systematic reviews (Adermark 2021 [53], Baenziger 2021 [54], Chan 2021 [55], O'Brien 2021 [56], Zhang 2021 [57], Khouja 2021 [58], Aladeokin 2019 [59], Glasser 2019 [60], Soneji 2017 [61]), of which two (Baenziger 2021 [53], Ademark 2021 [54]) included the large number of studies. Beazinger et al., provided an analysis of three systematic reviews, one review reported among young adults (<30 years) an adjusted OR 2.21 (95 % CI 1.72–2.84), while the other two reviews reported similar estimates [54]. Ademark et al., reported an stratified analysis per age group, from five studies including adolescents (<18 years) they reported an OR of smoking initiation of 2.33 (95%CI 1.69–3.23) [53].

The update search identified 27 observational studies (PRISMA Flowchart 4.3.2). Nineteen studies were prospective cohorts, three were retrospective cohorts, three studies used a propensity score analysis, one used a Markov model, and one was a post hoc analysis using the cohorts from a randomized controlled trial (RCT). Overall, most of the studies (n = 23) reported an association between the use of e-cigs and smoking initiation in adolescents, regardless the effect measure considered. Nine studies included adolescents, according either to the means or to the descriptions (Martinelli 2021 [62], Ortega 2021 [63], Barrington-Trimis 2021 [64], Dobbs 2020 [65], Evans-Polce 2020a [66], Evans-Polce 2020b [67], Kang 2020 [68], Melka 2020 [69], Odani 2020 [70]), among them, five estimated adjusted by potential relevant confounders reporting aOR from 1.30 (95%CI 1.03–1.63) to 8.01 (3.08–20.83).

3.1.2. Secondhand smoke

Based on the most recent available evidence on SHS as an established carcinogen, recommendation 2 of the Code is: "Make your home a smoke-free place. Respect and promote laws that ensure smoke-free spaces to protect our health." Even though smoke-free workplace laws have become the norm in LAC (first region of the world to be covered by these policies), enforcement remains a challenge. [4,71] Therefore, both employers and employees should promote and advocate for the implementation of smoke-free workplaces and enforce existing ones. In addition, SHS exposure at home also increases the risk of cancer. Consequently, we recommend homes also be smoke-free to decrease the risk of cancer among non-smokers at home.

3.1.3. Alcohol

Regarding alcohol, recommendation number 6 of the LAC Code Against Cancer, 1st edition states that "Avoid drinking alcoholic beverages. This helps prevent several types of cancer". For cancer prevention "avoiding" alcohol consumption is a better choice than "limiting consumption" [72], because the available evidence yields that, even at low doses, alcohol drinking is associated with cancer of the oral cavity and pharynx, esophagus, and female breast [33,39,40]. Therefore, it can be concluded that there is no safe level of alcohol consumption in relation to cancer.

3.2. Recommendations for policymakers

3.2.1. Effectiveness of tobacco and alcohol control policies

The WHO Global Action Plan for the Prevention and Control of Non-Communicable Diseases (NCDs) 2013–2020 proposed "a 30 % relative reduction in prevalence of current tobacco use in persons aged 15 + years" and "at least 10 % relative reduction in the harmful use of alcohol" [73]. Unfortunately, there was little progress in most countries [74] and therefore in 2021 these goals were extended to 2030 [75]. In order to achieve these goals the WHO published evidence-based interventions ("Best Buys") ranked according to an average cost-effectiveness ratio in low- and middle-income countries to prioritize implementation [76]. These include articles from the WHO Framework Convention on Tobacco Control (WHO-FCTC) and MPOWER to reduce tobacco consumption [77,78]. Regarding alcohol, measures from the Global Strategy to Reduce the Harmful Use of Alcohol/SAFER initiative to reduce alcohol related harms are included [79,80].

In LAC even though most countries have ratified the FCTC [4] and made progress in its implementation, the decline in smoking prevalence has not been proportional to the severity of the epidemic. Tobacco remains as a leading cause of cancer and e-cigs represent a new challenge in the region [81]. Regarding alcohol, the SAFER action package includes 5 cost-effective strategies to reduce alcohol-related harm and include **S**trengthen restrictions on alcohol availability, **A**dvance and enforce, drink-driving counter measures, **F**acilitate access to screening, brief interventions and treatment, **E**nforce bans or comprehensive restrictions on alcohol advertising, sponsorship and promotion and **R**aise prices on alcohol through excise taxes and other pricing policies [3,80].

Tobacco and alcohol control policies are often hindered by their corresponding industries' influences. Therefore, these policies are often delayed or not implemented at all leading to additional burden from both risk factors [82–84]. Therefore, policy implementation depends on evidence available but also on the political will to protect them from vested interest of both industries. Consequently, to be effective these policies need strong political will to translate science into policies particularly those that go against economic interests of the tobacco and alcohol industries.

3.2.2. LAC Code Against Cancer as an ally to overcome challenges to tobacco and alcohol control policies

Based on this, we propose a set of tobacco and alcohol control recommendations for policymakers as part of the LAC Code Against Cancer, 1st edition. The Code targets the general population, while recognizes the social, political, and economic determinants of these two risk factors and the need of political will and commitment to strengthen WHO- FCTC and MPOWER, and SAFER implementation in the region (Fig. 3).

By raising awareness about the importance of reducing smoking and alcohol use for cancer prevention, the LAC Code Against Cancer, 1st edition, can help boosting the implementation of WHO-FCTC [77], a health treaty encompassing a set of evidence-based measures, which implementation is also supported by WHO-MPOWER, a policy package measures to reduce tobacco demand [78]. Moreover, this Code can also help strengthening the Global Strategy to Reduce the Harmful Use of Alcohol which implementation is supported by the SAFER initiative [80]. (See Supplementary material II).

3.3. Messages for primary healthcare professionals

Health education is key to ensure individuals are informed about evidence-based actions they should undertake to prevent and reduce their cancer risk. Primary care healthcare professionals play a key role in

Tobacco, weight, physical activity, diet, alcohol, and breastfeeding[1,2,3,4,5,6,7,8]

- Implement tax policies, considering best practices, aimed at discouraging the use of tobacco, e-cigarettes, alcohol, and unhealthy foods and beverages.
- Implement health warning labels for the containers of tobacco, e-cigarettes, alcohol, and unhealthy foods and beverages. For foods and beverages, it is recommended to implement warning labels that include the PAHO nutrient profile model.
- Create healthy environments in the community, schools, educational centers and public buildings: ban the use of products that contain tobacco and generate emissions in shared environments, as well as the use of e-cigarettes, which are a gateway for tobacco use; prohibit alcohol use in these settings; decrease the availability of unhealthy foods and beverages and increase the availability of healthy foods and beverages; promote the creation of spaces for physical activity, as well as spaces to facilitate breastfeeding, and ensure access to drinking water.
- Include quality physical education classes in curricula, promote physical activity at recess, and encourage active transportation to and from school.
- Ban advertising, promotion, and sponsorship of tobacco, e-cigarettes, alcohol, and breastmilk substitutes; and ban the advertising of unhealthy foods and beverages to children.
- Implement communication, education, and counseling programs to encourage behavioral changes in the population regarding the use of tobacco, e-cigarettes, alcohol, and unhealthy foods and beverages, and to promote physical activity, healthy eating, and breastfeeding.
- Safeguard the design, implementation, and evaluation of these policies from potential conflicts of interest.
- Adopt the international codes and conventions related to the recommendations above, and ensure that they are correctly implemented:
  - WHO Framework Convention on Tobacco Control.
  - International Code of Marketing of Breast-milk Substitutes.
  - The WHO Technical package SAFER to prevent and reduce alcohol-related death and disability.
  - The International Labour Organization Maternity Protection Convention and related recommendations.

1 Pan American Health Organization. PAHO Nutrient Profile Model. Washington, D.C.: PAHO; 2016. Available from: https://iris.paho.org/bitstream/handle/10665.2/18621/9789275118733_eng.pdf.

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3 World Cancer Research Fund International. Driving action to prevent cancer and other non-communicable diseases: a new policy framework for promoting healthy diets, physical activity, breastfeeding and reducing alcohol consumption. London: WCRF; 2018. Available from: https://www.wcrf.org/wp-content/uploads/2021/07/POLICY-FRAMEWORK-web.pdf.

4 World Health Organization. WHO Framework Convention on Tobacco Control. Geneva: WHO; 2003. Available from: https://apps.who.int/iris/rest/bitstreams/50793/retrieve.

5 World Health Organization. International Code of Marketing of Breast-Milk Substitutes. Geneva: WHO; 1981. Available from: https://www.who.int/publications/i/item/9241541601.

6 World Health Organization. The technical package SAFER. A world free from alcohol related harms. Washington, D.C.: PAHO; 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/330053/9789241516419-eng.pdf.

7 United Nations Children's Fund. Breastfeeding and Family-Friendly policies: an evidence brief. New York: UNICEF; 2019. Available from: https://www.unicef.org/media/95071/file/UNICEF-Breastfeeding-Family-Friendly%20Policies-2019.pdf.

8 International Labour Organization. Maternity Protection Convention. Geneva: ILO; 1919. Available from: https://www.ilo.org/dyn/normlex/en/f?p=1000:12100:0::NO::P12100_INSTRUMENT_ID,P12100_LANG_CODE:312148,en:NO.

Fig. 3. Latin America and the Caribbean Code Against Cancer 1st edition: Recommendations for policymakers on lifestyle

cancer prevention since they are population's first contact with the healthcare system and, thereby, health education should be embedded in these professionals' daily practice [85]. The LAC Code Against Cancer, aims to contribute to enhance knowledge and skills among care healthcare professionals to discuss effective preventive measures with patients and their family with this objective it includes a knowledge output: an online competency-based microlearning program. The curriculum of this e-learning program builds capacity on how primary healthcare professionals can help their community prevent or reduce their risk of cancer [9].

1. Tobacco and nicotine-related products. Primary care health professionals should ask all their patients and their families whether they smoke or vape, inform them about the harms of smoking and vaping, and promote tobacco and nicotine related products cessation strategies among users. Since quitting benefits health at any age and increases life expectancy by up to 10 years.

2. Secondhand smoke . Primary care health professionals should inform about the harms of exposure to SHS, especially among children, and promote smoke-free environments through the following arguments since they are proven to protect the health of the entire population (smokers and non-smokers), to prevent young people from starting to smoke and, in workplaces, to reduce absenteeism, increase productivity, and staff satisfaction.
3. Alcohol. Primary care health professionals to help prevent alcohol use by their patients and their families should be prepared to explain the risks of alcohol drinking; use structured and tested tools to assess the level of risk for alcohol use disorders in all patients/people, and to apply brief counseling intervention programs to support alcohol drinking cessation in primary care [86]; and refer for specialized treatment patients with alcohol dependence, or harmful consumption.

Health professionals also should understand that cessation and prevention of smoking and alcohol consumption will be much more successful in an social environment where there are laws and regulations limiting tobacco and alcohol advertising and promotion, prohibiting smoking in public places, support pictoral health warnings on tobacco package and front of package labeling on ultra-processed foods, making these products less accessible through sales restrictions, and less affordable through taxes and prices policies. In this regard health professionals also should be prepared to advocate for the implementation of populational measures from WHO-FCTC, the MPOWER and SAFER policy packages in their community and country. (See Supplementary material II).

4. Conclusions

The LAC Code Against Cancer, 1st edition, aims to raise awareness among the general population and primary care professionals about tobacco and alcohol as leading modifiable cancer risk factors, emphasizing that there is no safe level of consumption for both.

It also aims to support WHO-FCTC, the MPOWER and SAFER policy packages to reduce population exposure to these risk factors taking into account that through the implementation of these policies resulted in some regional progress. Both risk factors still remain as leading causes of cancer and new challenges are being faced with the dissemination of e-cigs and with the interference of the tobacco and alcohol industries to block or slow policies in the region and worldwide.

The LAC Code Against Cancer also seeks to encourage primary care professionals to identify tobacco and alcohol consumption among their patients and offer support for them to quit, understanding that both initiatives are respectively core measures of WHO-FCTC, the MPOWER and SAFER policies. Also recognize the importance of policies to create a supportive social environment to change attitude, behavior and social acceptability related to tobacco and alcohol consumption.

CRediT authorship contribution statement

Luz Myriam Reynales, Conceptualization, Methodology, Investigation, Writing- Original draft preparation, Writing - Review & Editing. **Joaquin Barnoya**, Investigation, Writing- Original draft preparation, Writing - Review & Editing. **Tania Cavalcante**, Investigation, Writing- Original draft preparation. **Tania Aburto**, Investigation, Writing - Review & Editing. **Isabelle Romieu**, Investigation, Writing - Review & Editing. **Mariana C. Stern**, Investigation, Writing - Review & Editing. **Simón Barquera**, Investigation, Writing - Review & Editing. **Camila Corvalán**, Investigation, Writing - Review & Editing. **Pedro C. Hallal**, Investigation, Writing - Review & Editing. **Ariadna Feliu**, Methodology, Supervision, Writing - Review & Editing. **Carolina Espina**, Conceptualization, Supervision, Project administration, Writing - Review & Editing. **Carlos Canelo-Aybar**, Methodology, Formal analysis, Writing - Review & Editing. **Rosa Alvarado-Villacorta**, Methodology, Formal analysis, Writing - Review & Editing. **Juan A. Rivera**, Conceptualization, Writing - original draft.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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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.2023.102413.

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