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Latin America and the Caribbean Code Against Cancer 1st Edition: Medical interventions including hormone replacement therapy and cancer screening☆

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ABSTRACT

Prostate, breast, colorectal, cervical, and lung cancers are the leading cause of cancer in Latin America and the Caribbean (LAC) accounting for nearly 50% of cancer cases and cancer deaths in the region. Following the IARC Code Against Cancer methodology, a group of Latin American experts evaluated the evidence on several medical interventions to reduce cancer incidence and mortality considering the cancer burden in the region. A recommendation to limit the use of HRT was issued based on the risk associated to develop breast, endometrial, and ovarian cancer and on growing concerns related to the over-the-counter and without prescription sales, which in turn bias estimations on current use in LAC. In alignment with WHO breast and cervical cancer initiatives, biennial screening by clinical breast examination (performed by trained health professionals) from the age of 40 years and biennial screening by mammography from the age of 50 years to 74, as well as cervical screening by HPV testing (either self-sampling or provider-sampling) every 5–10 years for women aged 30–64 years, were recommended. The steadily increasing rates of colorectal cancer in LAC also led to recommend colorectal screening by occult blood testing every two years or by endoscopic examination of the colorectum every 10 years for both men and women aged 50–74 years. After evaluating the evidence, the experts decided not to issue recommendations for prostate and lung cancer screening; while there was insufficient evidence on prostate

Abbreviations: ASR, age-standardised rate; BSE, breast self-examination; CBE, clinical breast examination; CCEI, Cervical Cancer Elimination Initiative; CIN, cervical intraepithelial neoplasia; FIT, faecal immunochemical test; GBCI, Global Breast Cancer Initiative; gFOBT, guaiac faecal occult blood test; HBV, hepatitis B virus; HCV, hepatitis C virus; HICs, high-income countries; HIV, human immunodeficiency virus; HPV, human papillomavirus; HRT, hormone replacement therapy; IARC, International Agency for Research on Cancer; LAC, Latin America and the Caribbean; LDCT, low-dose computed tomography; LMICs, low- and middle-income countries; NMSC, non-melanoma skin cancer; PAHO, Pan-American Health Organization; PCR, polymerase chain reaction; PSA, prostate-specific antigen; RCT, randomised controlled trial; VIA, visual inspection of the cervix with acetic acid; WHO, World Health Organization; WLWH, women living with HIV.

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cancer mortality reduction by prostate-specific antigen (PSA) testing, there was evidence of mortality reduction by low-dose computed tomography (LDCT) targeting high-risk individuals (mainly heavy and/or long-term smokers) but not individuals with average risk to whom recommendations of this Code are directed. Finally, the group of experts adapted the gathered evidence to develop a competency-based online microlearning program for building cancer prevention capacity of primary care health professionals.

1. Introduction

Nearly 20 million new cases and 10 million deaths from cancer occur annually worldwide [1]. About 7% of cases (1.4 million) and 8% of deaths (705k) take place in LAC in a ratio of ~1:1 between men and women [1,2]. In men, prostate, lung, colorectal, and gastric cancers are the most common cancers in LAC, accounting for at least 50% of cases (~380k) and deaths (~176k), while in women the most frequent are breast, colorectal, cervical, and lung cancers, also representing at least 50% of cases (~378k) and deaths (~160k) (Fig. 1). Although lung cancer in women ranks fourth in LAC, it is the second leading cause of cancer death (Fig. 1). Considering both sexes, the five cancers with highest age-standardised rates (ASR) for incidence and mortality in LAC are prostate (ASR incidence: 59.2, ASR mortality: 14.2), breast (51.9, 13.5), colorectal (16.6, 8.2), cervical (14.9, 7.6), and lung (12.0, 10.5) (Fig. 2). These five cancers also have the highest incidence worldwide, but mortality rates of liver (8.7) and stomach (7.7) cancers are higher or at least equal to those of the prostate (7.7) and cervix (7.3) (Fig. 2).

About 40% of cancers are preventable by adopting primary prevention strategies aimed at reducing exposure to well-established carcinogens [3–5]. For instance, anti-tobacco policies for encouraging smoking cessation, promotion of healthy lifestyles (such as physical activity and avoiding alcohol and red/processed meat consumption), or regulation of hormone replacement therapy (HRT) use to prevent lung, colorectal, and breast cancers [6–10]. Also, as infectious agents are responsible for approximately 13% of cancers worldwide [11], several evidence-based primary prevention strategies have been developed to prevent cervical, liver, and gastric cancers such as vaccination against human papillomavirus (HPV) and hepatitis B virus (HBV), antiretroviral treatment of HBV and hepatitis C virus (HCV), and *H. pylori* eradication therapy [12–17]. Conversely, secondary cancer prevention, meant to stop or inhibit the development and spread of cancer, thereby preventing death from cancer, can be remarkably useful, especially when risk factors are poorly understood or non-modifiable. Cancer screening and early diagnosis followed by effective treatment are the main tools of secondary prevention of cancer [18]. While cancer screening aims at detecting disease in asymptomatic/healthy population (i.e., individuals at average risk), early diagnosis is focused on detecting cancer in symptomatic patients at the earliest opportunity [18]. However, cancer screening and early diagnosis strategies are recommended only when their benefits outweigh the potential induced harms [18]. Therefore, it is important to carefully evaluate the risks and benefits of any cancer screening or early diagnosis strategy before recommending it. Cancer screening guidelines are regularly updated to reflect new evidence and changes in clinical practice.

Under the overall umbrella of the World Code Against Cancer Framework [19,20], 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 [21], the 1st edition of the Latin America and the Caribbean (LAC) Code Against Cancer has been developed by experts of LAC, in collaboration with the Pan-American Health Organization (PAHO/WHO) (Fig. 3) [22]. The LAC Code Against Cancer consists of a set of evidence-based cancer prevention recommendations targeted to the general population, suited to the epidemiological, socioeconomic, and cultural conditions of LAC, and tailored to the availability and accessibility of health-care systems, provided by a supplementary set of

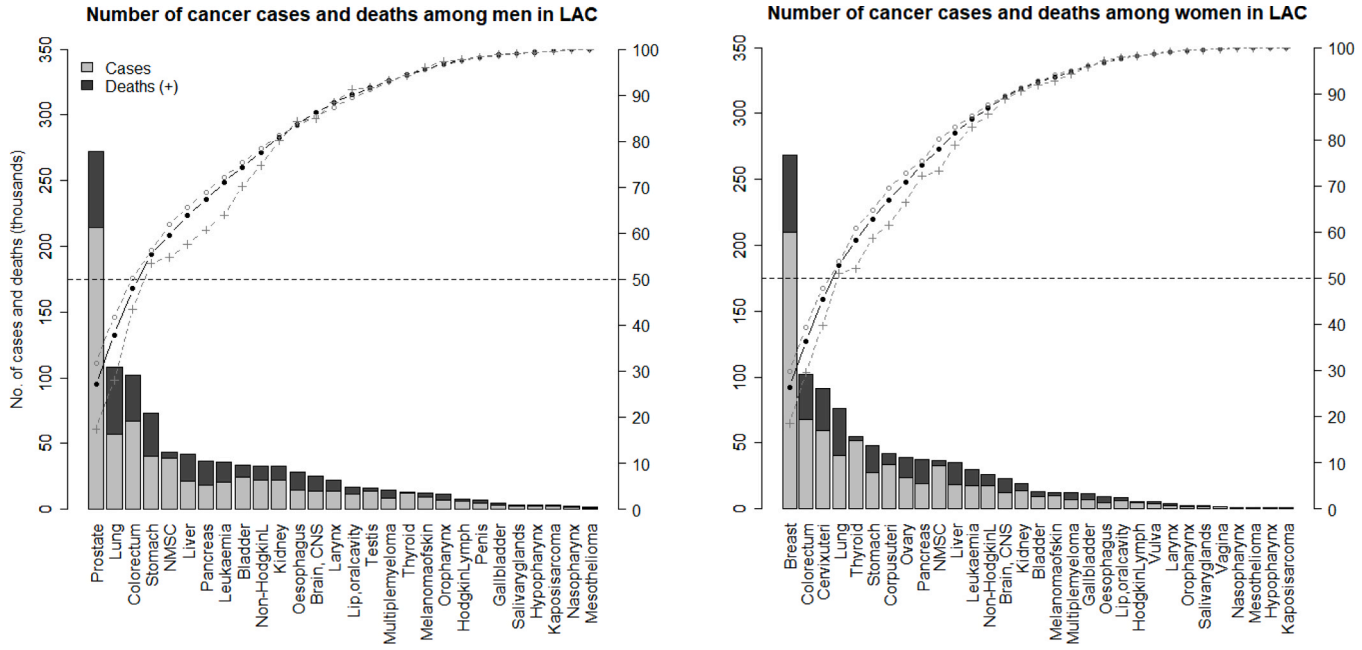

Fig. 1. Number (left axis) and cumulative proportion (right axis) of cancer cases and deaths among men and women in LAC. Black continuous line: cumulative proportion of cases plus deaths (black circle). Gray dashed lines: cumulative proportion of cases (gray circle) and deaths (cross). NMSC: non-melanoma skin cancer. Data Source: Globocan 2020 – IARC/WHO. Graph production: authors' creation.

recommendations to policymakers (Supplementary material). In addition, the LAC Code Against Cancer includes 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 their patients and families on evidence-based actions on primary and secondary prevention of cancer [23].

In this manuscript we address the benefits and risks and harms of HRT use in menopausal women and screening and early diagnosis of breast, cervical, colorectal, prostate, and lung cancer as part of the LAC Code Against Cancer 1st edition. Other medical interventions such as HPV and HBV vaccines and *H. pylori* eradication, as well as the adoption of good lifestyle habits, are addressed in other manuscripts of the LAC Code Against Cancer [7,10,24].

2. Methods

Methods used to generate recommendations targeting individuals of the general public to prevent cancer are described elsewhere [22]. Briefly, within the group of experts, considering the burden of cancer in LAC, the evidence available for (i) using HRT and risk of different cancers, and (ii) screening of breast, cervix, colorectal, prostate and lung cancers to reduce incidence and mortality of these cancers, was evaluated. Systematic reviews, meta-analyses and current international guidelines were revised, and whenever group members were aware of newly published or LAC-specific evidence, a new systematic review based on PICO questions developed by the group was commissioned to the Iberoamerican Cochrane Centre group following the IARC methodology applied to the European Code [25]. The Cochrane reviews consisted of two separate phases: (i) an overview of systematic reviews on the field and (ii) a systematic review of individual studies (to update the evidence identified from previous reviews). After deliberations on the strength of the evidence, the expert group decided to propose or not recommendations appropriately. Recommendations were then drafted, revised by an expert group on communications, and presented to the Scientific Committee and all experts groups' leaders to ultimately reach consensus on final recommendations [26]. Finally, group members adapted the gathered evidence on HRT use and cancer screening to develop a competency-based online microlearning program aimed at building cancer prevention capacity of primary care health professionals [23]. Although discussed, other medical interventions such as chemoprevention with aspirin were not included in the LAC Code Against Cancer as they did not fit the methodological criteria [22]. As new evidence arises, particularly for LAC, we anticipate that they will be addressed in future editions.

3. Results

3.1. Hormone replacement therapy and cancer

Health personnel recommends HRT to improve the quality of life of women by reducing peri and menopause symptoms. They recommend it

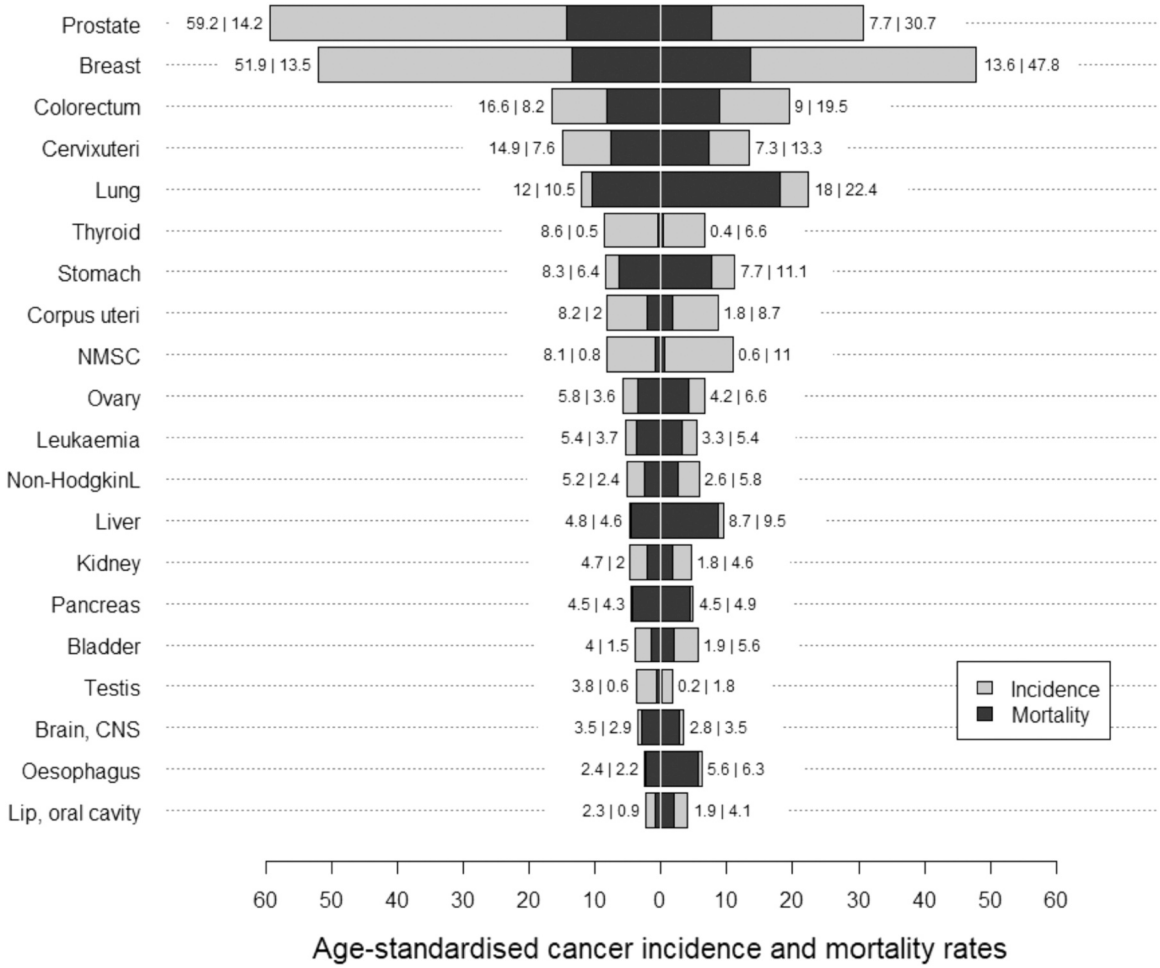

Fig. 2. Age-standardised cancer incidence and mortality rates in both sexes in LAC (left) and worldwide (right). Rates are expressed as "Incidence|Mortality" for LAC and "Mortality|Incidence" for the world. NMSC: non-melanoma skin cancer. Data Source: Globocan 2020 – IARC/WHO. Graph production: authors' creation.

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

particularly to treat vasomotor symptoms and genitourinary syndrome of menopause. They also prescribe it to prevent and treat osteoporosis. In cases of premature ovarian failure, they recommend it up to the average age at which menopause naturally occurs, regardless of symptoms. HRT dosage, formulas, and routes of administration are multiple. IARC has classified HRT (based on oestrogen or combined oestrogen and progesterone) as a carcinogen [5]. Any type of HRT, except vaginal oestrogens, increases the risk of breast cancer [27]. The Collaborative Group on Hormonal Factors in Breast Cancer (2019) analysed the risk of HRT for breast cancer using data from 24 prospective and 34 retrospective studies. A dose-response effect of HRT use over time was observed. Compared to women using HRT for less than one year, the risk of breast cancer was 17% higher for those who used oestrogen therapy for 1–4 years and 60% higher for those who used combined oestrogen-progestogen therapy for 1–4 years (relative risk 1.17, 95% CI 1.10–1.26 for oestrogen, and 1.60, 95% CI 1.52–1.69 for combined therapy). The risk was even higher among long-term users (i.e., 10–14 years of use) with a relative risk of 1.43 (95% CI 1.37–1.50) for oestrogen and 2.26 (95% CI 2.16–2.36) for combined therapy [27]. Additional evidence shows that more than one year HRT use also increases the risk of endometrial cancer, and at least five years of HRT combined therapy use increases the risk of ovarian cancer. It also increases the risk of cardiovascular diseases, thromboembolism, and stroke [5,28]. Therefore, HRT use should be individualized using the best available evidence to maximize benefits and minimize risks of continuing or discontinuing it. HRT use estimates range from 12% to 50% worldwide, with LAC being the region with the lowest use (~12%) [29]. However, the over-the-counter drug sale in LAC is of concern as it may lead to increasing and long-lasting use of HRT without medical supervision. Alternative methods to mitigate menopausal symptoms should be first considered (such as vaginal lubricant or moisturiser, physical activity, and a healthy diet) [9,30].

3.2. Cancer screening and early diagnosis

Screening methods have been proposed for breast (breast self-examination, clinical breast examination, mammography), cervix (cytology, visual inspection of the cervix after acetic acid, HPV detection), colorectal (occult blood tests, sigmoidoscopy, colonoscopy), lung (low-dose computed tomography), and prostate cancer (prostate-specific antigen detection) (Table 1). However, currently, only screening methods for breast, cervical, and colorectal cancers have proven evidence-based efficacy in reducing incidence and/or mortality in individuals at average risk with benefits outweighing harms [31–33]. Evidence on benefits (effectiveness) and harms (negative side effects) of several methods for cancer screening are described below (Table 1).

Table 1
Evidence on benefits of several screening methods for breast, cervical, colorectal, prostate, and lung cancer.

Screening method	Target population	Screening interval, y	Evidence on reducing incidence [(a)]	Evidence on reducing mortality [(a)]	Evidence on benefit/harm ratio [(a,b)]	Source of evidence
Breast cancer[(a)]						
Self-examination	W aged 40–74	Monthly	Inadequate	Inadequate	Inadequate	IARC Handbook
CBE	W aged 40–49	1–2	Limited	Inadequate/SLOE* †	Inadequate (but)* †	IARC Handbook/SR*
CBE	W aged 50–74	1–2	Limited	Inadequate/Limited (but)* ‡	Limited (but)* ‡	IARC Handbook/SR*
Mammography	W aged 40–49	2	Limited	Limited	Limited	IARC Handbook
Mammography	W aged 50–74	2	Sufficient	Sufficient	Sufficient (>>1)	IARC Handbook
Cervical cancer[(a)]						
VIA	W aged 30–49	3	Limited	Sufficient	Inadequate	IARC Handbook
Cytology	W aged 30–65	3	Sufficient	Sufficient	Sufficient (>1)	IARC Handbook
HPV testing	W aged 30–65[(c)]	5–10[(c)]	Sufficient	Sufficient	Sufficient (>>1)[(d)]	IARC Handbook
Colorectal cancer[(a,e)]						
gFOBT	M&W aged 50–74	2	Limited	Sufficient	Sufficient (>1)	IARC Handbook
FIT	M&W aged 50–74	2	Limited	Sufficient	Sufficient (>1)	IARC Handbook
Sigmoidoscopy	M&W aged 50–74[(f)]	10	Sufficient	Sufficient	Sufficient (>1)	IARC Handbook
Colonoscopy	M&W aged 50–74[(f)]	10	Sufficient	Sufficient	Sufficient (>1)	IARC Handbook
Prostate cancer						
PSA	M older than 40–50	1	Inadequate[ξ]	SLOE[ξ]	Inadequate (but) (<1)[ξ]	Literature search
Lung cancer						
LDCT	High-risk[(g)]	1	Inadequate[Ψ]	Sufficient[Ψ]	Inadequate[Ψ]	Literature search
LDCT	Never smokers	—	Inadequate	Inadequate	Inadequate	Literature search

[(a)]Adapted from IARC Handbooks on breast, cervical, and colorectal cancer. [(b)]Benefit/harm ratio: > >1 benefits substantially outweigh harms, > 1 benefits outweigh harms, < 1 harms outweigh benefits. [(c)]Women aged 30–49 years should be prioritised, particularly when screen-and-treat approaches are implemented; for women living with HIV (WLWH) start age is set at 25 years with an interval screening of 3–5 years. [(d)]Benefit/harm ratio for HPV is greater than for cytology and much greater than for VIA. [(e)]Evidence supported by recent systematic review (Lin et at. JAMA 2021). [(f)]Mainly recommended for subjects with positive occult blood test results. [(g)]Risk based on age and smoking history: individuals mainly aged 50–75 years who have at least 15–pack-year smoking history and currently smoke or have quit within the past 15 years. *Inadequate evidence*: data on incidence or mortality are lacking, or when the number or quality of studies does not permit a conclusion. *Limited evidence*: screening is associated with a reduction in mortality from the cancer or a reduction in the incidence of invasive cancer, or a reduction in the incidence of clinically advanced cancer; chance, bias, and confounding cannot be ruled out with reasonable confidence. *Sufficient evidence*: screening is consistently associated with a reduction in mortality from the cancer or a reduction in the incidence of invasive cancer; chance, bias, and confounding can be ruled out. *Evidence obtained from updated systematic review (SR) performed by the Iberoamerican Cochrane Centre commissioned by the LAC Code Against Cancer 1st edition; the updated SR identified two recently published RCTs in addition to those already included in previous systematic reviews. †In women younger than 50 years, CBE does not reduce mortality according to an RCT conducted in Mumbai, India (Mittra et al. BMJ 2021); however, based on a previous systematic review (Ngan et al., BMC Cancer 2020) and the Mumbai RCT, there is sufficient evidence that CBE shifts the stage distribution of tumours detected toward a lower stage (updated SR). ‡In women aged 50 years or older, there is limited evidence that CBE reduces breast cancer mortality as only the Mumbai RCT (Mittra et al. BMJ 2021) has shown a reduction of 29% (relative risk 0.71, 95% CI 0.54–0.94) while no effect on mortality reduction was observed in another RCT conducted in Trivandrum, India (Ramadas et al., Cancer 2022); however, based on the previous systematic review (Ngan et al., BMC Cancer 2020) and the two Indian RCTs (Mittra et al. BMJ 2021; Ramadas et al., Cancer 2022), it was confirmed that there is sufficient evidence that CBE shifts the stage distribution of tumours detected toward a lower stage (updated SR). [ξ]Based on five RCTs (Ilic et al., BMJ 2018), PSA-based screening cannot reduce overall mortality, and although it might reduce prostate cancer mortality, undesirable side effects triggered by overtreatment due to high PSA false positive rates outweigh the potential benefits. [Ψ]Based on a Cochrane meta-analysis including 8 RCTs; authors conclude that the certainty of the evidence is moderate. *Abbreviations*: CBE: clinical breast examination. FIT: faecal immunochemical. gFOBT: guaiac faecal occult blood test. HPV: human papillomavirus. LDCT: low-dose computed tomography. M: men. PSA: prostate-specific antigen test. SLOE: suggestive lack of effect. SR: systematic review. VIA: visual inspection of the cervix with acetic acid. W: women.

3.2.1. Breast cancer screening

3.2.1.1. Effectiveness. There is sufficient evidence supporting that mammography screening is effective in reducing breast cancer mortality in women aged 50 years and older; however, the evidence is limited for women aged 40–49 years, for whom mammography screening appears to offer no benefits [31].

Early diagnosis of breast cancer can be facilitated by clinical breast examination (CBE), which consists in identifying symptomatic women through periodical examination of the breast by trained clinicians. CBE has shown to be effective in downstaging diagnosed breast cancers in women 50 years and older, however, the evidence has been inconclusive for younger women [31].

The group of experts noted that it appears to be an increase in the proportion of breast cancers among women aged 40–49 [34], and in view of the lack of mammography screening programmes in most LAC countries, commissioned a systematic review of recent published evidence on the effectiveness of CBE for reducing breast cancer mortality and downstaging in both women 40–49 years of age and those 50 years and older. Results are summarised in Table 1. Briefly: (i) there is no evidence that CBE reduces mortality among women younger than 50 years (evidence based on a single RCT conducted in Mumbai, India, relative risk 0.93, 95% CI 0.79–1.09) [35]; (ii) there is sufficient evidence that CBE downstages tumours detected among women younger than 50 years (consistent evidence from a previous systematic review and the Mumbai RCT) [35,36]; (iii) there is limited evidence that CBE reduces breast cancer mortality among women aged 50 years or older (only the Mumbai RCT showed a significant reduction, relative risk 0.71, 95% CI 0.54–0.94; no effect was observed in another RCT in Trivandrum, India) [35,37]; and (iv) there is sufficient evidence that CBE downstages tumours detected among women 50 years and older (consistent evidence from previous systematic review and the 2 RCTs in India) [35,37]. Differences in mortality reduction between the 2 RCTs in India may be partially explained by differences in target populations (e.g., women aged 35–64 years in Mumbai vs. 30–69 in Trivandrum), screening rounds and intervals (four/biennially vs. three/triennially), and duration of follow-up (20 vs. 14 years).

Finally, breast self-examination (BSE) has not shown to be effective in reducing breast cancer mortality or downstaging [31,38].

3.2.1.2. Age range and screening interval. Mammography screening is recommended for women aged 50–74, as the greatest mortality reduction has been observed in this age group [31]. CBE is recommended along with mammography, particularly when mammography is used with early diagnosis purposes. Based on the new evidence on the effectiveness of CBE for downstaging, CBE can be used to screen women aged 40 and above [35,36]; nevertheless, women aged 40–49 years should consult about being screened in accordance with their breast cancer risk. Mammography and CBE are recommended biennially [31].

3.2.1.3. Negative side effects. The most common harms of mammography include pain and discomfort from breast compression, false-positive findings, overdiagnosis (range 1%−10%), complications associated with diagnostic methods, and the risk of radiation-induced breast cancer. However, benefits of screening mammography outweigh those harms [31]. Both CBE and BSE may increase unnecessary anxiety in women and unnecessary referrals to diagnostic procedures [31].

3.2.2. Cervical cancer screening

3.2.2.1. Effectiveness. Cervical cytology has been historically the most widely used cervical cancer screening method worldwide. Cytology has led to a decrease in the incidence and mortality rates of this cancer, thought particularly in high-income countries (HICs) where organised screening programs have been sustainably implemented guaranteeing high screening coverage, adequate monitoring of altered results, adequate quality assurance, and permanent training of personnel [39,40]. However, even under optimal conditions, high-quality cytology sensitivity for detection of precancerous cervical lesions, i.e., cervical intraepithelial neoplasia (CIN) grade 2 or worse (CIN2+), is only 50% [41,42]. To overcome this limitation, cytology-based screening intervals have been set in three years or even less. Because most low- and middle-income countries (LMICs) cannot afford screening programs based on good-quality cytology and proper follow up to anormal screen results, the impact on reducing incidence and mortality in these countries has been minimal [43–46].

As an alternative, visual inspection of the cervix with acetic acid (VIA) for primary screening of cervical lesions was proposed for settings with limited healthcare access. This visual technique facilitates immediate treatment of women with obvious cervical lesions reducing the likelihood of loss to follow-up. However, VIA is highly variable and unreliable, with sensitivities for CIN2+ detection widely ranging from 20% to 90% [47], missing a large proportion of women with cervical lesions that may eventually progress to cancer. Moreover, scaling and ensuring high quality VIA screening can also be challenging, which should be accounted while considering this modality for population-based screening.

Recognition that cervical cancer is caused by HPV infection has led to the development of effective primary and secondary prevention strategies, such as HPV vaccination and HPV-based screening tests [12,13,41,48]. Sensitivity of HPV for detection of CIN2+ (>90%) is far superior to that of cytology or VIA [49–59]. Therefore, HPV testing allows extending screening intervals (at least 5 years) being more efficient and cost-effective compared to other screening tests. Furthermore, HPV testing is the only cervical screening test so far that allows self-sampling without jeopardising its high performance if PCR-based tests are used, which may help increase access to screening [60]. Compared to cytology and VIA, HPV testing has proven to be more effective in reducing cervical cancer incidence and mortality (Table 1) being recommended by WHO as the primary screening test even for women living with HIV (WLWH) [33,61]. Finally, HPV-based screening allows the identification of high-risk HPV infected women who need treatment, and it is possible to implement a variety of approaches varying from treatment of all HPV-positive women (i.e., screen-and-treat) to treatment of women with histologically confirmed CIN2/3 diagnosed after colposcopy-directed biopsy.

3.2.2.2. Age range and screening interval. HPV prevalence in the young population is high and most of these infections are transient and disappear spontaneously after 1–2 years [62]. Therefore, WHO recommends HPV testing (self-sampling or provider-sampling) for primary screening in women over 30 years of age (Table 1) and every 5–10 years [61]. Priority should be given to women between 30 and 49 years, although among women aged 50–65 years, unscreened and under-screened women should also be prioritised. Among women over 50 years, WHO recommends discontinuing screening after two consecutive negative screenings. In WLWH, WHO recommends starting screening with HPV testing at age 25 with screening intervals of 3–5 years, prioritising WLWH aged 25–49 years [61].

3.2.2.3. Negative side effects. Regardless of the screening method (i.e., HPV testing, cytology, or VIA), sample collection involved in cervical screening may cause pain, feelings of shame, and discomfort [63]. However, self-sampling for HPV testing may attenuate such distasteful effects [64]. A positive HPV result can trigger feelings of stigma and shame because of its sexually transmitted infection connotation. Similarly, regardless of the screening method, a positive result increases anxiety and distress levels and may raise concerns about cancer [65,66]. Furthermore, diagnostic procedures and treatment following a positive cervical screen may trigger bleeding, infection, and other adverse

obstetric events [67].

Most HPV-positive women do not have cervical disease. Therefore, triage of HPV positives is recommended whenever possible to avoid unnecessarily overstretching gynaecological services, such as colposcopy [33,61]. WHO recommends cytology, VIA, partial genotyping of HPV16/18 (already included in some HPV tests) or colposcopy (most likely available in settings where cytology exists) as triage methods [61]. In settings where cytology or VIA are established such as in LAC [68], using these tests for triage may be suitable if quality assurance is guaranteed. However, in settings without capacity to adequately follow up women with negative triage results or with healthcare access constraints, HPV-based screen-and-treat strategies may suit better [61]. Although this approach may trigger overtreatment, there are available options such as ablative treatment of the transformation zone, namely, thermal ablation or cryotherapy. Ablative treatment is highly acceptable by targeted women, causes minimal discomfort, and minimises undesirable side effects like preterm birth delivery associated with other options such as excisional treatment [69,70].

3.2.3. Colorectal cancer screening

3.2.3.1. Effectiveness. Colorectal cancer screening by occult blood tests such as the guaiac faecal occult blood test (gFOBT) and faecal immunochemical test (FIT) followed by endoscopic examination of the colon and the rectum (i.e., sigmoidoscopy and colonoscopy) of screened positives, or by sigmoidoscopy or colonoscopy without previous testing, have shown to be highly effective in reducing colorectal cancer incidence and mortality (and even all-cause mortality) [71–78]. The greatest reduction of mortality is observed for colonoscopy (~68%), followed by sigmoidoscopy (~47%), FIT (~40%), and gFOBT (13%–18%) [32,79]. Colorectal screening can effectively detect not only colorectal cancer at an early stage but also non-malignant precursor lesions (i.e., neoplastic polyps or adenomas) that can be timely treated to prevent the onset of approximately 70% of colorectal cancers. In terms of accuracy, the sensitivity of occult blood tests for colorectal cancer detection is lower, particularly gFOBT, ranging between 16%–38% for gFOBT and 27%–91% for FIT, while the sensitivity of colonoscopy alone ranges between 75%–98% [32]. To compensate limitations in sensitivity, screening is offered at different screening intervals as described below.

3.2.3.2. Age range and screening interval. Regardless of the screening method, it is recommended to start colorectal screening in men and women and at the age of 50 and continue among average-risk adults in good health with a life expectancy of more than 10 years until the age of 74 [32,80–84]. Screening intervals vary depending on the method used. For those with limited sensitivity (i.e., gFOBT and FIT) the screening interval is biennial, while colonoscopy is recommended every 10 years [32]. However, given that endoscopic methods require highly specialised resources and infrastructure, they are recommended rather as diagnostic than screening methods. Therefore, people with positive screening results based on gFOBT or FIT must be referred to either sigmoidoscopy or colonoscopy for further clinical evaluation [82].

3.2.3.3. Negative side effects. No physical harm has been associated with the use of occult blood stool tests themselves [85,86]. However, false positive results may trigger unnecessary referrals to endoscopic and other medical procedures with their corresponding adverse effects, including overtreatment (i.e., detection and treatment of neoplastic polyps or adenomas that would never progress to cancer). Additionally, sigmoidoscopy and colonoscopy have been associated to bleeding (0.08–0.2 cases per 1000 procedures) and intestinal perforation (0.08–2.4 cases per 1000 procedures) due to user's own conditions and/or medical professional's expertise [32].

3.2.4. Prostate cancer screening

PSA testing, which detects prostate-specific antigen (PSA) levels in blood, is the most sensitive marker available for monitoring prostate cancer progression and response to therapy. PSA is a glycoprotein enzyme secreted by prostatic epithelial cells and is the most abundant protein in seminal plasma. Under normal conditions, only a small portion of the protein leaks into the blood. Elevated PSA levels are observed in the presence of neoplasms of the lower genitourinary tract (prostate, bladder, urethra) and in the presence of many conditions that alters the architecture of the prostate gland (including prostatic inflammation or infection, benign prostatic hyperplasia, sexual activity, or recent prostatic manipulation such as digital rectal examination) [87] limiting PSA testing specificity for prostate cancer detection leading to overdiagnosis and overtreatment [88–90]. Hence, the use of PSA in prostate cancer screening remains controversial. Furthermore, it has been shown that most cancers detected by PSA are of low risk that do not require treatment [91,92]. While prostate cancer screening by PSA may have a modest impact on prostate cancer-specific survival and/or mortality (no changes on overall survival for at least the first 10 years follow-up nor overall mortality), harms associated with screening (biopsy complications, overdiagnosis, and overtreatment) outweigh potential benefits [87,93,94]. Approximately 20%–50% of men with positive PSA test results will be over-diagnosed and most of them will receive cancer treatment. Erectile dysfunction, urinary incontinence, and bowel dysfunction are some of the long-term complications associated with overtreatment [94–96]. Therefore, prostate cancer screening with PSA is only recommended based on shared decision-making according to subjects' conditions such as presence of prostatic symptoms, family history of prostate cancer, and whether life expectancy is greater than 10 years [97,98]. So far, no benefit of screening with a PSA test has been shown in individuals with a life expectancy of 10 years or less [98].

3.2.5. Lung cancer screening

Low-dose computed tomography (LDCT) is proposed for early detection of lung cancer in heavy smokers. There is strong evidence that LDCT, compared with chest radiography or no screening, reduces lung cancer mortality in high-risk individuals (mainly aged 50–75 years who have at least 15–pack-year smoking history and currently smoke or have quit within the past 15 years) [99–102]. A recent Cochrane meta-analysis evaluated the efficacy of LDCT to reduce mortality in high-risk individuals (most included trials having an entry requirement of ≥20 pack-year smoking history). More than 90k participants aged 40 years or older from 8 trials were analysed. Pooled estimates showed that LDCT reduces lung cancer mortality by 21% (relative risk 0.79, 95%CI 0.72–0.87) and all-cause mortality by 5% (relative risk 0.95, 95%CI 0.91–0.99) compared to no LDCT [102]. False-positive rates of LDCT are high triggering unnecessary following examination, increase of 2.6-fold in invasive procedures (95%CI 2.4–2.8), overdiagnosis (18%), overtreatment, incidental findings, increases in distress, and although rarely, radiation-induced cancers [99,102]. Evidence regarding target population and screening intervals is continually being refined aiming at maximizing the benefit/harm ratio. Evidence on the effectiveness of LDCT screening in the general population remains inadequate [103,104].

3.3. Justification for recommendations to prevent cancer

Recommendations of the LAC Code Against Cancer for individuals are shown in Fig. 3. Table 2 summarises the rationale of the recommendations within the LAC context. In addition, the LAC Code Against Cancer provides specific recommendations for policymakers (Supplementary material) to guide countries developing the infrastructure needed to enable the public to adopt the recommendations (Fig. 4).

3.3.1. Reducing HRT use

Based on well-established evidence that HRT intake increases the

Table 2
Description of contextual characteristics of LAC in relation to the LAC Code Against Cancer recommendations.

Recommendation	Relevance for LAC	Guidelines	Programmes	Coverage	Components of the recommendation	Justification
Controlled HRT use Recommendation #14 (Fig. 3)	Limited regulations on over-the-counter HRT sales	No guidelines to control HRT use in LAC	No established policies to control HRT use in LAC	—	Do not use HRT	Long-term use of HRT causes breast, ovarian, and endometrial cancer. The risks of using HRT outweigh the benefits.
					Use it only if it is directed by your doctor	HRT users should ensure that it is under medical prescription.
Breast cancer screening Recommendation #16 (Fig. 3)	Most common female cancer in LAC | Global Breast Cancer Initiative (GBCI) compliance	Most LAC countries have national breast cancer screening guidelines	Most LAC countries have national breast cancer screening programmes (opportunistic)	Low coverage of breast cancer screening in LAC. Only 4 LAC countries have coverages > 70%	Visit a health care provider every two years for a clinical breast exam from age 40	CBE has proven effective to downstage breast cancers in women both younger and older than 50 years. In a randomosed control trial, CBE has proven effective to reduce breast cancer mortality in women over 50 years (Table 1).
					Get mammography every two years from age 50 up to age 74	There is vast evidence that mammography is effective in reducing mortality in women over 50 years (Table 1).
					Follow your health care professional's recommendations based on your results	Organised cancer screening programmes do not exist in LAC. Therefore, the LAC Code Against Cancer urges individuals to follow the recommendations of health professionals who must guide them to receive subsequent clinical procedures necessary after a positive screening result.
Cervical cancer screening Recommendation #17 (Fig. 3)	90% of cervical cancer in LMICs | 3rd most common cancer in women in LAC | Cervical Cancer Elimination Initiative (CCEI) compliance	Most LAC countries have national cervical cancer screening guidelines (based on cytology or HPV testing or both)	Most LAC countries have national cervical cancer screening programmes (opportunistic) but based on cytology. Only 1 LAC country has HPV-based screening	Low coverage of cervical cancer screening in LAC. Only 6 LAC countries have coverages > 70%	Visit a health care provider and ask for HPV testing at least every 5–10 years from age 30 up to age 64	HPV testing is being progressively introduced in LAC. In some countries, HPV testing is accessible under driven demand. HPV testing is the most effective cervical cancer screening method and current WHO cervical screening guidelines recommend it as the primary cervical test.
					Ask if you can collect the sample yourself	Self-sampling (only possible for HPV testing so far) may help implement the use of HPV testing as the primary cervical cancer screening method and increase screening coverage.
					Ask for the exam available if you do not have access to HPV testing	In most LAC countries, cytology (and VIA in some) continue being the primary cervical cancer screening method and while the transition to HPV testing occurs, cytology (or VIA) should be used.
					Follow your health care provider's recommendations based on your results	Organised cancer screening programmes do not exist in LAC. Therefore, the LAC Code Against Cancer urges individuals to follow the recommendations of health professionals who must guide them to receive subsequent clinical procedures necessary after a positive screening result.
Colorectal cancer screening Recommendation #15 (Fig. 3)	3rd most common cancer in LAC | Steady rise of incidence and	Most LAC countries have national	Colorectal cancer screening programmes in LAC are scarce (present only in a	Very low coverage of colorectal cancer	Visit a health care provider and ask for an early detection test for colon and rectal cancer (faecal occult	Both occult blood tests and colonoscopy (or sigmoidoscopy) have shown to be effective in reducing

(*continued on next page*)

Table 2 (*continued*)

Recommendation	Relevance for LAC	Guidelines	Programmes	Coverage	Components of the recommendation	Justification
	mortality rates in LAC	colorectal guidelines	quarter of LAC countries)	screening in LAC. Only 1 LAC country has a coverage > 70%	blood or colonoscopy) if you are between 50 and 74 years old	colorectal cancer incidence or mortality. Health professionals may provide either colonoscopy (full examination of the colon and rectum) or sigmoidoscopy (only the lower part of the colon and rectum) based on their criteria.
					Follow the health professional's recommendations according to your results	Organised cancer screening programmes do not exist in LAC. Therefore, the LAC Code Against Cancer urges individuals to follow the recommendations of health professionals who must guide them to receive subsequent clinical procedures necessary after a positive screening result.

risk of cancer, particularly breast cancer, and because policies on over-the-counter drug sales in LAC are relaxed, the first edition of the LAC Code Against Cancer recommends not to use HRT. Should it be necessary, the decision to use HRT should be based on a thorough discussion with a healthcare provider to weigh potential benefits and risks, and the therapy must be administered by prescription for the shortest time possible and at the lowest effective dose. The LAC Code Against Cancer recommends "*Do not use hormone replacement for menopause unless directed by your doctor. Hormone replacement can cause breast cancer*" (Fig. 3). It is worth noting that there are still no policies in place to control the use of HRT. Therefore, the LAC Code Against Cancer recommends developing agreed national guidelines in LAC countries on the tailored use of HRT including dose, regimen, and duration. Additionally, the LAC Code Against Cancer urges LAC countries to create public policies to prohibit the over-the-counter sale, without medical prescription, of HRT drugs (Fig. 4).

3.3.2. Cancer screening

Based on well-established evidence of benefits outweighing harms, the LAC Code Against Cancer recommends screening for breast, cervical, and colorectal cancer (Fig. 3 and Table 2). Conversely, the LAC Code Against Cancer does not recommend prostate cancer screening since benefits do not outweigh harms. The main approach to prevent this cancer is seeking medical advice for shared decision-making based on subject's conditions and individual risk. The LAC Code Against Cancer does not either recommend screening for lung cancer due to the limited evidence in the general population since LDCT has only shown to be effective in reducing mortality when targeting individuals with high-risk smoking habits. Additionally, the limited access to LDCT in LMICs, particularly LAC, may present challenges for targeted individuals in following a LDCT-based recommendation. The feasibility of implementing lung cancer screening must be evaluated within each national context, considering local epidemiology, infrastructure, resources, and costs. Avoiding smoking and anti-tobacco policies (e.g., MPOWER measures) remain as the main and most cost-effective prevention strategy [6,8,10,105].

For individuals, the LAC Code Against Cancer states that "*Cancer can be controlled and cured if it is detected and treated early*" and states the following recommendations.

3.3.2.1. Breast cancer screening. There is sufficient evidence that mammography reduces mortality in women over 50 years. As screening mammography may not be widely available in some countries in LAC [80], it may still be used as a diagnostic test for early diagnosis in symptomatic women triggered by CBE. There is sufficient evidence that CBE is effective in downstaging diagnosed breast cancers from the age of 40 years, and, although limited, there is evidence that CBE may reduce breast cancer mortality in women over 50 years. This evidence is relevant since many women, particularly in LMICs, may benefit of early diagnosis, in line with the Global Breast Cancer Initiative (GBCI). The GBCI aims to prevent premature deaths of 2.5 million women under 70 years of age by 2040 by adopting the following goals: (i) > 60% of breast cancers are diagnosed at stage I/II, (ii) breast cancer diagnosis is fully completed within 60 days, and (iii) > 80% diagnosed women undergo full courses of treatment and successfully return home [38,106]. While goals (ii) and (iii) are reachable by enhancing health care systems, goal (i) is related to downstaging diagnosed breast cancers. Consequently, CBE followed by diagnostic or screening mammography, as evidence-based effective strategies to prevent breast cancer, may help comply with the main aim of the GBCI. Therefore, the LAC Code Against Cancer recommends to the general population: "*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*" (Fig. 3). The LAC Code Against Cancer urges governments in LAC to guarantee access to mammography to improve coverage (Table 2) and meet the GBCI goals for timely diagnosis and treatment (Fig. 4).

3.3.2.2. Cervical cancer screening. Cervical cancer is one of the most preventable cancers. However, cervical cancer incidence and mortality rates remain high, particularly in LMICs [1]. There is sufficient evidence that HPV-based cervical screening is the most effective strategy to prevent cervical cancer incidence and mortality and it is considered one of the "Best buys" [6]. Despite cytology and VIA are also considered "Best buys", HPV testing is the only cervical screening test so far capable to detect > 90% of precancerous lesions, being the test with the highest performance, and more reproducible results. Also, HPV testing is the only screening test that allows the use of self-collected vaginal samples which may improve the chances of increasing coverage. In November 2020, WHO launched the Cervical Cancer Elimination Initiative (CCEI) aimed at reducing cervical cancer incidence to < 4 cases per 100k women by achieving the following goals by 2030: 90% of girls are fully vaccinated with HPV vaccine by age 15 years, 70% of women are screened with a high-performance test by age 35 years and again by age 45 years, and 90% of women identified with cervical disease receive treatment [107]. Because of its high performance and its possibility of self-sampling, HPV testing is the most suitable test to comply with the screening CCEI goal. Additionally, HPV testing could also help comply

Hormone replacement during menopause[22, 23,24]

- Develop consensus on national guidelines on the use of hormone replacement during menopause, as well as on customizing dose, regimen, and duration of treatment.
- Prohibit the over-the-counter sale (without medical prescription) of hormone replacement therapies for menopause.

Early detection of colon and rectal cancer[25]

- Implement secondary prevention programs for colon and rectal cancer. According to current scientific evidence, mortality from colon and rectal cancer can be reduced by a fecal occult blood test every two years followed by colonoscopy for patients who have a positive result, and by at least one colonoscopy in a person's lifetime between the ages of 50 and 74.
- Ensure a reasonable and regulated supply of fecal occult blood tests and colonoscopy services as needed for national programs.

Early detection of breast cancer[26, 27]

- Ensure the availability of quality mammograms and clinical breast examinations performed by health professionals with appropriate training, and discourage the use of breast self-examinations, as they have no benefit.
- Ensure timely diagnosis and treatment of patients with abnormal mammograms or clinical breast examinations. According to the WHO Global Breast Cancer Initiative, no more than 60 days should pass between first symptoms (or first interaction of the person with symptoms with the corresponding health system) (or detection of patients with abnormal results via screening) and complete diagnosis, including a comprehensive pathology report. Once cancer is confirmed, the best multimodal treatment available in the country should be offered.
- Adopt the recommendations for screening and early diagnosis in people at high risk of developing breast cancer.

Early detection of cervical cancer[28, 29, 30]

- Following the WHO cervical cancer elimination initiative, ensure that at least 70% of women over 30 years of age are screened with a high-performance test (such as the HPV test) at least twice in their lifetime, once before age 35 and again before age 45. Where HPV molecular testing is not available, continue to use the available test (cytology or visual inspection with acetic acid) until HPV molecular testing is implemented.
- Ensure that 90% of patients with precancerous lesions or cervical cancer receive treatment, regardless of the screening algorithm offered (e.g., screening followed by colposcopy, biopsy, and treatment of confirmed lesions, or screening and treatment of patients with abnormal results).
- Ensure the availability of early detection tests, triage, diagnosis, treatment, and follow-up, according to the national program.

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Fig. 4. Latin America and the Caribbean Code Against Cancer 1st Edition: Recommendations for policymakers on medical interventions.

with the treatment CCEI goal since this test allows screen-and-treat approaches with the capacity of treating almost 100% of the lesions present among HPV-positive women. Therefore, the LAC Code Against Cancer recommends to the general population: "*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. 3). Nevertheless, HPV testing is not yet implemented in most LAC countries (Table 2) [68,80]. Therefore, the LAC Code Against Cancer urges governments in LAC to adopt strategies to comply with the CCEI goals by 2030 (Fig. 4).

3.3.2.3. Colorectal cancer screening. Compared to HICs, age-standardised colorectal cancer incidence and mortality rates are lower in LAC. However, during the last decades, these rates have been declining in most HICs, particularly mortality, while in LAC they are increasing [2,108]. For the next 20 years, it is estimated that colorectal cancer incidence and mortality rates in LAC will increase up to 76% and 84%, respectively [1]. The increase in incidence in LAC is mainly attributed to increased life expectancy and lifestyle changes, while the increase in mortality could be associated with low rates of early detection and treatment [109]. There is sufficient evidence that colorectal cancer mortality could be reduced by screening with faecal tests followed by endoscopic evaluation (i.e., sigmoidoscopy and/or colonoscopy). Therefore, the LAC Code Against Cancer recommends colorectal screening by faecal blood tests as follows: "*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 (faecal occult blood test or colonoscopy). Based on the results, follow your health professional's recommendations promptly*" (Fig. 3). However, both colorectal cancer screening programmes and awareness on colorectal cancer screening, particularly in LAC, are scarce, and existing programmes have very limited coverage (<40%) [32,71,80,81]. Thus, the LAC Code Against Cancer urges governments in LAC to strengthen initiatives to implement colorectal cancer screening programmes (Fig. 4).

3.4. Building capacity on cancer prevention of primary care health professionals

Knowledge transfer of evidence-based interventions, such as HRT use and cancer screening, in healthcare delivery via counselling is challenging. Primary healthcare professionals are key actors to rise public literacy and awareness on early detection interventions. However, they often lack knowledge and skills to provide advice on these interventions to eligible subjects. Therefore, enhancing capacity in cancer prevention is needed to empower healthcare professionals. Hereto, the LAC Code Against Cancer 1st edition, includes an online competency-based microlearning program aimed to boost healthcare delivery of cancer prevention messages, and to advance their knowledge and practice on evidence-based cancer prevention actions. The e-learning program includes four modules on medical interventions (i.e., HRT use and cancer screening), one for each of the recommendations of the LAC Code Against Cancer, in which the authors of this manuscript present these interventions in the LAC context, explaining their benefits and risks [23]. In addition, this program also includes a module for the two interventions that was not recommended (i.e., prostate and lung cancer screening).

4. Conclusions

In this manuscript we compile the evidence behind the LAC Code Against Cancer recommendations for HRT use and cancer screening following the World Code Against Cancer Framework methodology. In summary, there is strong evidence that long-term use of HRT increases the risk of cancer, particularly breast cancer. Data on HRT use, whether medical prescribed or not, is limited in the region. However, it is of concern the growing easiness of buying over-the-counter multiple drugs (possibly including HRT) in the region calling for needed drug sales regulation. There is sufficient evidence supporting breast, cervical, and colorectal cancer screening in the region. Recommendations on breast and cervical cancer screening are aligned with WHO's initiatives and together with colorectal screening respond to the needs of the LAC population.

The main strength of the LAC Code Against Cancer 1st edition, is that recommendations were agreed upon by a group of LAC experts, knowledgeable on cancer prevention and control and aware of country and regional contextual factors, who comprehensively evaluated the evidence using robust methodology supported by systematic reviews as needed. After several meetings, group members were able to achieve recommendations on consensus.

The recommendations covered in this first edition target individuals of the general population who are informed and empowered to take preventive measures, and who unfortunately may face challenges when requesting cancer prevention services, particularly for screening, as these may not be readily available. Nevertheless, these recommendations will increase cancer awareness and may trigger appropriate in-country health services capacity and delivery improvement. In addition, the e-learning platforms developed by the LAC Code Against Cancer targeting primary care professionals will further catalyse capacity building for cancer prevention.

CRediT authorship contribution statement

Armando Baena: Formal analysis, Investigation, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Melisa Paolino:** Investigation, Validation, Writing - review & editing. **Cynthia Villareal-Garza:** Investigation, Validation, Writing - review & editing. **Gabriela Torres:** Investigation, Validation, Writing - review & editing. **Lucia Delgado:** Investigation, Validation, Writing - review & editing. **Rossana Ruiz:** Investigation, Validation, Writing - review & editing. **Carlos Canelo-Aybar:** Investigation, Validation, Writing - review & editing. **Yang Song:** Investigation, Validation, Writing - review & editing. **Ariadna Feliu:** Conceptualization, Methodology, Writing – review & editing. **Mauricio Maza:** Investigation, Validation, Writing - review & editing. **Jose Jeronimo:** Investigation, Validation, Writing - review & editing. **Carolina Espina:** Conceptualization, Funding acquisition, Methodology, Project administration, Supervision, Writing - review & editing. **Maribel Almonte:** Formal analysis, Investigation, Supervision, Validation, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Disclaimers

The authors alone are responsible for the views expressed in this manuscript. Where authors are identified as personnel of the International Agency for Research on Cancer / World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer / World Health Organization.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2023.102446.

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