

Cervical cancer screening programs in Latin America: current recommendations for facing elimination challenges

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Abstract

Objective. To describe current cervical cancer screening program guidelines in Latin America. **Materials and methods.** We searched official recommendations for the general population and women living with HIV (WLHIV) by reviewing official sources from 19 countries; these data were supplemented with a consultation carried out by the WHO with the Ministries of Health. **Results.** Screening policies vary significantly in regard to target populations, primary tests, and screening intervals. Sixteen countries have recently updated their recommendations; however, cytology remains the primary screening test for most countries. Eleven countries have introduced HPV tests, and eight countries have implemented screen-and-treat algorithms; only three countries have developed evidence-based guidelines. All countries but Costa Rica have specific recommendations for WLHIV. **Conclusions.** Although most countries have updated their screening policies, only a few are properly aligned with the WHO elimination strategy. Recommendations for WLHIV require better integration with cervical cancer screening programs.

Keywords: uterine cervical neoplasms; papillomavirus infections; mass screening; public policy; HIV; Latin America

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Resumen

Objetivo. Describir directrices vigentes en los programas de tamizaje de cáncer de cuello uterino en Latinoamérica. **Material y métodos.** Se buscaron recomendaciones oficiales en instituciones de gobierno de 19 países, tanto para la población general como para mujeres viviendo con VIH (MVIH). Se complementó la información mediante consulta de la OMS a los Ministerios de Salud. **Resultados.** Las recomendaciones varían ampliamente entre países respecto a población objeto, pruebas e intervalos de tamizaje. Dieciséis países tienen recomendaciones actualizadas; sin embargo, la citología continúa siendo prueba primaria en la mayoría. Once países introdujeron las pruebas de VPH y ocho tienen estrategias de ver y tratar. Todos los países, excepto Costa Rica, tienen recomendaciones específicas para MVIH. **Conclusión.** A pesar de recientes actualizaciones, pocos países tienen abordajes adecuadamente alineados con la estrategia de eliminación de la OMS. Las recomendaciones para MVIH requieren mejor integración con los programas de tamizaje.

Palabras clave: neoplasias del cuello uterino; infecciones por papilomavirus; tamizaje masivo; política pública; VIH; América Latina

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Cervical cancer remains the main cause of cancer death among women in 36 countries, most of them low-income and lower-middle-income.¹ Given its preventable condition, the elimination of cervical cancer is considered a priority under the agenda of the World Health Organization (WHO). Key elimination targets are to achieve, by 2030, full vaccination against HPV of 90% of the girls by age 15, over 70% screening coverage using a high-performance test for women aged 35 to 45 years, and treatment of 90% of cervical disease.² Modeling estimates show that vaccination alone would take longer to achieve the elimination goal, namely global incidence below 4 per 100 000 by the year 2060.³ Thus, the manner in which countries organize screening is fundamental to reduce cervical cancer incidence mortality.

Latin America and the Caribbean has the second-highest cervical cancer mortality worldwide, with the highest rates in the Caribbean (8.2 per 100 000), followed by South America (7.8 per 100 000) and Central America (6.8 per 100 000).⁴ Cervical cancer screening was introduced in Latin America in the late 1950s;⁵ since then, intensive research has prompted the development of new technologies and new programmatic approaches. Previous studies have described the cervical cancer screening programs in the region, revealing different extents of coverage, organization levels, and effects on cervical cancer incidence and mortality.⁶ However, information about the integration of new evidence into public health practice is scarce. Although WHO periodically reports on the existence of screening programs, no detailed report about program characteristics is provided, and the available data is gathered through self-reported questionnaires with low reliability.⁷

The proper definition of target populations, screening tests, screening intervals, and clinical pathways (including diagnostic work-up and treatment) are crucial for screening programs to be effective.^{8,9} Accordingly, the Pan American Health Organization (PAHO) recommends the introduction of new technologies in "screen and treat" or "screen, triage, and treat" approaches to reduce inequalities, overcome follow-up barriers, and improve detection and treatment rates.¹⁰ In addition, quality assurance as part of organized programs helps ensure the successful implementation of screening programs;¹¹ however, information gaps undermine monitoring and evaluation, and, ultimately, quality assurance programs. Thus, information about current characteristics of screening programs helps in assessing countries' preparedness to incorporate the cervical cancer elimination strategy of the WHO—a critical issue in regions such as Latin America, which have a high cervical cancer incidence and mortality, that constitutes

a significant burden for underserved women as a result of socioeconomic inequalities.^{4,12}

In this study, we aimed to describe current guidelines/recommendations for cervical cancer screening in Latin America, both for the general population and for women living with the human immunodeficiency virus (WLHIV), as an indicator of preparedness to reduce the disease burden, in agreement with the WHO cervical cancer elimination strategy.

Materials and methods

We conducted a structured review of official documents in order to retrieve information regarding the current national cervical cancer guidelines/recommendations for the general population and for WLHIV.

Search strategy

From August 2019 to October 2020, we scrutinized websites from Ministries of Health in 19 Latin American countries defined as Spanish and Portuguese-speaking countries of the Caribbean and Central and South America. Puerto Rico was excluded due to the influence of US guidelines because its self-governing commonwealth association.

We collected all available official documents and information regarding cervical cancer screening from governmental websites in every country. In addition, we carried out a Google search using the terms: country [name], Latin America, cervical cancer, mass screening, early detection of cancer, diagnostic screening programs, up-to-date screening, guidelines, protocols, norms, regulation, legislation, recommendations.

We identified and retrieved the most recent national laws, sectoral regulations, ministerial guidelines and recommendations, and program protocols. Guidelines or recommendations not having explicit support of the respective countries' Ministry of Health (*i.e.*, guidelines by scientific societies or governmental institutions other than the Ministry of Health); and documents outlining regional or local programs instead of national programs were excluded.

In addition, we searched information about recommendations for cervical cancer screening among WLHIV in documents either from HIV or cervical cancer screening programs. To supplement the available information from screening programs, we searched official websites for HIV programs and conducted a Google search using the terms: country [name], Latin America, cervical cancer, HIV guidelines, women living with HIV. When discrepancies among sources were observed, HIV guidelines prevailed.

From November 2020 to February 2021, the WHO carried out a consultation with the Ministries of Health aimed at verifying, supplementing, or amending the initial data collected. A template was provided to each country with the data sources found, resulting in two countries providing additional information on screening policies and updated official documents.

Data collection and management

We retrieved information about the existence of current public screening policies, year of update, primary screening and triage tests used (alone or combined), target populations and screening intervals for every test, existence and characteristics of screen-and-treat and self-sampling strategies, process of implementation (rollout), and entity responsible for the screening program (organizer). To characterize recommendations for WLHIV, we retrieved the same information as for the general population, with the exception of rollout and organizer data.

All data were independently obtained by two researchers and subsequently verified by other members of the research team. Inconsistencies were subject to group discussion before the final registration in the database. Whenever different documents were found describing the same country and program, the data were independently collected for every document and registered with the corresponding publication date.

All retrieved information was cross-checked with information from the WHO's 2019 NCD Country Capacity Survey.

Analysis

For each country we describe the year of update and screening tests with their corresponding target populations and intervals for both the general population and WLHIV. Accordingly, we classified program approaches based on the definition of unique or multiple target populations for a given test, or shared target populations for different screening tests; this information is summarized in a figure (map) specifying the tests under description. Furthermore, for the general population we describe follow-up strategies considering triage testing for HPV positives and screen-and-treat approaches.

Results

Screening recommendations for 18 countries were found in official documents associated to national plans, national laws, or health sector regulations. In the case of Venezuela, the data were retrieved from an indexed publication.⁶ A total of 14 countries have specific cervi-

cal cancer screening guidelines or protocols, but only Brazil, Chile, and Colombia have evidence-based guidelines.¹³⁻¹⁵ During the last decade, 16 out of 19 countries updated their recommendations for cervical cancer screening (figure 1), and the most frequent changes were the introduction of Human Papillomavirus (HPV) tests and screen-and-treat algorithms.

The recommendations vary significantly between countries in terms of the concurrent use of different screening tests, the target populations, and the screening intervals (figure 2). We did not find reports on program performance or implementation status (rollout).

3.1 Screening tests

Eleven countries introduced HPV testing as part of their recommendations, with cytology as the main triage test (figure 2; table I). All countries except Honduras are still recommending cytology as the primary test either as the only choice or as an optional primary test. The concurrent use of HPV testing and cytology or direct visual inspection is recommended for different target populations in 3 out of 11 countries, while the remaining countries recommend these tests in various combinations for the same target population. Notably, Mexico introduced HPV testing for women aged 35 to 64 as a stand-alone test in 2007,¹⁶ but changed the recommendation to cytology or HPV testing in 2013.¹⁷ Only Panama recommends HPV and cytology co-testing.¹⁸

Four countries consider HPV self-sampling to be part of the recommendations for under-screened women or to overcome social and cultural barriers (Argentina, Colombia, Guatemala, and Honduras).^{15,19-21}

3.2 Target populations

Compared to previous recommendations, screening starts at older ages in most countries. Only six countries recommend screening under age 25 (table I), and Colombia, Nicaragua, and Paraguay keep an option for the screening of adolescents based on the age of sexual onset (appendix A).²² The Dominican Republic recommends starting screening at the age of 35 years. Regarding HPV testing, only Panama recommends its use in women under 30 years of age; most countries recommend starting at age 30, although Mexico recommends starting at age 35 (table I). The age to stop screening is between 64 and 69 years of age for all countries, but Guatemala stops screening at age 54.

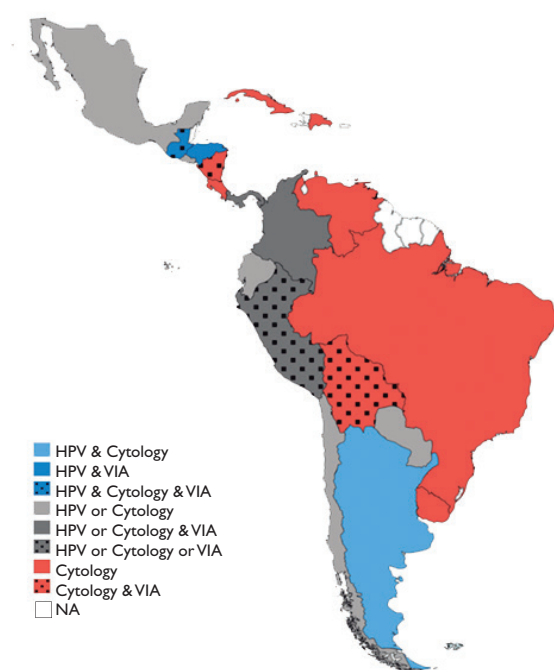
3.3 Screening intervals

The most frequent screening intervals are five years for HPV testing and three years for cytology and visual



No available information for Venezuela

FIGURE 1. TIMELINE OF CERVICAL CANCER SCREENING GUIDELINES UPDATE IN LATIN AMERICA, 2021



HPV: Human Papillomavirus test
VIA: Visual inspection with acetic acid
NA: Not applicable

* Denotes concurrent use of screening tests for different target populations
or: Denotes concurrent use of screening tests indistinctly for the same target population
Panama recommends co-testing with HPV and cytology

FIGURE 2. CURRENT USE OF CERVICAL CANCER SCREENING TESTS IN LATIN AMERICA, 2021

inspection. Three countries in Central America recommend cytology every two years, and only Panama recommends HPV testing every three years. However, Colombia shortens the screening interval for HPV testing to three years if done by self-collection, given the potential lower sensitivity of vaginal samples compared with cervical samples.¹⁵

3.4 Screen-and-treat strategies

Eight countries include screen-and-treat in their official recommendations (table I). Most countries (n=5) use visual inspection with acetic acid (VIA) followed by cryotherapy for positive findings; alternative approaches include complementary inspection with lugol iodine and HPV testing followed by immediate treatment (table I). Furthermore, in Colombia, Nicaragua and Paraguay, screen-and-treat strategies are restricted to specific populations with limited access to health care, whereas for the remaining countries, the recommendation covers the general target population.

3.5 Cervical cancer screening recommendations for WLHIV

All countries except Costa Rica have specific recommendations for cervical cancer screening among WLHIV, mainly described in HIV guidelines. Chile, El Salvador, Honduras and Peru set up recommendations in both HIV and cervical cancer guidelines; however, the recommendations differ between them.

Compared to the recommendations for the general population, the most common variations in WLHIV include the age for the initial screening test (linked

to age of HIV diagnosis), a shorter screening interval (annual), and the combination of screening tests. Cuba and Brazil specify strategies based upon patient's immunological status, and only Mexico and Colombia introduced HPV testing as part of the recommendations for WLHIV (table I).

Discussion

This paper summarizes the current national recommendations for cervical cancer screening in 19 Latin American countries. During the last decade, 16 out of 19 countries updated their recommendations to introduce new screening tests or alternative programmatic ap-

proaches; however, cytology remains the main screening test. Our findings provide essential baseline information about the preparedness of the region to implement the WHO's strategy for cervical cancer elimination, including actions oriented toward WLHIV.

In general, we found low variability for recommendations on HPV primary screening as most countries follow international standards regarding age of screening start and screening intervals. Only 1 out of 11 countries that feature HPV testing recommends starting screening before age 30 and a shorter interval. By contrast, six countries using cytology as primary screening test recommend starting before age 25, and four make screening for adolescents optional (table I).

Table I
CERVICAL CANCER SCREENING POLICIES IN LATIN AMERICA

Country	Recommendations for the general population						Recommendations for WLHIV			Sources*
	Year of update	Screening test	Target population (age)	Screening interval	Triage for HPV positive women	Screen and treat strategies	Year	Screening strategy	Screening interval	
Argentina	2015	Cytology HPV test	25-29 30-64	3 y 5 y	Cytology	No	NA	Cytology and colposcopy	6 m (first year) - 1 y	A1, A2, B1
Bolivia	2009	Cytology VIA [‡]	25-64 N/A	3 y N/A	No	VIA and cryotherapy	2017	Cytology and colposcopy	NA	A3, B2
Brazil	2016	Cytology	25-64	3 y	No	No	2016 [§]	Cytology	6 m (first year) - 1 y If CD4 < 200: 6m	A4
Chile	2015	Cytology HPV test	25-64 30-64	3 y 5 y	Cytology or HPV genotyping	No	2013 [#]	Cytology	1 y	A5, B3
Colombia	2019	Cytology HPV test VIA-VILI [¶]	25-69 30-65 [∞] 30-50	3 y 5 y 3 y	Cytology	VIA-VILI and cryotherapy [¶]	2014	Cytology and HPV test	1 y	A6, A7, B4
Costa Rica	2007	Cytology	>20	2 y	No	No	NA	NA	NA	A8, A9
Cuba	2018	Cytology	25-64	3 y	No	No	2018 [§]	Cytology Immunosuppressed: Cytology and Colposcopy	3 y Immunosuppressed: 1 y	A10
Dominican Republic	2010	Cytology	35-64	3 y	No	No	2018	Cytology	1 y	A11, B5
Ecuador	2017	Cytology HPV test	21-65 30-65 [∞]	3 y 5 y	Cytology	No	2019	Cytology	Sexually active: 1 y Menopause: 6 m (first year) - 1 y	A12, B6
El Salvador	2015	Cytology HPV test	20-65 30-59 [∞]	2 y 5 y	No	HPV and cryotherapy	2020*	Cytology	6 m	A13, B7

(continues...)

(continuation)

Guatemala	2020	Cytology HPV test VIA	25-29/ 50-54 30-39 40-49	3 y 5 y 3 y	VIA or cytology	HPV/VIA and cryotherapy/ LEEP	2019	Cytology	1 y	A14, B8
Honduras	2015	VIA HPV test	25-29 30-64	3 y 5 y	VIA	VIA and cryotherapy	2017 [#]	Cytology	6 m (first year) - 1 y	A15, B9
Mexico	2013	Cytology HPV test	25-64 35-64	3 y 5 y	Cytology	No	2018	HPV test Triage: Cytology or genotyping	5 y	A16, A17, B10
Nicaragua	2010	Cytology VIA ^{&}	25-64 30-50	3 y 1 y	No	VIA and cryotherapy ^{&}	2016	Cytology	1 y	A18, A19, B11
Panama	2017	Cytology HPV test	21-70 25-64 [∞]	2 y 3 y	Cytology	No	2016	As the general population		A20, B12
		Co-testing HPV test/ Cytology	30-64	3 y						
		VIA ^{&}	NA [°]	NA						
Paraguay	2015	Cytology HPV test	21-65 30-65	3 y 5 y	Cytology	Colposcopy and LEEP ^{&}	2015 [§]	Cytology	6 m	A21, A22, A23
Peru	2019	Cytology HPV test VIA	25-64 30-49 [∞] 30-49	2 y 5 y 2 y	Cytology or HPV geno- typing	VIA and cryotherapy/ thermoco- agulation	2019 ^{#,§}	Cytology or VIA	6 m (first year) - 1 y	A24
Uruguay	2014			3 y	No	No	2018	Cytology	6 m (first year) - 1 y	A25, B13
Venezuela	NA			3 y	N/A	N/A	2016	Cytology	1 y	A26, B14

HPV: human papillomavirus; VIA: visual inspection with acetic acid; VILI: visual inspection with lugol iodine; N/A: not available; LEEP: loop electrosurgical excision procedure; WLHIV: women living with HIV; "y": years, "m": months

* Appendix A & B²²

[‡] When there is no cytopathology laboratory available

[§] Recommendations from the cervical cancer screening guideline

[#] Recommendations in the cervical cancer screening guideline differ from HIV guideline's recommendations

[&] In women from rural, distant areas or with limited access to health services

[∞] Screen with HPV test if possible

[°] Recommended until menopause

Cervical cancer screening programs were introduced into the region during the 1950s; throughout the following decades, most attempts to improve screening relied on morphology-based testing such as computer-assisted cytology, direct visual inspection, colposcopy, and cervicography.²³ Research into HPV testing as a screening method started in the 1980s, and consolidated evidence of their superior accuracy and capability to reduce cervical cancer mortality has been available since the early 2000s.²⁴

Despite the extended commercial availability of HPV testing, the implementation of molecular technologies as primary screening tests has not occurred broadly in most areas of the world. Nowadays, only a

few countries have introduced the technology in their national programs. Although several countries have developed pilot projects or implemented HPV testing on a small scale, cytology remains the basic screening test in national guidelines.²⁵⁻²⁷

The inclusion of HPV testing in current recommendations reflects the affordability for national economies and the need to overcome some limitations of screening programs.⁸ Besides high coverage, cytology-based screening requires strong quality assurance and several visits along the clinical pathway that challenge follow-up of positive-screened women, particularly in low- and middle-income settings. The inclusion of HPV

testing in national recommendations of more than half of Latin American countries represents an opportunity to enhance the performance of screening programs, and consequently, a greater chance of controlling cervical cancer in the region.

In addition to their higher accuracy, HPV tests offer the possibility of increasing participation rates among reluctant women through the option of self-sampling; this may also reduce losses to follow-up among positive-screened women by reducing the number of visits involving point-of-care tests,²⁸⁻³⁰ as indicated by some reports from the region.³¹ Despite these advantages, additional visits or the use of low-sensitive triage tests to correct the lower specificity of HPV testing deserves careful consideration because it might hinder the follow-up of positive-screened women.^{8,24} Screen-and-treat strategies in one or two visits have been proposed to overcome some of these limitations, yet direct visual inspection remains the predominant screening technique for this approach. Although HPV testing and treatment has been proposed as an alternative strategy within this scenario,⁸ only Guatemala and El Salvador have implemented it in Latin America. Some countries recommend VIA for screen-and-treat despite recommending HPV testing for the regular program; thus, the rationale behind the VIA recommendation is likely to be related to concerns about overtreatment and logistics of HPV testing in screen-and-treat scenarios rather than concerns around affordability.^{6,8}

Although the potential advantages of molecular screening, deficient program organization and quality assurance should be tackled to achieve the expected population impact. The implementation of updated guidelines in Latin America differs from Europe and North America because there is no planned roll-out process. Usually, national recommendations in Latin American countries are mandatory for the public health system, and a deadline to achieve full implementation is defined after recommendations development. Nevertheless, the characteristics of the health systems as well as the current status of screening coverage might play a major role in the implementation process. Most Latin American countries have segmented health systems with different organizational structures, serving different population groups, and under different rules and benefit packages.³² Under this model, health care is provided to the poorest population through public hospitals, employees are served by social security institutions, and the richest segment is privately insured; thus, policies for cancer control are separated and unequal, challenging the universal implementation of organized cervical cancer screening.

We retrieved information about screening recommendations from official sources providing more detailed information than did the WHO survey on cancer country profiles.⁷ We also found some differences in the data reported; these are likely due to the data-collection methods used, as we directly reviewed official documents, whereas the WHO survey is self-reported; however, we include information gathered through a WHO consultation process in order to approach both sources of data. Most countries reported to the WHO that they had organized screening, but we found no reports on program performance, which prevented us from defining the status of the guidelines' implementation (rollout). We consider this situation critical because, beyond the inclusion of new alternatives in current recommendations, their final impact on cervical cancer elimination depends upon the achievement of the defined goals related to HPV vaccination, screening coverage, and CIN detection and treatment rates, which are essentially the result not only of the selected algorithms but also of their level of implementation.

The HIV disease burden in Latin America has increased. Incident cases augmented by 21% since 2010, and approximately 780 000 women were living with HIV in Latin America and the Caribbean in 2019. This number is expected to increase due to the decreased mortality and the increased availability of anti-retroviral treatment.^{33,34} Considering that some countries with the highest cervical cancer incidence and mortality are also areas of high HIV prevalence,^{4,34} and given the higher risk for HPV infection and progression,^{35,36} WLHIV have been defined as a special target population for cervical cancer elimination. We found 18 countries that have specific recommendations for cervical cancer screening among WLHIV, most of which were derived from the HIV guidelines. Currently, cervical cancer screening is recommended for sexually active girls and women as soon as they test positive for HIV and regardless of their age. Because the higher prevalence of high-risk HPV will result in a reduced specificity of HPV testing, a careful review of the age for starting screening and triage algorithms for HPV-positive women is highly desirable to achieve an optimal harmonization of cervical cancer screening and HIV guidelines, as well as a better coordination of the corresponding programs.³⁷

Conclusion

Latin American countries have a long tradition with cervical cancer screening; however, the level of program

organization is not clear, and the region continues to bear a significant burden of disease. Cervical cancer screening recommendations vary significantly among Latin American countries in terms of target populations, screening tests, and screening intervals. The differences observed might be related to variations in the methods used for assessing evidence, the influence of opinion leaders, and contextual factors such as affordability and accessibility.

Although the introduction of HPV testing continues to evolve, cytology remains the main screening test, and only three countries defined HPV testing as the exclusive choice for the corresponding target populations. We retrieved information from the last updated recommendations, and we do not know the time elapsed between policy updates; however, a long time until the next revision could be expected, and consequently, the concurrent use of cytology along with HPV testing might defer the full introduction of molecular screening.

The Covid-19 pandemic introduced additional challenges to cervical cancer screening; however, its final impact remains to be established, given the lack of accurate official reports. Despite the challenges faced by the introduction of new technologies, the existence of alternative programmatic approaches such as screen-and-treat strategies and HPV self-sampling in a considerable number of Latin American countries suggests that, given the new evidence, they are incorporating it into their national recommendations to help overcome socioeconomic barriers and improve screening coverage and follow-up. Our findings reveal the status of the recommendations for cervical cancer screening in Latin America, contributing to the design of strategies aimed at advancing the WHO's cervical cancer elimination agenda.

Ethics approval

Since this is a study based on documentary sources, no ethical clearance was required.

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Data sharing

Additional data and project related documents are available upon request.

Contributors

Study design: FDG, SB, BL, DSS, CJS, MR. Data collection: FDG, SB, CMM, RE. Data analysis and interpretation: FDG, SB, BL, MR. First manuscript draft: FDG, MR. Manuscript draft editing and review: FDG, CMM, SB, BL, MR. All authors reviewed and approved the final version of the manuscript.

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