HPV Vaccination

Toward the Elimination of Cervical Cancer in the Caribbean Countries

Virtual Meeting Report
22–23 and 29–30 October 2020

PAHO
Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

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PAHO Pan American Health Organization World Health Organization Regional Office for the Americas

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OBJECTIVE

Discuss strategies and share experiences toward the elimination of cervical cancer in the Region of the Americas by improving coverage for human papillomavirus (HPV) vaccination, introducing HPV testing, and increasing screening coverage and treatment rates.

PARTICIPANTS

Participants included representatives from the ministries of health from the Caribbean subregion, experts from the Pan American Health Organization / World Health Organization (PAHO/WHO), and professionals from various other institutions, including the Institut Català d'Oncologia (Spain), George Mason University (United States), Population Services International (PSI) Caribbean (Trinidad and Tobago), the National Institute of Infectious Diseases (Argentina), and The Cancer Centre Eastern Caribbean (TCCEC) (Antigua and Barbuda), among others.

DAY 1:
UPDATES, OVERVIEW, AND FUNDING FOR HPV VACCINATION

The meeting officially opened on October 22 with welcoming remarks by Andrés de Francisco and Anselm Hennis from PAHO. The first day largely focused on HPV vaccination in the Americas.

Session 1: Updates on Strategies for the Regional and Global Elimination of Cervical Cancer

Moderator: Cuauhtémoc Ruiz Matus, PAHO

1. Global Update on HPV Vaccination and Coverage

Speaker: Paul Bloem, WHO, Switzerland

Global strategy to accelerate the elimination of cervical cancer as a public health problem: A global strategy will be launched on 17 November 2020 as a call to all countries to take action to eliminate cervical cancer, setting a threshold of 4 per 100,000 women-years for elimination as a public health concern. To reach and maintain this incidence rate by the end of the century, the following 2030 control targets were defined: 90% of girls fully vaccinated with the HPV vaccine by age 15; 70% of women screened with a high-precision test at 35 and 45 years of age; and 90% of women identified with cervical cancer disease and receiving treatment.

Strategies and characteristics of the HPV vaccine: With high coverage of the HPV vaccine globally, elimination can be reached within a century. Vaccinating girls is central to this effort, and can avert 45 million deaths from HPV over the next century. Introducing two lifetime screens could shorten the elimination timeline by a decade and prevent another 14 million deaths. The HPV vaccine has an excellent safety profile, with a lower number of adverse events following immunization (the acronym ESAVI, which is used in the region, corresponds to the acronym AEFI) than many other vaccines. The vaccine's duration of protection is a key factor, as reaching elimination requires an assumption of lifelong protection. The number of strains contained in the vaccine is less important, since those that are contained most commonly cause cervical cancer.

Recommendations of the 2019 Strategic Advisory Group of Experts on Immunization (SAGE): Because girls in low- and middle-income countries (LMIC) lack HPV vaccine access, SAGE recommends that countries temporarily postpone implementation for boys until all countries have access to the vaccine and there is no risk of low supplies in the market. Vaccinating boys has not been shown to improve coverage overall, nor among girls, so gender-neutral vaccination is not a remedy for low coverage. New, alternative strategies were also proposed, including an extended 1+1 schedule, with the second dose being given 3-5 years apart in cases of serious supply issues.

Challenges and solutions: Dropout is significantly higher for HPV vaccines than childhood vaccines, particularly in LMIC, likely due to affordability issues. Coverage is higher in schools than in facilities, but school strategies are expensive. There is a lack of trust in the vaccine, which must be rebuilt to avoid hesitancy, including among medical professionals. Confidence in health workers themselves must also be rebuilt, and all stakeholders must be onboard regarding vaccine safety. Programs must budget for continued communication for years after vaccine introduction.

The future: Demand is currently higher than supply, and supply is expected to grow slowly in the short term but will ramp up steeply after 1-3 years. There is no major forecasted impact of the COVID-19 pandemic. New market entrants could help with supply challenges and potentially affect prices in the long term. There is a growing belief that a single dose of the HPV vaccine may be sufficient, and trials are underway to determine if one dose maintains a strong and stable immune response, protects against cervical infections from HPV 2/3, and prevents cancer in the long term.

2. Advances in the Introduction of HPV Vaccines in the Americas

Speaker: Lúcia Helena de Oliveira, PAHO

HPV vaccines: The bivalent vaccine is composed of HPV strains 16 and 18, which are the two most oncogenic types. The quadrivalent vaccine contains HPV 6, 11, 16, and 18. The nonavalent vaccine contains HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58. All three licensed vaccines are very safe and offer comparable immunogenicity, efficacy, and effectiveness for cervical cancer prevention. All should be administered before the onset of sexual activity.

Vaccination introduction: In the Region of the Americas (including the Caribbean), 43 countries and territories have introduced the vaccine. As of 2019, 13 countries reported gender-neutral vaccination: Antigua and Barbuda, Argentina, Barbados, Bermuda, Brazil, Canada, Chile, Montserrat, Panama, Puerto Rico, Saint Kitts and Nevis, Trinidad and Tobago, and the United States of America. The most commonly used vaccine is the quadrivalent vaccine.

Vaccination coverage: Achieving high HPV vaccine coverage is a challenge. An analysis of coverage in 52 countries from 2014 to 2016 found that 27% of countries had ≥80% coverage and 25% of countries had <50% coverage. This indicates that achieving high coverage requires adopting a number of vaccination strategies, with priority given to school vaccination.

Recommendations of the Technical Advisory Group (TAG) on Vaccine-preventable Diseases: At a 2019 meeting, TAG members emphasized the importance of meeting the needs of countries to reduce the cervical cancer burden, and called on the global public health community to challenge HPV vaccine manufacturers to respond ethically to global vaccine delivery needs and align with the PAHO/WHO call to eliminate cervical cancer. Vaccination should be prioritized for girls, with 80% coverage to create a herd immunity that would protect both boys and girls, and communication and vaccination plans should be implemented in schools.

Key examples of PAHO 2019 technical cooperation:

- Regional meetings: HPV Vaccination Toward Cervical Cancer Elimination
- Vaccine coverage calculation guide
- Measuring the HPV vaccine impact
- Measurement document (in progress)
- Support to countries in introduction plans and crisis situations due to adverse events following immunization.

3. Immune Response to HPV Vaccines

Speaker: Malda Kocache, PhD, George Mason University, United States of America

The body's natural immune response to infection with the HPV virus is slow and not very strong. The virus does not induce inflammation that would alert the immune system to infection. The antibodies are weaker, with low titers and low avidity. Only about 70% to 80% of women seroconvert, and men do not seem to produce protective antibodies. Natural infection is controlled by the cell-mediated response more than the antibody response. The cell-mediated response is important to control viral infections, but the neutralizing antibody response is important to stop infection from occurring.

Unlike innate immunity, the immune response to the vaccine is extremely robust and effective. Immunity with one dose is nine times higher than with the response to natural infection. There are three available HPV vaccines, all subunit vaccines made from the antigenic L1 capsid protein. The L1 protein generates virus-like particles, which mimic the virus enough to induce a strong immune response but are not infectious or oncogenic themselves, since they do not actually contain DNA. Once the vaccine is introduced intramuscularly, the antigen-presenting cells and the innate immune response kick in; B cells and helper T cells become activated; and B cells differentiate into long-living plasma cells (LLPCs). These LLPCs produce neutralizing antibodies, thereby inducing highly effective immune memory, inhibiting infection, and preventing the disease from developing.

Doses are separated by at least six months to give memory B cells time to develop. The second dose is what activates the B cells to produce high-affinity antibodies. The immune response is highest in girls aged 9-14, and a two-dose schedule is very effective in this age group. Studies have shown that the long-term effect of the HPV vaccine will significantly reduce the prevalence of high-risk lesions, resulting in a reduction in cervical cancer.

4. Discussion

Is there a maximum time frame between the first and second dose? We often get questions from parents who missed the second dose at six months and want to know if they have to start over.

There is no maximum time frame between doses. The vaccine is licensed with the six-month interval, but research shows that, particularly for younger girls, the immune response is even stronger with a longer interval—optimally one year or more. Currently, **WHO** proposes that countries consider annual vaccination, both for programmatic reasons and for this strong response. If an individual misses the second dose and comes back some time later, WHO guidance is not to restart, but to finish out the course. Typically, only optimum time is discussed but, in principle, there is no maximum time frame, If the question comes up often, it can help to have a formal policy that can bring clarity to health workers who are asked these questions by parents.

Can a woman receive the vaccine after age 26?

It depends on the country's license; for example, the vaccine is licensed up to age 45 in the United States of America, but a policy of vaccinating older women is not recommended. The first goal is to reach cervical cancer elimination, so most of the effort must go toward vaccinating girls between the ages of 9 and 14 and to reach high coverage in this age group. A woman who is 26 years of age has likely been sexually active for some time, and if she had a prior infection with either HPV 16 or 18 (the primary oncogenic strains) the vaccine will no longer protect against them. The other important factor relates to immunology: the younger the girl, the better her immune response. Not only does delaying vaccination not protect as well against the most common oncogenic strains, but there is actually a plateau after 10 years. There is a higher neutralizing antibody titer when girls are vaccinated younger.

What is the role of the vaccine in patients already diagnosed with pre-invasive or invasive cervical cancer?

The vaccines are preventative, not therapeutic, and are licensed as such. There are no data showing that the vaccines work to induce any type of reversal. While you can control the replication of the virus by the cell-mediated response, the vaccine is actually creating neutralizing antibodies, which will inhibit the infection. But for women with pre-invasive and invasive cervical cancer, that infection has already occurred. This is another example of why it is so important to administer the vaccine early in life.

5. Plan of Action for Cervical Cancer Prevention and Control and Summary of the WHO Regional Consultation on Cervical Cancer Elimination

Speaker: Silvana Luciani, PAHO

Cervical cancer in the Americas: In the Americas, more than 72,000 women are diagnosed and more than 34,000 die from cervical cancer each year. The Caribbean subregion has the highest mortality rate in the Americas. An integrated approach to cervical cancer control must be implemented across the life course, with HPV vaccination for adolescent girls, screening and treatment of women in middle years, and cancer diagnosis and palliative care for all women who

need it but particularly for those women in their later years. Countries are encouraged to move away from low-sensitivity tests such as cytology and visual inspection with acetic acid (VIA) and toward high-performance tests such as HPV testing delivered with or without triage.

Regional plan of action: The Region of the Americas has adopted a Plan of Action for Cervical Cancer Prevention and Control 2018–2030. It has four main interventions and strategies:

1. Strengthen program organization, governance, information systems, and cancer registries;
2. Invest in primary prevention;
3. Strengthen screening and pre-cancer treatment;
4. Improve access to diagnosis, treatment, rehabilitation, and palliative care services.

National cervical cancer elimination plans: Developing a country plan for cervical cancer begins with political and technical commitment and an empowered program manager working with a multidisciplinary committee. Next, a situation assessment should be conducted; and goals and targets for elimination created. Updated screening guidelines and the training of providers and lab personnel are also important elements. Education and communication activities should be planned, and an information system set up to monitor targets.

PAHO technical and financial support: PAHO has significant technical knowledge and tools available (see www.paho.org/cancer). PAHO also has two types of funds available to facilitate the acquisition of vaccines and HIV tests: the Revolving Fund for Access to Vaccines, which includes HPV vaccines; and the Strategic Fund for Public Health Supplies, which includes the three prequalified HPV tests. Countries are encouraged to utilize the Strategic Fund because it allows for one unique price regardless of purchase size, for all countries in the Region.

6. PAHO's Revolving Fund Update on HPV Vaccines

Speaker: John Fitzsimmons, PAHO

The Revolving Fund for Access to Vaccines is an important mechanism for HPV introduction in the Region. In his presentation, John Fitzsimmons discussed some of the ongoing and upcoming challenges with supply and demand, and the work that the Revolving Fund is doing to ensure consistent supply.

Supply/demand overview: In the Americas, the 2020 total demand of the HPV vaccine was 2.8 million doses, with 1.8 million purchased and an additional 1 million pending. Demand is expected to increase in 2021, but the supplier has only agreed to provide 2.5 million doses. PAHO will continue to push for the full 2.8 million doses required. Of the 1.8 million doses purchased in the Region, the total supply procured by the Caribbean subregion was 97,680. Various Caribbean countries are also in the process of switching from the bivalent to the quadrivalent vaccine.

Supply/demand management and 2021 projections: Some countries in the Region have a healthy number of months projected for vaccine utilization, while others are projected to have low supply levels. To avoid the risk of stockouts, PAHO will work closely with countries to help them manage their inventories. They will also continue to follow up on countries' current supply levels in order to target discussions with the supplier and manage supply and demand. These meetings have been a very effective tool for targeting supply in a constrained environment.

HPV market perspective: Given the constrained market conditions, supply is not going to be sufficient to meet global demand until at least 2023, and only with tight management and careful planning. Several countries eligible for support from Gavi as well as self-financing countries had to postpone HPV vaccine introductions and multi-age cohort campaigns. Many factors could affect the supply/demand balance.

Next steps: Looking ahead to the market, the WHO-prequalified products include GlaxoSmithKline's Cervarix and Merck's Gardasil and Gardasil 9.

There are also other suppliers in the wings. WHO prequalification is expected toward the end of 2021 or into 2022.

7. Discussion

Should an individual with genital warts be given the HPV vaccine?

Yes, an individual with genital warts should be given the HPV vaccine because the strains that cause genital warts are not oncogenic. Even if an individual already has either HPV6 or HPV11 (the strains that cause genital warts), vaccines **containing these serotypes will protect against some** other wart-forming strains and the majority of cancer-causing strains. Vaccination will not, however, have any effect on an individual's existing warts.

Can you expand on the cross-protections against other strains not included in the HPV vaccine?

Usually, if the strain is not in the vaccine preparation, there is less cross-coverage. That said, cross-protection has been demonstrated to some degree for all three currently licensed HPV vaccines. Cervarix, in particular, has particularly strong cross-protection against other strains. In fact, some effectiveness studies have indicated that protection against high-grade lesions **goes far beyond the projected rate** of approximately **70%**, instead landing much closer to 90%. **A study from Scotland, for example, indicated that Cervarix's total protection was closer to that which Gardasil 9 provides. Gardasil 4 provides some cross-protection as well, although generally to a lesser extent. As per the WHO position, the current vaccines available right now—even with bivalent strains—could offer protection of up to 85%.**

Is there any word on when the new dosing interval updates will come out in writing?

On the question of a **six**-month interval versus a longer interval, the WHO guidance has been six months at minimum for many years now, with no maximum. The 2017 guidance suggested a maximum of approximately 12-15 months be used. Last year, WHO did a special analysis on duration for SAGE, and the systematic review revealed that the 12-month immune response is better and higher than the six-month response. This means that there is now some flexibility, which is why in 2019, SAGE announced the ability to have intervals up to 2, 3, or 5 years, or longer. Quebec, a province in Canada, recently decided to move to an interval of 5 years between the two doses.

This SAGE recommendation is quite new, however, and PAHO has not had a TAG meeting since the update to discuss which intervals would be best for the Region. Although the literature has indicated the ability to use longer intervals, there are concerns about increasing intervals to 3 or **4 years when the Region already struggles to reach coverage targets with the existing six-month intervals.** Longer intervals require an extremely well organized program in terms of logistics and the ability to **locate girls** to complete their second dose.

At the close of Day 1, Silvana Luciani emphasized the importance of a multidisciplinary approach. John Fitzsimmons's update on the supply issues undoubtedly brings up questions and concerns around how cervical cancer can be eliminated without a sufficient supply of the HPV vaccine, which is critical for elimination. Therefore, it is crucial to reinforce the notion that this will take a comprehensive approach. And while the issue of HPV vaccine supply is solved, everyone should be thinking about HPV testing, screening, and treatment access, as well as how to increase quality and scale up those strategies.

DAY 2: SCREENING AND TREATMENT

While the first day focused on HPV vaccination in the Americas, the second day, 23 October, switched the focus to the screening and treatment of pre-cancerous lesions and invasive cancer. The day contained a review of the evidence, a talk about the increased risk of cervical cancer in women living with HIV, and a panel of presenters who shared their experiences in several Caribbean countries to improve access to HPV testing and screening, and access to cancer treatment.

Session 2: Screening and Treatment of Cervical Cancer

Moderator: Silvana Luciani, PAHO

1. HPV Testing for Cervical Cancer Screening and Program Monitoring

Speaker: Nathalie Broutet, WHO, Geneva, Switzerland

Nathalie Broutet provided an overview of the global HPV guidelines and shared WHO's work to support strategies to introduce HPV testing in national programs. Many countries have not reached the 2030 elimination strategy targets of 70% screening and 90% treatment of pre-cancer, so an updated guideline—which advocates for simpler screening and treatment algorithms—is being created on screening and treatment.

A systematic review found that HPV testing as a primary screening test yields the greatest reductions in cervical cancer incidence mortality, improves equity, and is more cost-effective and acceptable to women and providers. The updated guideline therefore recommends that countries start by introducing HPV testing or adapting existing cytology-based programs toward the HPV test. Implementation recommendations include health system interventions, patient-targeted strategies, provider-targeted strategies, and new self-sampling strategies. Ancillary guidelines also are being developed by WHO to support the introduction of these new recommendations.

The only three prequalified HPV tests are careHPV (Qiagen), GeneXpert (Cepheid), and Abbott RealTime High Risk HPV; two cobas tests (Roche) are also under evaluation.

An existing toolkit, titled *Improving Data for Decision-making: A Toolkit for Cervical Cancer Prevention and Control Programmes,* is a comprehensive but difficult-to-use guidance document that covers monitoring and surveillance. This tool is being reviewed in order to simplify and restructure the content, and to identify gaps. A surveillance framework is also being developed to address surveillance and monitoring, as well as a simple framework to monitor the strategy and Cervical Cancer Elimination Initiative (CCEI) targets.

Overview of strategic actions:

- Price-reduction strategies are required for a sufficient supply of screen-and-treat technologies and products.
- There must be a national scale-up of screen-and-treat approaches using the HPV test with a simple algorithm, followed by immediate treatment or with triage.
- The quality and coverage of service delivery must be increased.
- Progress must be monitored and evaluated by strengthening governance and accountability, setting country-specific targets, developing or improving cancer registries, tracking patients through the continuum of services, and disaggregating data by equity stratifiers.

2. Screening and Treatment in Women Living with HIV

Speaker: Bernardo Nuche, PAHO

Worldwide in 2019, there were approximately 38 million people living with HIV, 1.7 million new infections, and 0.69 million HIV-related deaths (including cervical cancer). In the Caribbean, new infections of HIV have decreased over the last 20 years, as have AIDS-related deaths. Unfortunately, there is a growing population of at least 160,000 women living with HIV (WLHIV) aged 15+ in the Caribbean, with approximately 71% receiving antiretroviral therapy (ART).

Women living with HIV (WLHIV) have a higher risk of HPV acquisition than the general population. There are many possible reasons for this but approaches to reducing HPV mortality must take cervical cancer into account, and approaches to cervical cancer must take the needs of HIV+ women into account. Synergistic interventions can help to control both infections and can be much less costly than non-integrated services. For example, ART reduces HPV risk, HPV vaccination prevents HIV infection, and the follow-up of cervical cancer screening and HIV control can be combined. Furthermore, many lessons from the HIV response can be adapted for cervical cancer intervention, including setting specific disease-response targets, combining intervention approaches, competing for prices in generic drug markets, engaging with civil society, and mobilizing the community.

Per the WHO Cervical Cancer Screening and Treatment Recommendations for WLHIV, any of the three screening tests (HPV test, VIA, or cytology) can be used, and women and girls who have initiated sexual activity should be screened as soon as they test HIV positive, regardless of age. HIV-positive women who screen negative should be retested within 3 years, and women who have been treated for pre-cancerous lesions should receive 12-month post-treatment follow-up. Baseline CD4 counts should be a key element of care for WLHIV and done as one of the initial evaluative tests.

Some regional next steps to improve and integrate HPV and HIV programs include supporting the rollout of the Global STI Strategy and the regional Plan of Action for Cervical Cancer Prevention and Control 2018–2030, updating the epidemiological situation for cervical cancer in WLHIV, and supporting countries to address data gaps. In all countries, the Ministry of Health must continue procuring cervical cancer-related supplies as part of the full package of services needed in HIV programs.

Session 2.1: Screening and Pre-cancer Treatment Experiences and Challenges

3. Trinidad and Tobago: Results of a Pilot Project on HPV Testing

Speaker: Moira Lindsay, PSI Caribbean, Trinidad and Tobago

PSI Caribbean's pilot project on HPV testing was the first project in Trinidad and Tobago fully dedicated to preventing cervical cancer. The pilot aimed to reduce cervical cancer morbidity and mortality and ensure that Trinidad and Tobago is on track to meet the WHO 2030 global elimination targets. The primary outcome was increased uptake of HPV vaccine and screening coverage. The overall project goal was to screen 1,500 women using the careHPV test, which provides a simple positive or negative result for HPV. The target population was women between 30 and 65 years of age, to be followed up with a Papanicolaou (Pap) smear and no self-sampling.

Methods: PSI Caribbean formed a global partnership with Qiagen, the manufacturers of careHPV, and a local partnership with a regional health authority. Implementation started at the beginning of 2019, when a team from Qiagen trained the laboratory staff. The samples were then collected between March and November 2019.

Results: PSI Caribbean did not meet the full target of 1,500, but was able to test 1,300 women.

There were 1,200 numbers analyzed for the pilot, of which 140 were HPV positive (i.e., a positivity rate of about 11.7%). Of those positive results, 115 were referred for Pap smears.

Accomplishments and challenges: The project introduced a high-performance screening test into the public system, increased screening coverage, and identified issues to address before scale-up. There were also some challenges. PSI Caribbean did not have the tax exemptions in place before the machine shipped. There were also persistent challenges regarding the collection of samples due to a high rotation of people involved in the pilot, and procurement delays that required a pause on sample collections. There were challenges delivering information, education, and communication (IEC) to patients, as well as issues with the data-collection process. Finally, COVID-19 led to delays in final Pap smear and colposcopy follow-ups.

Next steps: The Ministry of Health has indicated plans for a national scale-up of HPV testing, and to use the lessons learned from the pilot for future planning. Health systems strengthening will need to be emphasized before scale-up. The Ministry of Health also secured several polymerase chain reaction (PCR) machines for COVID-19 that can be used for HPV testing.

4. The Bahamas: Challenges to Incorporating HPV Testing into the Screening Program

Speaker: Philip Swann, Ministry of Health, Bahamas

Cervical cancer is the second leading cause of death in the Region of the Americas. In the Bahamas, the incidence rate of cervical cancer has decreased, there is an improved cervical cancer prevention program, and vaccination is indicated for girls and boys aged 9-12 years. Philip Swann presented some common HPV testing challenges and opportunities, and how these have applied as the Bahamas works to create a strategy to eradicate cervical cancer in partnership with PAHO/WHO and Rotary International.

Currently, most of the Bahamas' HPV testing is outsourced to other countries. The public sector has at least two platforms that can perform HPV testing, so part of the eradication plan is to assess both platforms, to choose which one better meets the country's needs. The national screening need is for approximately 130,000 women, so cost is an important consideration.

HPV testing is the gold standard in the Bahamas, but this test is only available in the private sector. A promising opportunity is the National Health Insurance (NHI) program primary benefits package for the NHI Initiative, a liquid Pap test that includes HPV testing. To handle wider introduction of HPV testing, there will need to be a revision of testing recommendations and an investment in staff and equipment. Successful HPV testing also requires good information technology, and thus the additional benefit of the NHI approach is an electronic health record, along with incentives to providers to meet certain targets. The ability for laboratory information system integration is also key.

Plans were made to add screening and prevention messaging to cervical cancer educational campaigns, but this has taken a back seat due to COVID-19. The COVID-19 era has, however, had the benefit of increasing channels of communication for digital platforms, thereby significantly driving down campaign costs. There is a low rate of Pap smears being done in the public sector, owing to numerous factors, but there is strong evidence to support the usefulness of self-screening methods to increase access to HPV screening and remove some of the screening barriers.

Session 2.2: Opportunities to Improve Cancer Treatment

5. How Cancer Care Was Improved in Jamaica

Speaker: Nadine Dietrich-Badal, Jamaica

Nadine Dietrich-Badal's presentation provided an overview of an integrated, comprehensive approach to cancer care. Starting from the genetic structure of the virus, she gave a short lesson on HPV and oncogenesis, including the important role of the E6 and E7 oncoproteins, and then touched on primary prevention through HPV vaccination. She spoke about screening with high-performance tests such as the HPV DNA test, and emphasized the importance of cervical tissue biopsy and pathological review with histopathological confirmation to diagnose disease. She discussed the use of radiotherapy and high dose rate (HDR) brachytherapy to treat advanced cervical cancer disease; and informed participants that oncospecific treatments at lower doses can be used with palliative intent.

After this comprehensive look into the stages of oncology, Nadine spoke about cancer care regionally. In Jamaica, cervical cancer is the second most frequent cancer among women between the ages of 15 and 44 years. Every year, approximately 486 women are diagnosed with the disease and about 361 die. The country faces many cancer-treatment barriers. There is a high demand and wide unmet need for advanced oncology and surgical services such as HDR brachytherapy. Long waiting times for radiotherapy services hamper effective treatment implementation. As well, there is a lack of dedication to research due to the burden of patient/doctor volume and absence of a computerized database.

In spite of these challenges, Jamaica has seen phenomenal improvements in cancer care, even in just the past several years. Most notable is the recent development of screening guidelines for cervical cancer, as well as the initiation of a National Cancer Registry and the inclusion of HPV vaccination in the national vaccination schedule (despite uptake challenges). Palliative care has significantly improved the scope of Jamaica's services and accessibility, and the Hope Institute, an oncology and palliative care unit in Jamaica, was chosen as a PAHO regional site for a WHO palliative care project.

Moving forward, the PAHO-supported cervical cancer elimination plan will be developed in 2021. This will be a comprehensive cancer control plan that covers prevention, screening, diagnosis, treatment, and palliative care. It will require an increase in funding, educational campaigns on the importance of HPV vaccines, improved organized screening programs, increased palliative care services, participation improvement, the ability to record cancer incidence and mortality, computerized database collection, and contribution to research.

6. How Antigua and Barbuda's Cancer Center Is Creating Shared Services in the Caribbean

Speaker: Henry Hazel, TCCEC, Antigua and Barbuda

Henry Hazel spoke about his work at The Cancer Centre Eastern Caribbean, which increases access to cancer screening and cancer care services in Eastern Caribbean countries. The institution is headquartered in Antigua but operates in the rest of the countries in the Organisation of Eastern Caribbean States (OECS) as well. Henry provided some background on TCCEC's development and the Partnered Care Model, which was based off of an arrangement with three sectors—private, government, and user—to ensure equity and access to care.

The OECS countries formed a collective agreement called The Caribbean Cancer Center Network (TCCCN) to offer convenient cancer care for OECS residents. At the center is the Cancer Centre Eastern Caribbean in Antigua, which houses the radiation facility; any cancer patient who needs radiation services flies to Antigua to for care. Antigua is also outfitted to deliver

chemotherapy, and although no single OECS country would have been able to afford the initial investment of US$ 15 million for chemotherapy delivery, it became economically feasible with the combined population of TCCCN, and Antigua officially became the Caribbean's provider of both radiotherapy and chemotherapy. Outside of Antigua, there are independent island clinics in the various countries, and OECS created a way to facilitate the movement of patients in need of critical care from their particular countries into Antigua and then back home again.

Prices at TCCEC are competitive, with various pricing categories to ensure equity and access. The Five-Domain Model was eventually created to guide TCCEC's evolution, and the Partnered Care Model has evolved to now include the industrial and philanthropic sectors in addition to the three already included. TCCEC ensures quality care, measures outcomes, and improves the cancer control system. Its vision for the future is to become a comprehensive and academic center as well as a cancer treatment center.

7. Discussion

Can the tests be purchased through the Revolving Fund?

PAHO's Strategic Fund for Public Health Supplies is actually the one used for medicines and technologies, and therefore yes, the tests can be purchased through the Strategic Fund. PAHO's Revolving Fund for Access to Vaccines is for vaccines, including HPV vaccines.

Should the HPV vaccine be given to HPV-negative women?

Yes. Negative or positive, every girl should receive the HPV vaccine.

Should all clients who have had the HPV vaccine get the HPV test as well?

Yes. The vaccines cover the most common carcinogenic serotypes, but they do not cover all types. Even if a woman already knows she has had an HPV infection, she should still get the vaccine because she may have one strain of HPV, but after vaccination will be protected against other types.

HPV vaccination is recommended for girls <15 years old, with the goal of achieving 90% vaccine coverage, especially in the 9-14-year age range. With screening, the recommended age range for HPV testing is women between 35 and 45 years of age. This is the target population in which testing must be prioritized to reach 70% coverage. Hence, all women aged 35-45 years should receive HPV testing.

At what age should the HPV test be done?

For the general population of women, the age to start screening with HPV tests is 30. For women with HIV, we may recommend 25, although the literature is still being reviewed.

Does the HPV test replace cytology?

The HPV test may replace cytology-based screening in the future, so the short answer is yes, PAHO is recommending HPV testing as the primary test. This will be even more important when the girls now being vaccinated reach screening age.

Is the HPV vaccine protective against all oncogenic strains?

All of the vaccines protect against the most important oncogenic strains: HPV16 and HPV18. There have also been many studies that show cross-protection with the bivalent and quadrivalent vaccines. As well, the bivalent vaccine, which only contains strains 16 and 18, still protects against 70% of most oncogenic cancers. Therefore, WHO considers all three currently licensed vaccines to be efficacious against cervical cancer.

DAY 3: COVERAGE AND IMPLEMENTATION

On the third day, 29 October, the focus moved from screening and treatment of pre-cancerous lesions to the topic of coverage, and the issues of HPV vaccine implementation in the Caribbean.

Session 3: HPV Vaccination
Moderator: Martha Velandia

1. Challenges of the HPV Vaccination Program
Speaker: Lillia Middleton, Ministry of Health, Belize

Lillia Middleton shared a comprehensive look at the HPV vaccination program in Belize, which was launched in November 2016 using the quadrivalent vaccine for girls aged 9-15 (and boys in 2018) in standard 4 classes. The strategy was to introduce the HPV vaccine in the National Schedule, and delivery was school-, health facility-, or campaign-based.

The program had a robust communication plan that included meeting with leaders and experts to train, sensitize, and prepare them; coordinating with community leaders and the media to disseminate information; and giving lectures and private trainings to health care professionals, parents, teachers, and students. It created a crisis plan and delivered accurate information to counter anti-vaccination groups, providing evidence-based data before, throughout, and following the program's launch. It also developed a vaccination consent form for parents to sign.

A key component of the program's successful introduction was to start preparing schools for the program in a sequential manner—starting with school principals, then teachers, then parents, and finally students—before administering the vaccines. Areas that adopted this approach had better or full uptake of the vaccine, while areas that took shortcuts had lower uptake.

Challenges to reaching 80% coverage included myths, misinformation, and the influence of anti-vaccination groups; principals and teachers not accepting the program; poor coordination with some schools; poor parental attendance at meetings; consent forms not being signed; difficult work load for maternal and child health staff; and school closures due to COVID-19. Strengths of the HPV vaccination program included integration into existing school health programs; annual training of principles; full funding by the Government of Belize; strong data recording and sharing of vaccine administration with public health nurses; and full support from community leaders, Ministry of Education, civil society organizations, and nongovernmental organizations.

2. Challenges of the HPV Vaccination Program
Speaker: Nurse Florestine Lewis and Mignon Rolle Shillingford, Coordinator, Health Promotion, Ministry of Health, Dominica

Dominica launched its HPV vaccination program in 2019, introducing the quadrivalent vaccine to a targeted population of 849 students in grade 6 in all the country's primary schools. The delivery strategy was primarily school-based but also used health centers under certain circumstances. Annual coverage was 83%, and the first dose had 94% coverage, indicating wide access to the vaccine. The second dose dropped to 81% coverage during the COVID-19 pandemic.

The program had some challenges reaching 90% coverage for girls aged 15 years:

Opposition to the vaccine from some parents
Solutions:

- Early and continued buy-in from health care workers, the media, teachers, and other stakeholders

- Numerous education sessions with all stakeholders
- Trainings for principals/teachers and media workshops. Resistant teachers were given targeted education sessions
- Parent-teacher association meetings held with all schools
- Training sessions for all district- and national-level staff, whether involved in vaccine administration or not

Several cases of absenteeism of children at school
Solutions:

- Absent students were asked to visit the nearest health center with their parents. Most were subsequently immunized

COVID-19 pandemic delayed second dose administration due to lockdowns and school closures
Solutions:

- Committed Expanded Program on Immunization (EPI) staff communicated with school principals, who arranged specific dates for all grade 6 students to come to school for second-dose immunization

Issues with consent forms
Solutions:

- Parents who had not returned forms for their children were called; verbal consent was given
- Since the education act mandated vaccination for every child at school, some teachers stood in as proxies for students whose parents did not return consent forms
- Some parents took their children to health centers to be immunized
- No reports of adverse reactions from any of the schools, boosting parents' confidence in the vaccine

Other strengths of the HPV vaccination program included political commitment to the program; prior planning for challenges and roadblocks; technical and funding support for all aspects of implementation thanks to PAHO, CPO, and the Dominica Ministry of Health; and the highly effective strategy of combining cervical cancer prevention and education activities with vaccine introduction.

3. Discussion

Lúcia Helena de Oliveira started off the discussion by thanking the countries for their presentations, and reminding them that hearing about their problems and how those problems are solved helps PAHO and others to learn how they can help. She then moved into a question-and-answer period about the use of consent forms in HPV vaccination programs:

> ***Using vaccination consent forms can make it difficult to get children vaccinated, and consent forms are not typically used for other vaccines. Why are you using consent forms for HPV?*** *(Lúcia Helena de Oliveira)*

> In Belize, we decided to use the consent form because HPV was a new vaccine at the time. However, we have since realized the barriers these forms pose to vaccinating girls, and are currently rethinking whether the consent form is truly necessary, since we do not ask for consent with other vaccines.
> ***Lillia Middleton (Belize)***

> In Dominica, we have always had a practice of handing out consent forms in schools for diphtheria-tetanus (DT) and polio vaccines, especially for schools in cities where affluent parents often complained if they were not given the opportunity. Since we have always used these forms, we simply continued the practice, so as not to upset anyone. One of the strengths of our program, however, was that the education act mandated that everyone at school be vaccinated, so some of the principals and teachers stood in as proxies for children even if the parent had not sent in the consent form.
> ***Nurse Florestine (Dominica)***

> In Grenada, the consent form is also one of the strategies we have adopted. It is not used for the other vaccines because they are administered at the clinic. Because parents

are not at the schools, parental consent is a must, however.
Guest: EPI Manager (Grenada)

Are there any plans in Belize to adapt your strategy due to COVID-19? *(Paul Bloem)*

To continue giving the vaccine throughout the COVID-19 pandemic, Belize has started a drive-through: the child comes in with their parents, gets the vaccine, and then leaves right afterward. We have also connected with principals: since most of the children are doing online classes, principals send texts to the parents so the students in the standard 4 class can still get the vaccine. A third strategy is calling parents so that they can bring their child to the health center for the vaccine.
Lillia Middleton (Belize)

Joining various vaccines in the same class is convenient and a great opportunity to limit costs. In your countries, are the DT and polio boosters and HPV vaccines all given on the same day? Is there a combination of the first dose of the HPV vaccine plus DT and the second dose of the HPV vaccine plus others? *(Paul Bloem)*

In Belize, we go to the schools to give the vaccines twice a year. The first dose begins in November, and the second in May. In addition to the HPV vaccines, we also provide vitamin A, deworming, tetanus, vaccinations, and other services. This helps us give more vaccines in one session.
Lillia Middleton (Belize)

In Dominica, we go to the schools twice a year. The first visit is to give the children vaccinations and a complete physical examination, including vision and hearing assessments. Because we were introducing the HPV vaccine for the first time, we did not give the DT or polio vaccines in combination with the first dose of the HPV vaccine. Moreover, if there were any adverse events, we would not have been sure which vaccine was the real culprit. So we wait until the second dose of the HPV vaccine to combine it with the DT polio. For this new academic school year, however, we are already giving out vaccinations, and are giving both doses. And for the first time, we are combining the HPV vaccine with the first dose of DT and polio.
Nurse Florestine Lewis (Dominica)

In both your countries, people could go to the health facility and get the vaccine if they missed it at school. But if there are girls next year who were not reached in the previous year and have already moved to a higher grade, can they still get the vaccine, or do you use a different strategy for them? *(Paul Bloem)*

In Belize, when we go to the classrooms, children who have missed the second dose for HPV and are in a higher grade can still get the vaccine. They can come from whatever class they are in to the class where we are giving the vaccine.
Lillia Middleton (Belize)

In Dominica, we are in the process of going into the high schools and finding the children who have received the first but not the second dose, so that we can complete this second round of the vaccine.
Nurse Florestine Lewis (Dominica)

Is there a legal issue if the consent forms are not used? *(Guest)*

WHO did a review on this issue several years ago and published a guidance document on consent. No, it is not illegal. What legislation often asks for is an informed consent procedure, which, at minimum, consists of informing parents of the vaccine. This can be done through the information given to the public announcing that the vaccine has now been introduced, or via other means, such as through teachers. Information is a key part of consent. Providing consent also depends on the country's norms and experiences. Many countries use more informal ways of acquiring consent. Many assume that when parents present their child for vaccination, that action is consent. Things are slightly different for adolescents, as their parents are not present. The assumption is that if information has been publicized and the child is present, then consent has been given.
Paul Bloem (WHO)

In general, countries in Latin America (not including the Caribbean) do not use vaccine consent forms. This is not only the case with HPV: there are huge vaccination campaigns against rubella, measles, and other diseases, none of which ever use consent forms. The HPV vaccine has had more issues with myths, anti-vaccination groups, and misinformation among religious groups than almost any other vaccine. Therefore, even before using consent forms, HPV vaccination already faced many challenges. A consent form only introduces another complication for vaccination.
Lúcia Helena de Oliveira (PAHO)

> ***What are PAHO/WHO recommendations regarding "opt-out" versus "opt-in" measures? The required parental permission seems to be less common in other regions, even in Latin America, and especially when the vaccine is included in the national vaccination schedule.*** *(Moira Lindsay)*

Evidence shows that procedures that use an opt-out process will attain the highest coverage. This has nothing to do with whether opting out is better from a legal or ethical perspective, but a great deal of behavioral research indicates that when individuals are given an option, they will normally go with the option being proposed. Thus, if the option being proposed is "Your child will be vaccinated unless you take an extra step," then most people will accept the vaccination, resulting in higher acceptance. Conversely, when done the other way around (i.e., "If you sign this form, only then will your child be vaccinated"), this invites parents to potentially not sign or hand the form in, resulting in lower coverage. As such, everyone is always recommended to review their forms, and, at a minimum, make them opt-out ways of providing consent rather than opt-in measures.
Paul Bloem (WHO)

4. Global Analysis of HPV Vaccination Coverage

Speaker: Paul Bloem, WHO, Geneva, Switzerland

Paul Bloem reviewed vaccine coverage indicators within the global health context, looking at relevant global strategies. Compared with other childhood vaccines—for which it is fairly easy to express coverage—HPV vaccine coverage is different because there are multiple variations between countries and over time within countries. Variations include things such as schedule, age and timing of vaccination, eligible cohorts, and so on. These variations complicate the work of measuring HPV vaccine coverage, and also make it hard to create a universal indicator or even to define the denominator. There are also concerns that coverage estimates may reflect program performance from up to five years earlier.

There is a need to refine the methodology in order to have a realistic coverage rate. Paul used an example from Botswana to demonstrate how to calculate indicators in the WHO/UNICEF Joint Reporting Form (JRF), as well as how program coverage changes over time, and which data points are important and helpful for creating indicators. He explained that the best strategy to obtaining high coverage is to vaccinate in schools, and explained what is done at a global level with the data that countries send.

Key messages on vaccine coverage included the following:

- Countries should collect data by age and dose.
- Consistency and quality of JRF reporting is extremely important.
- HPV coverage data are continuously updated and improved based on feedback from countries, so it is crucial to continue reporting and giving feedback.
- Countries should use coverage data and analysis to improve their program performance. Data should be used to figure out which strategies, structures, or ways of delivering are doing well, especially at a subnational level. Countries should also be conducting equity analyses looking at poverty, race, ethnicity and other factors, to know which subpopulations need stronger communications.

5. Guidelines for the Calculation of HPV Vaccination Coverage

Speaker: Martha Velandia, PAHO

This presentation reviewed the main points of the document prepared by PAHO, *Methodology to Calculate HPV Vaccine Coverage in the Region of the Americas*. The goal of this document is to establish a standard methodology to follow up on vaccine recipients and calculate HPV vaccine coverage in the Americas, allowing for the measurement of vaccination progress of the target population by country, defined strategies to reach equitable coverage, and the ability to make comparisons between countries and regions. The document is available in Spanish, English, and Portuguese, and uses the third Sustainable Development Goal as a reference framework: Indicator 3.b.1: "Proportion of the target population covered by all vaccines included in their national program."

In addition to presenting some regional data, Martha Velandia closely reviewed problems and challenges in estimating vaccine coverage, such as the incorrect use of numerators and denominators, incorrect reporting of the target population, failure to report the doses administered, lack of data, and inconsistent monitoring strategies. The key variables used to measure coverage are:

- Month and year vaccination began
- Target population
- Age (in years) at vaccination
- Sex of the vaccinated individual
- Changes in schedule/dose/age
- Strategy (school and/or health facility)
- Dose administered
- Vaccination dates

An interactive activity demonstrated to meeting participants how to calculate indicators such as access, annual coverage, annual dropout, and HPV coverage for girls at 15 years old. Martha also demonstrated in detail how to work with the JRF. She encouraged countries to use the vaccination coverage calculation methodology to monitor their coverage, and emphasized the importance of quality and completeness of data. "Quality and completeness" means being consistent in data reporting, collecting data on age and gender, and identifying the entire target population, not just those enrolled for the first dose.

6. Discussion

Lúcia Helena de Oliveira kicked off the discussion session by posing a question that led to a conversation on information systems: Have any participants from the Caribbean had challenges measuring HPV coverage in their countries?

A pediatrician from Antigua and Barbuda shared her experience with her country's first introduction of the vaccine, and the challenges she encountered measuring coverage. Due to having a surplus of doses set to expire shortly, the program had to expand its target population and create three different gender-neutral age categories: younger (primary target), middle, and older. Vaccine acceptance was highest in the oldest population, and uptake was low among the youngest primary target group. Successful communication and advocacy strategies helped Antigua and Barbuda use up a majority of its dose surplus. Unfortunately, assessing uptake was difficult, as they could not calculate how many people would have been a certain age during specific time periods. It was easier to calculate how many younger children were in a particular cohort and then decide on the target.

Key discussion points

- Countries must be careful when registering the doses. Antigua and Barbuda had to increase its target population just to make sure that all the vaccines were used, underscoring the importance of the registry. Countries in the planning process of introducing the vaccine must think carefully about the information systems they use.

- Countries put a lot of effort into setting a primary target—which is an acceptable strategy on its own—but they then find complementary strategies to expand vaccination to other cohorts, and sometimes those extra efforts are not translated in the programmatic coverages. It is crucial that countries report on the number of administered doses stratified by age, and record it in their Joint Reporting Forms, regardless if the individual(s) was vaccinated as a primary objective or via catch-up. Data on sex and strategy are also essential. This is how vaccination efforts can be translated into the estimates.
- Recording these data is not just important on a regional and global level, but also at the local level. Local programs must review their own data and make decisions based on those data. Any problems or changes should be reported. This helps to create a better understanding of a country's landscape.
- With so many Caribbean countries having low coverage, it could be valuable to strategize on how to increase uptake. There are many common barriers with countries' strategies, especially regarding parental consent.

A conversation on the Revolving for Access to Vaccines followed:

Have any countries experienced pushback from medical health care providers—especially obstetric gynecologists—due to Gardasil 9 being available but not being procured through the Revolving Fund? Are there any plans to assist in procuring the nonavalent instead of the quadrivalent vaccine in the near future?

Key discussion points

- Public health programs should justify why they choose a certain program and certain product instead of others.
- Gardasil 9 is a very similar product to Gardasil. WHO considers both vaccines highly effective at preventing cervical cancer, and their characteristics are extremely similar despite the number of strains being different, partially because of the cross-protection.
- The manufacturer is not offering the nonavalent vaccine to the Revolving Fund. The production of the nonavalent vaccine is lower than the quadrivalent vaccine, so manufacturers offer it to countries that pay much more for their doses. They are not willing to let go of the comfortable price margin they can make on these products.
- In the future, many more products will come onto the market. Several new bivalent and quadrivalent vaccines will be introduced in the next two to three years, along with a new series of nonavalent vaccine. This will make these vaccines easier to purchase.
- It is more important to obtain the two vaccines available through the Revolving Fund and to be fully covered than to be concerned about the differences between the vaccines.
- In the next year, the rotavirus and pneumococcal vaccines will also be available through the Revolving Fund at a much more affordable price than is currently available. This will be an opportunity for the Caribbean countries to rethink their vaccine introductions, especially rotavirus, as most of the countries in the Caribbean have not yet introduced the rotavirus vaccine.

DAY 4:
HPV VACCINATION IMPACT

Session 4: Impact of the HPV Vaccine
Moderator: Maria Tereza da Costa

1. HPV ESAVI and the Impact of Sociogenic Events on HPV Vaccination
Speaker: María Tereza da Costa, PAHO

María Tereza Da Costa gave a presentation about ESAVI that have been attributed to the HPV vaccine. Among local vaccine-related events, injection site reactions consist of pain (up to 80% of cases), swelling and erythema (25% for both), and severe pain that is spontaneous or prevents normal activities. The most frequent systemic reactions related to the vaccine are headaches (33%) and fever (10%). Dizziness, myalgia, arthralgia, and gastrointestinal symptoms are other possible vaccine-related reactions. The risk of anaphylaxis is comparable to other vaccines (approximately 1.7 cases per one million doses), and no other adverse events have been identified.

Syncope is considered a common anxiety- or stress-related reaction to an injection (it is not exclusive to injection with the HPV vaccine). Risk factors for syncope include fasting, low fluid intake, hot environments, and prolonged standing.

There are many myths about the HPV vaccine, including that it stimulates early sexual activity, causes infertility, or leads to serious health problems such as - autoimmune conditions. There is extensive scientific evidence disproving these myths, but rumors questioning the vaccine's safety nonetheless have a negative impact on coverage, leading to its withdrawal from some national immunization programs. Health professionals play an essential role in avoiding the spread of rumors and myths, and educating on the HPV vaccine's safety.

Finally, María Tereza spoke about collective sociogenic events from HPV vaccination, or clusters of adverse events following immunization. She gave an example from Brazil, and encouraged countries to be prepared to respond to any event that may damage trust in vaccines and cause a negative media response. To manage these crises, countries must have action plans in place for crisis response. Giving patients medical care is essential. The four immediate steps to take when responding to an event that may erode trust are: (1) Gather your inner circle; (2) understand the problem; (3) liaise with key stakeholders; and (4) communicate externally. The right response, taken promptly, can limit or even prevent the consequences of a crisis.

2. The Impact of Vaccination against HPV in Argentina
Speaker: Alejandra Picconi, National Institute of Infectious Diseases, Argentina

Alejandra Picconi described the first study to monitor HPV vaccination in Latin America and the Caribbean. She began her presentation with an overview of the HPV vaccination situation in Argentina, and then discussed the local HPV surveillance and the first data that came out on the evaluation of the impact of HPV vaccination in the country. In 2011, Argentina launched a comprehensive government-funded national HPV and cervical cancer prevention approach. In 2012, a meeting in Argentina for the development of a regional framework for the evaluation of the HPV vaccine set out its objectives: (1) to assess the impact of vaccination against HPV in the short term; and (2) to estimate vaccine efficacy for vaccine genotypes and potential cross-protection against related HPV types.

Two consecutive cross-sectional studies were performed in sexually active adolescent girls in the country, with identical procedures in both. One looked at vaccinated girls and the other at

unvaccinated girls, and information was gathered on HPV type-specific distribution for each group. Both studies were then compared to get an estimation of the HPV vaccine's effectiveness.

The studies found that, over the first seven years post-HPV vaccine introduction in Argentina, the prevalence of vaccine-type HPV 16 and 18 decreased by >93% in vaccinated sexually active girls, which demonstrated high effectiveness. There were also significant reductions in HPV 31 and 45. For HPV 16, 18, 31, and 45 combined, the vaccine effectiveness was 89.3%. This significant drop in non-vaccine genotypes related to HPV 16 and 18 would indicate cross-protection, which could increase the success of vaccination.

The study was presented in an oral session at the International Papillomavirus Conference in 2020, and has been accepted for publication in Papillomavirus Research. The available data so far from the study came from high-income countries where there may be different epidemiology of HPV, sexual behavior, and disease co-factors; thus, information cannot be directly and accurately extrapolated to LMIC. This information is valuable for the creation of the best public policy decisions for sustaining and optimizing immunization. Continued surveillance for HPV infection in quadrivalent-vaccinated cohorts will be critical to deepen knowledge and support actions.

3. PAHO Proposal to Evaluate the Impact of HPV Vaccines in Latin America and the Caribbean

Speakers: Lúcia Helena de Oliveira, PAHO, and Laia Bruni, Institut Català d'Oncologia

Lúcia Helena de Oliveira and Laia Bruni presented the PAHO proposal to evaluate the impact of HPV vaccines in Latin America and the Caribbean. The proposal originated from a regional meeting held in Guatemala in October 2017 that focused on lessons learned from the introduction of the HPV vaccine and later led to a PAHO collaboration with a team of multidisciplinary experts, with the goal of developing a guidance document to assess and measure the impact of HPV vaccination in Latin America and the Caribbean. The document's objectives were to present an overview of the possible designs for assessing the impact of HPV vaccination, prioritize the outcomes by relevance for immunization programs, and propose study designs for each outcome and note considerations.

The speakers covered several topics:

- The special aspects, study design considerations, and outcome measures for assessing HPV vaccination impact;
- Indicators for measuring impact on cervical cancer, high-grade pre-cancerous lesions, HPV infection, and genital warts;
- Prioritization of indicators; and
- An algorithm for selecting outcomes for impact assessment.

Key conclusions included the following:

- There are challenges inherent in impact assessments of the HPV vaccine.
- There is a need for collaboration networks and coordination with other teams and programs.
- There is a need for methodological, statistical, and technical advice on designing studies.
- Existing resources can be leveraged for impact assessments.
- When resources are limited, efforts must be focused on increasing HPV vaccination coverage, screening, and treatment.

4. Discussion

General discussion on measuring impact

- Measuring impact requires good data, and knowing exactly what is being compared using standard methods. This is not something every country will be able to do, and that is not the idea. It would be great if some PAHO member countries set up this kind of study in the future, but there are many challenges inherent in vaccine impact assessments, including

data quality, vaccination coverage, and laboratory issues. The costs associated with these studies are high, especially if the outcome requires the use of a laboratory.

- It is up to each country to decide which strategy to choose. Realistically, however, countries sometimes have to support the vaccination decision of the political majority. Hence, it is important that each country plan some kind of study to obtain more data for sustaining and improving vaccination, appropriate to the country context.

- Providing impact data is very important for encouraging Ministries of Health to invest in efforts to keep coverage high—and for program sustainability. Countries need local data to support their own HPV programs.

Several Caribbean countries have small populations, and cancer in general is a rare event (even as cervical cancer is relatively frequent, it is still rare), meaning there will be a relatively small number of cases. Does this have an implication for measuring impact? Is it more difficult to show impact, and does this mean that certain impact indicators may be better suited for such small territories than others? *(Paul Bloem)*

With small numbers of cases, an impact on measurement is quite possible. The concern with small countries is about sample sizes and the precision of the estimate. For example, for measuring outcome in places with few cervical cancer cases, countries can keep track of the very few cases they will have in the future. This will make it easier to pick specific cancer cases and look for the HPV types causing the cancer than to set a more complicated surveillance system on genital warts or another HPV infection service. It depends on available resources and the infrastructure of the country. Some countries may consider working together to share resources, such as a network of countries sharing cancer care resources.

Can somebody have full doses of the HPV vaccine but still be affected by cervical cancer?

Yes, but there are several factors to consider: first, the age of vaccination and whether a girl received the vaccine before becoming sexually active or after. The older one receives the vaccine, or if they received it after becoming sexually active, the more the impact of the vaccine drops. The younger a girl receives the vaccine (before age 15) the more protection she gets. The second factor is that none of the current vaccines, despite offering cross-protection, give 100% protection against cervical cancer. There will always be a small fraction of cancers that will not be prevented by HPV vaccination. The aim is to reduce this number enough that it become a very rare event, but it is not possible at this stage to expect to see no cervical cancer cases at all.

5. Conclusion and Next Steps: Building National Elimination Plans

Speakers: Silvana Luciani, PAHO; Lúcia Helena de Oliveira, PAHO; Cuauhtémoc Ruiz Matus; PAHO; and Paul Bloem, WHO

Four experts from PAHO and WHO wrapped up the final day by thanking everyone who participated in the meeting and leaving participants with some closing words.

Collaborative approach

- It is essential to work together. Meeting the 90-70-90 targets is a large task requiring combined efforts.
- A comprehensive approach to eliminating cervical cancer includes ensuring that the screening and treatment parts of the program are closely linked to the HPV vaccination part of the program.
- There is a great deal of support available to Caribbean countries from a large community that wants to collaborate, provide technical assistance and funding support, and help countries raise their coverage rates.

- These meetings provide an opportunity to share experiences on how to execute new strategies to maintain commitment levels. Continuing to meet and collaborate will set countries up for success in the future.

Coverage

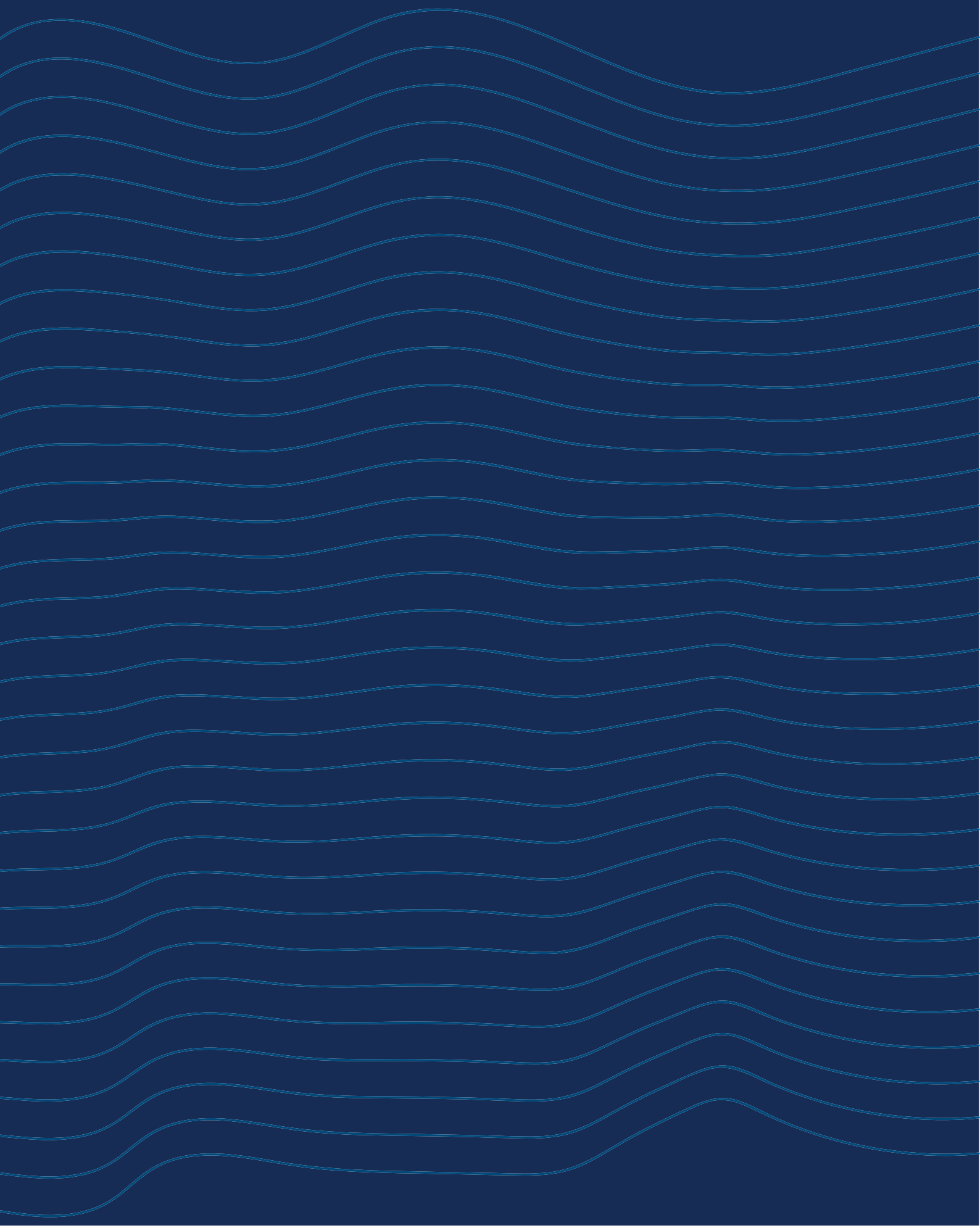
- The condition to reaching elimination is high vaccine coverage. Having a strong but expensive vaccine can only be justified if that vaccine is reaching the girls who must be reached.
- Maintaining high coverage will continue to be a ubiquitous challenge for countries everywhere, and must be worked on very seriously.
- This highlights the need for coverage improvement plans, or communication plans for restarting the whole program. It will need to be a collective effort.

COVID-19 considerations

- The moment to administer the vaccine is now. The vaccine's impact is not immediate, so there is only a small window, and waiting 10+ years means countries lose the chance to have a strong impact. This concern is more important now than ever, given the unique challenges the pandemic poses.
- COVID-19 created more obstacles for already existing HPV vaccination problems. The majority of countries in the Americas use school-based vaccination strategies, but in 2020 the schools were closed. This caused coverage to fall short in many countries, and therefore countries must consider how to recover these numbers in 2021.
- This is an opportunity to maintain confidence in the vaccination program. The HPV vaccine is always surrounded by myths and misinformation, and the myths surrounding the coming COVID-19 vaccine may exacerbate these challenges. But sharing correct information and evidence about HPV vaccination for lay audiences is a necessary effort.

Global strategy to accelerate elimination

- The Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem will be launched globally by WHO on 17 November 2020.
- This global launch is a great political opportunity in the Americas. It will raise awareness of cervical cancer, including the best prevention methods, and highlight the essential role that HPV vaccination plays in the long term toward elimination.
- It will also include expressions of commitment to the Region from governments and partner organizations around the 90-70-90 elimination goals.
- As a frontrunner, the Region of the Americas has a lot to teach the rest of the world.



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