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

PAHO

HPV Vaccination
Towards the Elimination of Cervical Cancer in the Caribbean Countries
22,23,29, and 30 October 2020

The meeting aims to discuss strategies and share experiences towards the elimination of cervical cancer in the Region of the Americas, by improving coverage for HPV vaccination, introducing HPV testing, and increasing screening coverage, and treatment rates.

Meeting agenda

October 22- Day 1 - Session 1: Updates in the Strategies for the Regional and Global Elimination of Cervical Cancer Moderator: Cuauhtemoc Ruiz-Matus		
10:00–10:15	Opening and Welcoming Remarks	Andrés de Francisco - PAHO Anselm Hennis - PAHO
10:15–10:25	Global Update on HPV Vaccination and Coverage	Paul Bloem - WHO
10:25 –10:35	Advances in the Introduction of HPV Vaccines in the Americas	Lúcia Helena de Oliveira - PAHO
10:35–10:50	Immune Response to HPV Vaccines	Malda Kocache - George Mason University USA
10:50–11:20	Discussion	
11:20–11:30	Regional Plan for Cervical Cancer Prevention and Control and Summary of the WHO Regional Consultation on Cervical Cancer Elimination	Silvana Luciani - PAHO
11:30 – 11:40	PAHO's Revolving Fund Update on HPV Vaccines	John Fitzsimmons - PAHO
11:40 – 12:00	Discussion	

525 23rd St. NW
Washington, DC 20037
www.paho.org

October 23 - Day 2 Session 2: Screening and Treatment of Cervical Cancer Moderator: Silvana Luciani		
10:00–10:20	HPV Testing for Cervical Cancer Screening and program monitoring	Nathalie Broutet - WHO
10:20 –10:35	Screening and Treatment in Women Living with HIV	Bernardo Nuche - PAHO
10:35–11:05	Screening and precancer treatment experience and challenges: Trinidad & Tobago: results of pilot project on HPV testing Bahamas: challenges to incorporating HPV testing into the screening program	Moira Lindsay, PSI Caribbean Dr. Phillip Swan, Bahamas
11:05–11:35	Opportunities to improve cancer treatment: - how cancer care was improved in Jamaica - how Antigua and Barbuda's cancer center is creating shared services in the Caribbean	Dr. Nadine Badal, Jamaica Mr. Henry Hazel - Cancer Centre Eastern Caribbean Antigua &Barbuda
11:35- 12:00	Discussion	

October 29- Day 3 Session 3: HPV vaccination Moderator: Martha Velandia		
10:00 – 10:15	Challenges of the HPV vaccination program	Belize
10:15 – 10:30	Challenges of the HPV vaccination program	Dominica
10:30 – 11:00	Discussion	
11:00 – 11:20	Global Analysis of HPV Vaccination Coverage	Paul Bloem - WHO
11:20-12:40	Guidelines for the Calculation of HPV Vaccination Coverage	Martha Velandia - PAHO Laia Bruni - Institut Català d'Oncologia
12:40- 1:00	Discussion	

October 30- Day 4 Session 4: Impact of the HPV vaccine Moderator: Maria Tereza da Costa		
10:00 – 10:20	HPV ESAVI and impact of Sociogenic Events on HPV Vaccination	Maria Tereza da Costa - PAHO
10:20 - 10:40	Impact of Vaccination against Human Papillomavirus in Argentina	Alejandra Picconi - National Institute of Infectious Diseases- ANLIS "Dr. Malbrán"-Argentina
10:40 – 11:00	PAHO Proposal to Evaluate the Impact of HPV Vaccines in Latin America and the Caribbean	Laia Bruni - Institut Català d'Oncologia-Spain
11:00– 12:00	Discussion	
	Conclusion and next steps: building national elimination plans	Silvana Luciani - PAHO Lúcia Helena de Oliveira - PAHO Cuauhtémoc Ruiz Matus - PAHO Paul Bloem – WHO

DAY 1

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Global Update on HPV Vaccines and Coverage

Paul Bloem
HPV vaccine strategy lead
WHO IVB EPI, Geneva

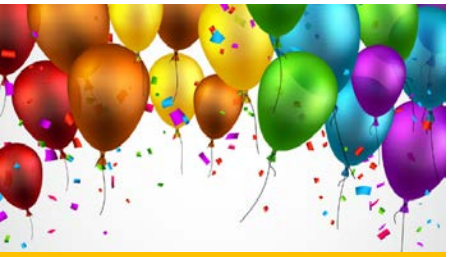
Caribbean Meeting on Cervical Cancer elimination, Oct 2020

World Health Organization

Global Strategy towards the Elimination of Cervical Cancer

VISION: A world without cervical cancer

THRESHOLD: All countries to reach < 4 cases 100,000 women years



Launch
17 November 2020
During WHA

2030 CONTROL TARGETS

90%
of girls fully vaccinated with HPV vaccine by 15 years of age

70%
of women screened with an high precision test at 35 and 45 years of age

90%
of women identified with cervical disease receive treatment and care

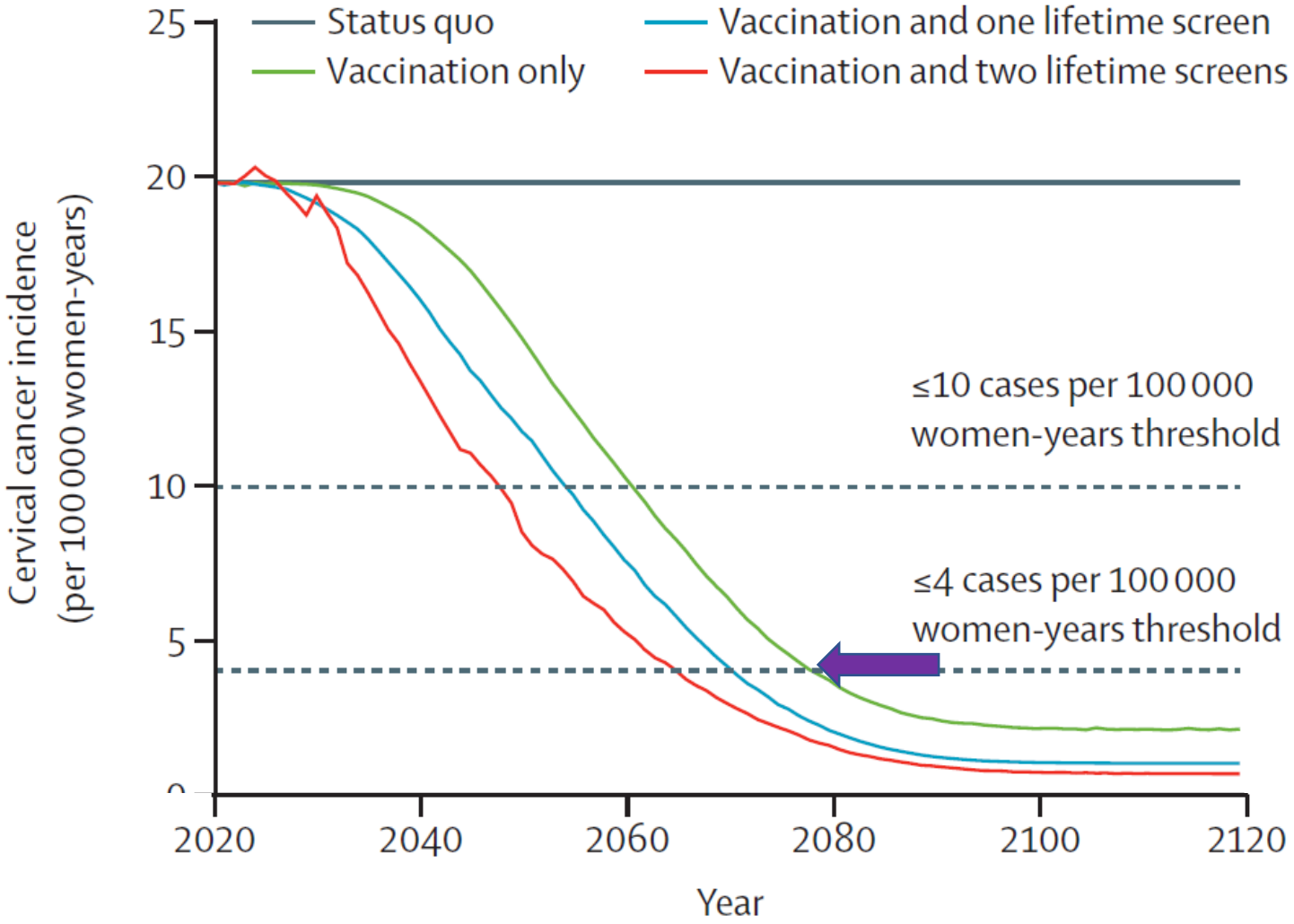
SDG 2030: Target 3.4 – 30% reduction in mortality from cervical cancer

World Health Organization

HPV vaccination of girls key for elimination

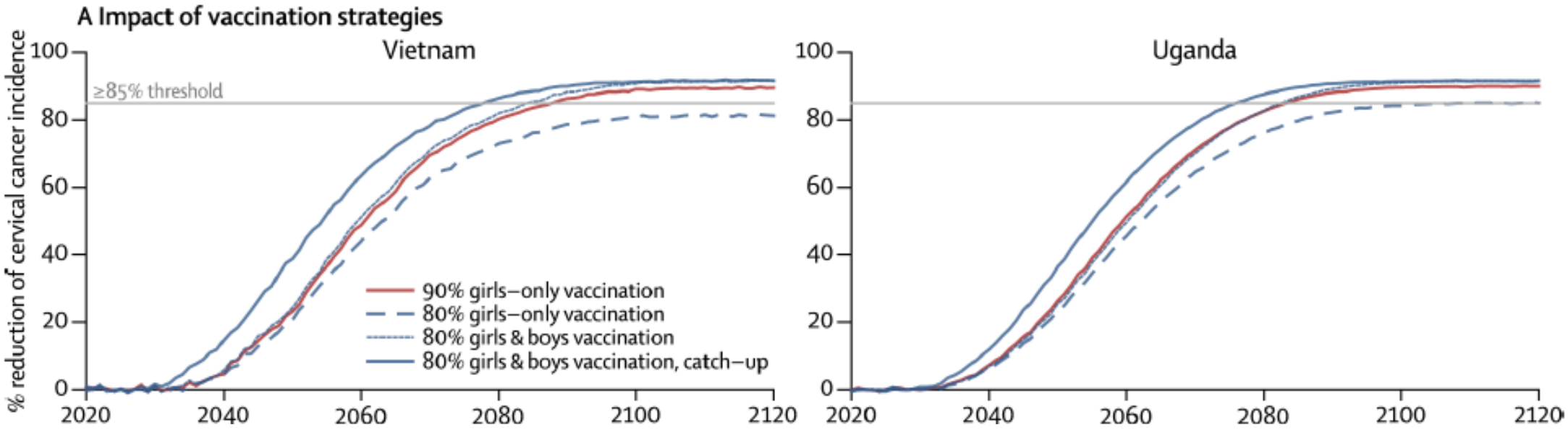
In LMICs

- ü High coverage HPV vaccination can achieve elimination within this century
- ü >45m deaths can be averted over the next century by vaccination of girls
- ü Adding 2 lifetime screens would prevent a further 14m death and help to achieve elimination a decade earlier



Source: Brisson, Canfell et al, Lancet 2020

Sensitivity analysis: 1) strategies (girls/boys)
2) characteristics of the vaccine



Source: Brisson, Canfell et al, Lancet 2020

>350M doses Globally by 2020

"Excellent Safety profile"

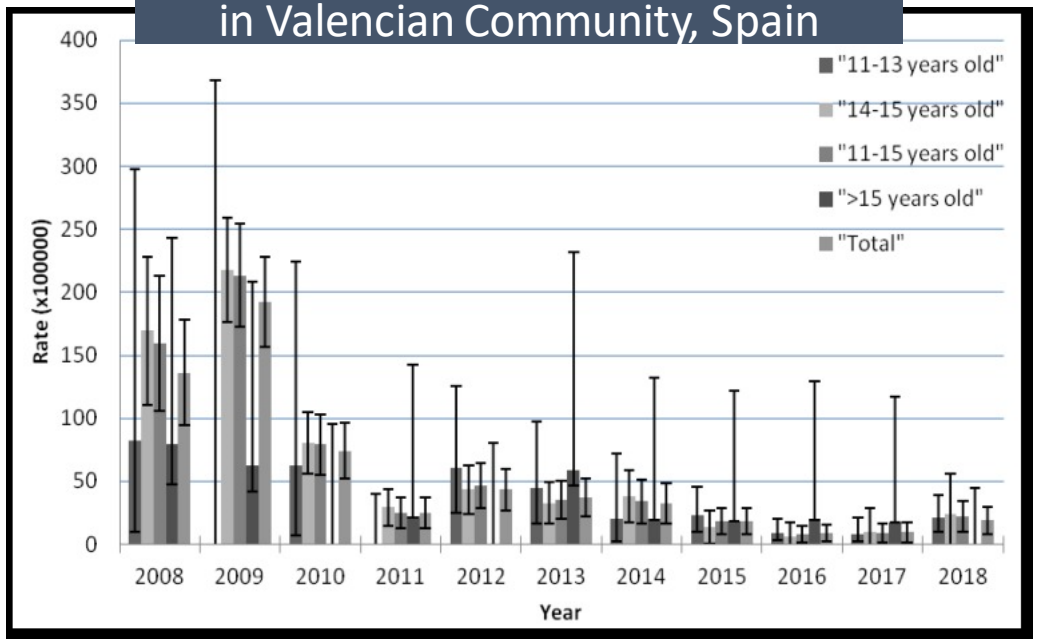
WHO Global Advisory Committee on Vaccine Safety (GACVS)

Statement on the continued safety of HPV vaccination (2017)

"Since licensure of HPV vaccines, GACVS has found no new adverse events of concern based on many very large, high quality studies. The new data presented at this meeting have strengthened this position."

- ü Latest GACVS review (Dec 2019) * confirmed HPV not linked with infertility
- ü AEFI for HPV vaccines not more frequent than for other vaccines - actually, lower reported numbers of AEFI in the longer term *(Egoavil, 2020)*

Reported AEFIs for HPV vaccine in Valencian Community, Spain



* https://www.who.int/vaccine_safety/committee/topics/hpv/en/

WHO Position on HPV vaccines (2017)

For the prevention of cervical cancer the use of HPV vaccines is recommended as per following schedule:

- Primary target: 9-14 years old girls, 2-dose schedule,

  Interval min 6m, no max - suggest 12-15m.

- HIV+ and females ≥15 years (3-dose schedule)

All three licensed HPV vaccines have excellent safety, efficacy, immunogenicity and effectiveness profiles, and are comparable for the prevention of cervical cancer.


2017, 92, 241–260

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

12 MAY 2017, 92th YEAR / 12 MAI 2017, 92e ANNÉE
No 19, 2017, 92, 241–260
http://www.who.int/wer

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Human papillomavirus vaccines: WHO position paper, May 2017

Introduction

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers on vaccines and vaccine combinations against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale immunization programmes. They summarize essential background information on the respective diseases and vaccines, and conclude with the current WHO position concerning their use in the global context.

The papers are reviewed by external experts and WHO staff, and reviewed and endorsed by the WHO Strategic Advisory Group of Experts (SAGE) on immunization (http://www.who.int/immunization/sage/en/). The GRADE methodology is used to systematically assess the quality of available evidence. The SAGE decision-

Vaccins contre les papillomavirus humains: note de synthèse de l'OMS, mai 2017

Introduction

Conformément à son mandat, qui prévoit qu'elle conseille les États Membres en matière de politique sanitaire, l'OMS publie une série de notes de synthèse régulièrement mises à jour sur les vaccins et les associations vaccinales contre les maladies ayant une incidence sur la santé publique internationale. Ces notes, qui portent essentiellement sur l'utilisation des vaccins dans les programmes de vaccination à grande échelle, résument les informations essentielles sur les maladies et les vaccins associés et présentent en conclusion la position actuelle de l'OMS concernant l'utilisation de ces vaccins dans le contexte mondial.

Ces notes sont examinées par des experts externes et des membres du personnel de l'OMS, puis évaluées et approuvées par le Groupe stratégique consultatif d'experts sur la vaccination (SAGE) de l'OMS (http://www.who.int/immunization/sage/fr). La méthodologie GRADE est utilisée pour évaluer de manière systématique la qualité des données dispo-

SAGE recommendations on HPV (Oct 2019)

ü Countries should temporarily postpone implementation of boys, older age group (≥15 years) and multi-age cohort HPV vaccination strategies until all countries have access to HPV vaccine. This will significantly relieve supply constraints in the short term and enable allocation of doses to high-burden countries currently planning to introduce this vaccine.

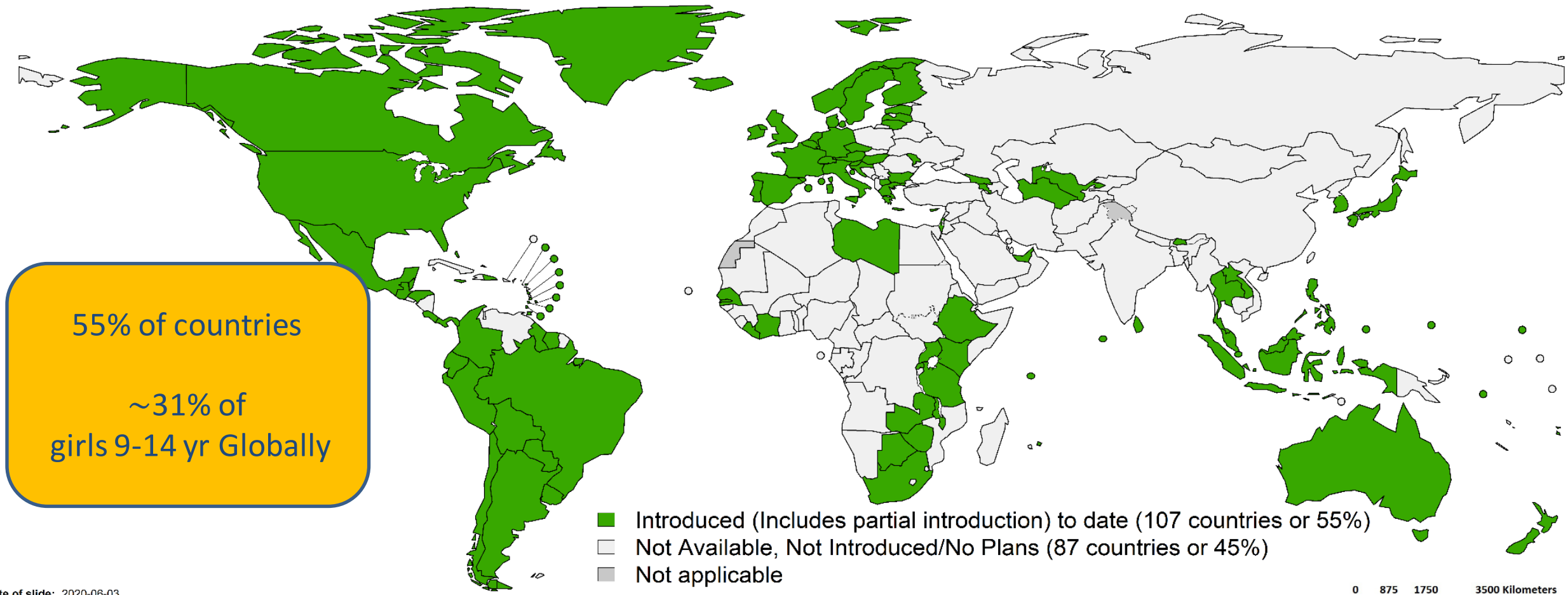
Alternative strategies:

Ç In order to retain the disease impact of MACs, target an older cohort of girls (e.g. those who are 13 or 14 years old or in a higher school grade)

Ç In order to reduce vaccine supply needs, adopt a "1+1" schedule with an extended interval of 3-5 years between doses for younger girls (e.g. 9 or 10 years old or lower school grade)

Source: https://www.who.int/wer/2019/wer9447/en/

Countries with HPV vaccine in the National Immunization Programme



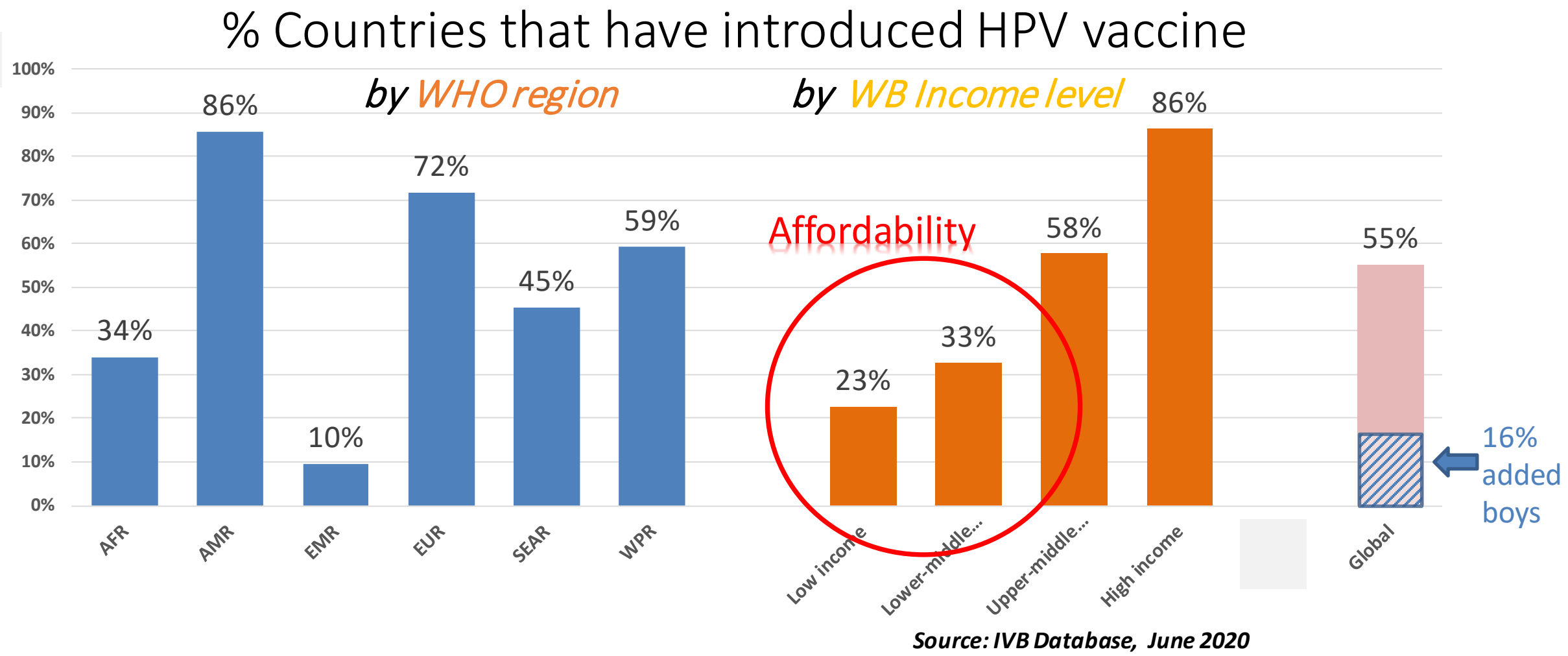
Date of slide: 2020-06-03
Map production: Immunization, Vaccines and Biologicals (IVB), World Health Organization(WHO)
Data source: IVB database as at 2nd June 2020

Disclaimer:

The boundaries and names shown and the designations used on this map do notimply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area nor of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

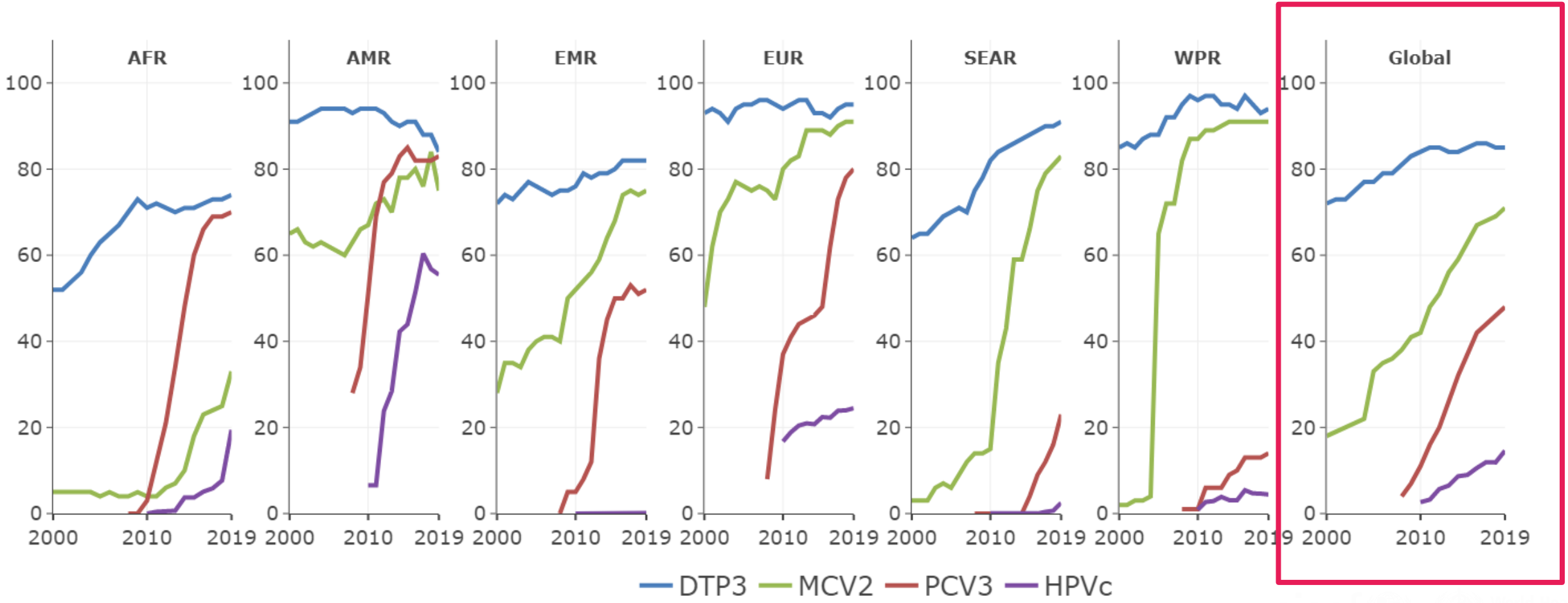
World Health Organization

Girls in low and middle income countries lack access



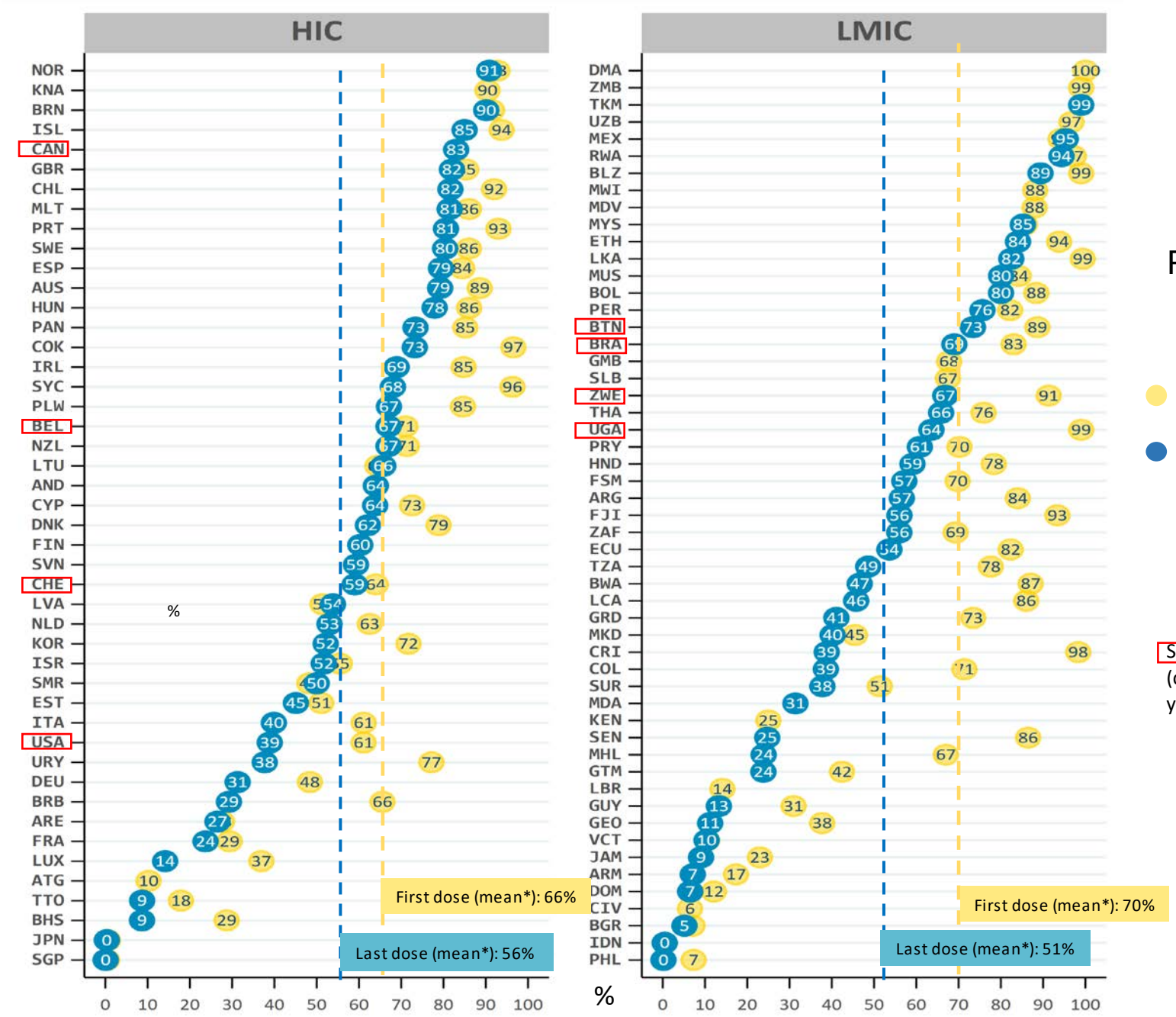
Source: IVB Database, June 2020

Vacunation and life course: Regional progress in HPV



SDG Indicador 3.b.1

2019 WHO/UNICEF HPV Vaccine coverage estimates by income level



HPV Programme indicator

- First dose
- Final dose

Survey data available (current or previous years)

* Full introduction countries only

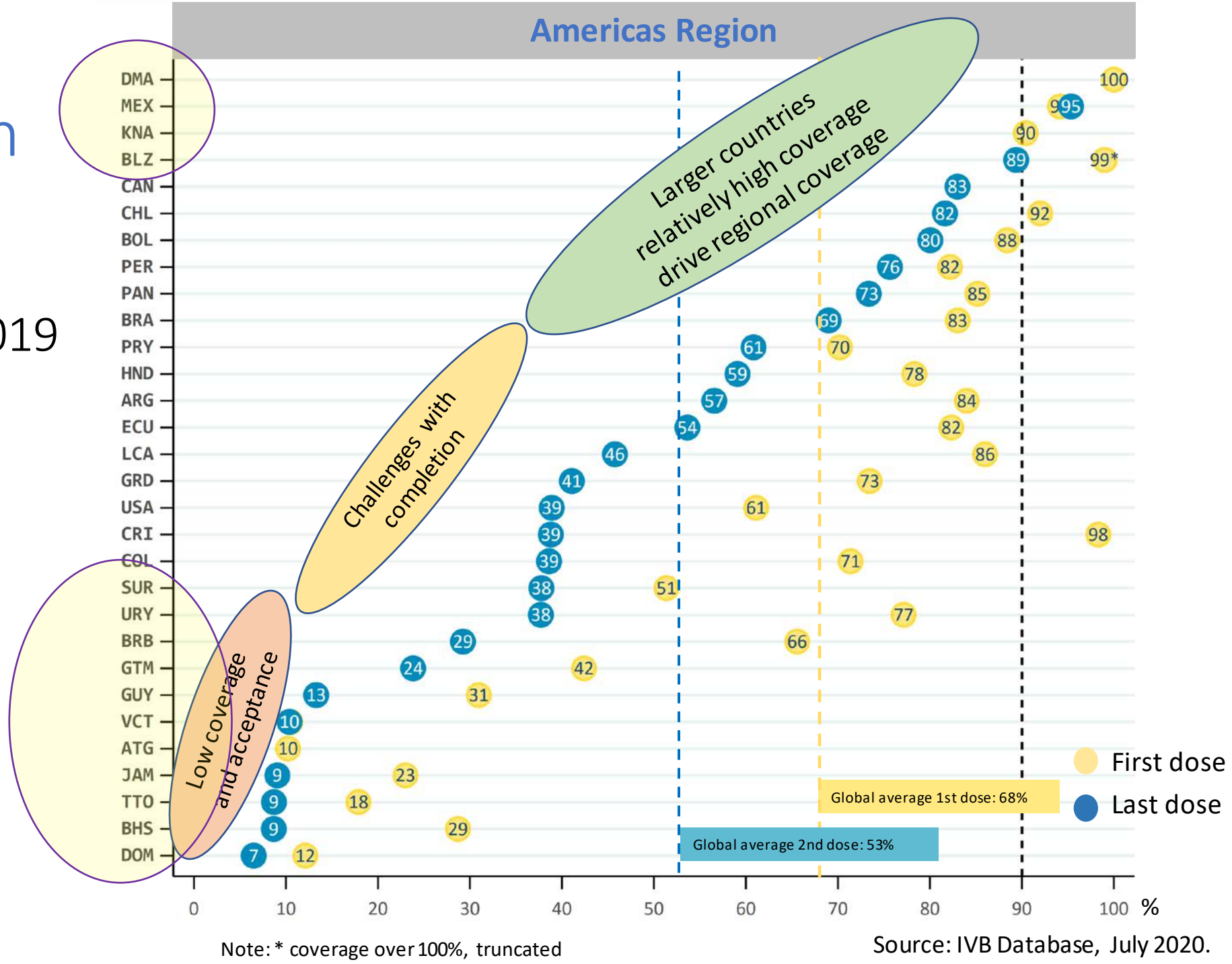
Some countries in HIC as well as LMIC reach the 90% coverage target but too many girls living in countries that provide HPV vaccination are not reached or not fully protected

Strategy?
Demand?
Confidence?
Hesitancy?

unicef World Health Organization

Americas Region

HPV vaccine
coverage estimates 2019
Program indicator

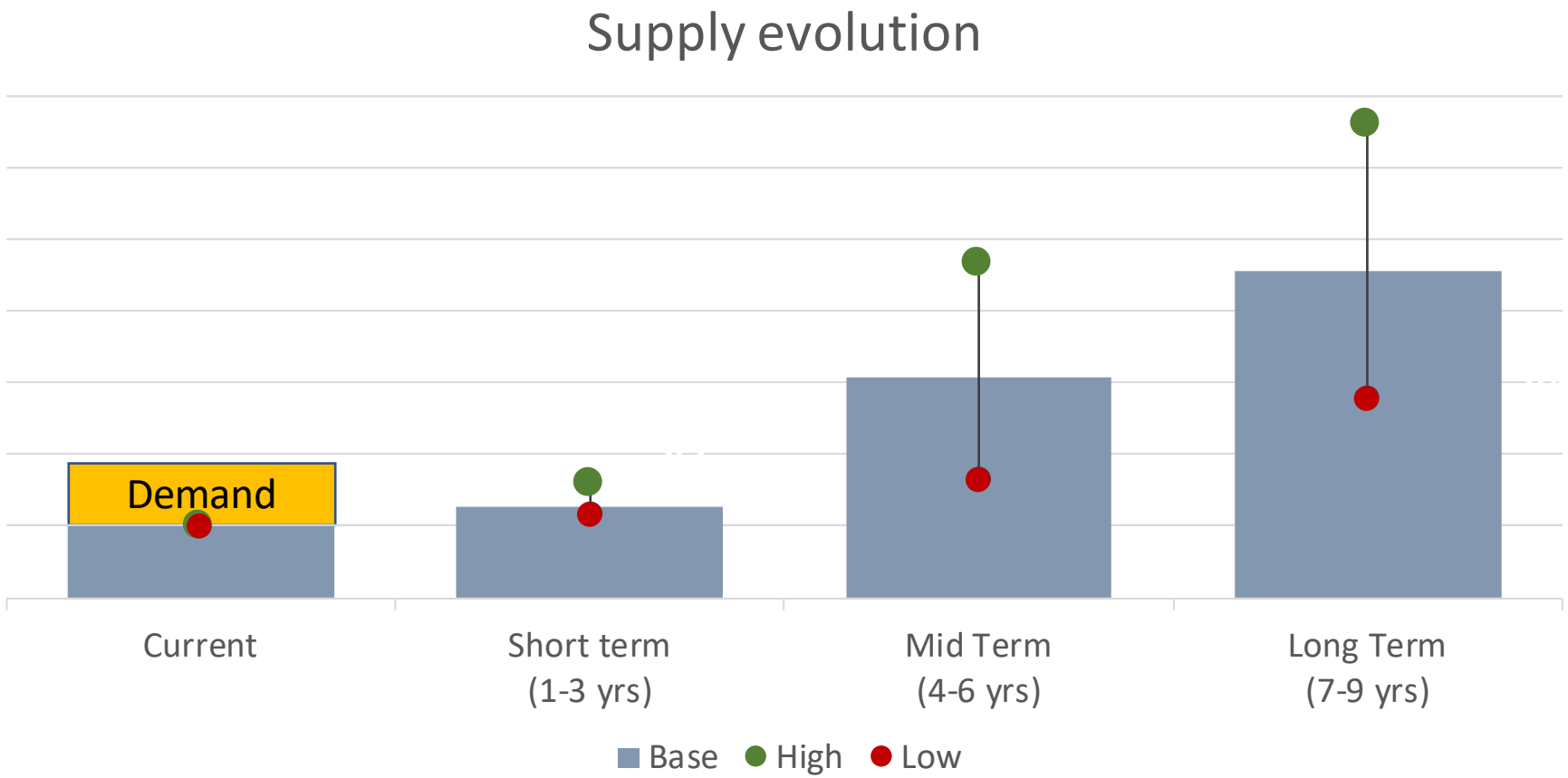


Note: * coverage over 100%, truncated

Source: IVB Database, July 2020.

Demand currently higher than supply

Supply to slowly grow in short term - steep ramp up from year 5



- Available supply may vary by +/-50% driven by manufacturers decisions and success in development/scale-up

- No major impact of the COVID-19 pandemic is forecasted

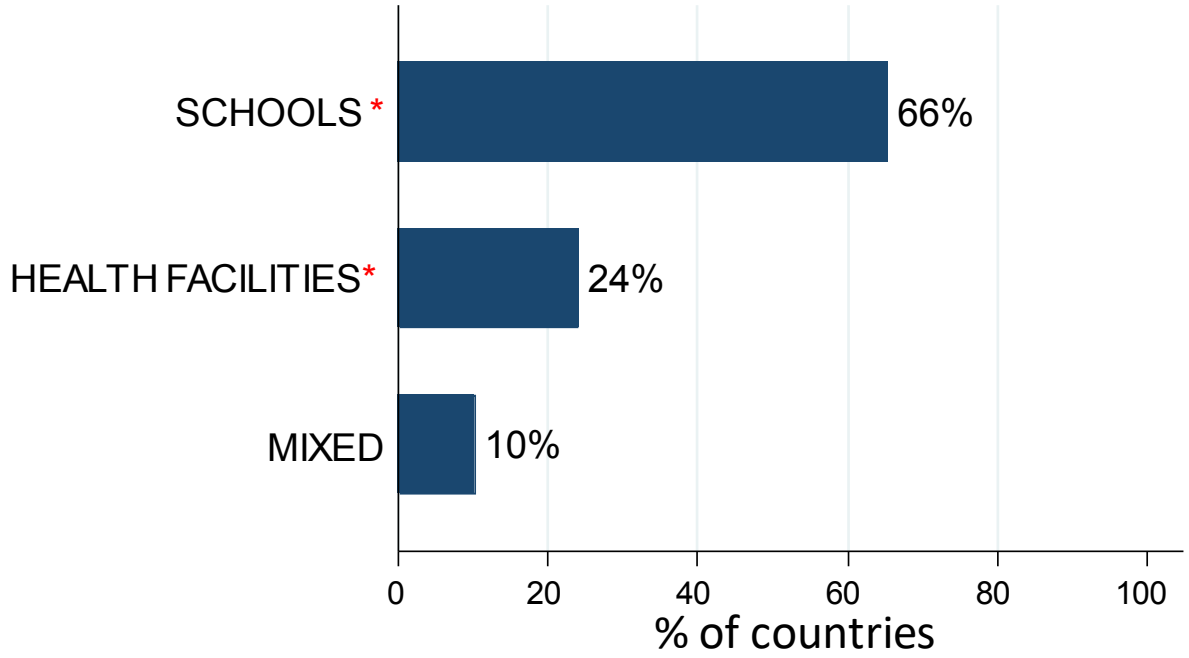
New market entrants

- Cecolin licensed in China and under PQ (early 2020) reviews
- Several other products could reach market by 2025

Source: MI4A market study, December 2019

HPV VACCINE DELIVERY STRATEGIES, COVERAGE & SUSTAINABILITY

PRIMARY DELIVERY STRATEGIES (2018)



* Note: These strategies are not always "exclusive"

Sustainability:

- Many countries are reviewing and revising their delivery strategy, in order to have high performing & sustainable strategies : Annual vaccination, changes in Age (range), from HF to School

Source: IVB Database, 1 June 2019. Preliminary data

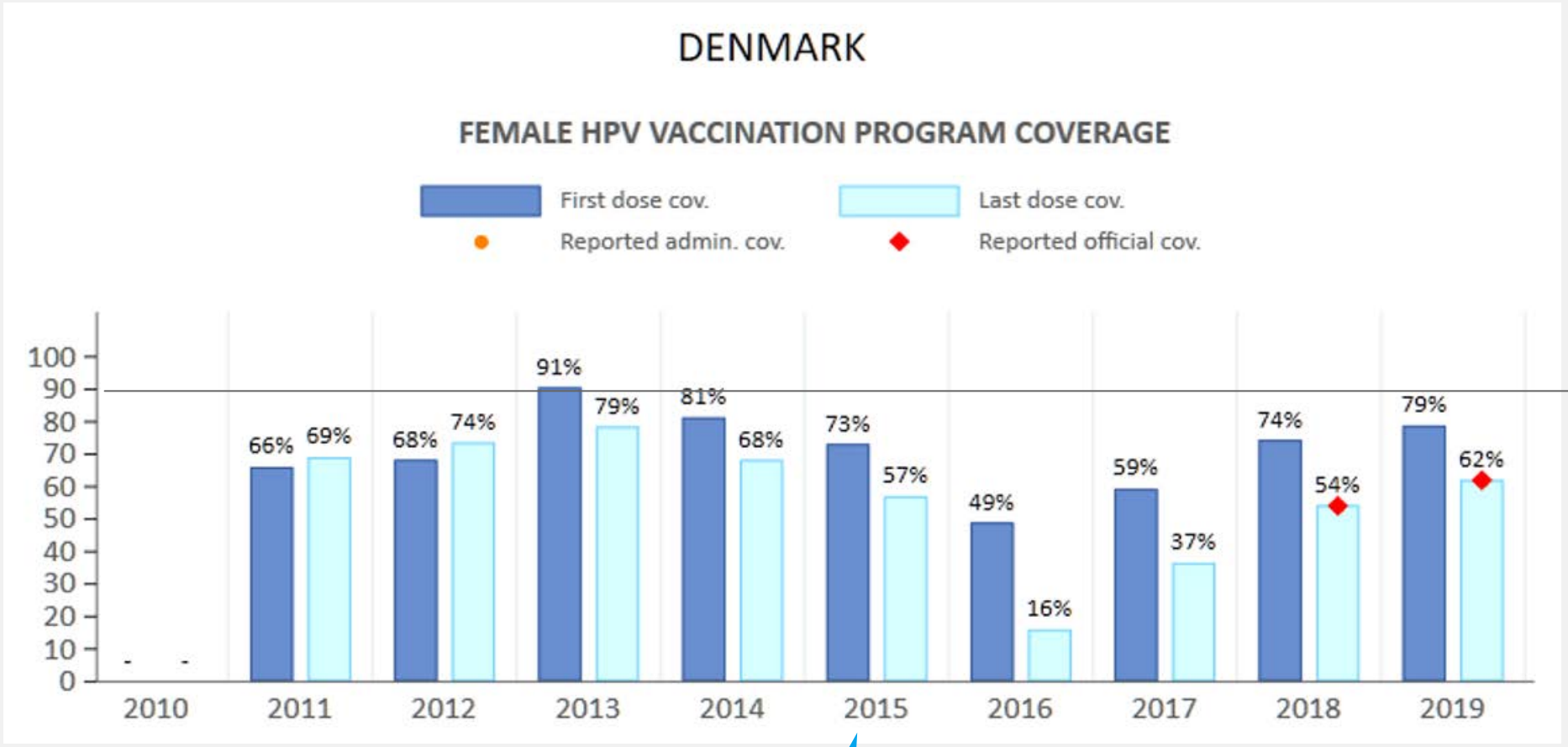
World Health Organization

Quality of demand generation/mobilization insufficient

- Low knowledge levels in parents & girls on Cx and HPV [1]
- Knowledge gaps and lack of trust in vaccine among vaccinators and other medical professionals [2]
- Lack of research into stakeholders and their perceptions to inform communication plans
- Suboptimal planning and implementation of communications plans, insufficient focus on key stakeholders[2], lack of continued communication efforts
- Coordination and engagement among all stakeholders insufficient to address rumors and safety events [3]

1. Perlman S. et al. Knowledge and Awareness of HPV Vaccine and Acceptability to Vaccinate in Sub-Saharan Africa: A Systematic Review. PLoS One. 2014; 9(3): e90912
2. Results from HPV PIEs in Georgia, Moldova and Armenia, 2018
3. GACVS, 5-6 June 2019 Report, WER 28 , 12 July 2019

(re-)Building vaccine confidence to prevent hesitancy

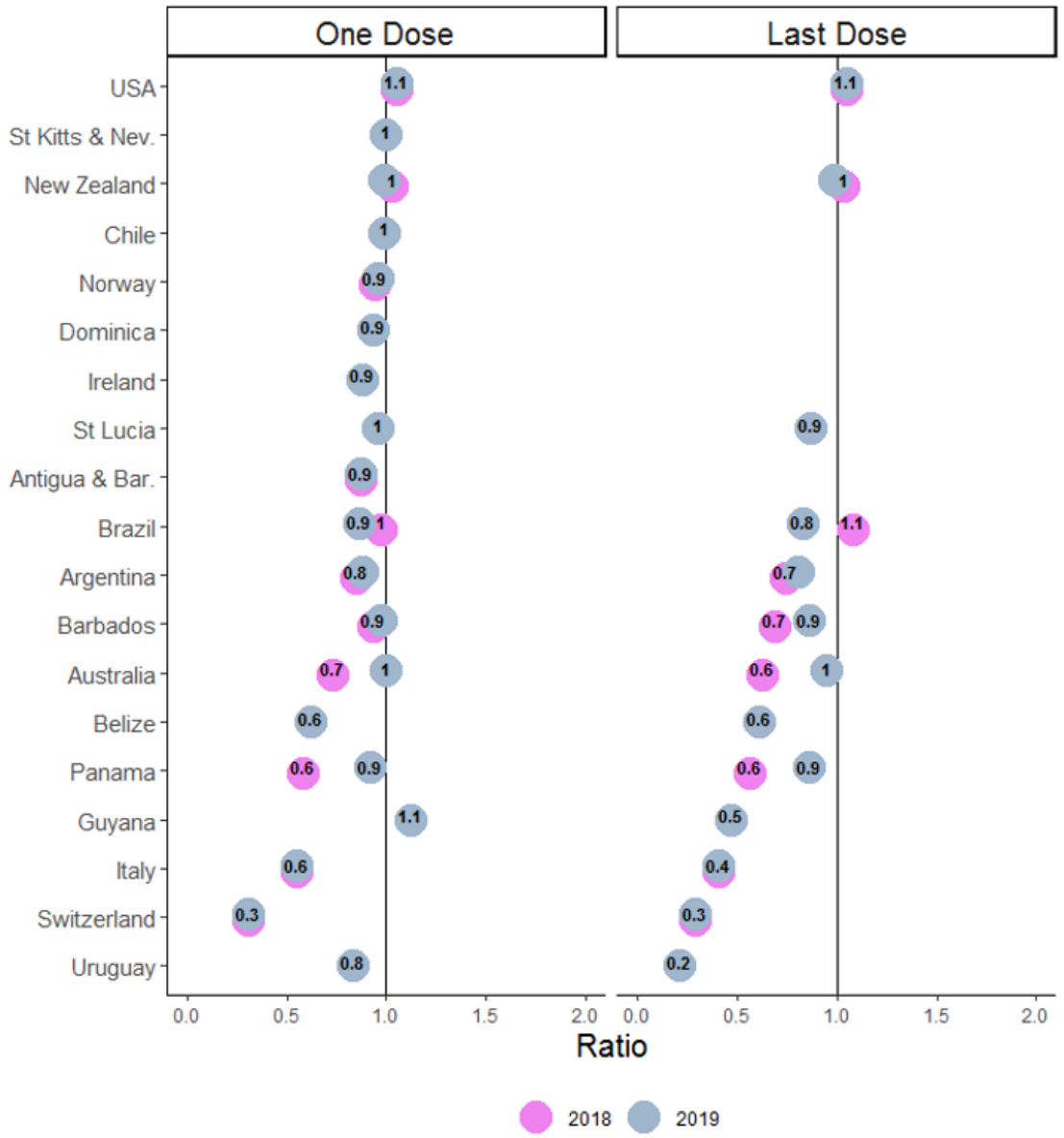


- Research
- Communication plan
- Involve all stakeholders
- Engage community & parents
- Build confidence among health workers
- Monitor….

AEFI

Source: IVB Database, 15 July 2020

Intra-country ratio of male to female HPV vaccine coverage



Source: Bruni et al., Publication under review

Male vaccination is normally well accepted and coverage quickly catches up with female coverage levels in most countries

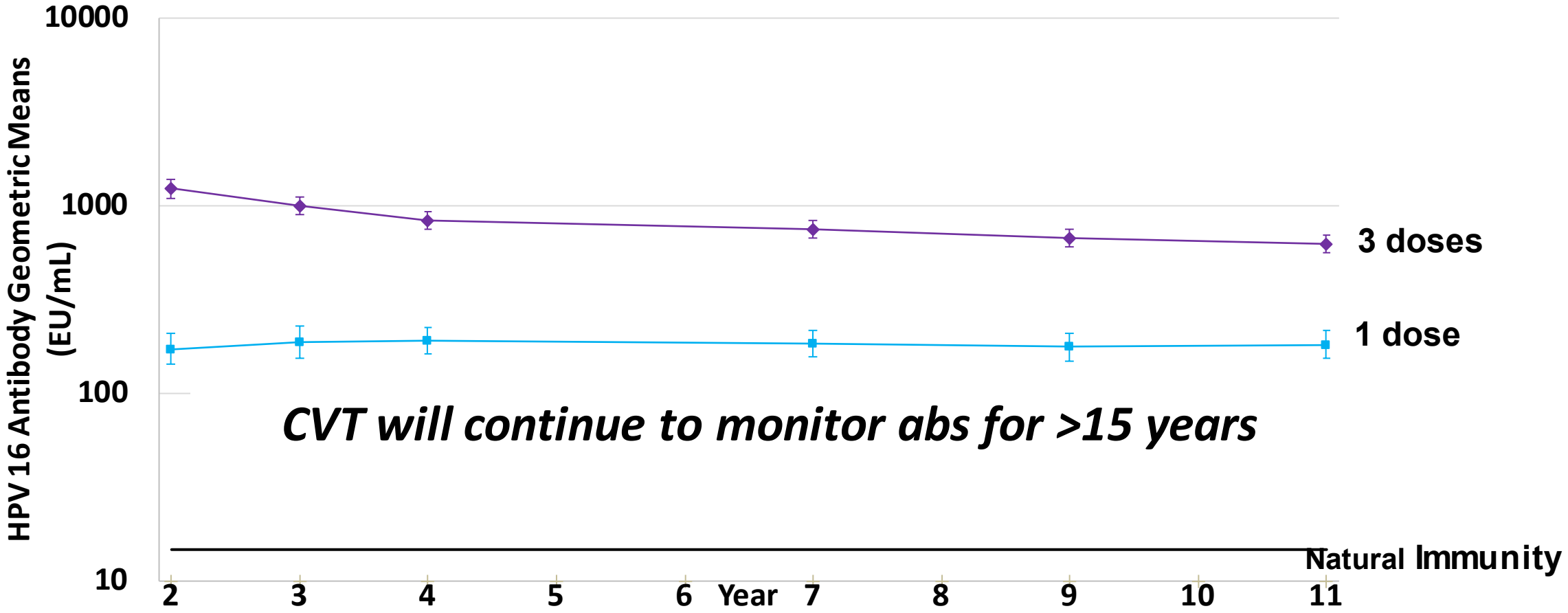
However, there are no indications that overall acceptance or coverage among the population is higher when boys vaccination is introduced.

unicef

World Health Organization

Does a SINGLE DOSE protect against Cx?

Costa Rica Vac Trial: Stable HPV16 serum antibodies for 11 years



Kreimer AR et al, Revise & resubmit

Thank You

HPV Vaccine Introduction Clearing House

Visit each area for related resources:

POLICY & DECISION-MAKING
Informing national decision-making for HPV vaccine introduction

PLANNING
Planning for HPV vaccine introduction

FINANCING
Budgeting and financing for HPV vaccine introduction

VACCINES & SAFETY
Characteristics, presentations and safety profiles of HPV vaccines

COMMUNICATION
Communicating effectively using research-based approaches

IMPLEMENTATION
Delivering HPV vaccination programmes

MONITORING & SURVEILLANCE
Monitoring the coverage and impact of HPV vaccine programmes

HPV PARTNERS
Links to HPV partners and resources

https://www.who.int/immunization/hpv/en/

World Health Organization

HPV Vaccination
Towards the Elimination of Cervical Cancer in the Caribbean Countries
22,23,29, and 30 October 2020

Advances in HPV Vaccination in the Americas

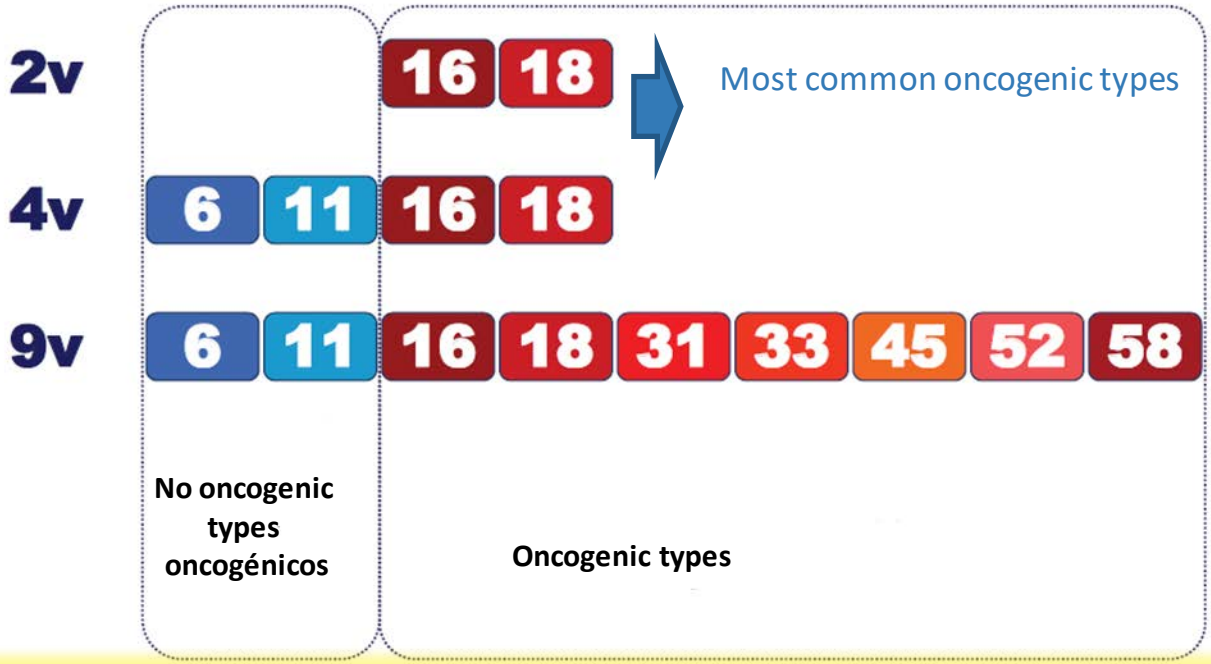
Lúcia De Oliveira, PhD, MSc
Regional Advisor on Immunization

Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas
Organización Panamericana de la Salud
Organización Mundial de la Salud
OFICINA REGIONAL PARA LAS Américas

Main topics

- HPV vaccines
- HPV vaccine Introduction and coverage
- TAG Recommendations
- Paho technical cooperation

Composition of HPV vaccines



All three vaccines should preferably be given before the onset of sexual activity

SAGE and TAG:
The three licensed vaccines are very safe, and offer comparable immunogenicity, efficacy and effectiveness for cervical cancer prevention which is mainly caused by HPV 16 and 18.

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Organización Mundial de la Salud
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Pan American Health Organization
World Health Organization
Regional Office for the Americas

HPV Vaccine Introduction in the American Region.

Caribbean

1. Anguilla (2016)
2. Antigua y Barbuda (2018)
3. Aruba (2014)
4. Bahamas (2015)
5. Barbados (2014)
6. Bermuda (2007)
7. Bonaire (2015)
8. Dominica (2019)
9. Granada (2019)
10. Guadalupe (2008)
11. Islas Caimanes (2009)
12. Islas Turcas y Caicos (2019)
13. Islas Vírgenes Británicas (2019)
14. Jamaica (2017)
15. Monserrat (2017)
16. Puerto Rico (2006)
17. Saba (2013)
18. San Martin (2013)
19. St. Lucia (2019)
20. San Eustaquio (2013)
21. San Kitts y Nevis (2019)
22. San Vicente y Granadinas (2017)
23. Trinidad y Tobago (2012)

43 and countries and territories

Americas

1. Argentina (2011)
2. Belice (2016)
3. Bolivia (2017)
4. Brasil (2014)
5. Canadá (2007-2009)
6. Chile (2014)
7. Colombia (2012)
8. Costa Rica (2019)
9. Ecuador (2014)
10. Estados Unidos (2006)
11. Guatemala (2018)
12. Guyana (2012 la mitad; 2017 todo el país)
13. Honduras (2016)
14. México (2012)
15. Panamá (2008)
16. Paraguay (2013)
17. Perú (2015)
18. República Dominicana (2017)
19. Surinam (2013)
20. Uruguay (2013)

With HPV vaccine

Without HPV vaccine

Source: PAHO/WHO UNICEF - JRF

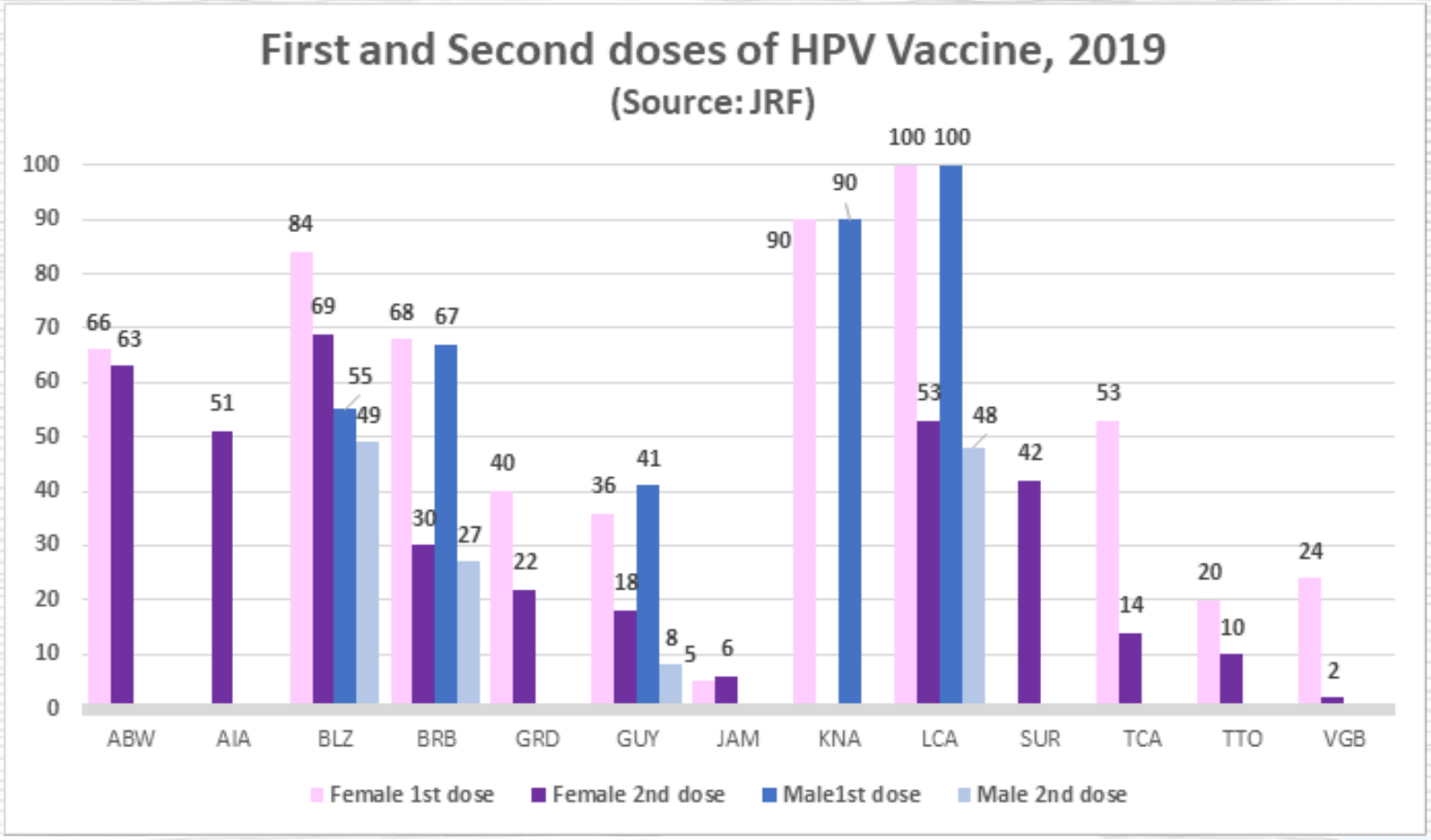
Organización Panamericana de la Salud
Organización Mundial de la Salud
Américas

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

HPV Vaccination In the America Region

- 90% of girls in the Region live in countries where the HPV vaccine has already been introduced into the national schedule
- The most commonly used vaccine is the quadrivalent vaccine.
-
- 2019: 13 countries report neutral gender vacination : Antigua and Barbuda, Argentina, Barbados, Bermuda, Brazil, Canada, Chile, United States, Monserrat, Panama, Puerto Rico, San Kitts and Nevis, Trinidad and Tobago (Joint Form for PAHO-WHO/UNICEF Notification - JRF, 2018 and Country Information).

HPV vaccine coverage, selected countries Caribbean, 2019.



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HUMAN VACCINES & IMMUNOTHERAPEUTICS
2020, VOL. 16, NO. 3, 573–580
https://doi.org/10.1080/21645515.2019.1661205

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

OPEN ACCESS Check for updates

Knowledge and awareness of Human Papillomavirus (HPV) and HPV vaccines among Caribbean youth: the case of the Bahamas

Clemon George [a], Robin Roberts [b], Delon Brennen [c], Lynette Deveaux [c], and Stanley E Read [d]

[a]University of Ontario Institute of Technology and Faculty of Medical Sciences, Oshawa, Ontario and the University of the West Indies, Cave Hill, Barbados; [b]UWI School of Clinical Medicine and Research, Nassau, The Bahamas; [c]Ministry of Health, Nassau, The Bahamas; [d]Division of Infectious Diseases, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

ABSTRACT

There is a high burden of cervical cancer in the Caribbean region, particularly in the Bahamas, yet there are few studies of Human Papillomavirus (HPV) and HPV vaccine in the region. The objective of this study was to assess the knowledge and awareness of HPV and the HPV vaccine among school-aged youth (15–18 years) living in the Bahamas.

Cross-sectional data were obtained from the "Getting to Zero" HIV study in the Bahamas conducted in 2014/2015 (n = 1553). The questionnaire elicited information on knowledge of HPV and HPV vaccines, using previously validated scales. Data analysis included Chi-square tests and Mann Whitney U test.

In this sample of school-aged youth, only 10.7% (146/1364) had ever heard of HPV. With respect to those who were sexually active (n = 685), only 10.7% had ever heard of HPV. For those who had heard of HPV, knowledge of HPV and HPV vaccines was assessed on an HPV Knowledge and HPV Vaccine Knowledge scale, respectively. There was no statistically significant difference in mean HPV knowledge score between males and females, or HPV vaccine knowledge scores, between males and females.

There was a general lack of awareness of HPV and HPV vaccines among school-aged youth in the Bahamas. This is an important gap in the HPV vaccine strategy and cancer prevention, as this is the age at which most people acquire HPV. It emphasizes the importance of developing a careful implementation plan, with an evaluation of knowledge and attitudes, in order to have an effective HPV vaccine uptake.

ARTICLE HISTORY
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KEYWORDS
Human Papillomavirus; knowledge; youth; Caribbean; Bahamas

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Lessons learned: It's a challenge to achieve high coverage with the HPV vaccine

A global analysis of HPV coverage between 2014 and 2016 showed that in 52 countries studied:

(14/52)

≥ 80%

(13/52)

< 50%.

Fuente: Brotherton JML, Bloem PN, Population-based HPV vaccination programmes are safe and effective: 2017 update and the impetus for achieving better global coverage, *Best Practice & Research Clinical Obstetrics and Gynaecology* (2017), http://dx.doi.org/10.1016/j.bpobgyn.2017.08.010

Analysis of vaccination coverage has shown that in order to achieve high coverage, a number of vaccination strategies must be adopted, and priority should be given to **vaccination in schools.**

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Organización Mundial de la Salud
Américas

Pan American Health Organization
World Health Organization
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Technical Advisory Group (TAG) on Vaccine Prevention Diseases, 2019

- TAG expresses its deep concern at the current challenges facing the provision of the HPV vaccine and stresses the importance of meeting countries' needs to reduce the burden of cervical cancer.

- TAG calls on the global public health community to challenge HPV vaccine manufacturers to respond operationally and ethically to global vaccine delivery needs and align with PAHO/WHO's call for cervical cancer elimination.
-
- In view of the current supply challenge, **all countries that administer vaccines to girls and boys should prioritize girls' vaccination, achieving HPV vaccine coverage of 80%. This will induce herd immunity and protect both girls and boys.**
-
- TAG encourages countries **to implement HPV communication and vaccination plans in schools to increase vaccine coverage and maximize the impact of vaccination**.
-

PAHO 2019 technical cooperation

- Regional Meetings: HPV Vaccination towards Cervical Cancer Elimination
- Vaccine coverage calculation guide
- HPV Vaccine Impact Measurement Document (in progress)
- Support to countries in introduction plans and crisis situations by ESAVIs

https://www.paho.org/es/temas/cancer-cervicouterino

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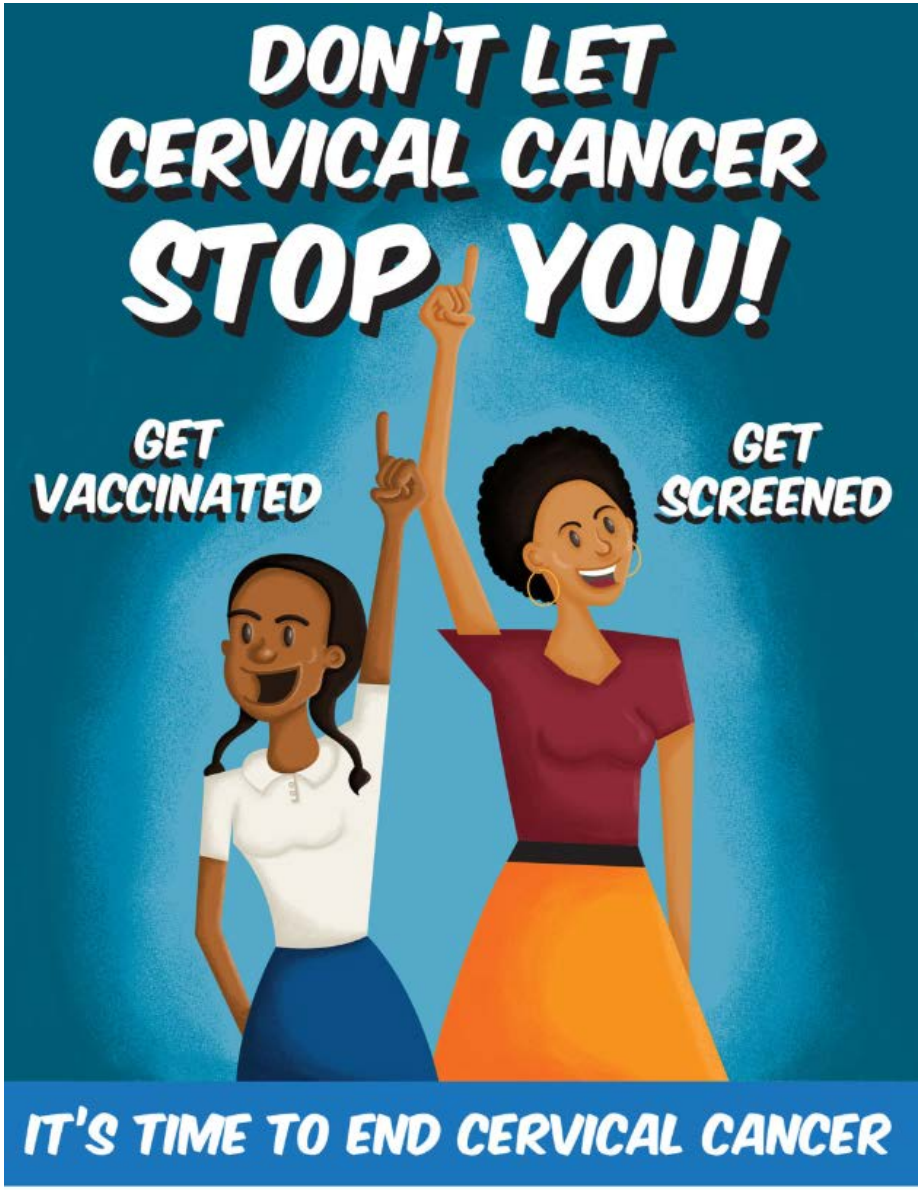

Pan American Health Organization
World Health Organization Americas

WWW.PAHO.ORG/FIN-CANCER-CERVICAL

Thanks

Maria Tereza da Costa

John Fitzsimmons

Thank you for your attention !

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Pan American Health Organization
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HPV ASSOCIATED DISEASES, AND IMMUNE RESPONSES.

Malda Kocache PhD
Professor, Biology Department
George Mason University
Fairfax, VA 22030

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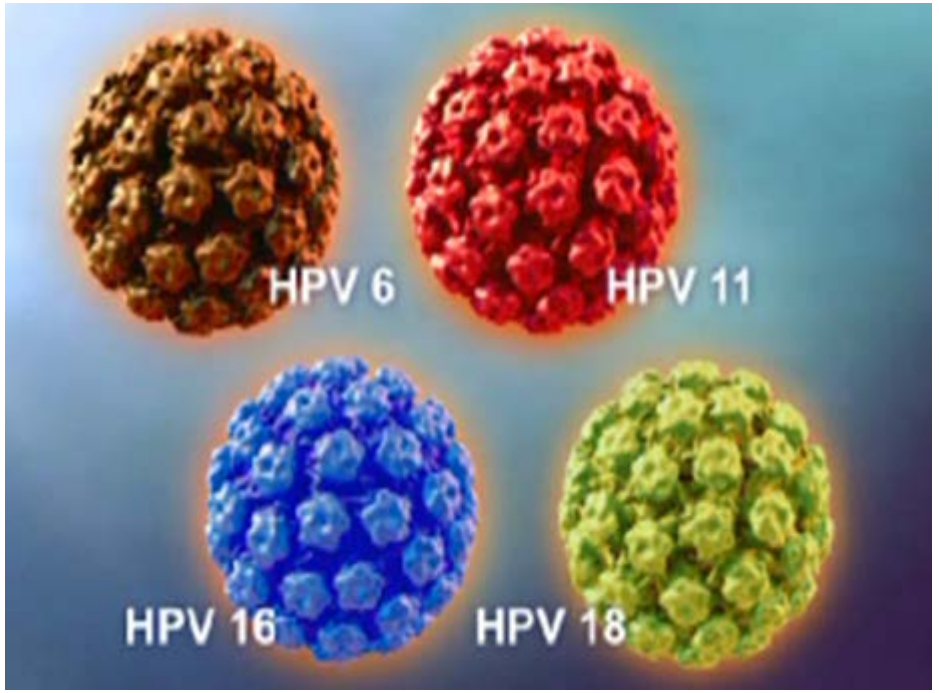
Presentation Outline

- Human Papillomaviruses (HPV)
- HPV Diseases and Cancers
- Natural Immune Responses to HPV
- Vaccine Induced Immune Responses
- Possibility of a One Dose HPV Vaccine?



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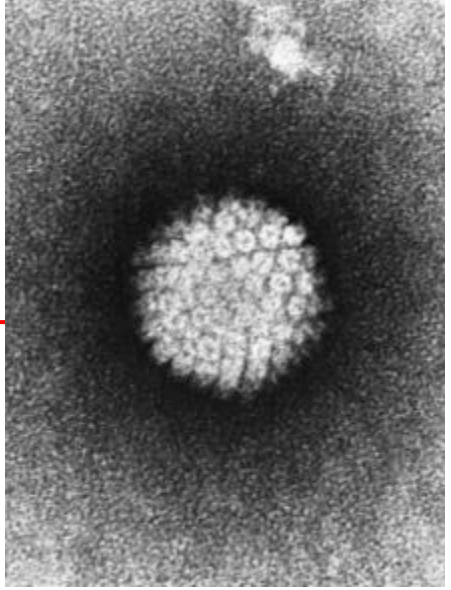
General Characteristics of HPV



- Family: Papillomaviridae.
- Human papillomaviruses (HPV's) are small, non-enveloped, icosahedral capsid viruses. (50 -60nm)
- Their genome is double stranded circular DNA of about 8000 bp.
- Over 150 types have been identified and grouped according to their preferred site of infection into either **cutaneous** or **mucosal** HPV.

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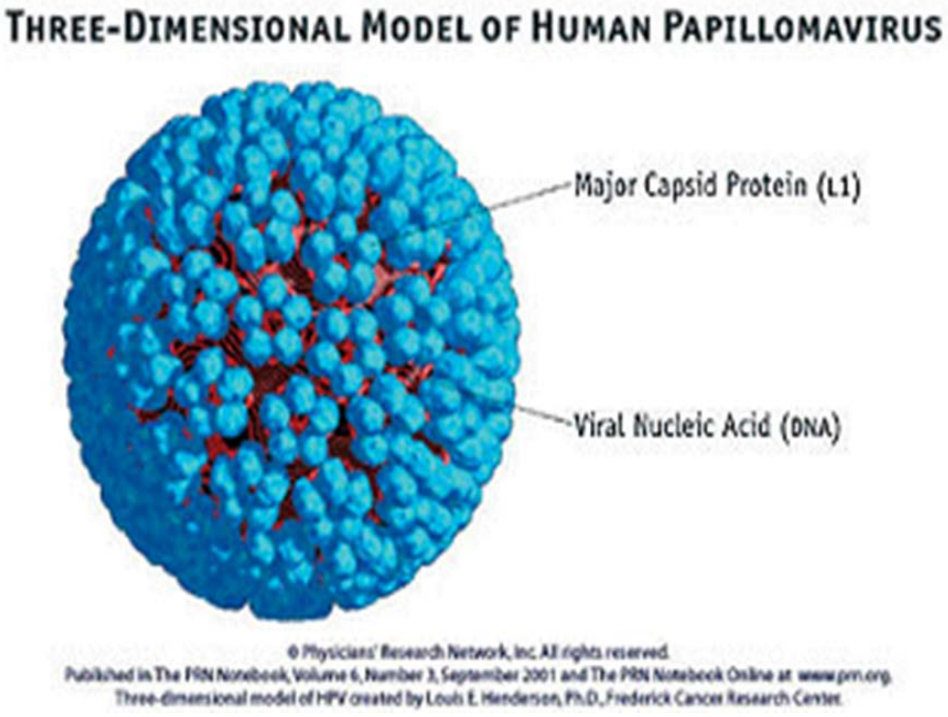
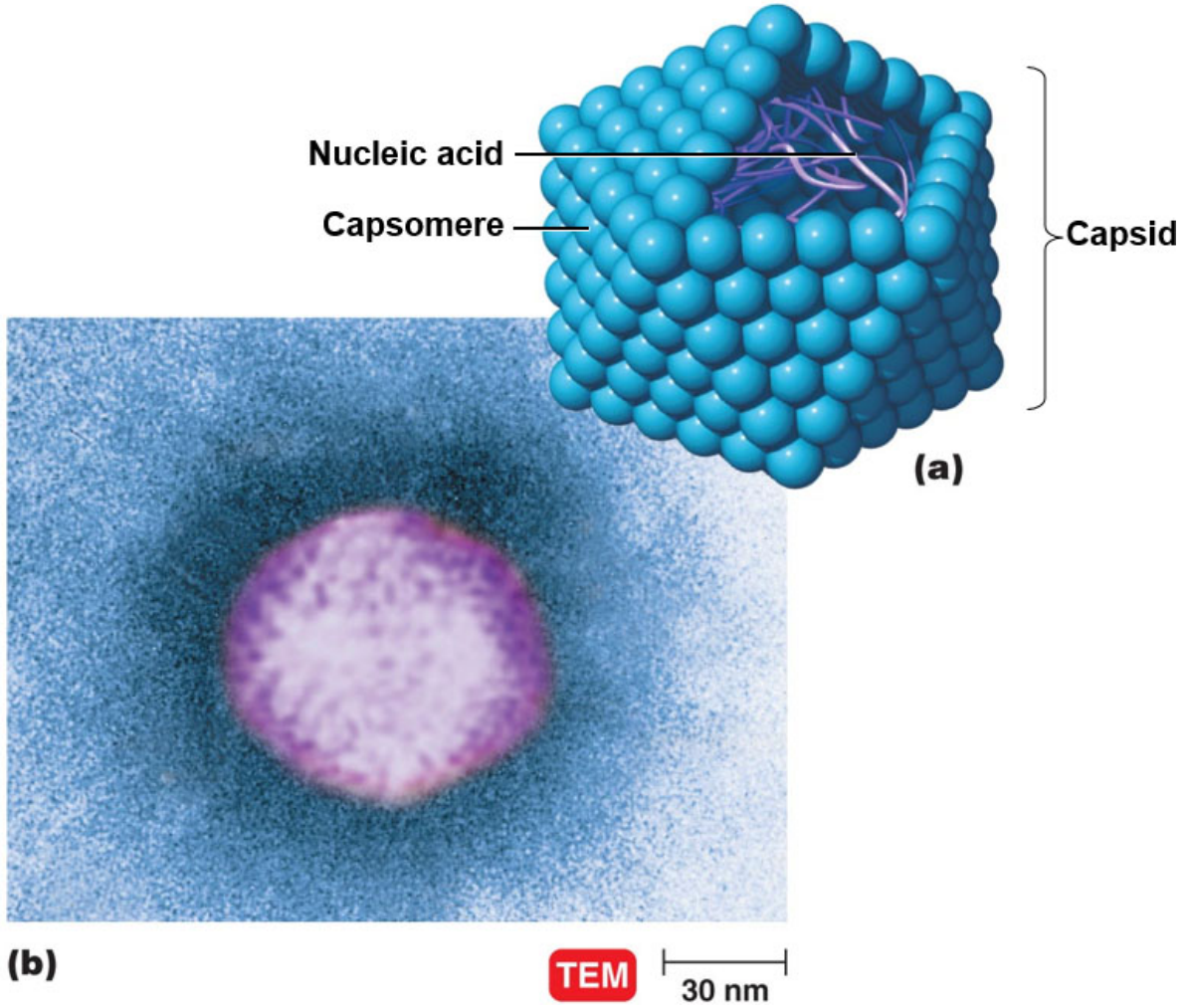
HPV Morphology





General Characteristics of HPV

- The genome encodes seven or eight early genes (E1 to E8), and two late structural genes (L1 and L2).

- **L1 is the viral attachment protein and one of the main capsid proteins. Highly antigenic and is used in vaccine preparation.**

- **Neutralizing antibodies: Attach to the receptor and neutralize infectivity**

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HPV Associated Diseases

- **HPV is the most common viral sexually transmitted infection in the world**
- **Cutaneous Infections**:
  - Common warts, plantar warts, flat warts, filiform warts, pigmented warts.

- **Condyloma acuminatum**: genital warts.
  - Appear on external genitalia, penis, vulva, and cervix.
  - Most commonly associated with low risk HPV-6 and 11

Reviews in Medical Virology
pages 2-23, 6 MAR 2015 DOI: 10.1002/rmv.1822
http://onlinelibrary.wiley.com/doi/10.1002/rmv.1822/full#rmv1822-fig-0003

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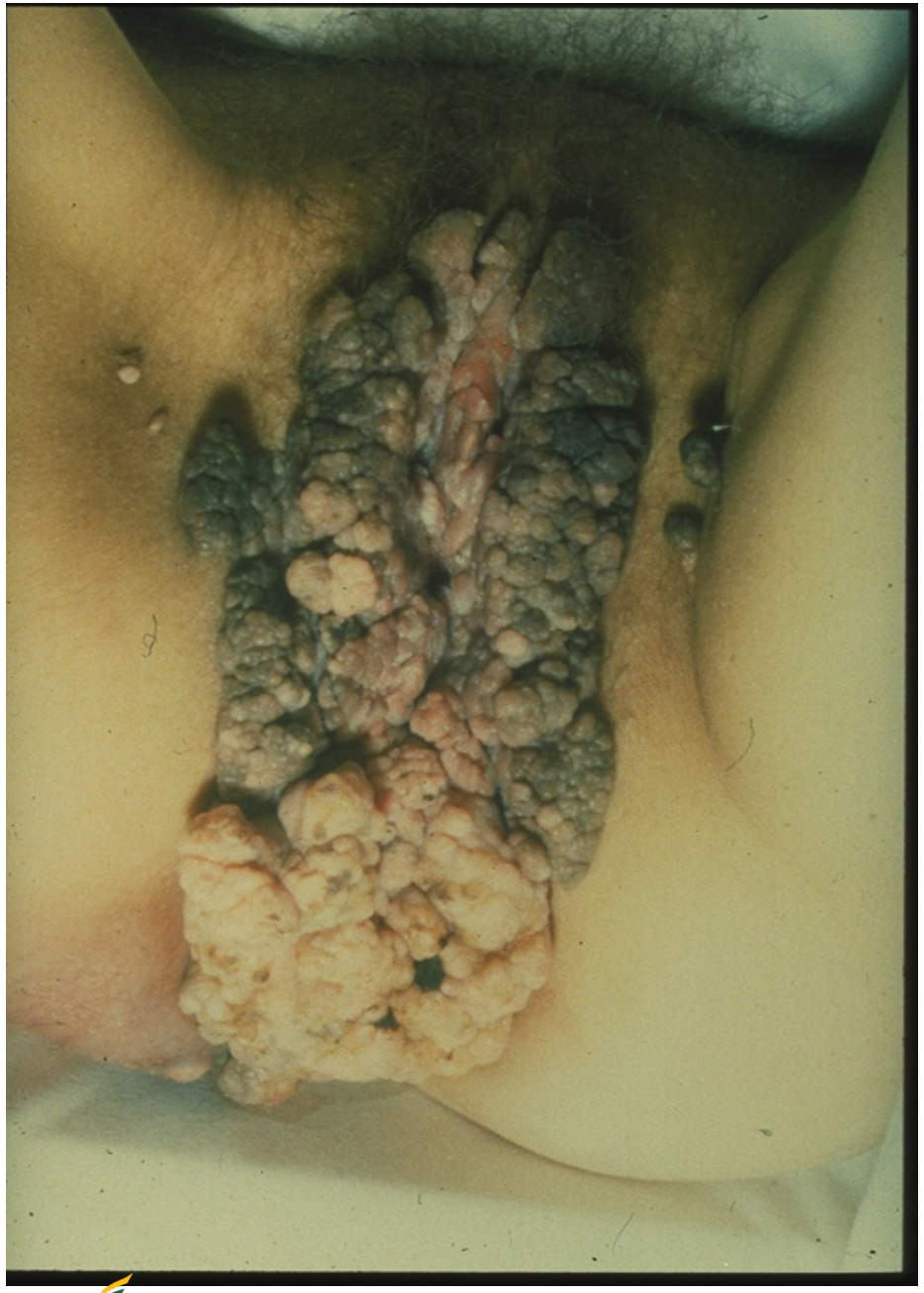
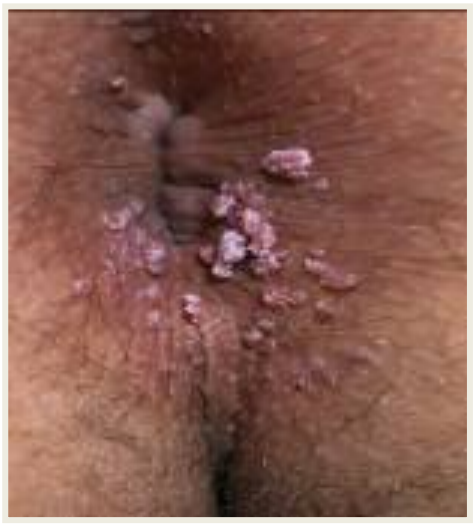
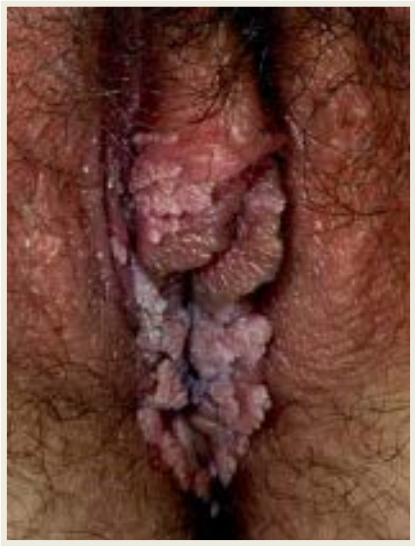
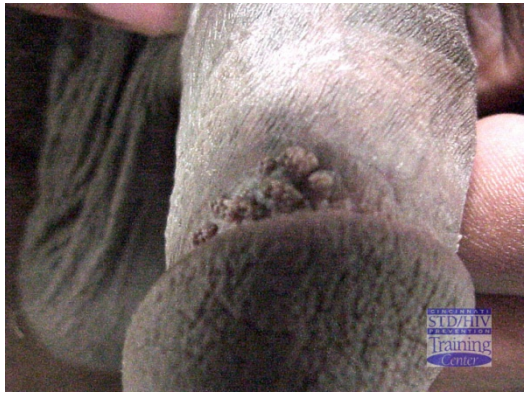
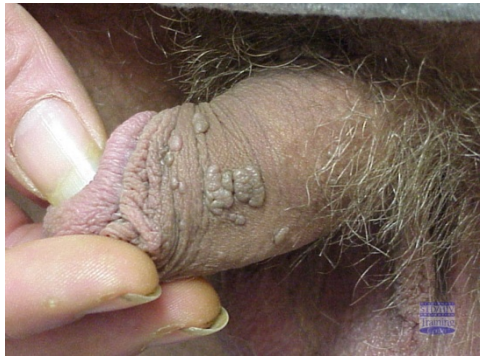


Genital Warts

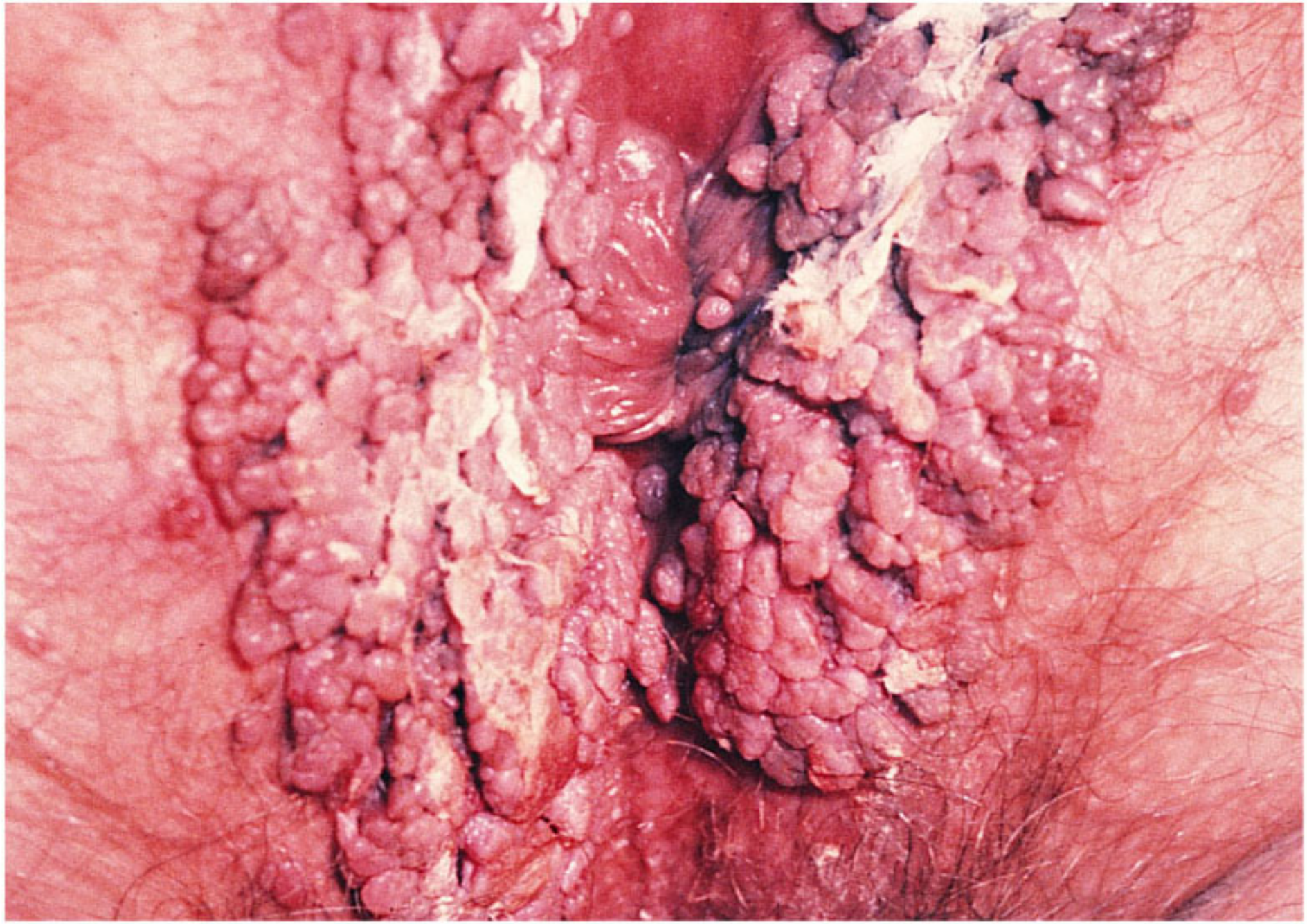








Cincinnati STD/HIV Prevention Training Center, at CDC. gov



HPV Associated Cancers

- **Anogenital cancers:**
  - Includes, vulva, vagina, penis, and anus.
  - HPV prevalence is 90% in vulvar intraepithelial neoplasia with HPV-16 most common followed by 18, 31, 33.

- **Head and neck cancers**:
  - HPV is a major risk factor for the development of these cancers.
  - **The incidence of HPV + ve oropharyngeal cancers has increased by 3 folds in the decade.**

Reviews in Medical Virology
pages 2-23, 6 MAR 2015 DOI: 10.1002/rmv.1822
http://onlinelibrary.wiley.com/doi/10.1002/rmv.1822/full#rmv1822-fig-0003

HPV Associated Cancers

- **Cervical neoplasia and Cervical Cancer:**
  - The extent of the abnormality has to do with how much of the poorly differentiated basal like cells extend toward the epithelial layer.
  - **HPV is detected in 99.7% of cervical abnormalities including cellular dysplasia to cervical cancer.**
  - **Most common types are HPV-16 and 18. Cause 70% of all cervical cancer cases**
  - Other subtypes are HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, 73, 82.

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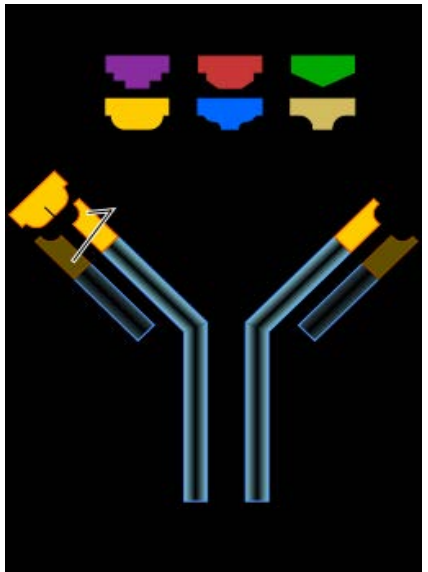
Reviews in Medical Virology
pages 2-23, 6 MAR 2015 DOI: 10.1002/rmv.1822
http://onlinelibrary.wiley.com/doi/10.1002/rmv.1822/full#rmv1822-fig-0003

Immune Response to HPV **Natural Infection**

- Seroconversion in 8-12 months. **SLOW**
- Response restricted to mucosal surfaces. No vigorous immune response.
- Antibodies are weak and of **low titers and low avidity**



Immune Response to HPV **Infection**

WHY?

- No virus induced cytolysis.
- No inflammation . Decreased innate immune response.
- No viremia. Infection is intraepithelial
- No proper presentation to the immune system. (Due to viral life cycle)

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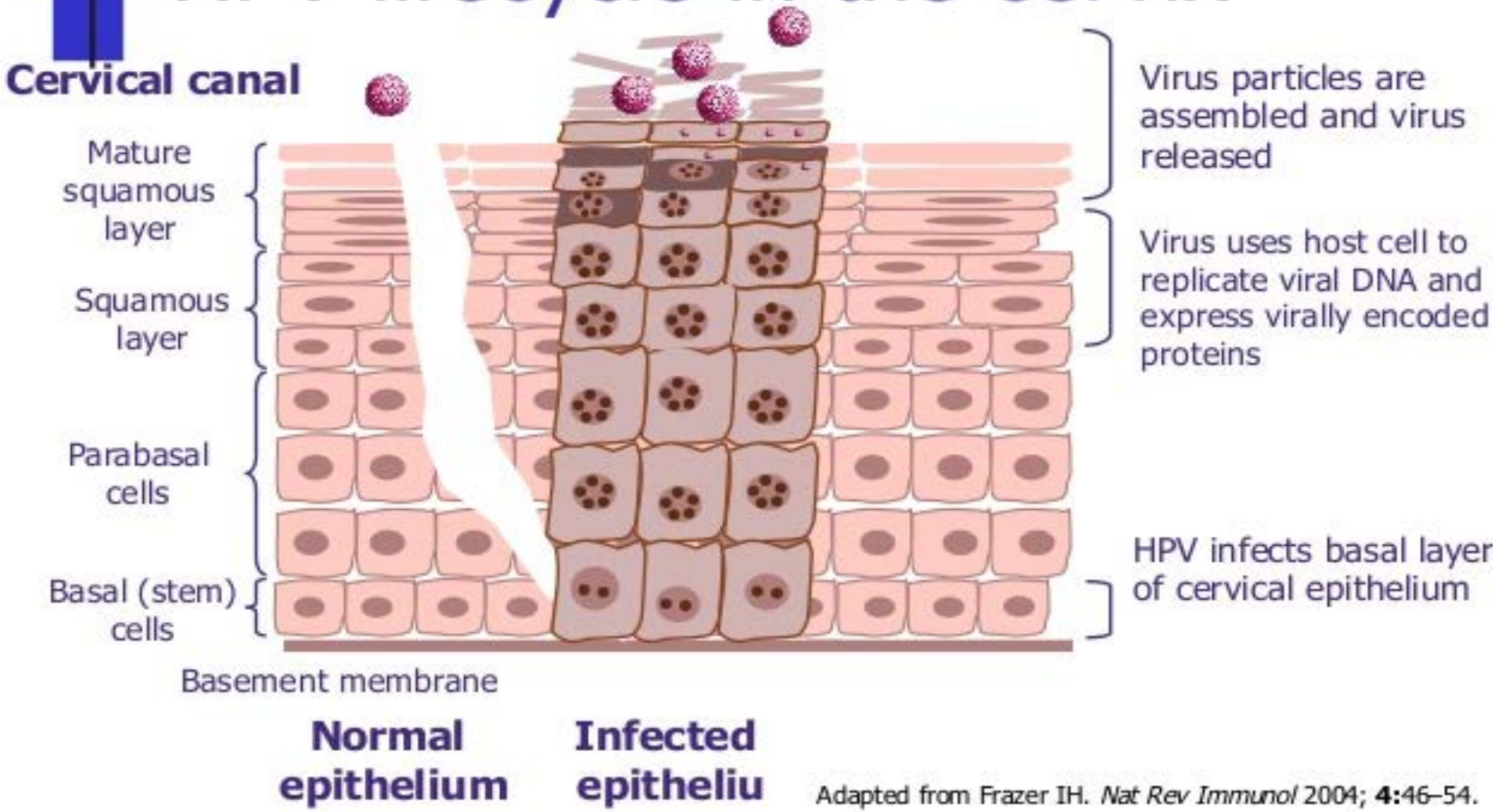
HPV lifecycle in the cervix



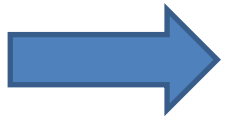
Adapted from Frazer IH. *Nat Rev Immunol* 2004; **4**:46–54.

Immune Response to HPV **Infection**

- 70%-80% of women seroconvert. Few men seroconvert and antibodies produced are not protective

- Control of infection is by CMI (cell mediated immunity)

- Ineffective CMI may lead to persistent infection
  Increased risk of progression to CIN2/3



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HPV Vaccines--- Ą Primary Prevention

- **Bivalent Vaccine**: prevention of premalignant genital lesions and cervical cancer
  - HPV-16 and HPV-18.
  - Intended for use in females ideally between the ages of 9-14 years old. (2 doses)
- **Quadrivalent Vaccine**: prevention of premalignant genital lesions, cervical cancer, and anogenital warts
  - HPV-6, 11, 16, and 18.
  - Indicated for use in both females and males from the age of 9 years old (up to 26 years). (2 or 3 doses)
- **Nonavalent Vaccine**: prevention of premalignant genital lesions, cervical cancers, ano-genital warts, and anal cancer
  - HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58
  - Administration for females (9-26 yr) and males (9-21 yr) (2 doses)

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HPV Vaccines: Subunit Vaccines

- All the vaccines are made from multiple types of HPV L1 capsid protein virus like particles (VLPs)
- L1 aggregates spontaneously into virus like particles that are highly immunogenic and produce effective neutralizing antibodies
- VLPs are non-infectious and non oncogenic making them extremely safe
- There is limited cross protection against non vaccine HPV types.

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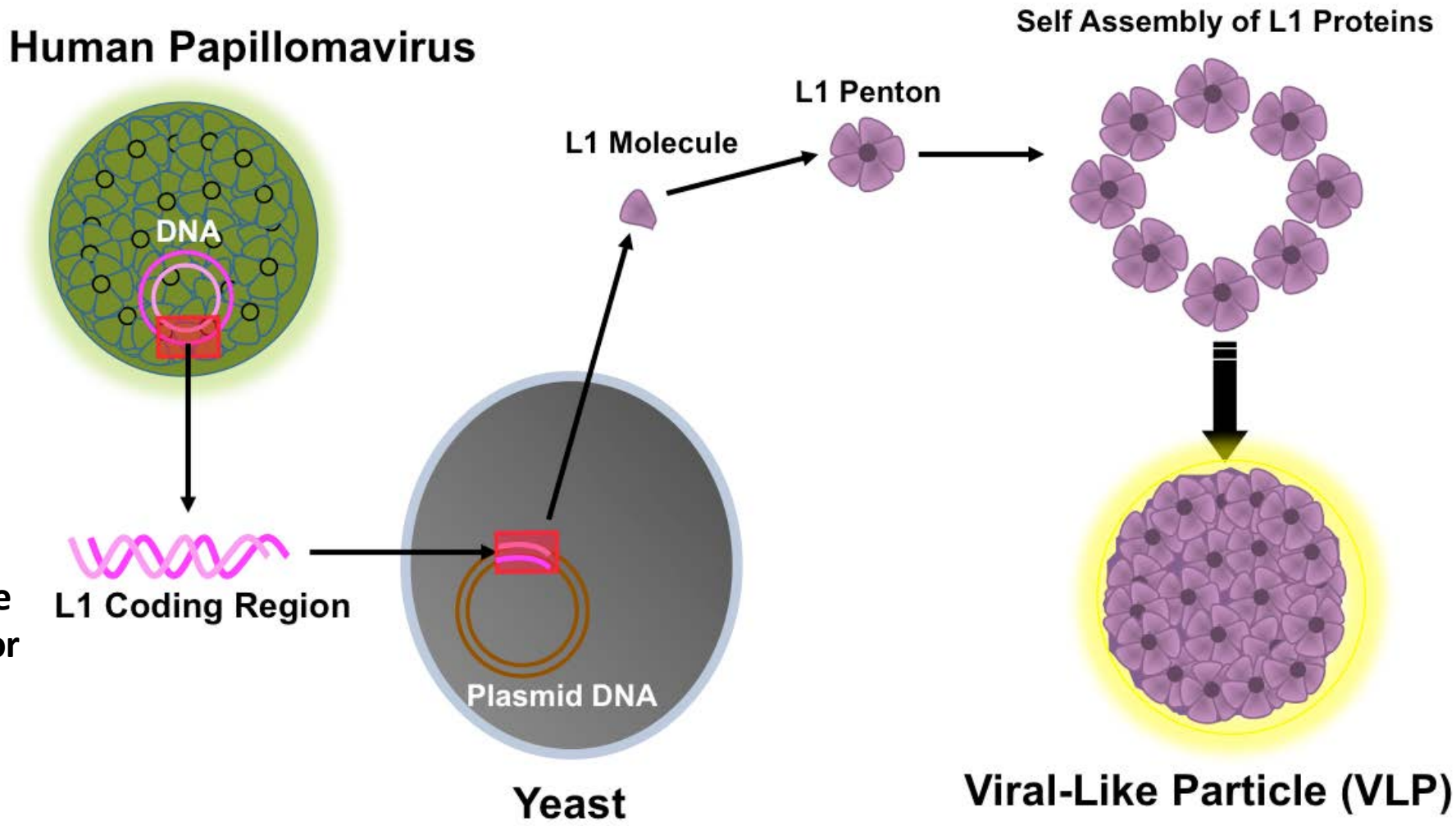
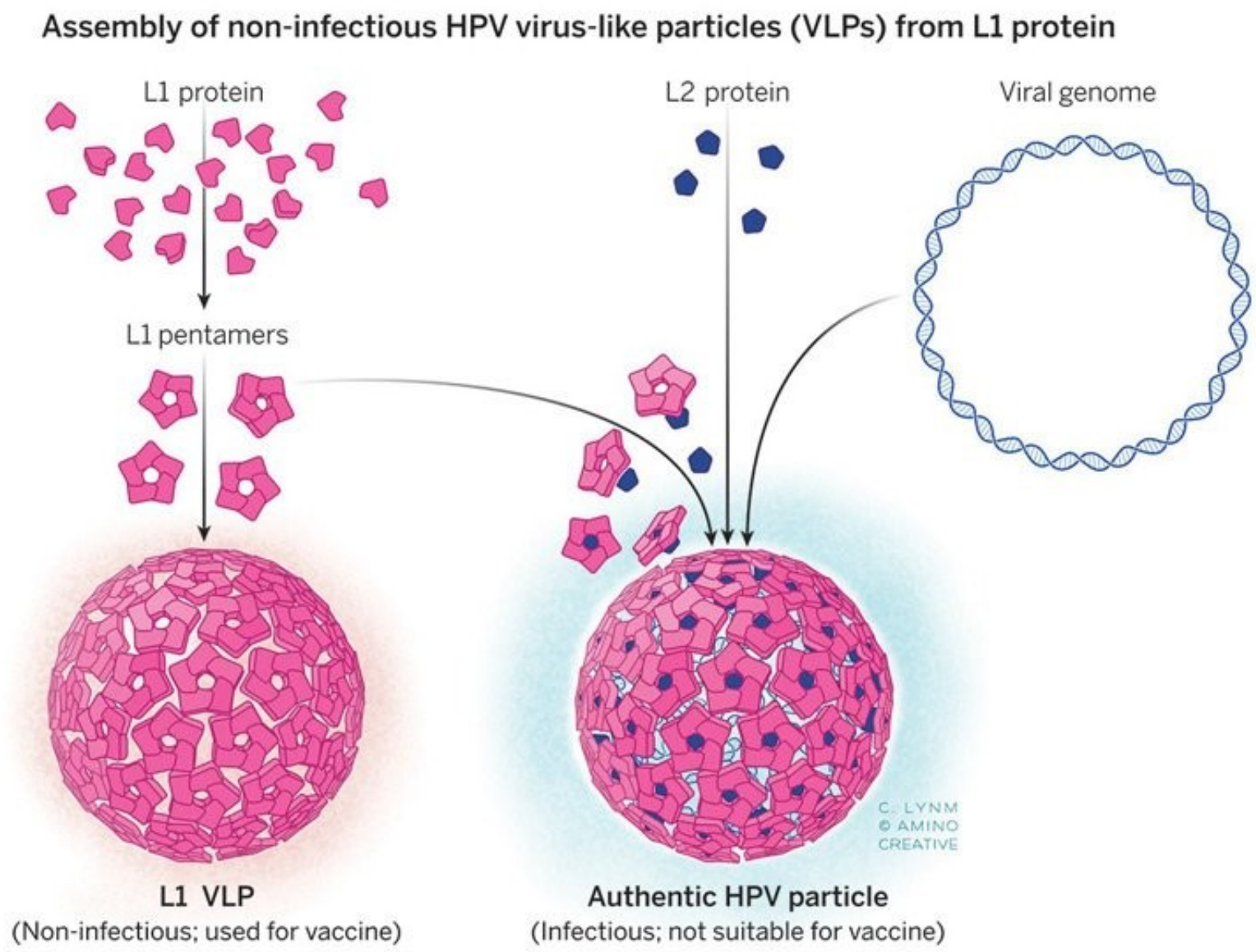
HPV L1 VLP Vaccine Synthesis





- High Repetitive L 1 aggregate
- 360 ordered protein subunits
- Induces excellent long-lived plasma cells (LLPC)

Immune Responses to HPV **Vaccination**

Advantages of the vaccine:

1. Resemble the actual virion.

2. Not infectious or oncogenic

3. Introduced intra muscularly ----- Ą much better access to lymph nodes and activation of B cells and Helper T cells

Immune Responses to HPV **Vaccination**

Advantages of the vaccine:

4. Higher dose of L1 antigen .

5. **Induces long lived plasma cells (LLPC)**

Result: Initiating an immune cascade that results in a robust T cell-dependent B cell response, which generates high levels of L1-specific serum neutralizing antibodies and immune memory.

Schiller, **Vaccine**. 2018 Aug 6;36

Viral Life Cycle
Highly Responsive to Antibody Responses

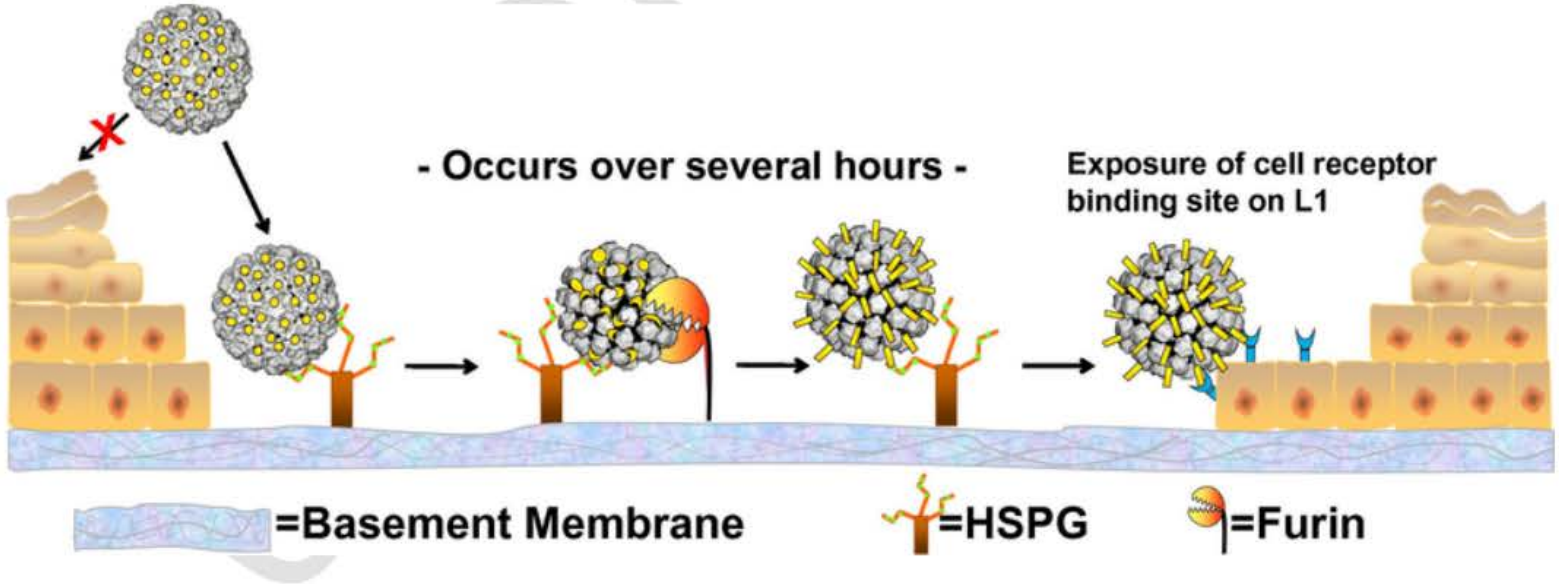


Fig. 3. Cervicovaginal HPV infection in a mouse model. A disrupted cerviovaginal epithelium is depicted. "X" indicates the inability of virions to bind the apical surface of intact epithelium. HSPG=heparan sulfate proteoglycan. The L1 capsid structure is depicted in grey. The L2 minor capsid proteins, cleaved by furin protease after a HSPG binding-induced conformational change in the capsid, are shown in yellow. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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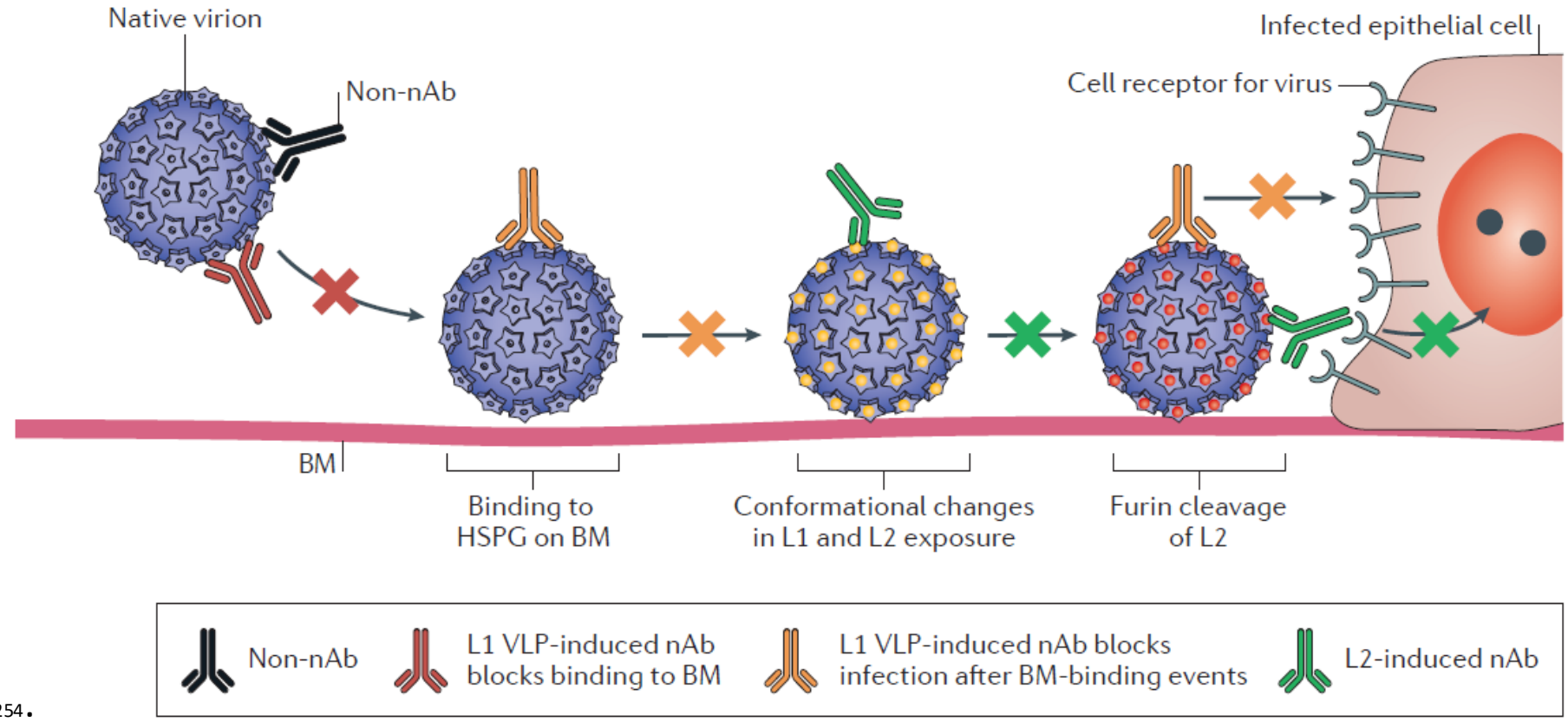
Neutralizing Antibody Blocking HPV Attachment



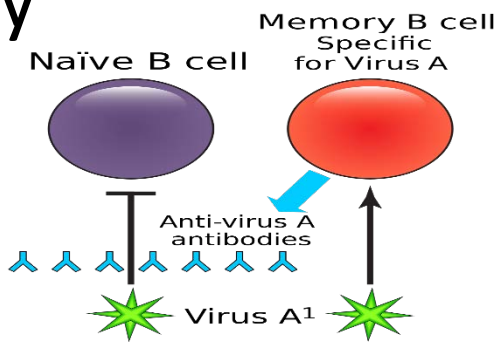
Nat Rev Cancer. 2018 Apr;18(4):240-254.

Immune Responses to HPV **Vaccination**

- Serological response is much higher (1-4 logs higher) as compared to natural infection

- Protection seems to be mediated by **polyclonal NEUTRALIZING** antibodies against the L1 surface protein.

- The antibodies produced have better affinity and avidity



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Why a 5-6 month wait?

- Memory B cells produced after 1 dose of the vaccine required **4-6 months** to differentiate into high affinity B cells.

- As such there needs to be at least a 6-month period between the 1st and 2nd dose of vaccine  to reactivate these high affinity B cells ----- Ą Plasma cells ----- Ą secrete **HIGH AFFINITY** antibodies

- This dosage recommendation will increase the duration of protection induced by the vaccine. **LONGER LASTING IMMUNITY**

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Immune Responses to HPV **Vaccination**

- The highest immune responses were seen in girls aged 9 – 15 years. (preferably before first sexual activity)
- Vaccine protection persists even with lower antibody titers.
- Suggests that vaccines may provide prolonged protection
- Studies show a high protective response up to 10 years post vaccination.
- No evidence that efficacy of the vaccine wanes over time.

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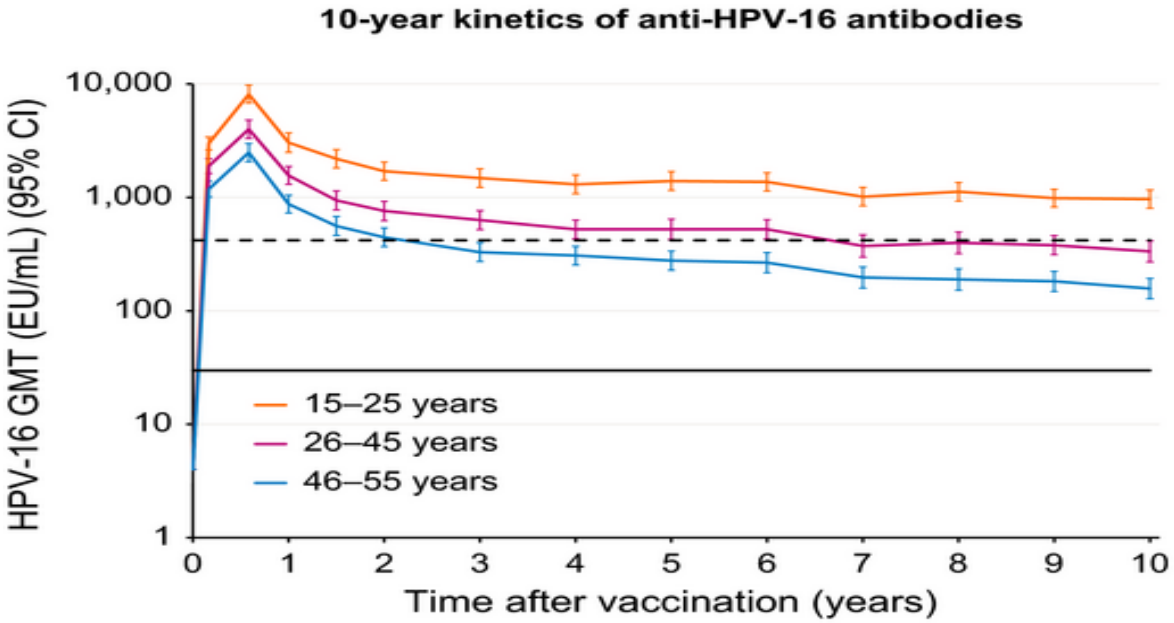
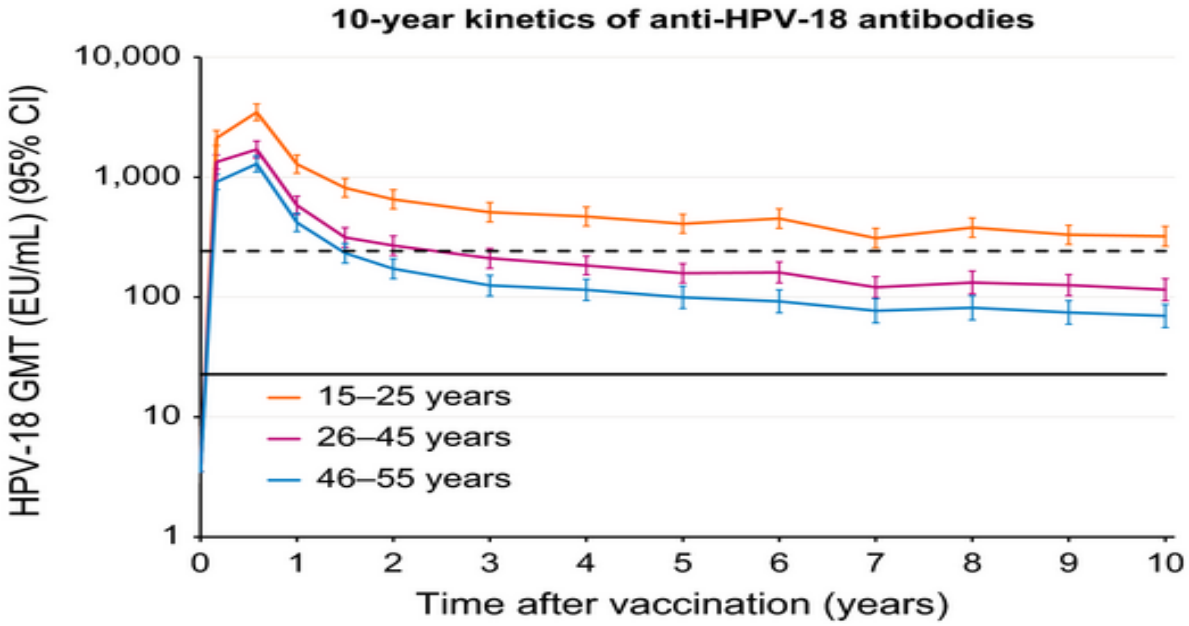
Ten-year immune persistence and safety of the HPV-16/18 AS04-adjuvanted vaccine in females vaccinated at 15–55 years of age





This study concluded that vaccinated females aged 15–55 years elicited sustained immunogenicity with an acceptable safety profile up to 10 years after primary vaccination, suggesting long-term protection against HPV.

Cancer Medicine, Schwarz et al
5 OCT 2017 DOI: 10.1002/cam4.1155
http://onlinelibrary.wiley.com/doi/10.1002/cam4.1155/full#cam41155-fig-0001

One vs Two or Three doses of HPV

- What we know:
  - 2 doses are as effective as 3 in the 9 – 14-year age group. Highly Supported Evidence.

- THE QUESTION:
  - **Can a one dose vaccine be effective??????**
  - **Rationale: Cost and Ease of delivery**

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Non-randomized observational data from clinical trials

1. The Costa Rica Vaccine Trial (CVT): 2vHPV

   - Only one dose of 2vHPV had similar efficacy as 3 dose after 4- and 7-years post vaccination.

   - Combined observation w PATRICIA showed similar efficacy of one vs 3 doses.

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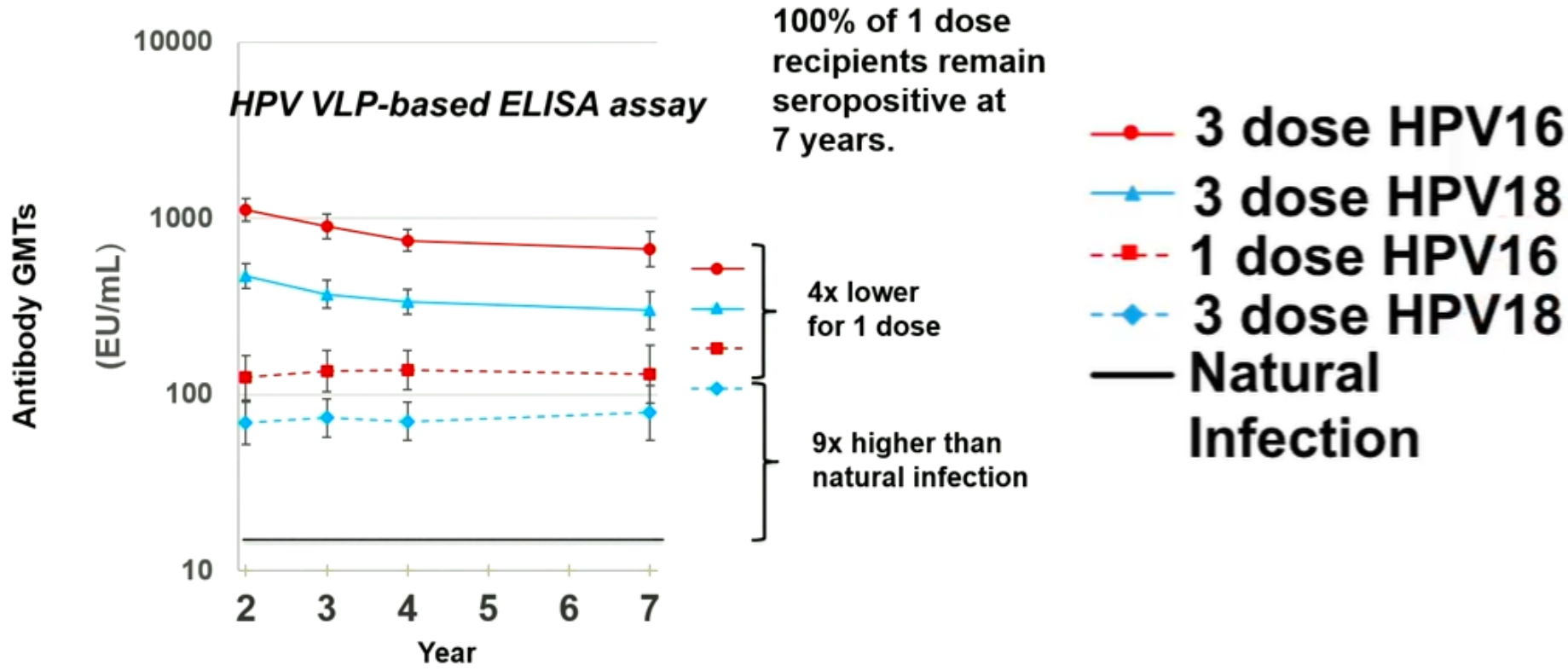
The Costa Rica Trial

Durability of VLP Ab Responds To 7 Years
Costa Rica Vaccine Trial



M Safaeian et al, J Nat Cancer Inst 110 (2), 2018.

Non-randomized observational data from clinical trials

2. India HPV Vaccine Trial : 4vHPV

- High vaccine efficiency against persistent HPV16/18 regardless of dosage compared to unvaccinated.

- Immune response **is inferior** in one compared to 2 or 3 doses

- Single dose groups had higher levels of immune responses than baseline values.

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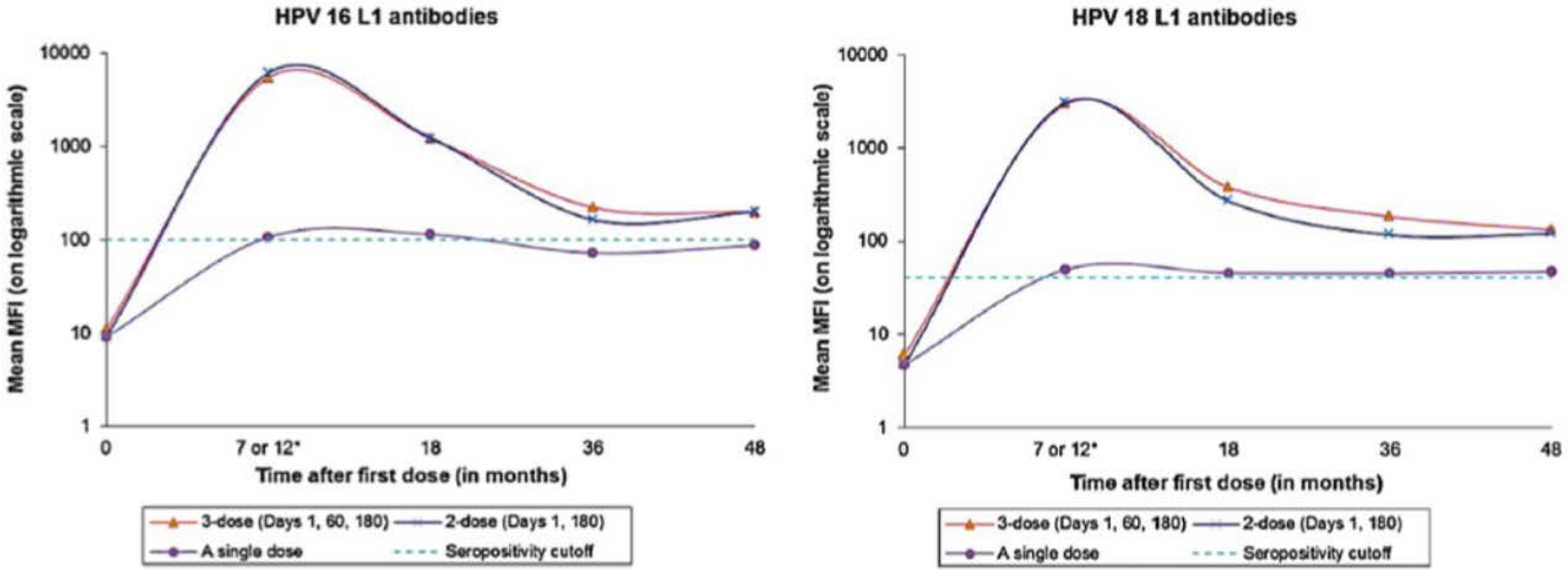
Figure 5. Mean MFI values for HPV types 16, 18, 6, and 11 L1 antibodies in the India HPV Vaccine Trial.



Mean median fluorescent intensity (MFI) values for HPV 16 and 18 L1 antibodies at different time points among girls who completed vaccination as per protocol (vaccination days 1, 60 and 180 (3-dose group) or days 1 and 180 (2-dose group)),

R. Sankaranarayanan et al./Vaccine 36 (2018) 4783–47914787

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Non-randomized observational data from clinical trials

3. Uganda Study: 2vHPV

   - GMT of one dose were inferior compared to 3 doses.

   - BUT, GMT levels in one dose group was higher than the Costa Rica

   - Immune responses in one dose were 4x higher than natural infection

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Non-randomized observational data from clinical trials

4. Fiji : 4vHPV

   - One dose recipients had significantly lower NAb titers than 2 or 3 doses.

   - Titers were 5 – 30x higher than unvaccinated.

   - A booster shot given after 6 years to one dose recipients increased NAb by 46-84 x suggesting strong anamnestic response

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Immune Responses to HPV **Vaccination**

CONCLUSIONS:

- Vaccination much better immune response than natural immunity.

- VLP vaccine is an excellent subunit vaccine with long lasting neutralizing antibody activity. LLPC (long lasting plasma cells)

- Vaccination significantly reduces the prevalence of high-risk HPV type in women ---- Ą Significant reduction in cervical cancer

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How I respond to Skeptics

- The HPV vaccine is a vaccine that prevents deadly cancers.
- If we had a safe vaccine that could prevent breast, lung, or colon cancer would anyone be objecting!!!!!

» HPV VACCINE

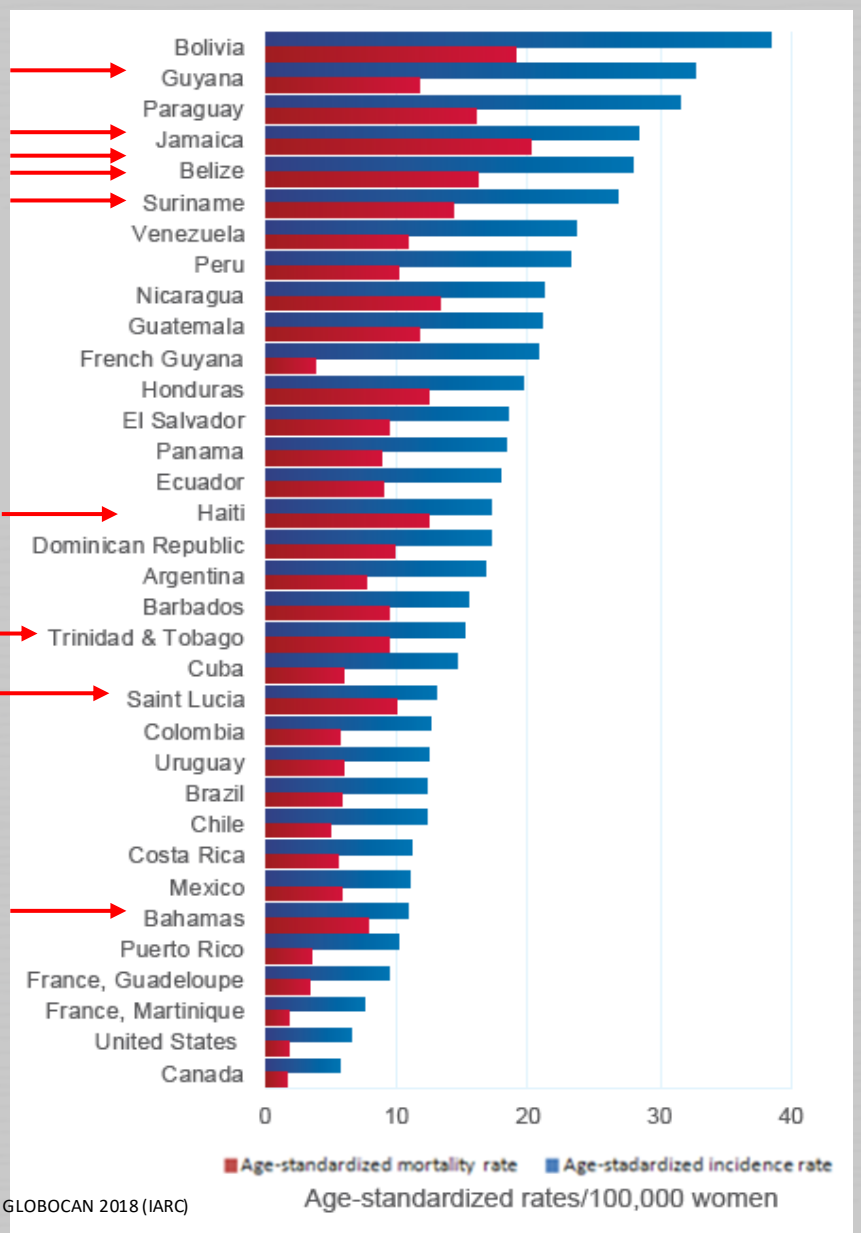
Regional Plan of Action on Cervical Cancer Prevention and Control

Silvana Luciani
Chief, Unit of Noncommunicable Diseases
Pan American Health Organization

Pan American Health Organization
World Health Organization
Americas

PAHO

Cervical Cancer in the Americas



Source: GLOBOCAN 2018 (IARC)

Approximately **72,000** women diagnosed, **and 34,000** women die each year from cervical cancer

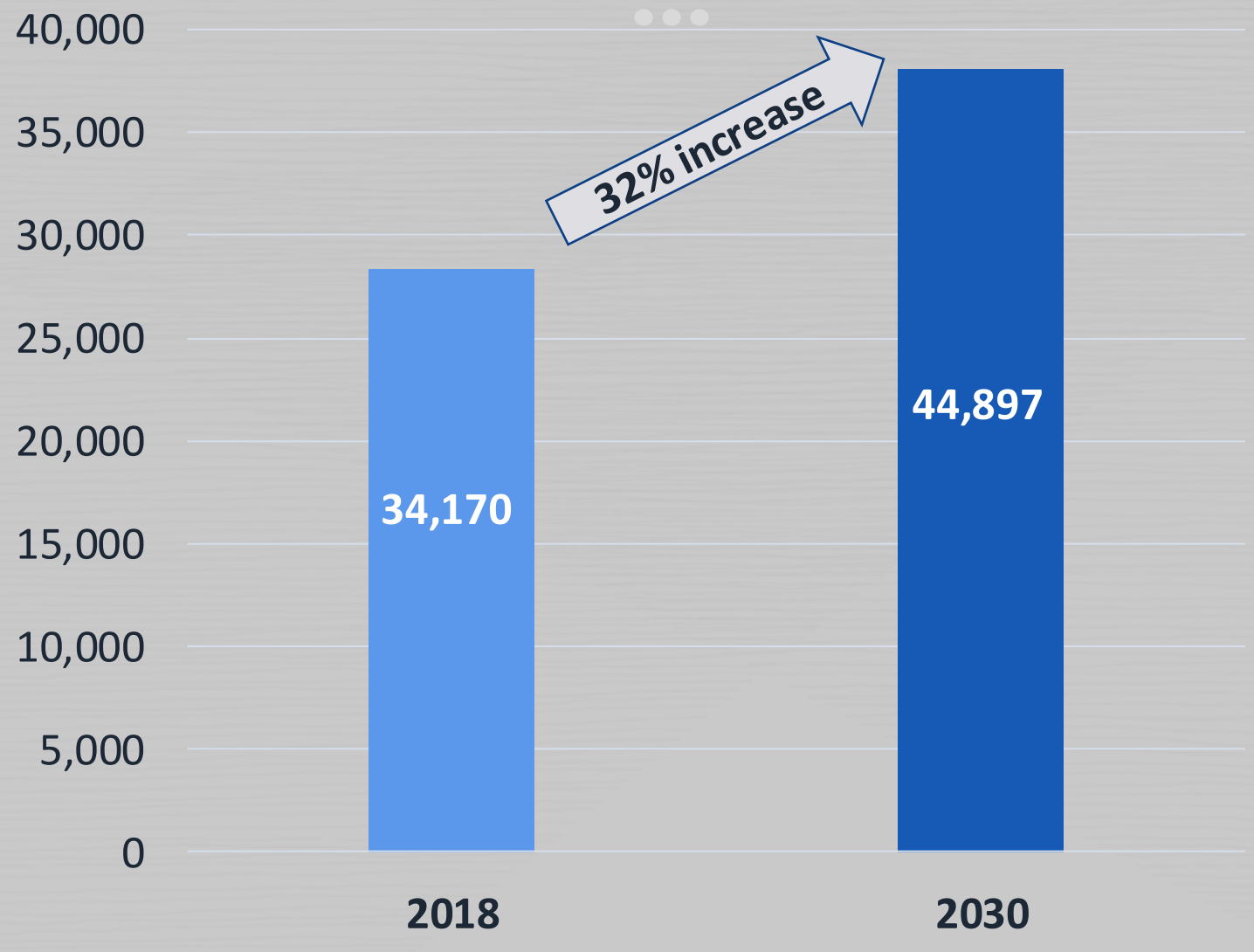
Mortality rates are highest in the **Caribbean,** where access to cancer treatment continues to be a challenge

Women living in vulnerable conditions have higher rates of cervical cancer

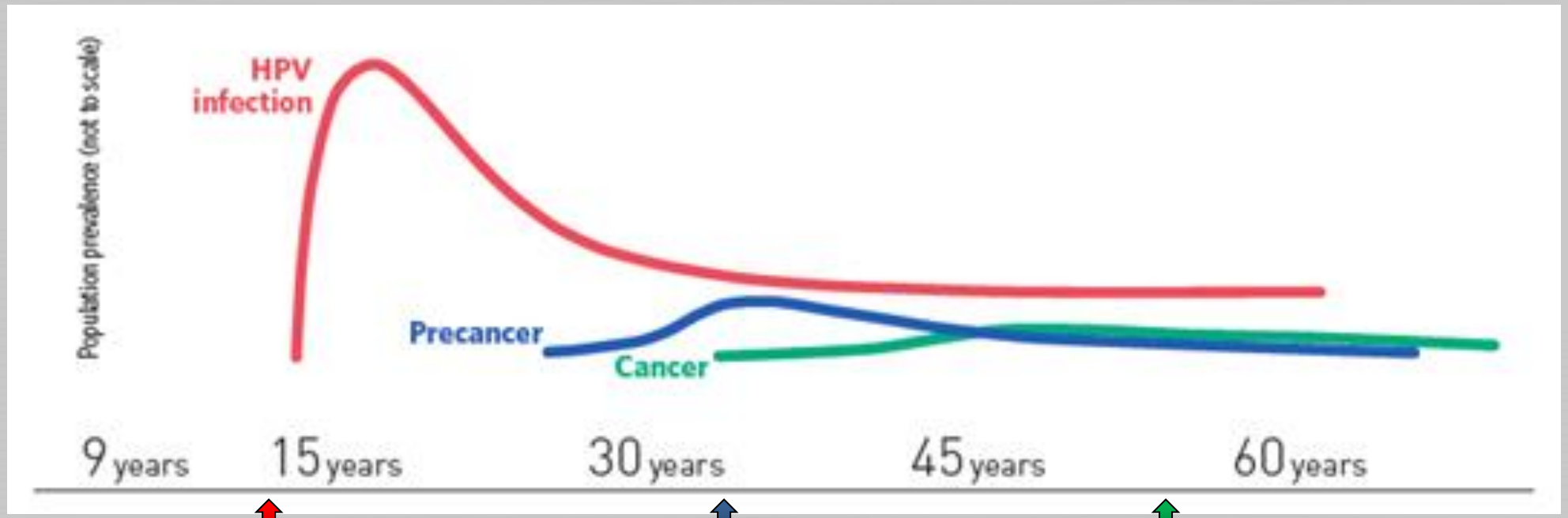
Women with HIV are at higher risk of developing cervical cancer

PAHO

PROJECTIONS IN CERVICAL CANCER MORTALITY IN THE AMERICAS



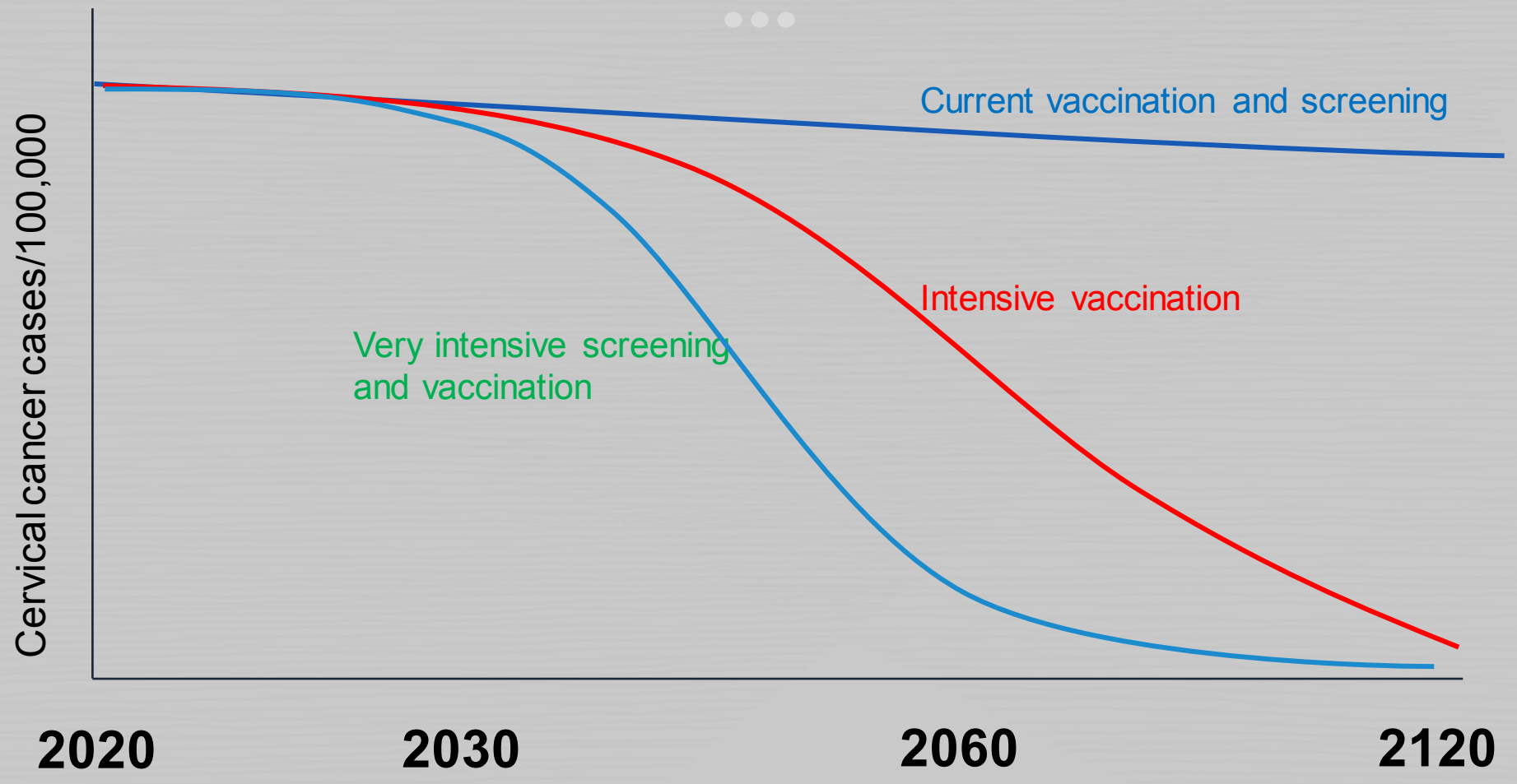
Comprehensive Cervical Cancer Control



HPV VACCINATION	SCREENING AND PRE-CANCER TREATMENT	CANCER DIAGNOSIS, TREATMENT, PALLIATIVE CARE
Girls 9-14 years	Women >30 years	All women as needed

Source: WHO, Comprehensive Cervical Cancer Control, 2014

Cervical Cancer Elimination: Conceptual Framework



PAHO

ELIMINATING CERVICAL CANCER

VISION: A world without cervical cancer

cervical cancer incidence < 4/100,000 women

HPV VACCINATION	SCREENING	TREATMENT
90% of girls fully vaccinated with HPV vaccine by 15 years of age	**70%** of women screened with an HPV test at 35 and 45 years of age	**90%** of women screened positive receive treatment for precancerous lesion or invasive cancer

CERVICAL CANCER SCREENING TESTS

Cervical Cancer Screening

Molecular

A. Nucleic Acid tests (NAT)
   - HPV DNA

   (e.g. Abbott, Roche Cobas, Qiagen, Cepheid Xpert, others)
   - mRNA

   (Hologic Aptima)

B. Protein biomarkers
   - HPV antibodies
   - Oncoproteins

   (e.g. OncoE6 / QIAsure)

Cytologic

A. Conventional PAP smear

B. Liquid-based cytology (LBC)

Visual Inspection

A. Visual Inspection with Acetic Acid or with Lugol Iodine (VIA / VILI)

B. Digital Imaging Approaches
   - i.e. Automated visual evaluation (AVE)

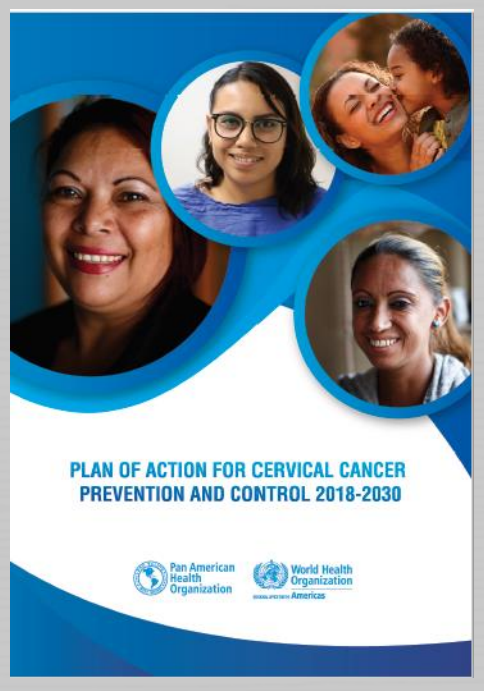
Move Toward High Performance Tests

Complex or Low-Sensitivity	High Performance Alternatives

Cytology:
Successful in high-resource countries, but implementing quality cytology screening is challenging in middle and low resource countries
 	
VIA:
Naked eye visual inspection with 3-5% acetic acid
	• **HPV Testing**
	  • **No triage**
	  • Followed by treatment with cryotherapy or thermal ablation
	
	• **HPV Testing**
	  • **Plus triage with Pap, VIA or other tests**
	  • Followed by treatment with cryotherapy or thermal ablation

PAHO Plan of Action for Cervical Cancer Prevention and Control

Goal: Reduce incidence and mortality rates by one-third by 2030



1. Improve cervical cancer program organization and governance, information systems, and cancer registries.
2. Strengthen primary prevention through information, education, and HPV vaccination.
3. Improve cervical cancer screening and precancer treatment through innovative strategies.
4. Improve access to services for cancer diagnosis, treatment, rehabilitation, and palliative care.

Develop the National Cervical Cancer Elimination Plan

Political and technical commitment

Empowered program manager and multi-disciplinary committee

Current situation assessment

National elimination plan, with goals, targets and resources

Updated guidelines

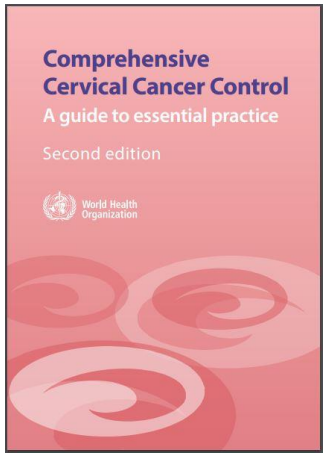
Training of health providers and lab personnel

IEC activities

Information system to monitor targets

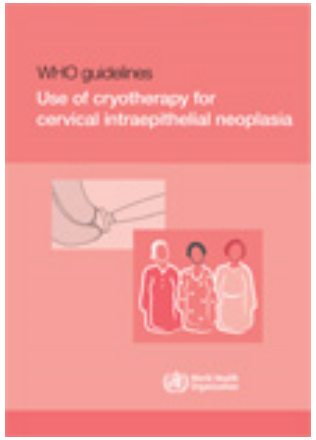
GUIDANCE TOOLS

www.paho.org/cancer

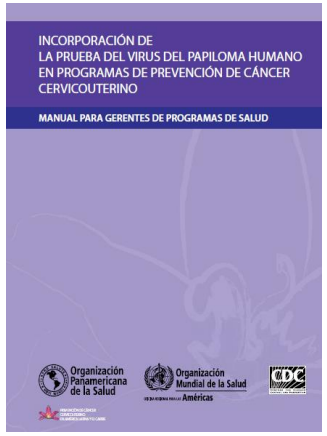


Cervical Cancer Guide

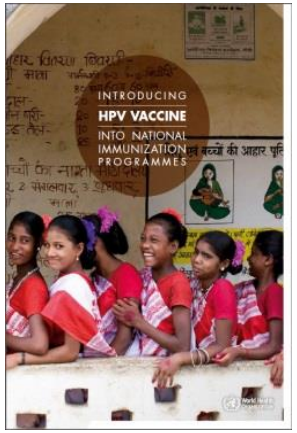
Screen & Treat Guide



Cryotherapy Guide



HPV Testing Guide



HPV Vaccine Guide

HPV Vaccine Communication

Strategic Fund + Revolving Fund

HPV vaccines

HPV tests:

Xpert HPV, Abbott RealTime High Risk HPV, CareHPV

Essential Cancer medicines

Morphine and palliative care medications

PAHO/WHO

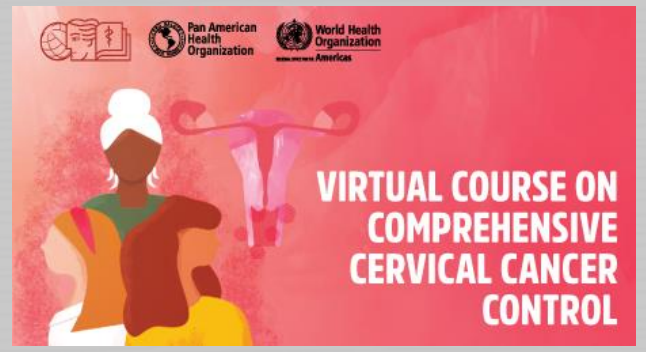
IT'S TIME TO END CERVICAL

Communication Materials + Virtual Course

www.paho.org/cancer

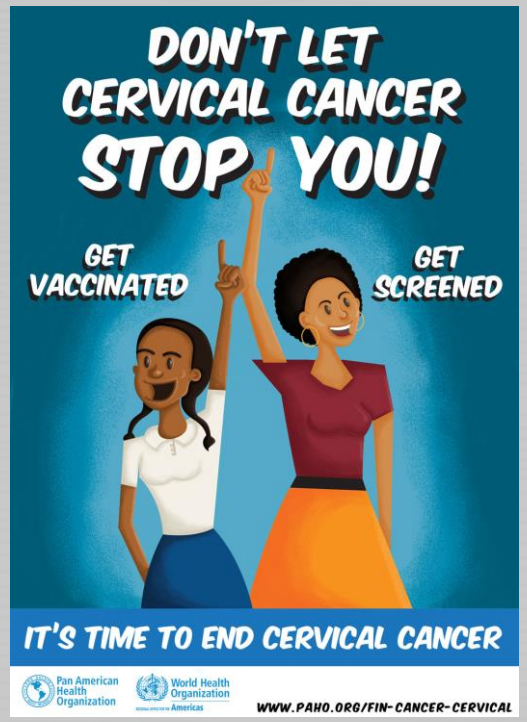
Campaign materials

Video



Virtual course

Factsheets



Poster

PAHO

HPV Vaccination: Towards the Elimination of Cervical Cancer in the Caribbean Countries

PAHO's Revolving Fund Update on HPV Vaccines

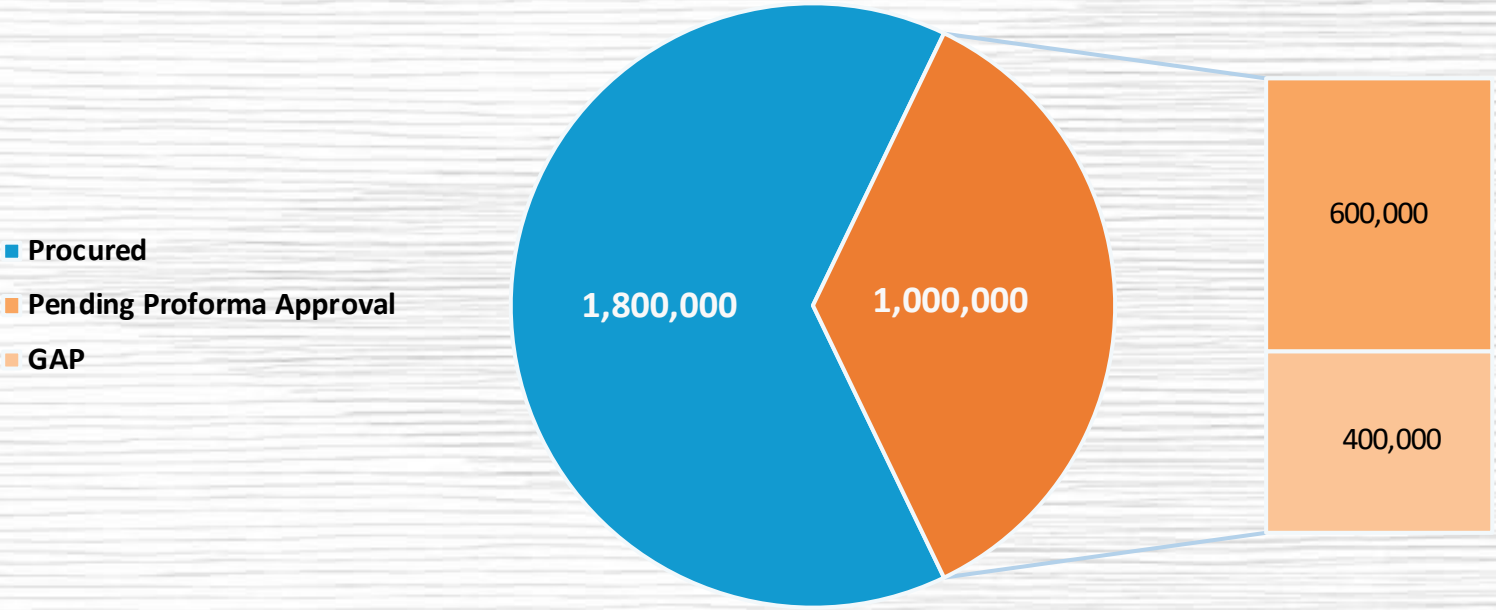
22 October 2020

Pan American Health Organization
World Health Organization
Americas
PAHO

Agenda

- Introduction
- Review of Regional Demand and Supply
  - Transitions from Bivalent to Quadrivalent Vaccine - 2019
  - Vaccine Uptake in the Caribbean - 2020
  - Country Stock Reach Q4 - 2020
  - Managing demand/supply in a constrained environment (PAHO/Merck) - 2020
  - Projected Demand 2021
- HPV Market Perspective
  - Constrained market conditions continue
  - Careful and reliable planning
- Next Steps?

HPV: Regional Demand vs Supply, October 2020



Total Demand 2020: 2.8 M Doses

2020 and 2021: Manufacturer keeps projecting maximum availability of 2.5 M ds / year

2021 DEMAND: 4 M ds (Includes 1.1 M ds from Mexico)

HPV: Summary of Demand vs Procurement 2020

Country	TOTAL HPV PROCURED 2020 (as of 20 Oct)	Total Demand PAHO 173 - 2020	Annual Requirements	Monthly Requirements	DELIVERY SCHEDULE					
					Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20
Anguilla *	0	0	264	22						
Antigua and Barbuda	4,000	4,000	2,308	192						4,000
Bahamas	15,000	15,000	15,152	1,263					7,500	
Barbados	3,000	5,000	5,000	417						2,000
Bermuda	500	500	606	51		500				
British Virgin Islands *	1,600	2,653	2,004	167						
Cayman Islands	600	1,000	1,000	83				600		500
Dominica	2,000	5,000	1,895	158			2,000			
Sint Maarten	200	200	600	50						
Grenada	0	0	1,900	158						
Jamaica *	8,000	0	30,612	2,551						8,000
Montserrat *	0	300	300	25						
Saint Kitts and Nevis	2,180	2,180	2,500	208		2,180				
Saint Lucia	5,000	5,000	5,556	463				5,000		
Saint Vincent and the Grenadines *	5,000	5,000	5,622	469						
Suriname *	25,000	25,200	18,000	1,500						
Trinidad and Tobago	25,000	51,000	105,263	8,772				25,000		41,000
Turks and Caicos *	600	470	1,000	83				600		
TOTAL CARIBBEAN	97,680	122,503								
TOTAL OTHER COUNTRIES	1,715,190	2,681,522								
GRAND TOTAL	1,812,870	2,804,025								

*Transitioned countries
Anguilla, BVI, Jamaica, Suriname, St. Vincent, Turks and Caicos
(Not sure about Monserrat: Procured bivalent until 2017. After that, nothing in 2018 and then, quadrivalent from 2019)

TOTAL REGIONAL DEMAND 2020: 2.8 M DOSES

Price Estimate in process

Pan American Health Organization
World Health Organization
Americas
PAHO

HPV: PROJECTED STOCK REACH 2020

Country	Projection Stock On Hand June-2020 (Source: PAHO- 173)	STOCK REACH PROJECTION (MONTHS) *						
		Jul-20	Aug-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20
Anguilla	246	10	9	8	7	6	5	4
Antigua and Barbuda	6,545	33	32	31	30	29	49	48
Bahamas	2,900	7	6	5	4	9	8	7
Barbados	4,549	10	9	8	7	6	10	9
Bermuda	54	0	9	8	7	6	5	4
British Virgin Islands	1,600	9	8	7	6	5	4	3
Cayman Islands	750	8	7	6	12	11	16	15
Dominica	135	0	-1	12	11	10	9	8
Sint Maarten	465	8	7	6	5	4	3	2
Grenada	2,280	13	12	11	10	9	8	7
Jamaica	14,500	5	4	3	2	1	3	2
Montserrat	88	3	2	1	0	-1	-1	-1
Saint Kitts and Nevis	421	1	10	9	8	7	6	5
Saint Lucia	463	0	-1	-1	10	9	8	7
Saint Vincent and the Grenadines	5,000	10	9	8	7	6	5	4
Suriname	6,460	20	19	18	17	16	15	14
Trinidad and Tobago	27,000	2	1	0	2	1	5	4
Turks and Caicos	353	3	2	1	7	6	5	4

- **Information of Stock on hand and Stock Reach Projections: For countries validation**

PAHO: HPV DEMAND SCHEDULE UPDATE (as of 13 October 2020)

CARRY-OVER 2019		
COUNTRY	QTY (ds)	PO
Paraguay	121,000	APO19-00032039
El Salvador	29,700	APO19-00032077
Panamá	150,000	APO19-00032046
Total Carry-Over	300,700	

13-Mar-20 MERCK SUPPLY PLAN

	20-Jan	20-Feb	20-Mar	20-Apr	20-May	20-Jun	20-Jul	20-Aug	20-Sep	20-Oct	20-Nov	20-Dec	TOTAL
GARDASIL Spanish Label		160,000	475,000	350,000	0	600,000	0	50,000	460,000	185,000	134,200	0	2,414,200
GARDASIL English Label	5,000	1,400	18,000	10,600	20,000	0	0	-	-	20,000	10,800	0	85,800
Calculation by Quarter	659,400			980,600			510,000			350,000			2,500,000
RECONFIRMED DEMAND PLAN	1,194,758			841,326			379,982			276,756			2,692,822

Quarter	Q1	Q2	Q3	Q4
Qty Available Merck (ds)	659,400	980,600	510,000	350,000
Balance Previous Quarter (ds)	0	313,080	333,440	543,840

PAHO ALLOCATIONS	Q1	Q2	Q3	Q4		
PRICE ESTIMATES	0	0	20,000	64,870	380,540	
PROCURED	346,320	960,240	279,600	185,610	0	0
TOTAL	346,320	960,240	299,600	631,020		
BALANCE	313,080	333,440	543,840	262,820		

TOTAL DEMAND 2020	TOTAL SUPPLY 2020 (As per Merck information)			
2,692,822	2,500,000			
	ISSUED ORDERS 2020 (as of 12 Oct) *	1,771,770	PENDING ALLOCATION / POs ISSUANCE	728,230

*Includes Orders in process for Belize and Bolivia

2021 PROJECTED DEMAND: UP TO 4 MILLION DS

Pan American Health Organization / World Health Organization Americas — PAHO

HPV WHO-PREQUALIFIED MARKET OUTLOOK
October 2020

Manufacturer	Country of Origin (NRA)	Commercial Name	Number of Doses per Vial	Schedule Requirement per person	Strains	WHO PQ Status	Shelf Life at Production	MDVP Applicable	Cold Chain Volume cm3/dose	Cold Chain Implications	Remarks
GSK	Belgium	Cervarix	1 dose vial	2 doses	HPV-16/18	Prequalified in 2009	60 months	Not Relevant	a)57.7 (Carton 1 vial); b)11.5 (Carton 10 vial); c)9.7 (Carton 100 vial)	2-8°C Storage	
			2 dose vial			Prequalified in 2009	60 months	No	a)28.8 (Carton 1 vial); b)5.7 (Carton 10 vial); c)4.8 (Carton 100 vial)		
Merck	EMA (UK)	Gardasil	1 dose vial		HPV-6/11/16/18	Prequalified in 2009	36 months	Not Relevant	a)74.7 (Carton 1 vial); b)15 (Carton 10 vial);	2-8°C Storage	
Merck	EMA (UK)	Gardasil 9	1 dose vial		HPV-6/11/16/19/31/33/45/52/58	Prequalified in 2018	36 months	Not Relevant	a)18.4 (Carton 10 single vials for UNICEF Supply); b)15.11 (Carton of 10 vials for PAHO Supply);	2-8°C Storage	
SHORT-TERM PIPELINE WHICH REACHED PHASE 2 CLINICAL TRIALS											
Xiamen Innovax	China		1 dose vial	3 doses	Bivalent	Licensed in China.					Prequalification can be expected in 2021.
Walvax	China		1 dose vial	3 doses	Bivalent	Phase 3 Clinical Trial					Prequalification can be expected in 2021 or 2022.
Serum Institute of India	India		1, 2 and 5 dose vial	2 or 3 doses	Tetravalent	Phase 3 Clinical Trial					Prequalification can be expected in 2021 or 2022.
CNBG Shanghai	China		1, 3 and 5 dose vial	3 doses	Tetravalent	Phase 3 Clinical Trial					Prequalification can be expected in 2022 or later.
Being Health Guard	China					Phase 2 Clinical Trial					
Bioleaders Corp	South Korea					Phase 2 Clinical Trial					
Janssen	USA					Phase 2 Clinical Trial					

HPV Vaccine: Overview of Global Supply and Demand

- Global supply is expected to be not sufficient to meet the global demand at least until 2023 (and then only with tight management and careful planning)
- Several Gavi eligible and self-financing countries had to postpone HPV vaccine introductions and multi-age cohort campaigns.
- Factors that could affect demand/supply balance
  - Increase in projected capacity does not materialize timely and in the expected size
  - Increase in global demand
  - Pipeline products do not reach market (or PQ) as forecasted
  - Prioritization of 9 valent production at the expense of UN market products
  - Additional developed countries extend immunization to boys and manufacturers prioritizing more profitable markets
  - Country introductions and coverage increases do not occur as planned

Next Steps

- Review demand projections by country for 2021
- Request updated national inventories information with reconfirmation demand process for Q1-Q2 2021
- Negotiations with supplier for 2021 underway
- Suggest placing Q1 2021 orders before end Dec 2020
- Other issues?


Thank you!

EXTRAS

HPV: Summary of Estimated Demand & Procured Doses, 2019

Oountry	Annual Requirements (PAHO 173-2019)	Monthly Requirements (PAHO 173-2019)	Total Demand (Purchase Plan PAHO 173 - 2019)	Jan-19	Feb-19	Mar-19	Apr-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19	TOTAL HPV PROCURED 2019
Anguilla	260	22	370												400	400
BVI *	700	58	0					1,400								1,400
Jamaica **	37,800	3,150	32,500	10,000							20,000					20,000
Suriname	10,500	875	11,400					10,500								10,500
St. Vincent	1,995	166	1,995													0
Turks and Caicos ***	625	52	190		600					190		300				490
			46,455													32,790

*British Virgin Islands: HPV Introduction in 2019. 1,400 ds planned in 2018 were purchased in 2019 (order issued under agreement extension until March 2019)

**Jamaica: 10K ds HPV Bivalent placed in late 2018 before supply agreement expiration (includes remaining balance of 400 prepaid ds)

** Turks and Caicos: Last order HPV2 (600 ds), issued in Dec 2018 and received in Feb 2019. Vaccine received in 2019 was HPV4 (490 ds)

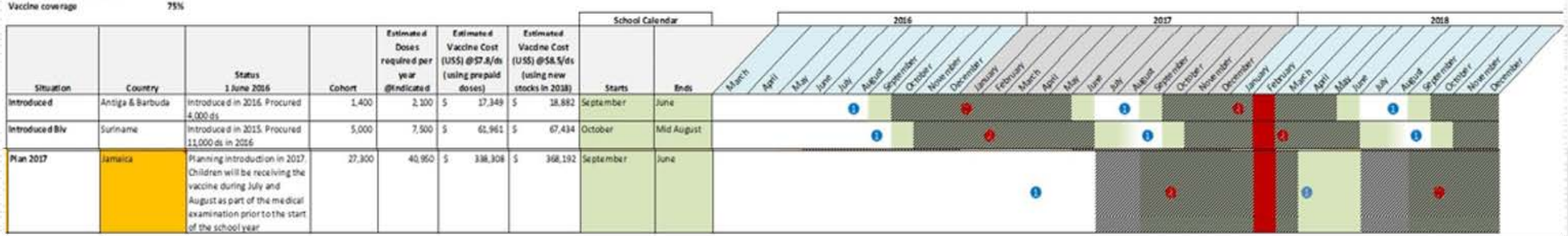
School Calendar 2016-2018
Pending update up to 2021

School Calendar and HPV vaccination in some countries in Latin America and The Caribbean

Timeline 2016 -2018

Vaccine coverage 75%

Situation	Country	Status 1 June 2016	Cohort	Estimated Doses required per year @indicated	Estimated Vaccine Cost (US$) @$7.8/ds (using prepaid doses)	Estimated Vaccine Cost (US$) @$8.5/ds (using new stocks in 2018)	School Calendar Starts	School Calendar Ends
Introduced	Antiga & Barbuda	Introduced in 2016. Procured 4,000 ds	1,400	2,100	$ 17,349	$ 18,882	September	June
Introduced Biv	Suriname	Introduced in 2015. Procured 11,000 ds in 2016	5,000	7,500	$ 61,961	$ 67,434	October	Mid August
Plan 2017	Jamaica	Planning introduction in 2017. Children will be receiving the vaccine during July and August as part of the medical examination prior to the start of the school year	27,300	40,950	$ 338,308	$ 368,192	September	June
	Anguilla	PENDING INFORMATION						
	BVI							
	St. Vincent							
	Turks and Caicos							



Pan American Health Organization
World Health Organization
Americas

PAHO

HPV Vaccine: PRICES

		PRICE/DOSE (US$)			
Manufacturer	**Pharmaceutical form**	**2017**	**2018**	**2019**	**2020**
GSK	Liquid: Ready to use	7.80 (I)	8.50	8.50	N/A
Merck	Liquid: Ready to use	9.80	9.58	9.58 (II)	9.98

(I) 2017: HPV Bivalent, Pre-paid doses , Price/dose: $8.50 - $0.70 discount

(II) 2019: HPV Quadrivalent, Price/dose: $9.98 – $0.40 discount

DAY 2

October 23 - Day 2 Session 2: Screening and Treatment of Cervical Cancer Moderator: Silvana Luciani		
10:00–10:20	HPV Testing for Cervical Cancer Screening and program monitoring	Nathalie Broutet - WHO
10:20 –10:35	Screening and Treatment in Women Living with HIV	Bernardo Nuche - PAHO
10:35–11:05	Screening and precancer treatment experience and challenges: Trinidad & Tobago: results of pilot project on HPV testing Bahamas: challenges to incorporating HPV testing into the screening program	Moira Lindsay, PSI Caribbean Dr. Phillip Swan, Bahamas
11:05–11:35	Opportunities to improve cancer treatment: - how cancer care was improved in Jamaica - how Antigua and Barbuda's cancer center is creating shared services in the Caribbean	Dr. Nadine Badal, Jamaica Mr. Henry Hazel - Cancer Centre Eastern Caribbean Antigua &Barbuda
11:35- 12:00	Discussion	

HPV testing for cervical cancer screening and program monitoring

World Health Organization

Dr Nathalie Broutet

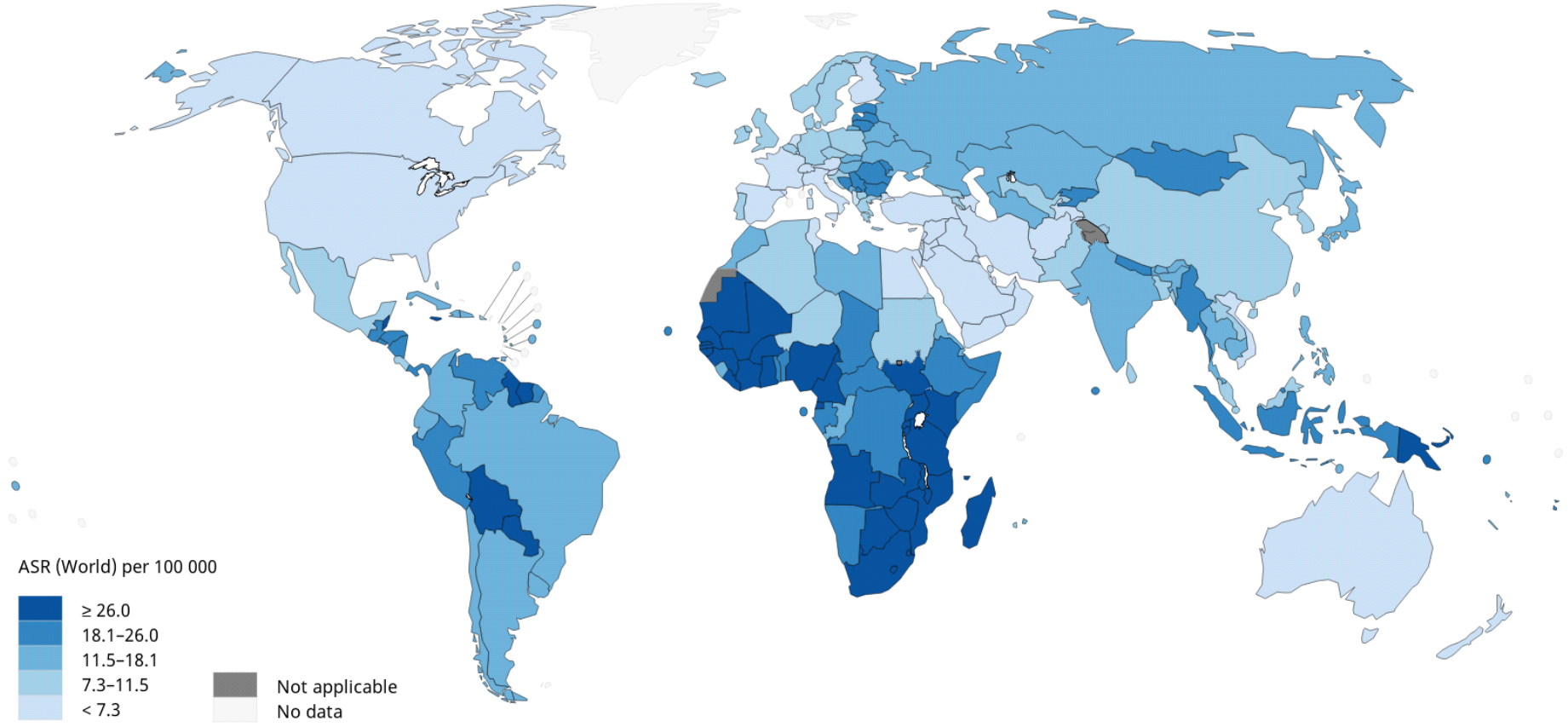
Sexual and Reproductive Health and Research Department

human reproduction programme hrp
research for impact
UNDP · UNFPA · UNICEF · WHO · THE WORLD BANK

The Growing Inequities in Cervical Cancer

Cervical Cancer Incidence Rates (Globocan 2018)

Estimated age-standardized incidence rates (World) in 2018, cervix uteri, all ages



World Health Organization

19 August 2020

The 73rd World Health Assembly adopted of the draft Global Strategy to accelerate the elimination of cervical cancer as a public health problem.

Photo credit: Chris Black

World Health Organization

Proposed Elimination Threshold and Targets

Threshold for Elimination as a Public Health Problem:
Age-adjusted incidence rate < 4 / 100,000 women

2030 Targets

90%
of girls fully vaccinated with HPV vaccine by 15 years of age

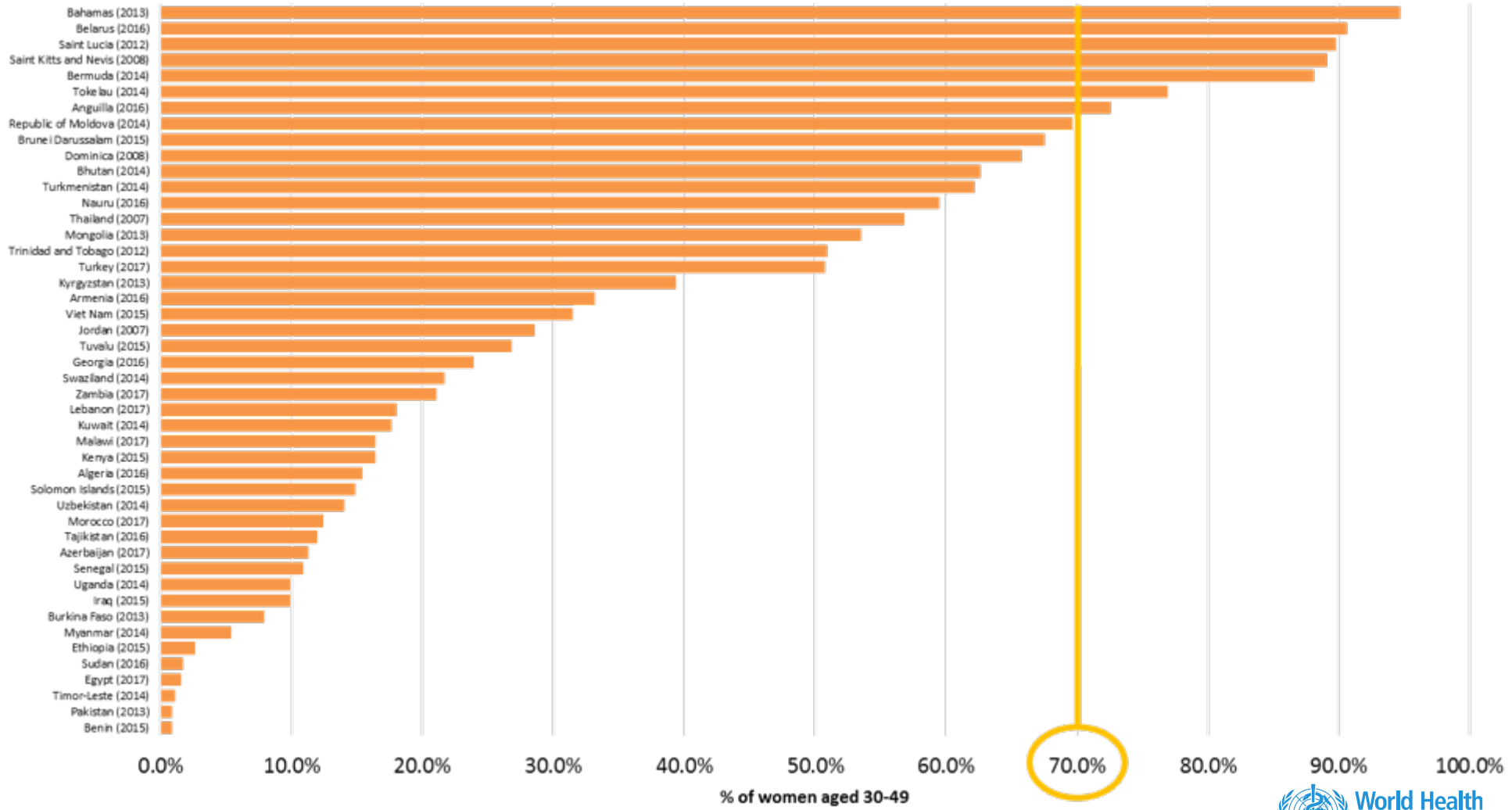
70%
of women are screened with a high-performance test by 35 and 45 years of age

90%
of women identified with cervical disease (precancer or cancer) receive treatment and care

SDG 2030 Target 3.4:
30% reduction in mortality from NCDs

World Health Organization

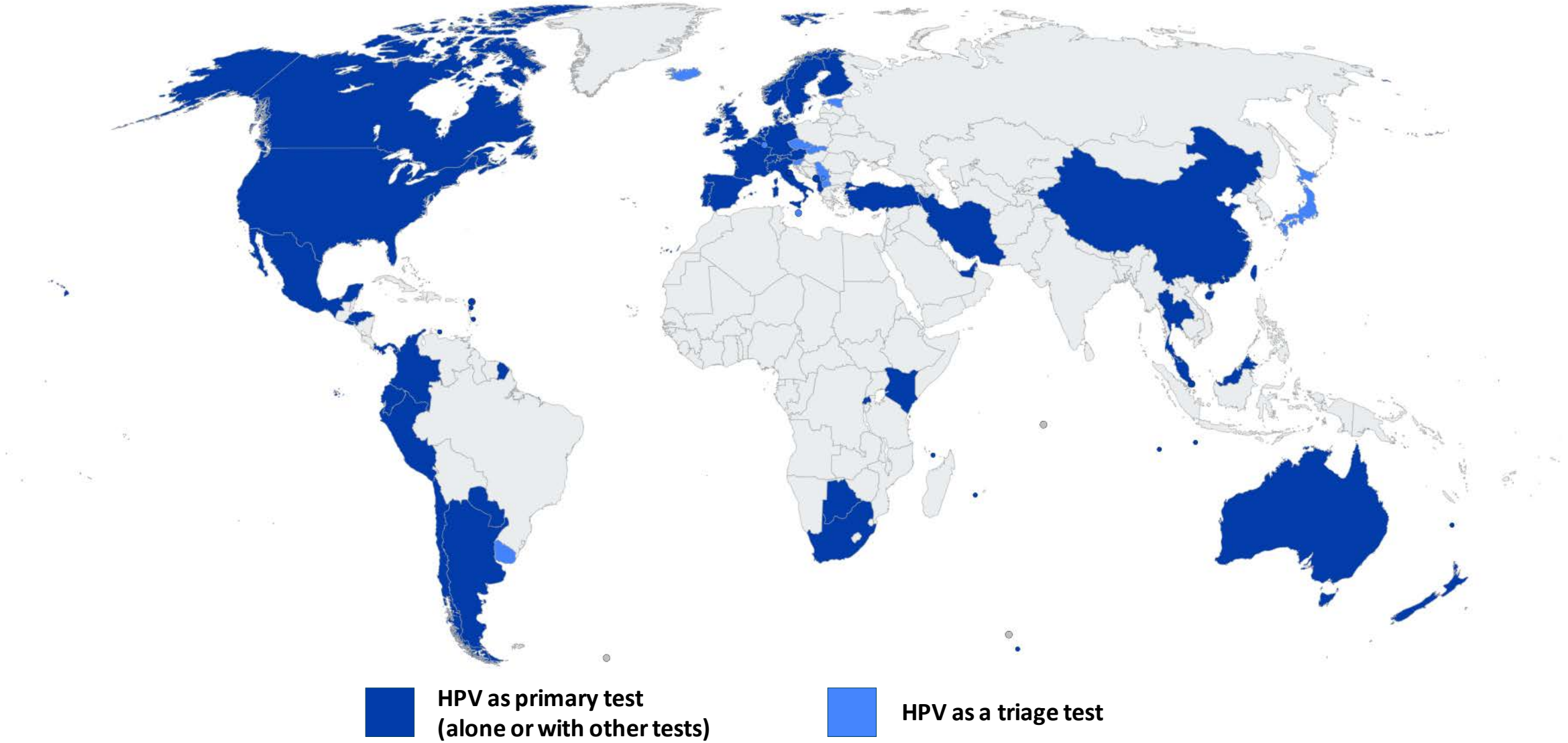
Proportion of Women Between 30-49 Screened for Cervical Cancer At Least Once



Source: WHO STEPS

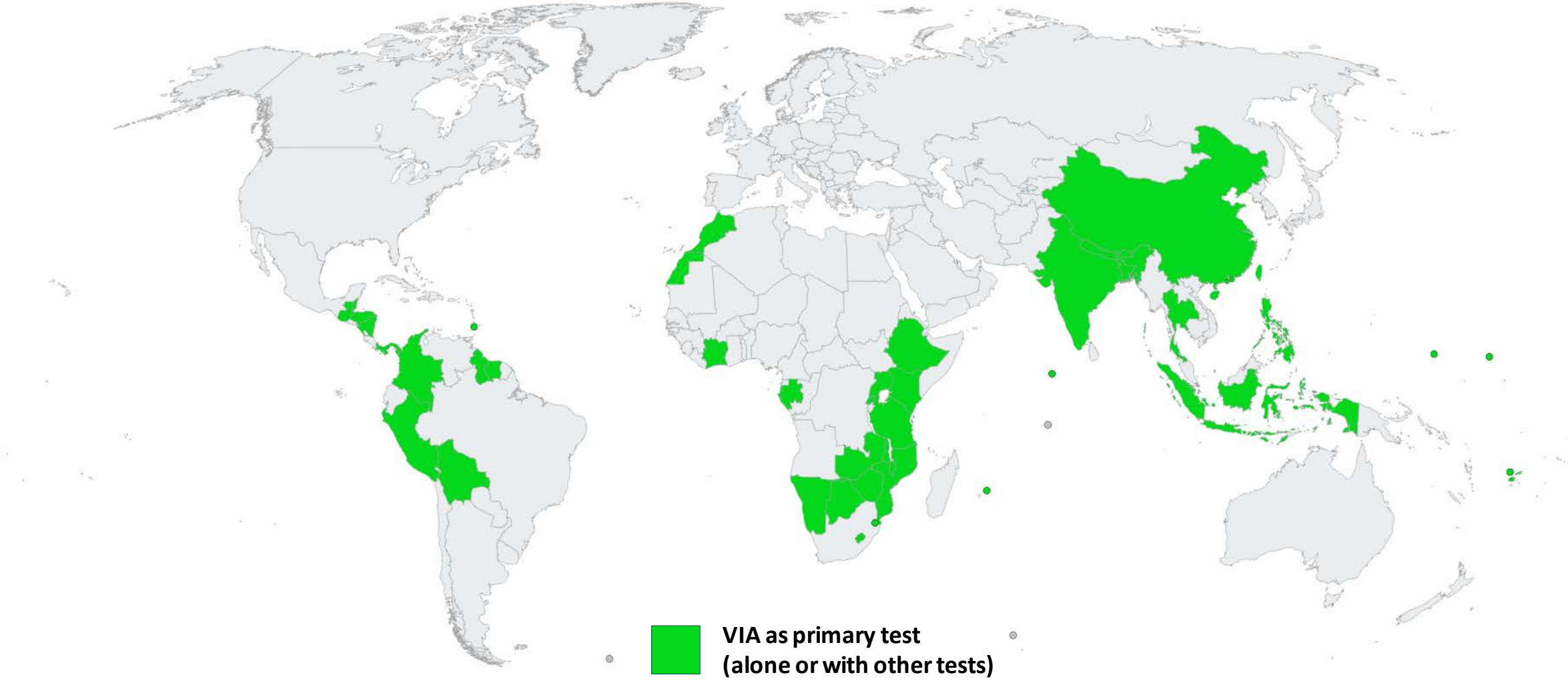
World Health Organization

OFFICIAL USE OF HPV TESTING IN CERVICAL CANCER SCREENING (preliminary results)



Cancer Epidemiology Research Program, Institut Català d'Oncologia (ICO), IDIBELL (Barcelona, Spain). ICO/IARC Information Centre on HPV and Cancer: www.hpvcentre.net - WHO

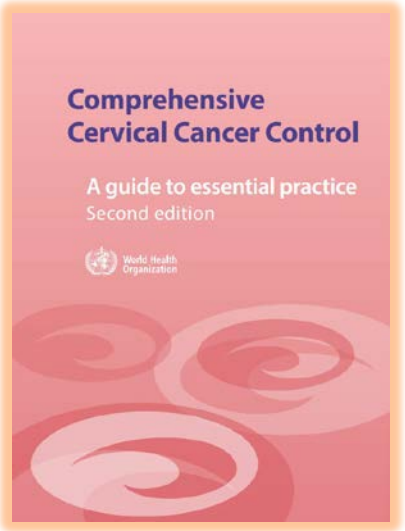
OFFICIAL USE OF VIA TESTING IN CERVICAL CANCER SCREENING (preliminary results)



Cancer Epidemiology Research Program, Institut Català d'Oncologia (ICO), IDIBELL (Barcelona, Spain). ICO/IARC Information Centre on HPV and Cancer: www.hpvcentre.net - WHO

Increasing access to screening and treatment to prevent cervical cancer

Updated guideline on screening and treatment of pre-cancer lesions for the prevention of cervical cancer, including women with HIV



Approaches to Cervical Cancer Screening and Future Tests
3 approaches to Cervical Cancer Screening

Cervical Cancer Screening

Molecular

A. Nucleic Acid tests (NAT)
   - HPV DNA
     (e.g. Abbott, Roche Cobas, Qiagen, Cepheid Xpert, others)
   - mRNA
     (Hologic Aptima)

B. Protein biomarkers
   - HPV antibodies
   - Oncoproteins
     (e.g. OncoE6 / QIAsure)

Cytologic

A. Conventional PAP smear

B. Liquid-based cytology (LBC)

Visual Inspection

A. Visual Inspection with Acetic Acid or with Lugol's Iodine (VIA / VILI)

B. Digital Imaging Approaches
   - i.e. Automated visual evaluation (AVE)

Agreed list of algorithms (priority: 1-7)

1. **VIA followed by treatment**
2. **HPV DNA** (self or clinician) **followed by treatment**
3. **Cytology Ą colposcopy and treatment decision**
4. **HPV DNA Ą HPV 16/18** (only when already part of the HPV test) **and VIA triage**
5. **HPV DNA Ą VIA triage**
6. **HPV DNA Ą colposcopy triage**
7. **HPV DNA Ą cytology triage - colposcopy**

Tests identified by GDG now moved to living guidelines

- AVE, HPV DNA E6/e7, HPV methylation markers,

Summary from systematic review (draft)

- HPV as a primary screening test likely results in greater (or similar) reductions in cervical cancer and deaths (and CIN 3+ lesions) with fewer treatments compared to
- HPV may be more cost effective when provided as a screening test
- It is probably as acceptable to women and providers, as feasible and may improve equity compared t

To Accelerate Access We Need to Move Toward High Performance Tests

Complex or Low-Sensitivity	High Performance Alternatives

Cytology:
Successful in high-resource countries, but implementing quality cytology screening is challenging in middle and low resource countries
 	
VIA:
Naked eye visual inspection with 3-5% acetic acid
	• **HPV Testing**
	  • **No triage**
	  • Followed by treatment with cryotherapy or thermal ablation
	• **HPV Testing**
	  • **Plus triage with HPV 16/18, VIA or other tests**
	  • Followed by treatment with cryotherapy or thermal ablation

World Health Organization

New Recommendation on HPV Self-Sampling

HPV self-sampling should be made available as an additional approach to sampling in cervical cancer screening services for women aged 30–60 years.

Source:

WHO Consolidated Guideline on Self-Care Interventions for Health: *Sexual and Reproductive Health Rights*

World Health Organization

Implementation Recommendations

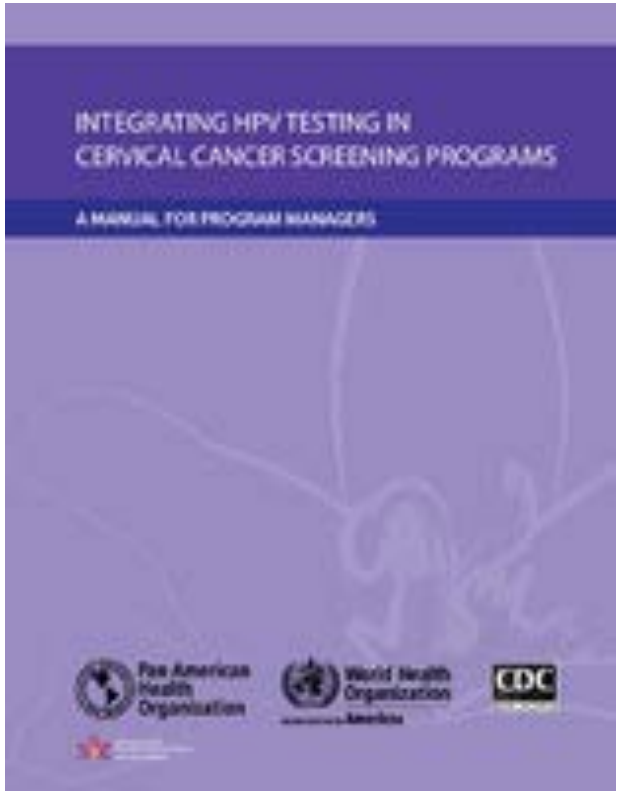
- What are the effects of health-system interventions to enable the adoption, implementation and scale up of effective screening approaches?
- What are the effects of patient-targeted strategies to support uptake of screening approaches and follow-up care?
- What are the effects of provider-targeted strategies to support the adoption of screening approaches and follow-up care?

Supporting introduction of HPV testing based strategy

- Tool to forecast global and national demand for HPV tests and treatments (with RPQ)
- **Guidance for programme managers and policy makers on implementation of screening and treatment for cervical cancer prevention as part of a Comprehensive National Cervical Cancer Prevention and Control Programme (modular format) (with IARC, NCD and IVB)**
- Tools for training of health and laboratory workers (with IARC and WHO Academy)
- Mapping of national coverage of screening and treatment services (with NCD / SMR)

- Establish governance and national committee of stakeholders
- ***How to introduce HPV tests for screening within a National Cervical Cancer Prevention and Control Programme (with RPQ and HHS)***
- Creating demand and advocacy for screening services
- Delivery of screening and treatment services, including through integration
- ***Costing tool for screening and treatment programme (w IVB)***
- Tool to monitor quality of screen & treat services

Integration of HPV testing in country programme



How to introduce HPV tests for screening within a National Cervical Cancer Prevention and Control Programme

How to guidance using a step by step approach

- Provide information on which test to choose
- Laboratory and quality control considerations
- How to plan logistical and practical aspects of HPV testing

Provide links to very specific and detailed guidelines for each of the aspect of the introduction

Highlight some country experiences

Scope of Guidance Document

Planning

- Stakeholder Engagement
- Information Gathering
- Screening Policy and Targets
- Build Delivery Model
- Review of Screening Capacity and Mapping of Services
- Program Costing and Resource Mobilization
- Product Selection

Rapid planning process

Implementation

- Implementation Roadmap
- Quality Management Systems Strengthening *including training and data management*
- Procurement Process
- Indicator Mapping

Expand services in phases

Monitoring and Scaling

- Implementation and Monitoring & Evaluation
- Adoption of Strategy

Learn as you go

There are currently only 3 Prequalified HPV tests

CareHPV™ (Qiagen)

GeneXpert™ (Cepheid)

Abbott RealTime High Risk HPV

https://www.who.int/diagnostics_laboratory/evaluations/pq-list/public_report_hpv/en/

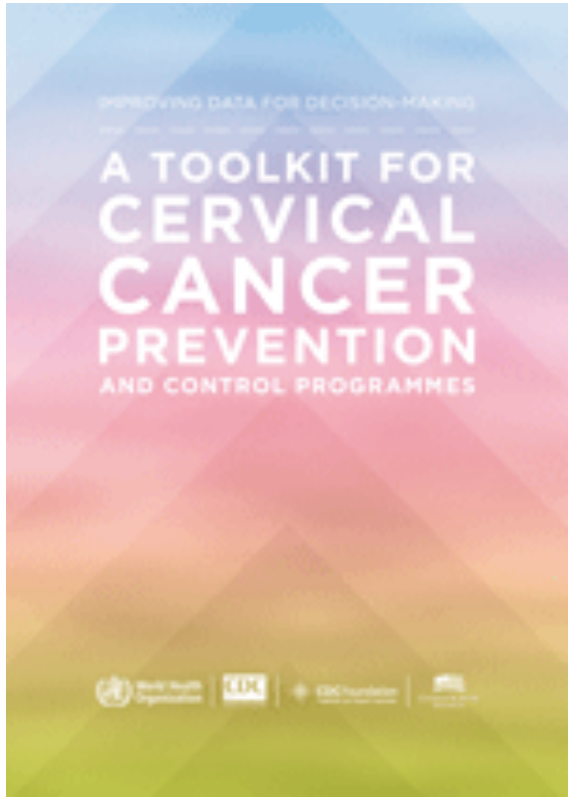
… and 2 under evaluation

Cobas 4800 HPV

Cobas HPV (for use on the Cobas 6800/8800 systems)

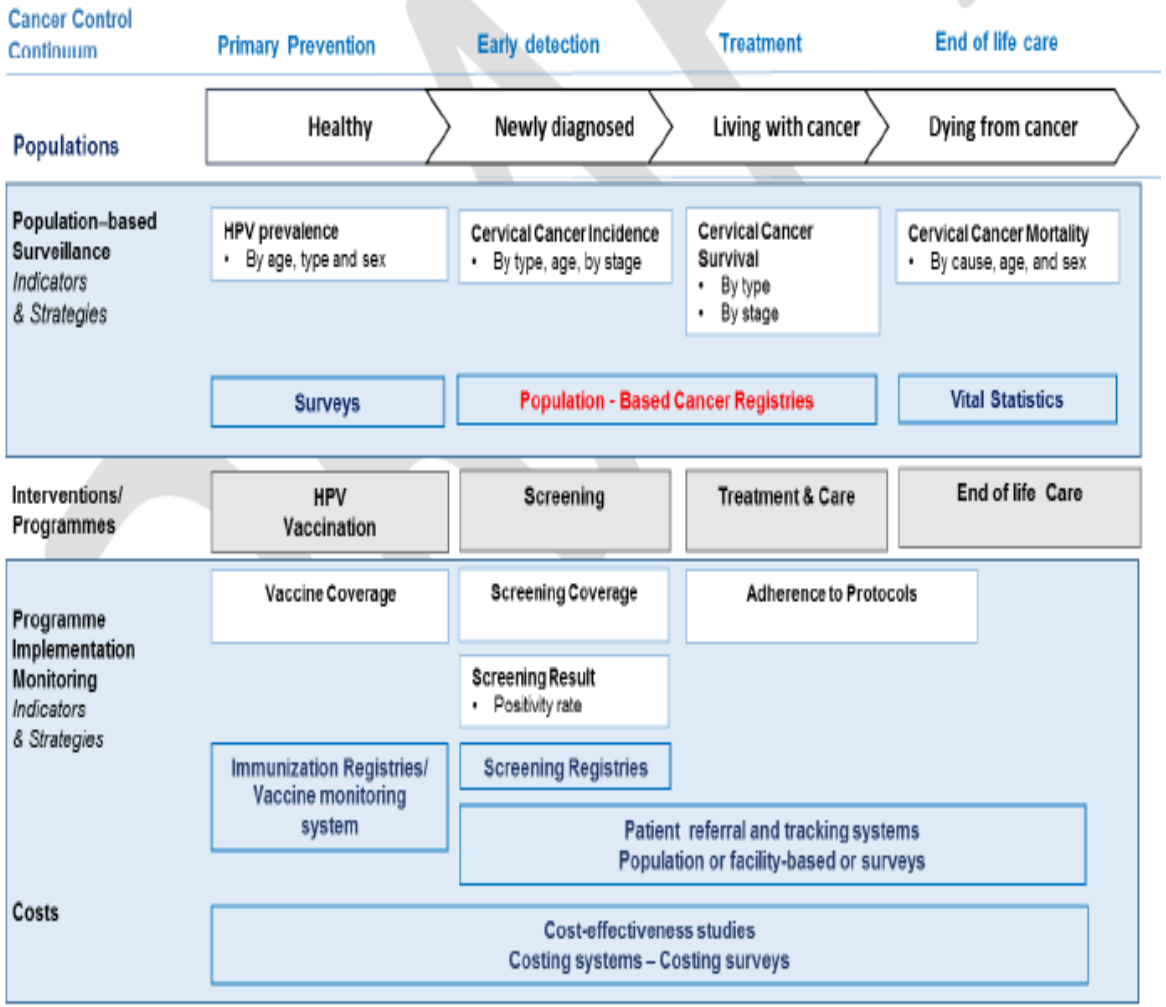
https://www.who.int/diagnostics_laboratory/hpv.pdf

Monitoring Framework to measure progress



- Review the current IDCCP tools – short modules
- Identify the gaps as per the agreed components of the surveillance and monitoring of the CCEI
- Ensure consistency with existing frameworks and tools
- Develop the framework for monitoring and evaluation of CCEI

Fig 10. Surveillance and monitoring for the elimination initiative



SECTION 1: RAPID SITUATIONAL ASSESSMENT OF DATA AND DATA SYSTEMS

How to identify opportunities for strengthening country data and data systems?

SECTION 2: POPULATION-BASED SURVEY MODULES

How to measure population coverage of cervical cancer screening and secondary prevention?

SECTION 3: PATIENT AND PROGRAMME MONITORING

How to routinely monitor patients and programs?

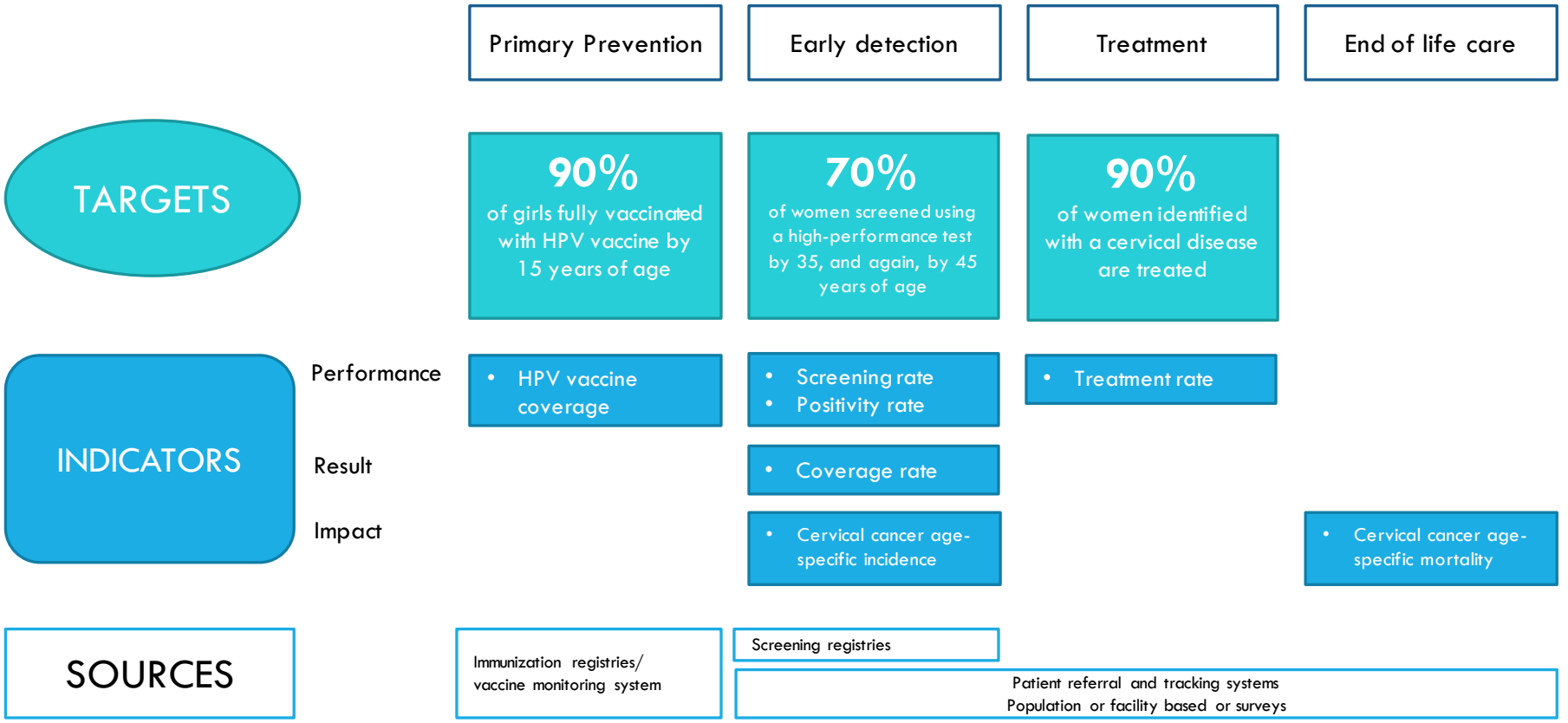
SECTION 4: FACILITY-BASED SURVEYS

How to survey facilities for service readiness, service availability, service quality?

SECTION 5: PREVENTION AND CONTROL COSTING

How to estimate costs of cervical cancer screening & treatment programs?

DRAFT FRAMEWORK FOR MONITORING AND EVALUATION OF THE CCEI



STRATEGIC ACTIONS FOR MONITORING AND EVALUATION

Strengthen governance and accountabilityof cervical cancer related programmes

Set country-specific targets, milestones, and indicators for monitoring and evaluating the National Cervical Cancer Elimination Programme.

Develop or improve population-based cancer registries to inform National Cervical Cancer Elimination Programmes and help track progress towards the goal of elimination.

Track patients throughout the continuum of services to ensure that women and girls in need are being successfully treated

Work towards disaggregation of data by equity stratifiers to enable detection of differences across population segments and set equity-oriented targets.

Achieving 70% Coverage of Screening and 90% Treatment of Precancer: Strategic Actions

- **National scale-up of screen & treat**
  - **Simple algorithms need to be introduced for different settings**
- **Sufficient, affordable supply of screen and treat technologies & products**
  - Prompt certification of new products
  - Price reductions
- **Increased quality and coverage of service delivery**
  - Countries detailed implementation plans to introduce and scale-up products and delivery models
  - Strengthen patient retention and linkage to treatment
- **Monitor progress**

World Health Organization

Quotes from Women

"In my country, there is no national program. Limited services in the public sector are free, in private sector are paid."

"If it is possible to have less intrusive diagnostic this would make it bearable. Also more information on possible side effects from the screening such as bleeding and discomfort should be given ahead of time in great detail as well as methods of reducing the discomfort"

Acknowledgements

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- Ahmadaye Ibrahim Khalil
- Iacopo Baussano

World Health Organization

The importance of cervical cancer screening and treatment in women living with HIV

Bernardo Nuche-Berenguer, MPH, Ph.D.

Pan American Health Organization

HPV Vaccination. Towards the Elimination of Cervical Cancer in the Caribbean Countries

23 October 2020

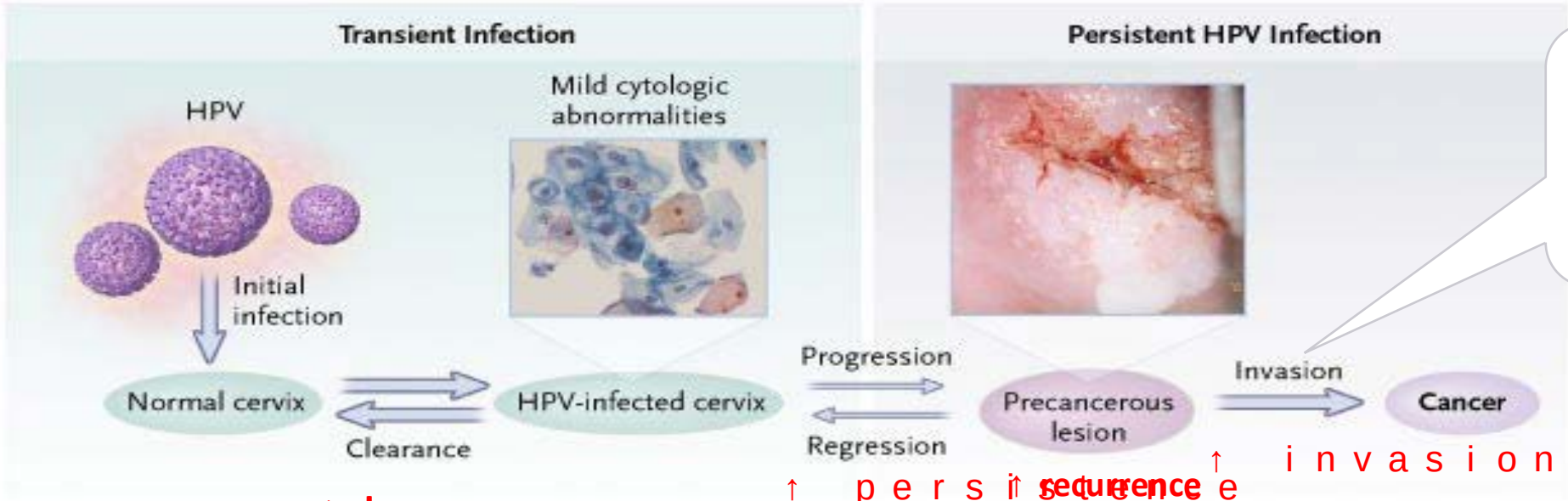
Pan American Health Organization
World Health Organization
Regional Office for the Americas

PAHO

Outline

- Epidemiological situation of HIV and of HPV/cervical cancer among WLHIV
- WHO recommendations for cervical cancer screening and treatment for WLHIV
- Lessons learned with the HIV response and opportunities for integration
- Regional next steps

Synergistic effects of HPV carcinogenic effect and HIV infection



Cervical cancer in an AIDS defining illness, (CDC-1993)

HIV/ AIDS

↑ **HPV acquisition**

↓ **clearance**

↑ **persistence**

↑ **progression**

↓ **regression**

↑ **recurrence after tx**

↑ **invasion**

Postulated mechanisms for the high burden of HPV in women living with HIV:

- Loss of control of the immune system
- Latent viral reactivation with immunosuppression / modulation / reconstitution
- Viral-viral interaction between HIV-HPV
- Correlated risk behaviors (↓ condom use, ↑ number of sexual partners)

Source: *Wright ,N Engl J Med 2003; V. Sahasrabuddhe, NYAS 2018; Kelly, Lancet 2018; Looker, JAIDS 2018*

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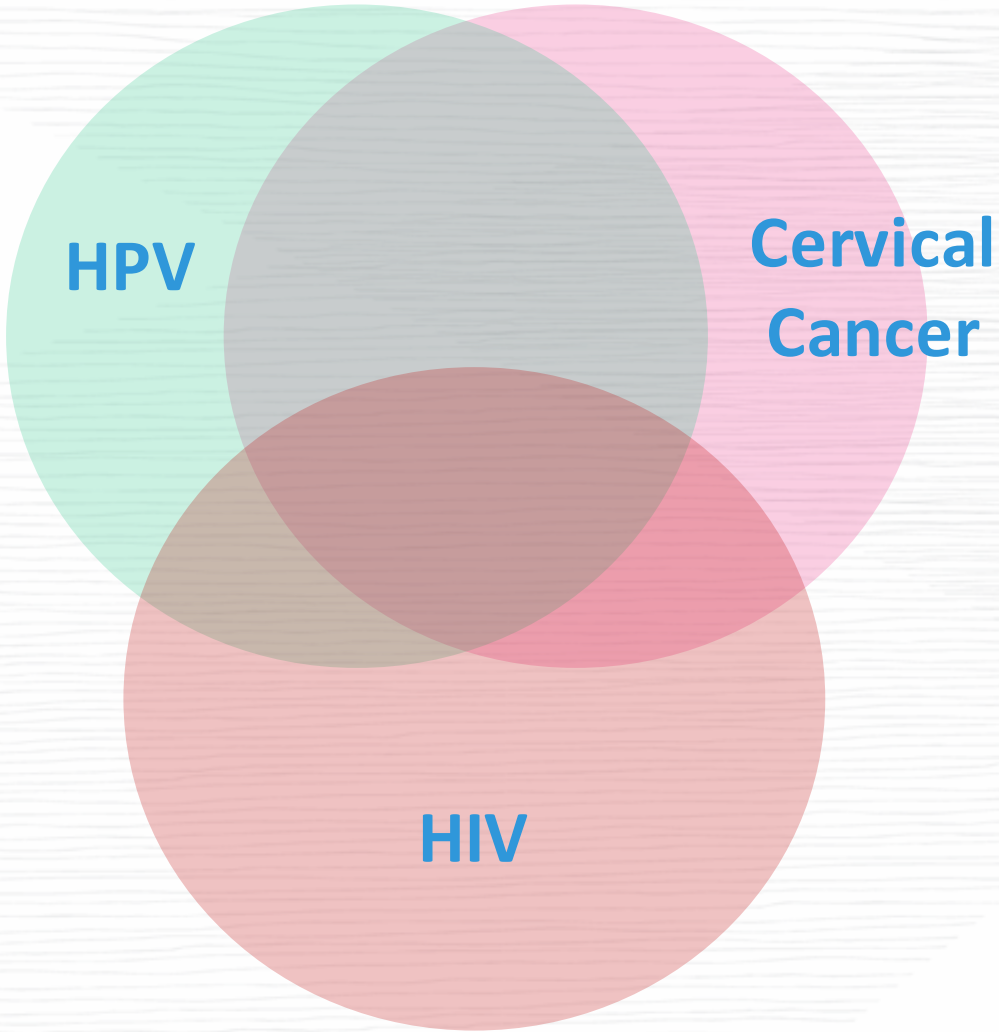
Double burden of disease: cervical cancer and HIV

- HIV + **4 to 10 times** more prone to develop cervical cancer than HIV negative women
- **30-80%** of HIV + women have prevalent carcinogenic HPV genotypes
- **10-40%** of HIV + women have prevalent cervical precancerous lesions
- **1.3-3.7%** of HIV + women are detected with cervical cancer at the time of screening

- Younger age at the time of cancer diagnosis, more aggressive clinical course, less responsiveness to treatment

Synergistic interventions to control HPV, Cervical Cancer Carcinogenesis and HIV infection



- ART reduces HPV incidence and prevalence

- HPV vaccine impacts on HIV acquisition

- Follow-up for CXCA screening or HIV control in WLWHIV

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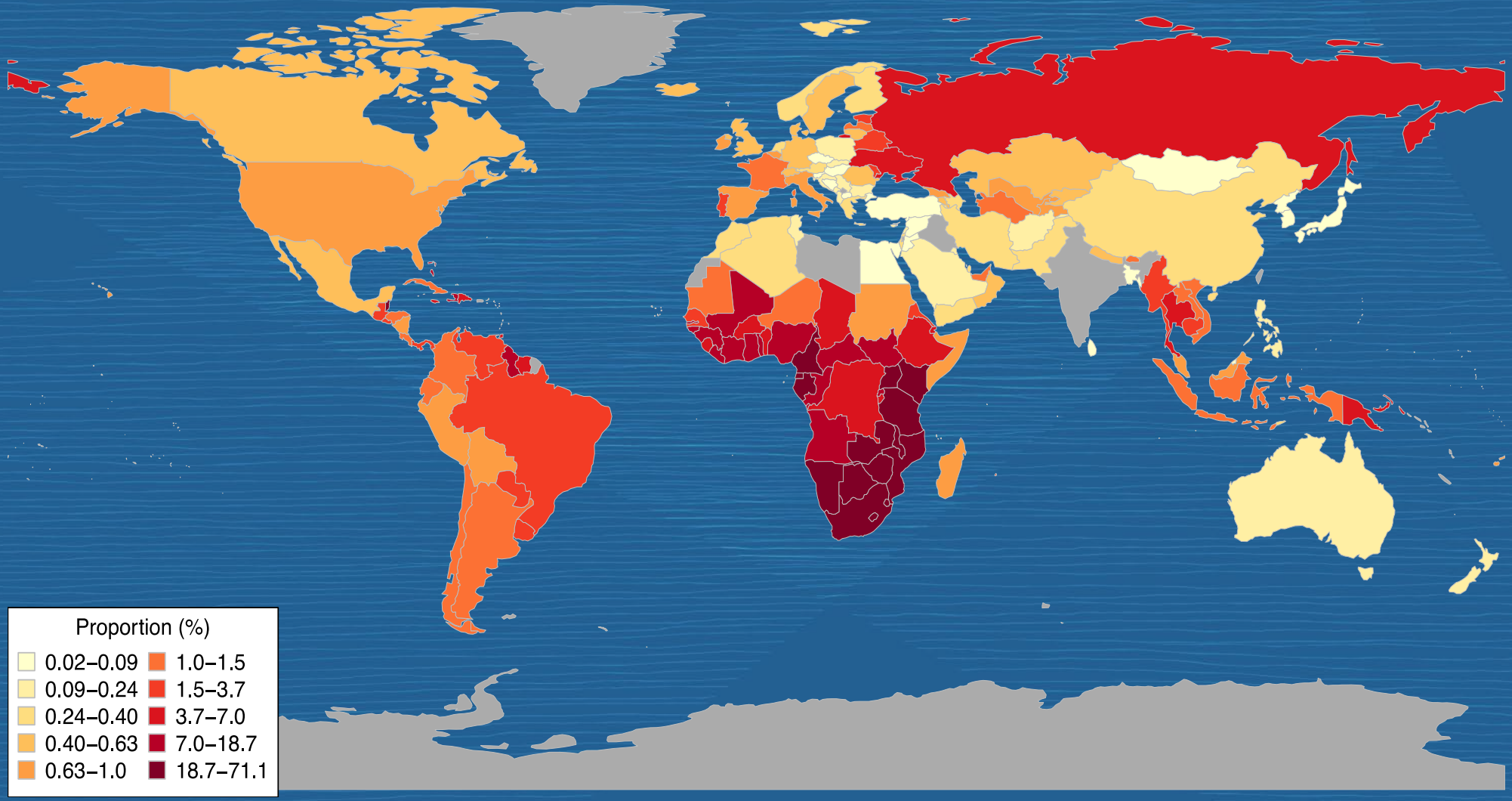
Estimated proportion of women with HIV among incident cases of cervical cancer



Note: preliminary data from WHO , 2019

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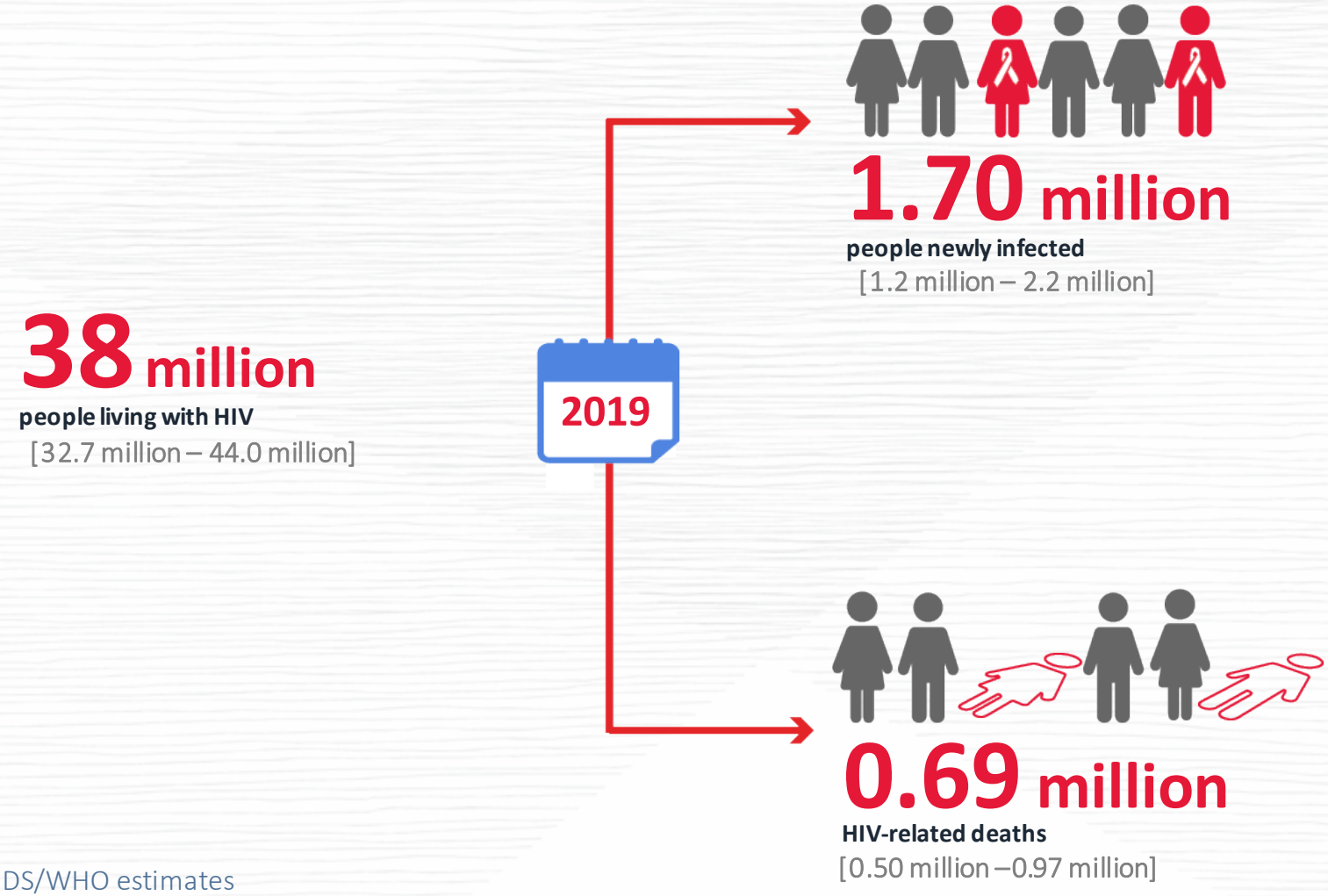
Summary of the global HIV epidemic (2019)



Source: UNAIDS/WHO estimates

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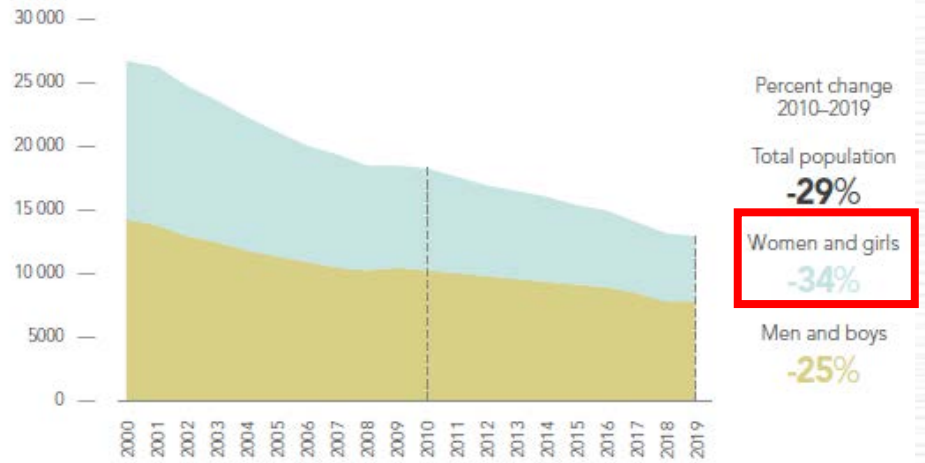
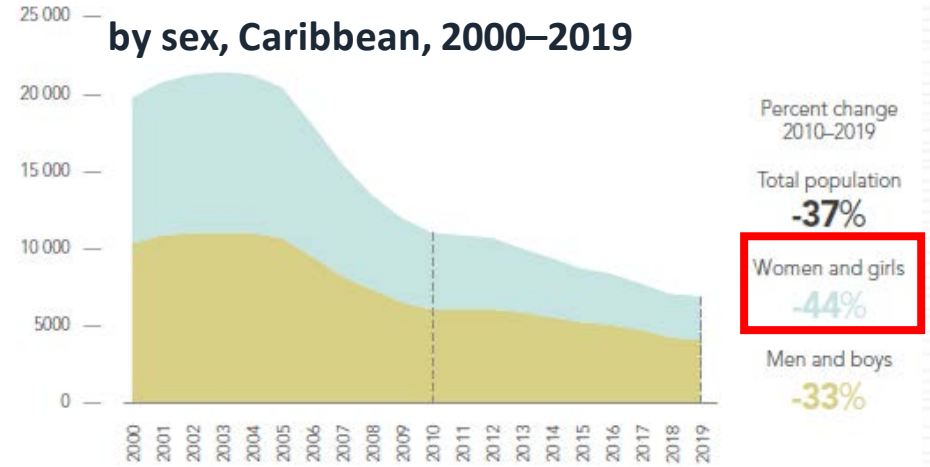
HIV epidemiological data in The Caribbean, 2019

New HIV infections by sex, Caribbean, 2000–2019

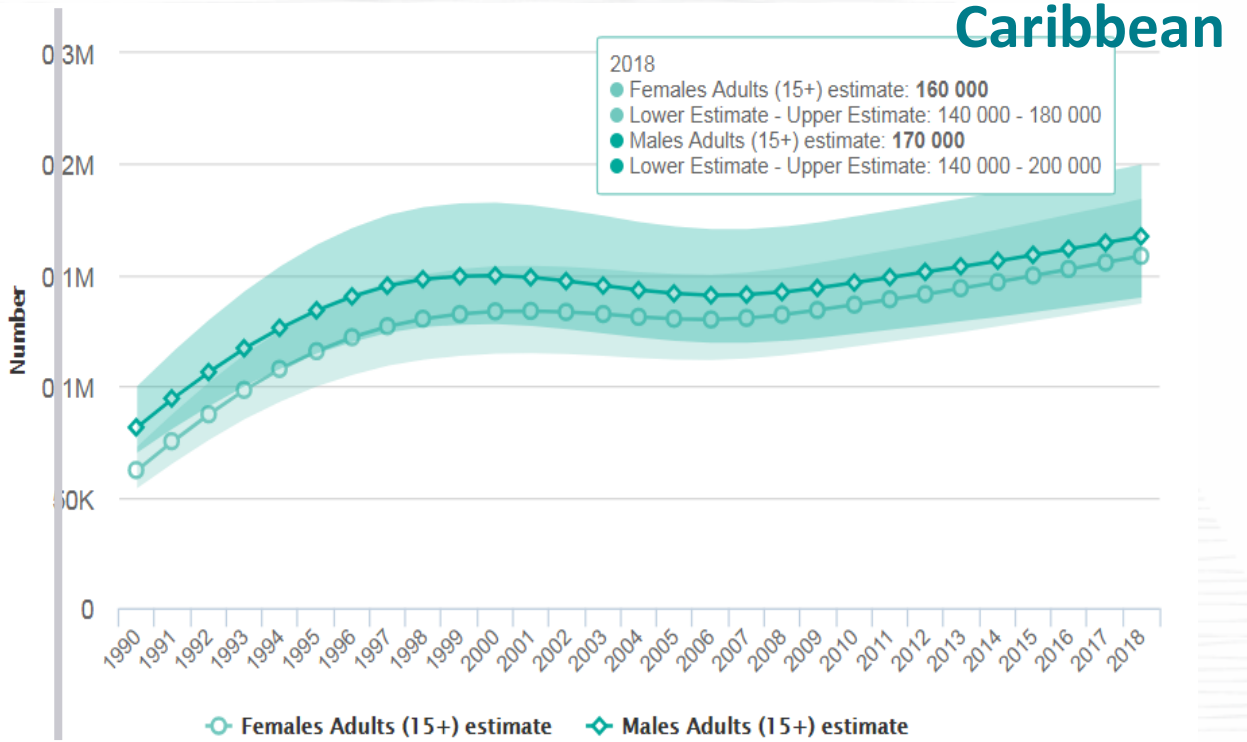


AIDS-related deaths by sex, Caribbean, 2000–2019



Source: UNAIDS/WHO estimates, 2019-2020

Est. 160,000 WLHIV (15+) in the Caribbean in 2018



Est. 71% of WLHIV (15+) were receiving ART in the Caribbean in 2019

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Cervical cancer screening among women living with HIV aged 30-49, last year available (Pap, VIA, HPV)

- *34 countries in the Americas report to the Global AIDS Monitoring (GAM) platform, Three countries in the Caribbean reported on this indicator:*

Country	Year	Indicator value (%)	Numerator	Denominator (est. % screened)	Estimated # WLHIV (15+), same year	Source (MOH)
Grenada	2017	**53.1**	17	32 (>16%)	<200	Clinical and pathology records
St. Lucia	2017	**5.8**	19	326 (>65%)	<500	Castries STI and Vieux-Fort STI data
Barbados	2018	**1.9**	17	899 (90%)	1,000	Users of Ladymead Reference Unit

Source: UNAIDS, Global Aids Monitoring

WHO recommendations on screening for women living with HIV

- **Any** of the three screening tests (VIA, HPV test, or cytology) can be used
- Begin screening for all women and girls who have initiated sexual activity as soon as they have tested positive for HIV, **regardless of age**
- HIV+ women screened negative (with no evidence of precancer) should be retested within a **maximum period of three years**
- HIV + women who have been **treated** for precancerous lesions **should receive a 12-month post-treatment follow-up**
- Management of abnormalities, including colposcopy and biopsy, **should not be modified** on the basis of a woman's HIV status.

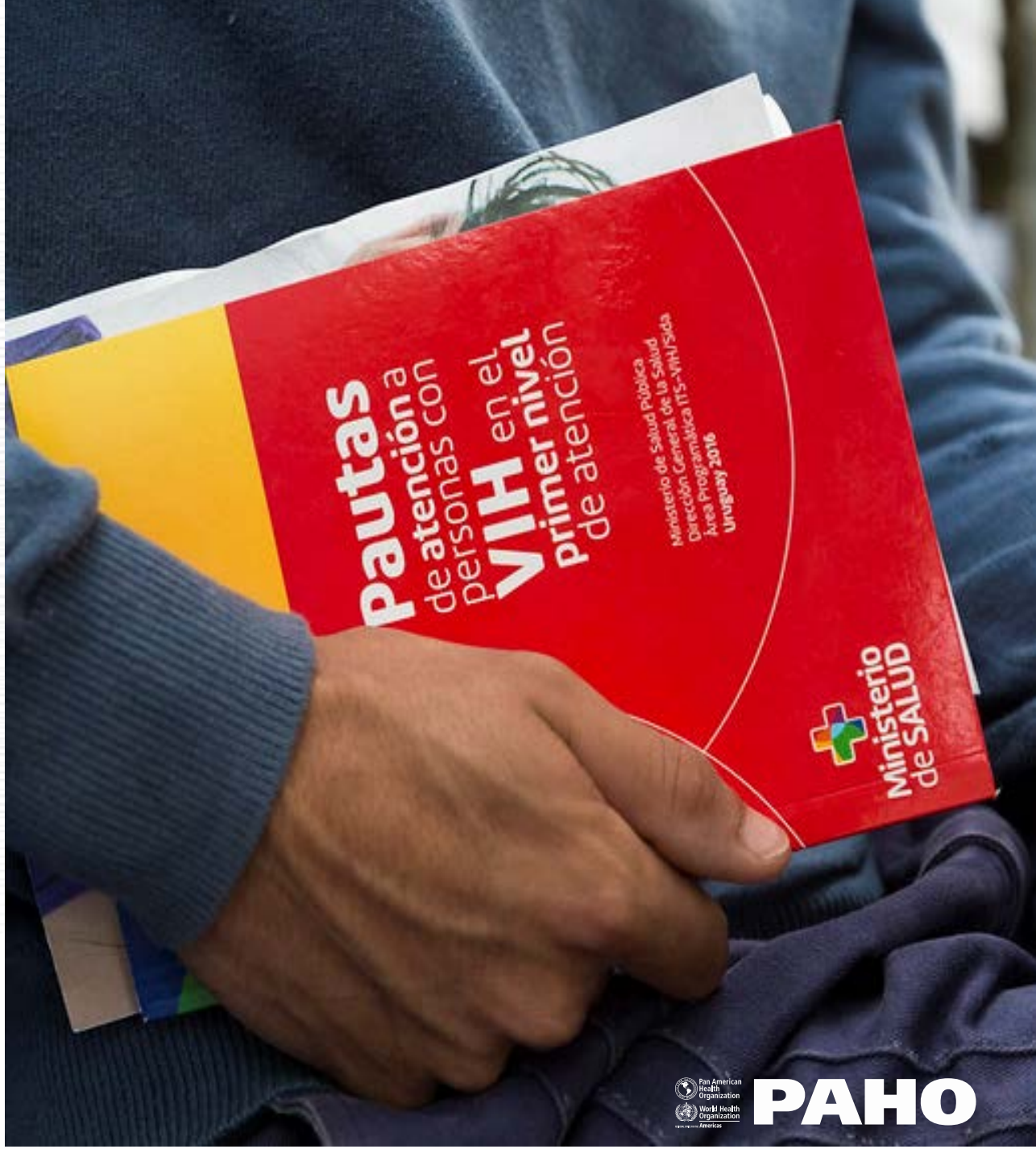
Comprehensive cervical cancer control A guide to essential practice - Second edition. Available at: https://www.who.int/reproductivehealth/publications/cancers/cervical-cancer-guide/en/

WHO Guidance on Treatment of precancerous cervical lesions for Women Living with HIV

No specificities for precancerous cervical lesions treatment for WLHIV

Any of the cryotherapy and loop electrosurgical excision procedure (LEEP) treatments can be used

The **screen and treat** recommendations apply to all women regardless of HIV status. However, some specific recommendations for screen and treat strategies for WLHIV



Comprehensive cervical cancer control A guide to essential practice - Second edition.
Available at: https://www.who.int/reproductivehealth/publications/cancers/cervical-cancer-guide/en/

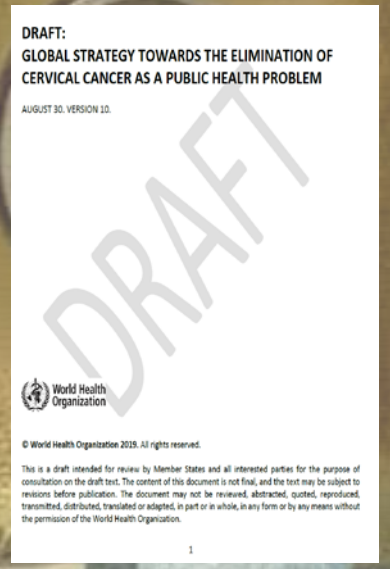
Good Practices on Treatment of invasive cervical cancer for Women Living with HIV

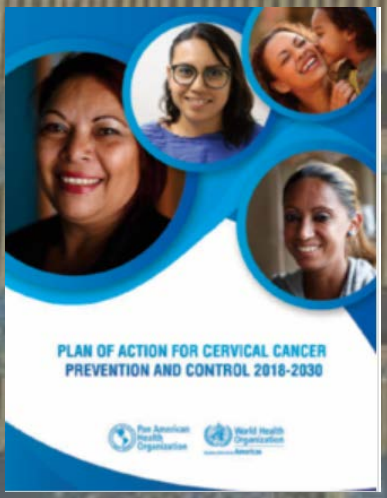
There are no evidence-based guidelines on this subject. However commonly used practices include:

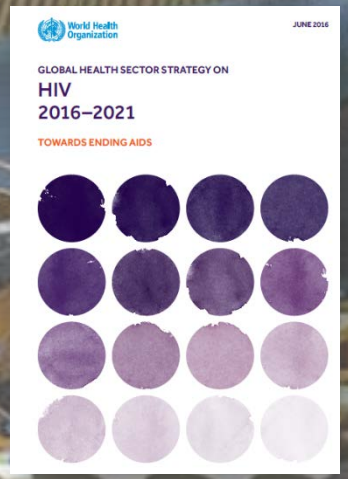
- Cervical cancer fully diagnosed, staged and treated at a tertiary-level institution with the appropriate expertise.
- A baseline CD4 count is a key element of care for WLWHIV and should be one of the initial evaluative tests obtained, regardless of the extent of the cancer.

Comprehensive cervical cancer control A guide to essential practice - Second edition. Available at: https://www.who.int/reproductivehealth/publications/cancers/cervical-cancer-guide/en/

Global and Regional Commitments towards ending AIDS and STI as a public health problem by 2030 that supports CxCa Elimination







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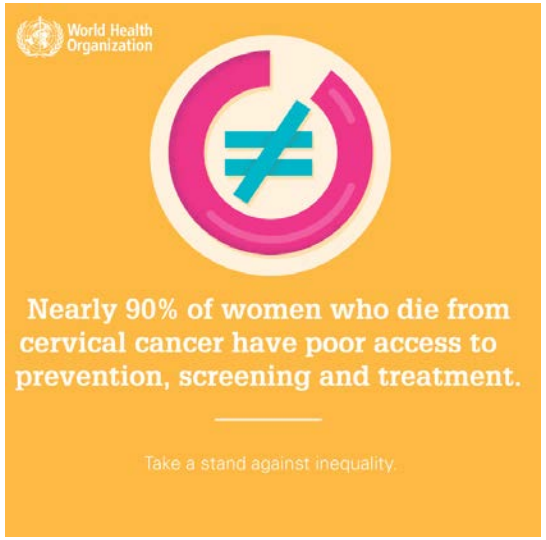
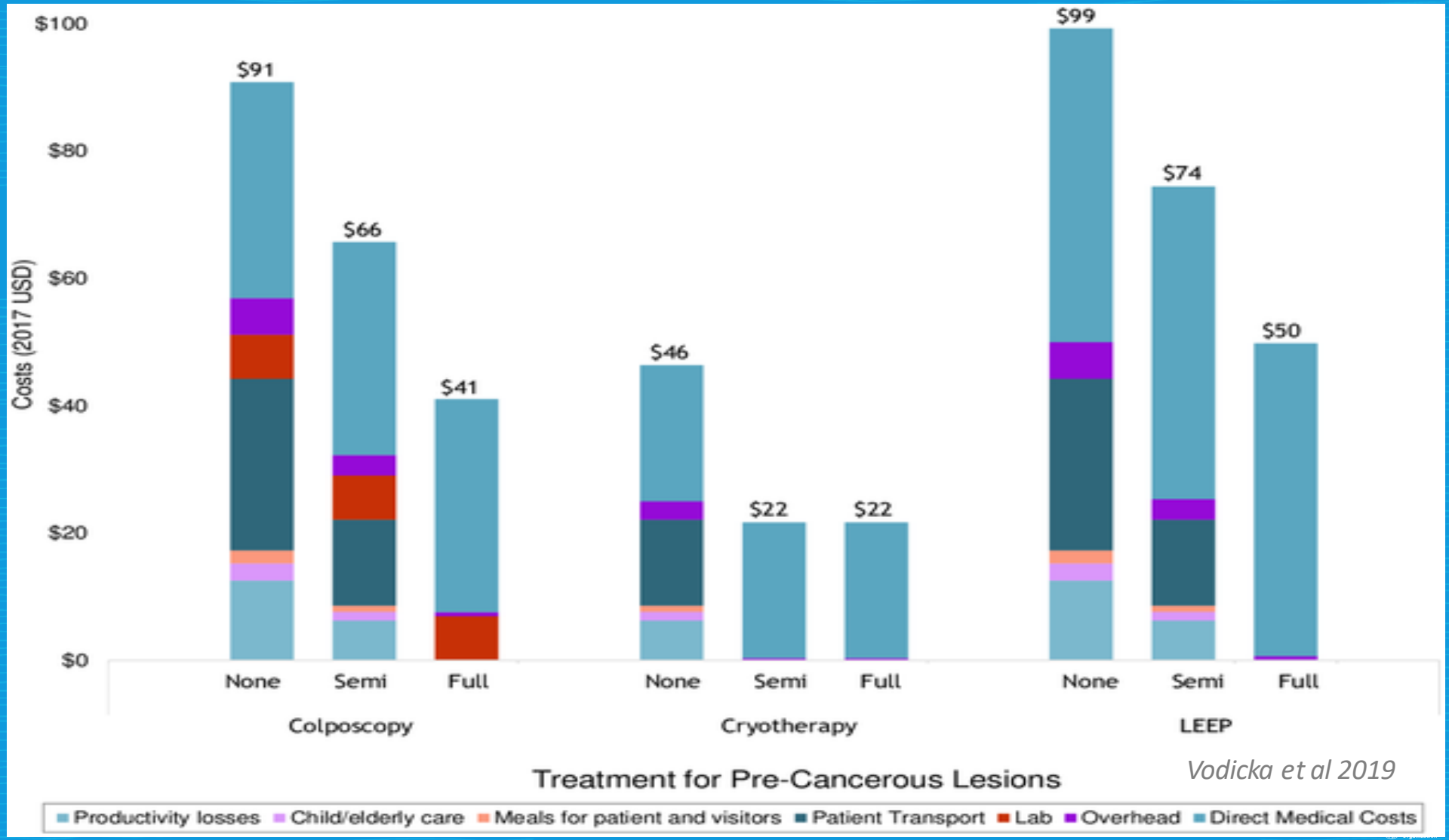
Opportunities for Integration

- Established HIV prevention and care services
  - effective strategies for linkage to care
  - **access to highly vulnerable populations**: WLHIV, female sex workers, transgender men, women who uses drugs, etc.
- SRH, STI and Adolescents' services
- EMTCT *Plus* initiative: use of maternal and child health (MCH) platform for screening
- Lab multiplex platforms and specimen referral

Universal health
Access and coverage for all



Comparison of integrated versus non-integrated HIV treatment costs for precancerous lesions by component of care (Kenya)



Vodicka et al 2019

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Lessons learned with the HIV response

- **Adaptability** to a fast changing environment
- Specific targets (90-90-90)
- Effective prevention efforts require a **combination approach of biomedical, behavioral and structural interventions**
  - Early diagnosis and immediate treatment
  - Differentiated models of care
  - Community and peer-led screening and treatment
  - Active linkage to care
  - POC diagnostics with simplified algorithms
  - Use of communication technologies (ex. SMS)
- Competition in **generics** drug markets
- **Meaningful engagement** of civil society from the start
- Strong community mobilization

Regional next steps

- Support the roll out and the monitoring of the Global STI Strategy & the Regional Plan of Action
- Complete regional mapping of policies and update epidemiological situation
- Support interprogrammatic work and service integration at country level
- Support countries to address data gaps
- Continue working in partnership with civil society organizations

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- Maeve de Mello
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- Shona Dalal
- Vikrant Sahasrabuddhe

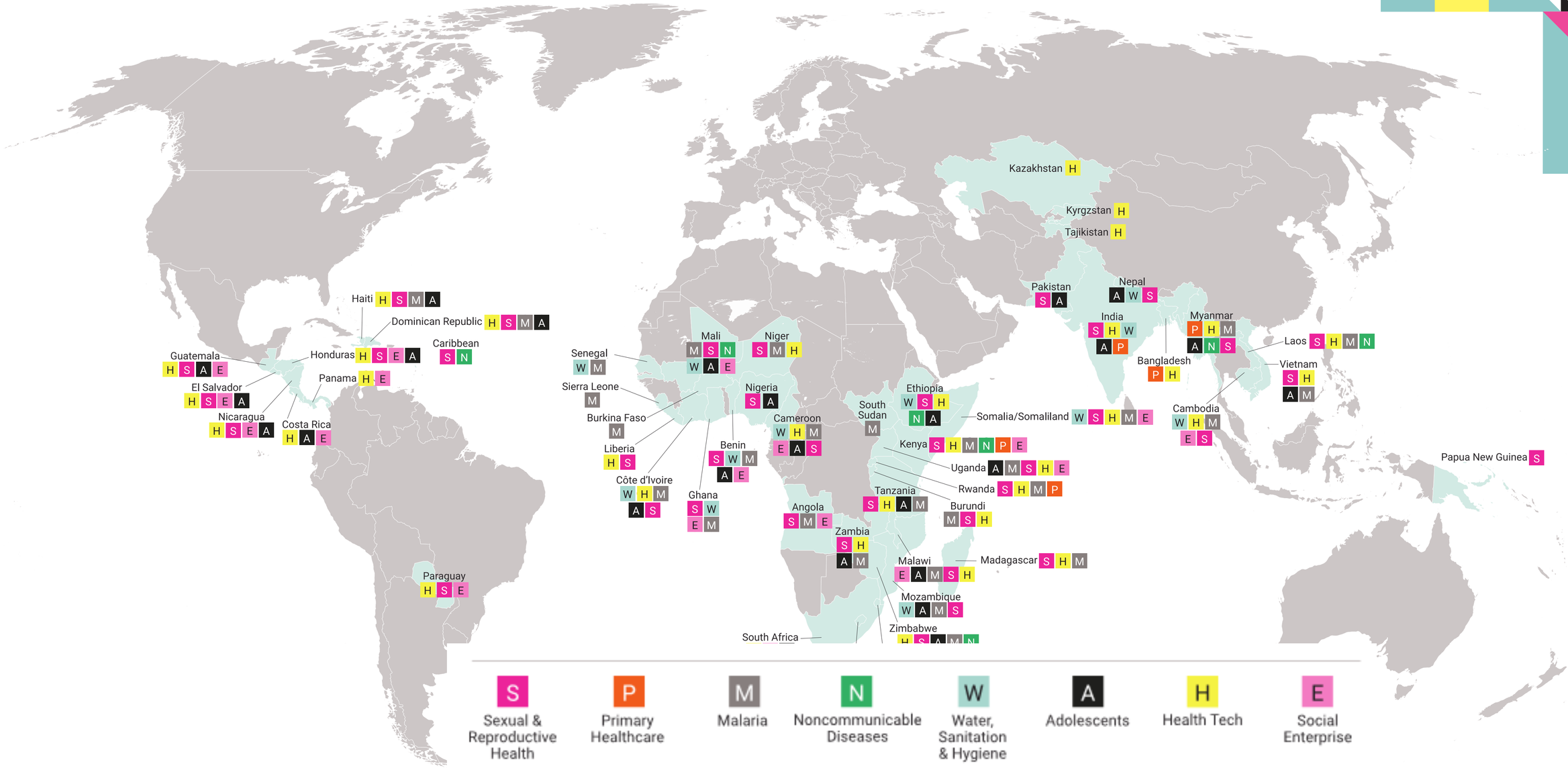
HPV Testing- Pilot Project

Trinidad & Tobago

Moira Lindsay
PSI-Caribbean

Population Services International (PSI)

PSI reimagines how to bring quality healthcare closer to those who need it most.



PSI-Caribbean established in 2005

PSI-Caribbean believes that getting the right products and services to vulnerable populations is key to helping people live healthy lives.

September 2017

Project Goal

Reduction in morbidity and mortality from cervical cancer;
Ensure T&T on track to meet WHO's 2030 Global Elimination Targets

- ü 90 % of girls fully vaccinated for HPV by age 15
- ü 70% of women screened with high performance test by 35 (and @45)
- ü 90% of women identified with cervical disease receive treatment

Project Primary Outcomes

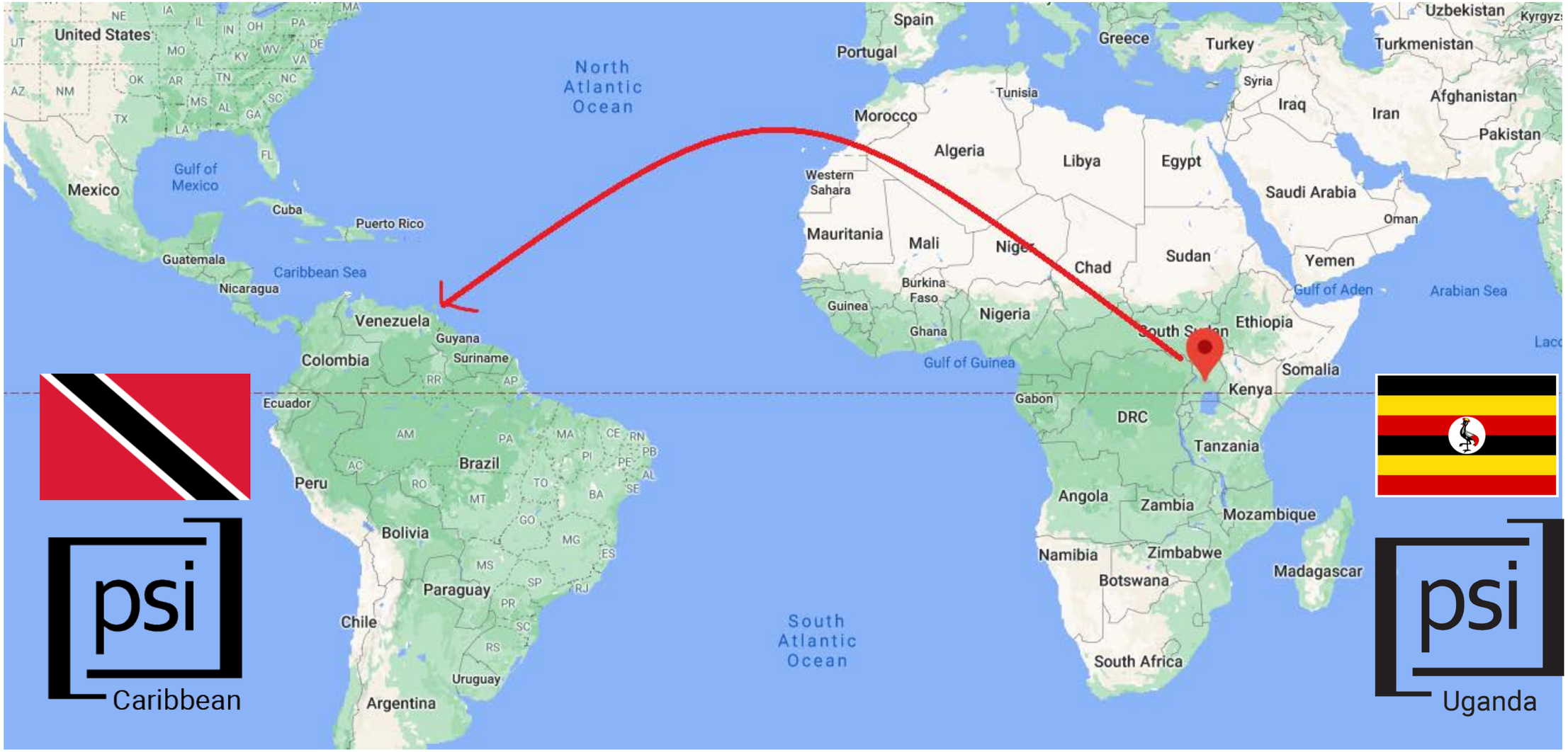
- Improved awareness, education, demand for HPV **vaccine** among parents/youth 9-15 years

- Increased **vaccine** coverage of T&T youth in school and facility-based screening programs

- Increased coverage of cervical cancer **screening** / preventive treatment ar years

#VACCINATESCREENTREAT.

2018-Opportunity via global partnership with QIAGEN



psi Caribbean

psi Uganda

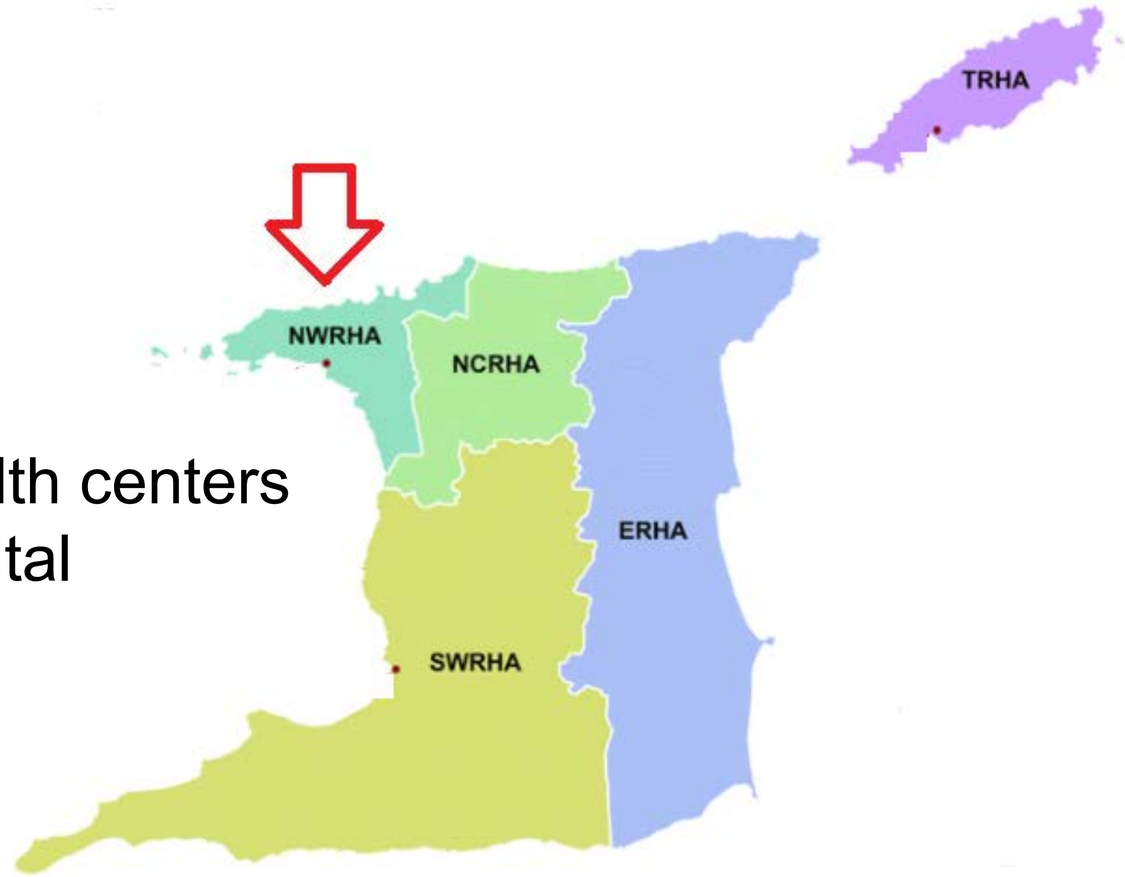
Local Partnership for HPV Pilot

Government of the Republic of Trinidad and Tobago
Ministry of Health

The North West Regional Health Authority

psi Caribbean

- 18 health centers
- 1 hospital



Protocol Overview

- Target: 1500 women
- HPV Test: careHPV test (QIAGEN)

  Uses Hybrid Capture 2- HC2- technology. Detects presence of 14 high-risk HPV genotypes. POS/NEG.
- Women 30-65 years. (no pregnant; no STIs; not doing treatment)
- Positive results to be followed up with Pap smear
- No self-sampling

Note: Took almost all of 2018 to completeMoU; Loan Agreements; Protocol; Algorithm; procurement of commodities; customs clearance of machine etc.

Feb 2019- Lab Training

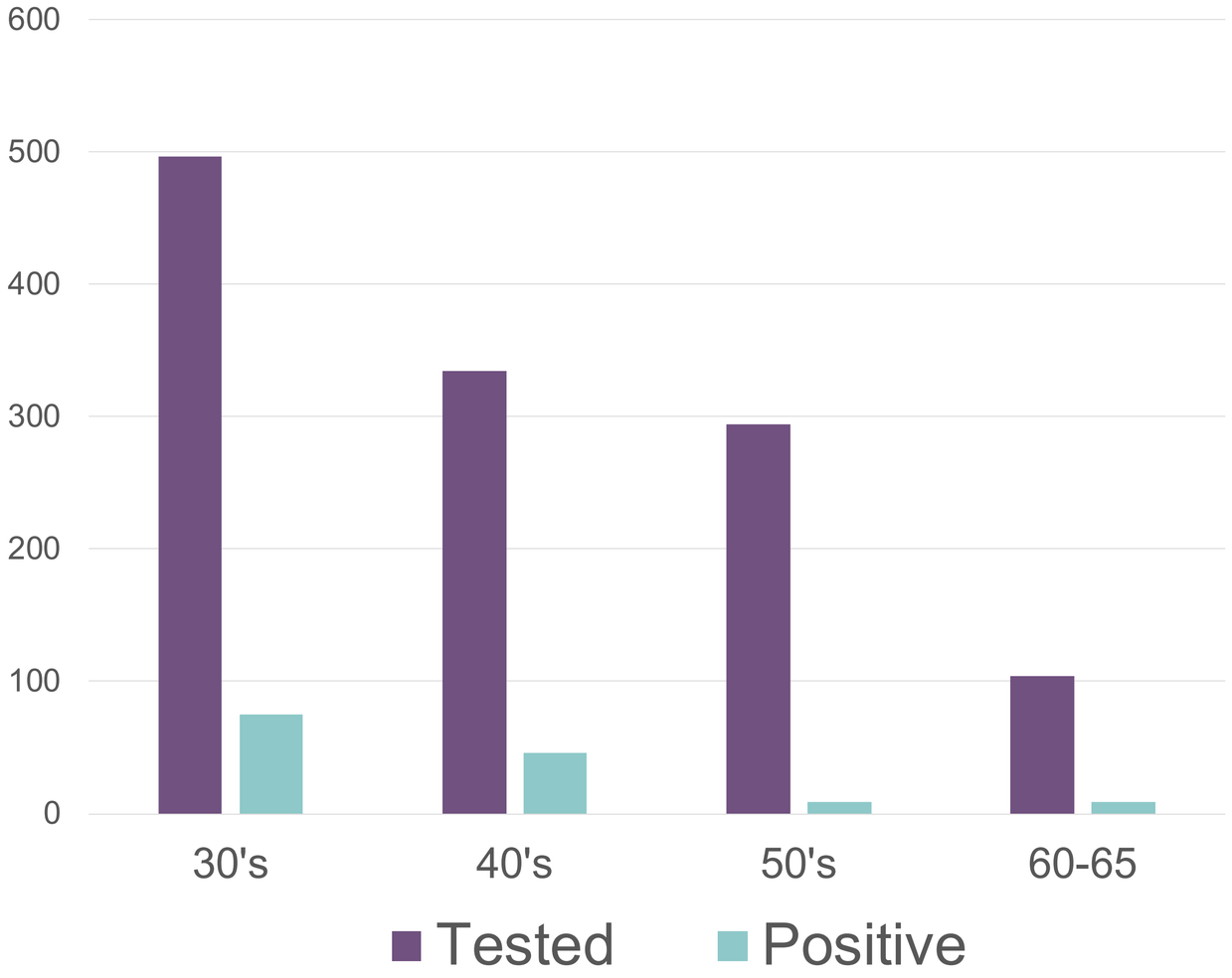
Timeline- pilot implementation

Mar-Nov 2019: Sample Collection& Analysis

Dec 2019-Present: Referral Follow Up

Pending: 11 Paps

Results



Total Tested	1306
Samples not eligible	104
Total (eligible) for pilot	1201
Total HPV positive	140

11.7%

Positivity Rate of Eligible Samples

Referrals

Total HPV Positive Results= 140

Referrals	Total
Referred for Pap	115
Pap completed	104
Scheduled and awaiting Pap	11
Referred to colposcopy	36

Reasons for lackof Pap Referral	Total
Unable to contact	14
Refused (against medical advice)	1
Co-tested (not in protocol)	4
Referred directly to colposcopy	4
Pap done at private facility	3

Colposcopy Results

Colposcopy Results	
CIN 1, 12	12
CIN 2, 23	7
CIN 3	4
Type 3 TZ	2
Cervicitis	2
Other (inflammation, benign)	3
Appointment rescheduled	4
Unreachable	2
Total	36

Note: Pending pap smear referrals will be included as data becomes available

Accomplishments

Introduced high performance screening test in the public system

Increase number of women screened

Identified issues to be addressed before scaling up

Increased Screening Coverage

Regional HealthAuthority (1 region)	2018	2019
Pap Smears at primary care facilities	2044	2610
HPV pilot		1305
Total	2044	3915

Includes repeat smears and total HPV samples collected

33%

Of women screened in 2019 via Pilot

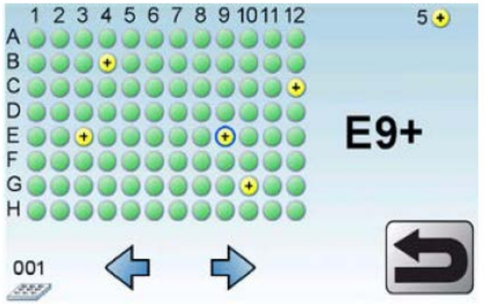
Takeaway: Figures increased significantly with a dedicated effort towards promoting screening

Challenges

- **Customs**
  - Did not have tax exemptions in place before machine was shipped resulted in long delays and high costs (non-issue for MoHs). Rectified before procurement of testing supplies.

- **Collection of samples**
  - Outside of age criteria; co-testing
  - Persisted throughout pilot as high rotation of persons involved in sample collection

- **Testing supplies and commodities**
  - Procurement- delays in local procurement resulted in pause on sample collection
  - Wastage- used 8% for reagents and 10% for brushes/collection medium. Insufficient if full tray is not used majority of time. (96 wells; 6 calibrators= 90 samples per tray)



Challenges

- **IEC info for patients**
  - Client card developed in early stages (emphasized importance of follow up) , but not widely distributed at health centers.
  - Pause on developing HPV testing materials endorsed by MoH until test available nationally.

- **Data Collection and Analysis**
  - No standardized data collection form at the beginning (using pap forms); inconsistent info collected at different testing sites.
  - Data information system at health authority crashed and had to be re-entered manually.

- **COVID and Parallel Health System**
  - Despite the Gov setting up a parallel health system during the COVID outbreak, health services have been affected due to lock down (Mar-May); ongoing staffing issues with rotation of staff etc.
  - Challenges to re-schedule pap and colposcopy appointments (some also due to patient fear/unwillingness to access facilities)

Beyond the Pilot

- MoH does plan to scale up HPV testing at a national level.
- Lessons from the pilot will be incorporated for future planning. Health systems strengthening must be emphasized.
- MoH has procured several PCR machines for COVID that can also be used for HPV testing.

CONNECT WITH US

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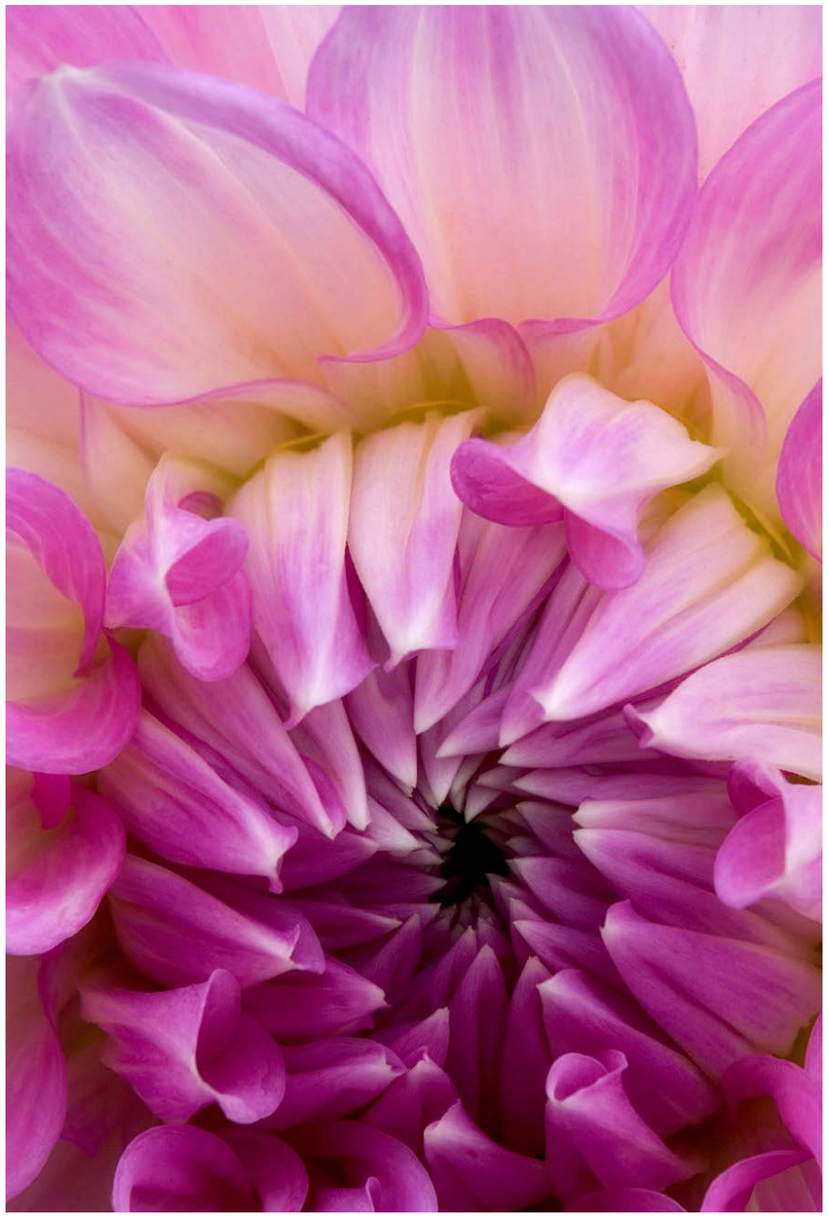
@PSCARIBBEAN

Moira Lindsay
mlindsay@psicarib.org



BAHAMAS: CHALLENGES TO INCORPORATING HPV TESTING INTO THE SCREENING PROGRAM

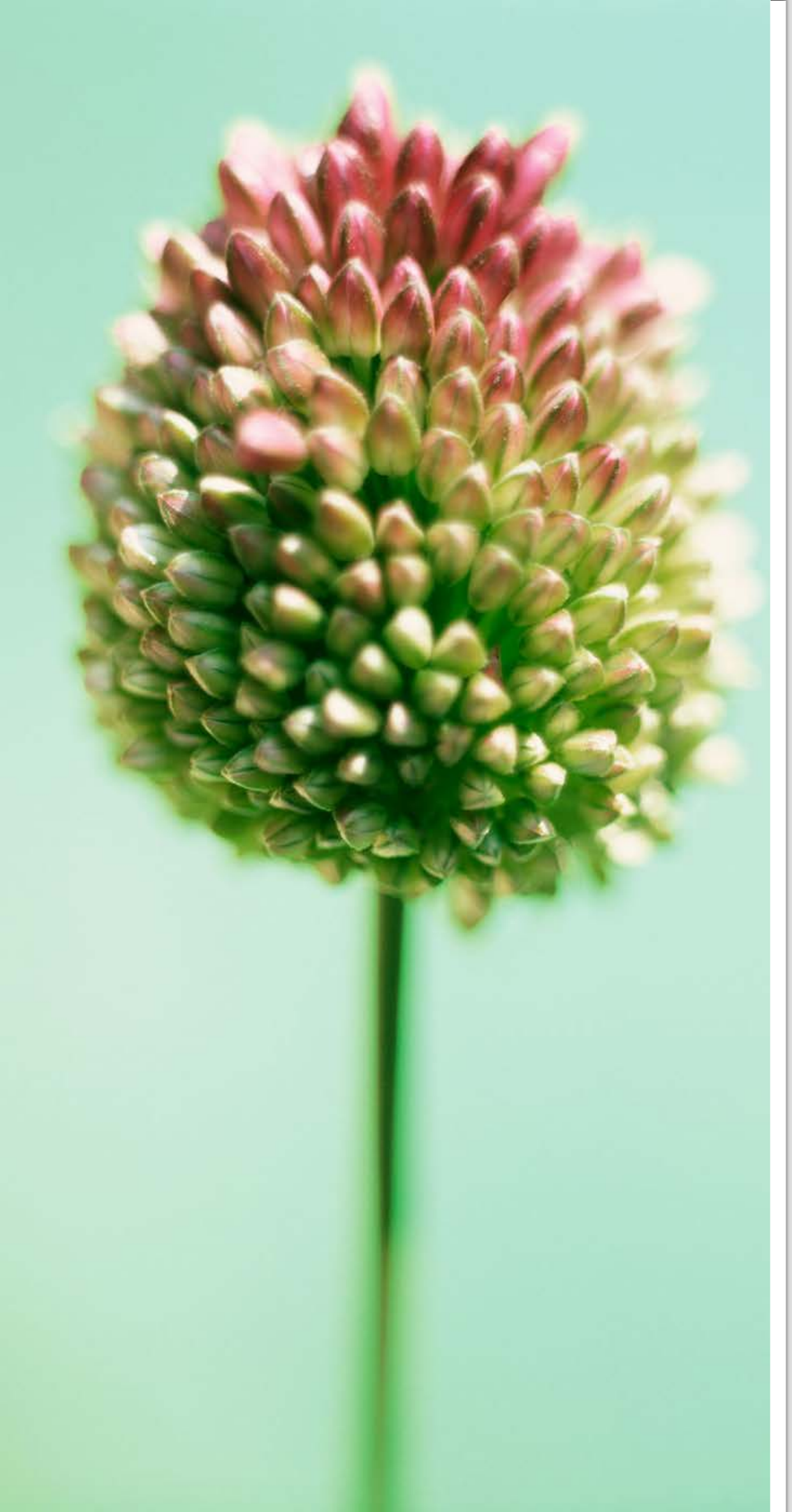
Dr. Phillip Swann,

Registrar, OCMO,

Ministry of Health

WHAT IS CERVICAL CANCER?

- Cervical cancer is preventable. It is one of the most common cancers among women in Latin America and the Caribbean. Its primary cause is the infection with high-risk human papilloma viruses (HPV).
- The HPV vaccine and the screening and treatment of precancerous lesions can prevent cervical cancer.
- The global cervical cancer elimination strategy proposes actions on community education and information, HPV vaccination, cervical cancer screening using HPV testing, treatment of women with pre-cancerous lesions and invasive cancer, as well as improving cancer registration, monitoring and evaluation.

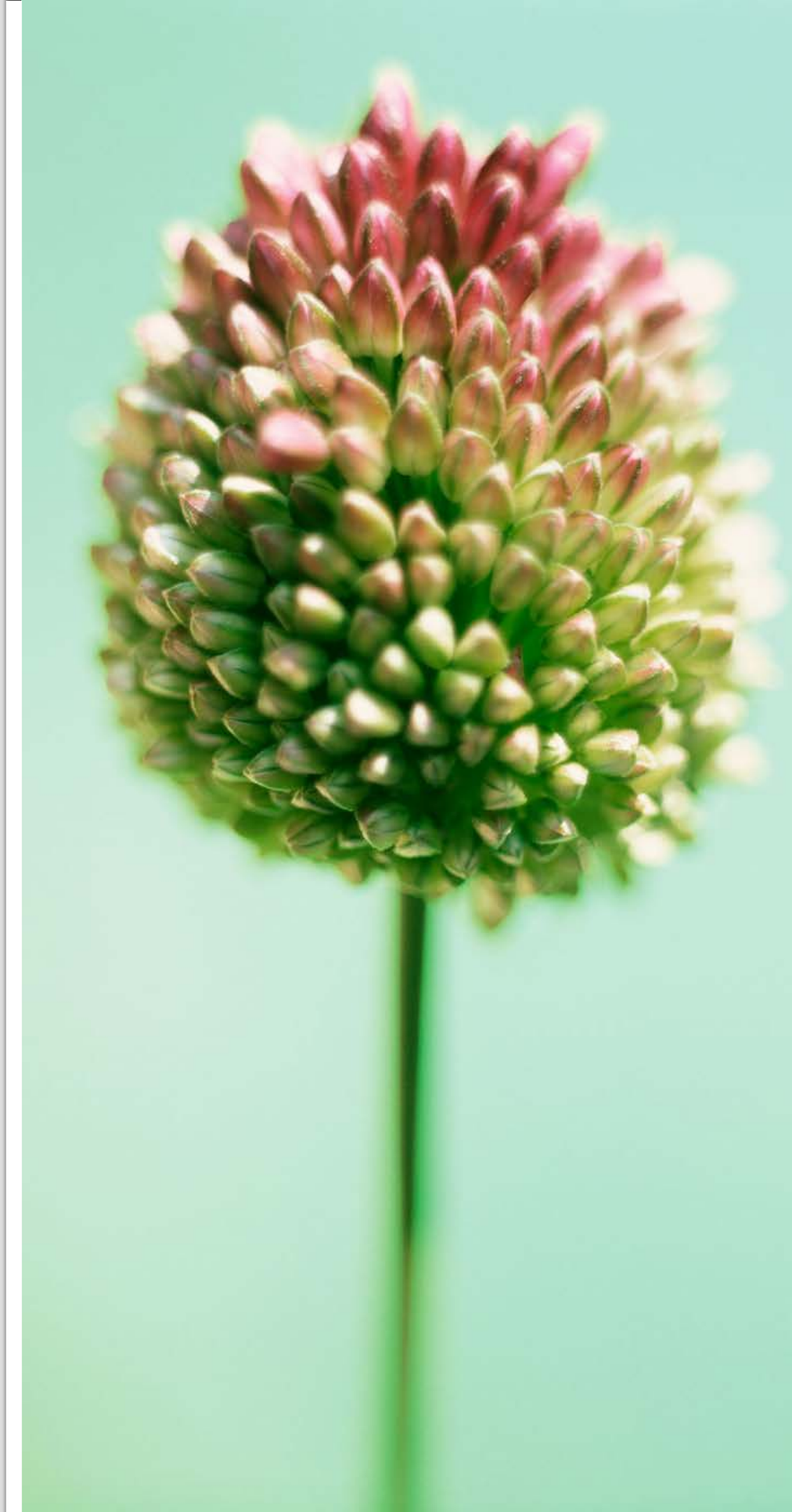


OVERVIEW OF CERVICAL CANCER

- Access to cancer prevention, early detection, and treatment services is an area of great need, in the Region where cancer is the second leading cause of death.
- Cervical cancer is largely preventable through community-based and primary care services that include HPV vaccination, screening, and treatment of precancerous lesions.

OVERVIEW OF CERVICAL CANCER

- In The Bahamas,
  - the incidence rate of cervical cancer has decreased from 22.4 per 100,000 population (2000) to 12.4 per 100,000 (2016).
  - Improved cervical cancer prevention program.
  - The national immunization schedule includes HPV vaccine for girls and boys 9-12 years of age,
  - Cervical cancer screening services are established and available in both private and public sector



WHAT ARE THE COMPONENTS OF A STRONG NATIONAL CAMPAIGN?

- Prevention
  - Education
  - Vaccination
- Screening
  - Pap smears
  - HPV testing
  - Colposcopy
- Diagnosis
  - Cytology
  - Imaging (late diagnosis)
- Treatment
  - Minor surgery
  - Hysterectomy
  - Adjuncts - radiation therapy, chemotherapy
- Post-treatment care
  - Counseling
  - Rehabilitation

WHAT ARE THE COMPONENTS OF A STRONG NATIONAL CAMPAIGN?

- Treatment
  - Minor surgery
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  - Adjuncts - radiation therapy, chemotherapy
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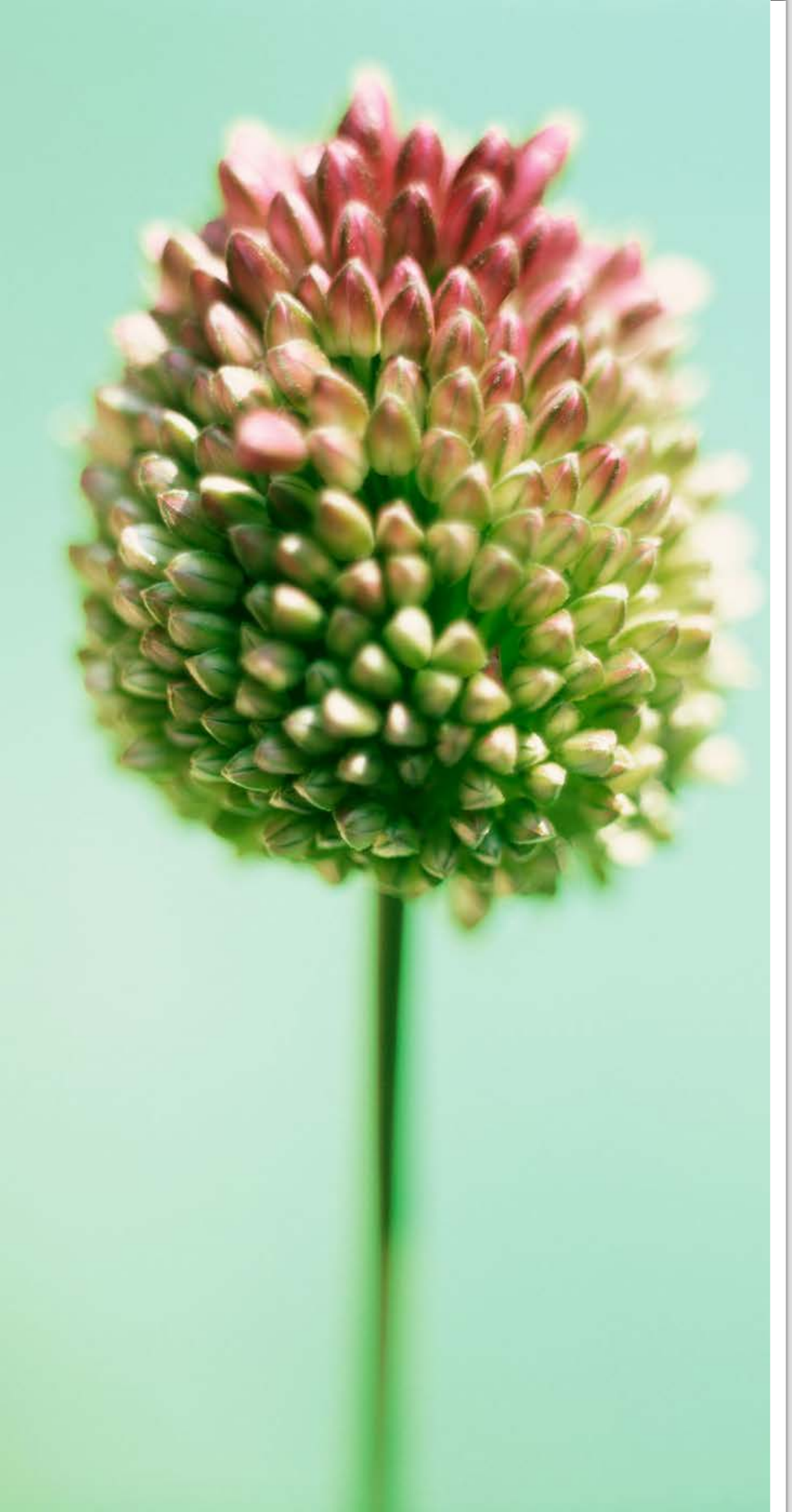
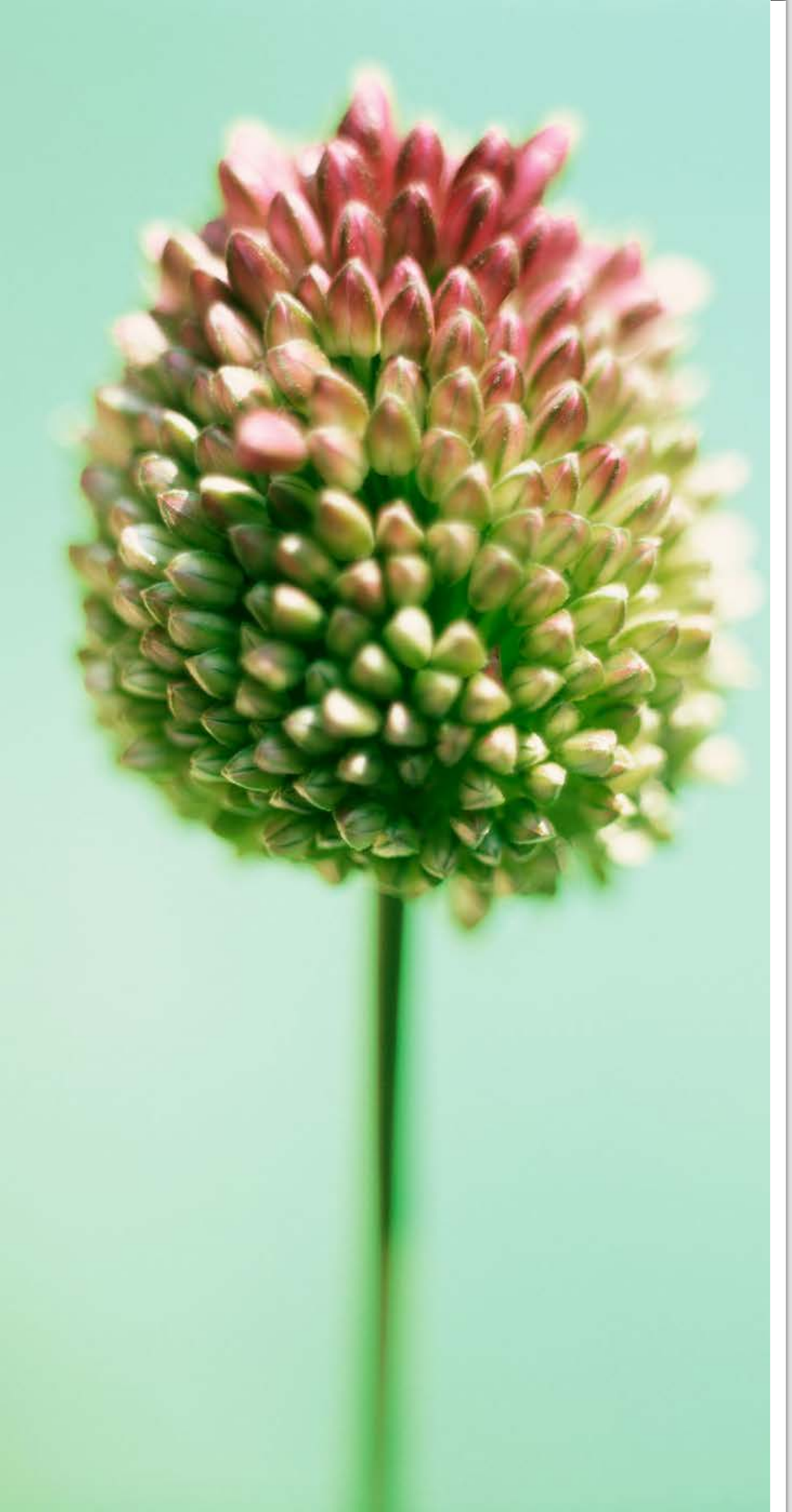


HPV TESTING

- Challenges
  - enhancing planning, funding and coordination,
  - • expansions in laboratory capacity, human resources, expertise and infrastructure,
  - • organized screening programmes,
  - • good information technology,
  - • enhanced educational campaigns and
  - • a consideration for self-sampling



HPV TESTING

- The Bahamas intends on eradicating cervical cancer.

- Partners - PAHO/WHO and Rotary International.

- Multi-pronged approach
  - prevention, early detection, early treatment, and palliation.

- Greatest benefits
  - coordination and planning.
  - funding

EXPANSIONS IN LABORATORY CAPACITY, HUMAN RESOURCES, EXPERTISE AND INFRASTRUCTURE,

- Presently - HPV testing is outsourced outside of the country.
- Public sector two platforms that can perform HPV testing,
- Plan to assess both platforms
  - anticipated needs for expanded testing services,
  - expanded access to testing and
  - turnaround time for results.
  - access to a sustainable and affordable inventory of testing supplies,
  - and little technical expertise required

EXPANSIONS IN LABORATORY CAPACITY, HUMAN RESOURCES, EXPERTISE AND INFRASTRUCTURE,

- Ideas for the creation of a national public health laboratory
  - to leverage existing laboratory-related expertise to efficiently address these national initiatives.
- Requires significant expansion of testing capacity
  - expansion in infrastructure,
  - acquisition of equipment,
  - recruitment of personnel and
  - reliable supply chains
- National screening need for target of approximately 130,000 women
- At present, consideration is that it would cost about US$100 in the public sector.

ORGANIZED SCREENING PROGRAMMES,

- Opportunistic screening for cervical cancer
- HPV testing is the gold standard in screening - only in the private sector.
- National Health Insurance programme primary benefits package for the NHI Initiative is a liquid pap test, which includes the HPV testing.
- National screening recommendations for The Bahamas being developed based on the national experience.
- Suggested cervical screening using pap smear is annually beginning at age 18 years, or age of sexual debut, whichever is earlier

ORGANIZED SCREENING PROGRAMMES,

- Abnormalities are managed with earlier re-screening and other interventions such as
  - cryotherapy,
  - colposcopy and
  - minor surgery
- HPV testing, will need to be a revision
  - overdiagnosis in a population less than 25 years, and
  - a decreased frequency in screening (NHI recommendation is once every three years).
- Cervical cancer eradication initiative requires
  - investment in staff and equipment

GOOD INFORMATION TECHNOLOGY

- NHI approach additional benefit is an electronic health record.
  - Enhances health intelligence and surveillance
- Coupled with incentives to providers to meet certain targets, such as increasing cancer screening
- The ability then for integration with a laboratory information system will be key as HPV testing has both a molecular and cytology component, which are usually independently reported on.

ENHANCED EDUCATIONAL CAMPAIGNS

- Currently, educational campaigns on cancer screening remain primarily purveyed by civil society.
- COVID-19
    - Hampered plans to augment messaging
    - Increased channels of digital communication platforms
  - Drove down costs for public awareness campaigns,
- Cervical cancer
  - ‘personal’ cancers
  - taboo topic in society.

CONSIDERATION FOR SELF-SAMPLING

- In The Bahamas, there is low rate of pap smears in the public sector,
- No data available for private sector
- Journal of the American Medical Association article by C Thomas et al entitled **HPV DNA Testing of Self-collected Vaginal Samples Compared With Cytologic Screening to Detect Cervical Cancer**
  - more than half of women developing cervical cancer in the United States have not had a Pap smear within the last 3 years, despite contact with the health care system in the majority of cases. And that "this is especially a problem for older women".
  - "inconvenience, time, and discomfort often involved with obtaining Pap smears in older patients"
  - the assumption that Pap smears are being obtained elsewhere, and
  - many male physicians feel uncomfortable obtaining Pap smears and taking sexual histories.

CONSIDERATION FOR SELF-SAMPLING

- Self-sampling may
  - "reduce underscreening in women who have access to health care"
  - "increase access to screening in many resource-poor areas."
-
- Self-sampling
  - "a facilitator to screening participation"
  - increases screening participation rates in those who are underscreened or never screened
  - more appealing to individuals who fear speculum examination
  - Removes concerns about privacy and modesty.

- Madzima et al - **Emerging role of HPV self-sampling in cervical cancer screening for hard-to-reach women** concluded "Convenience, privacy, ease of use, and, likely, cost-effectiveness of HPV self-sampling are driving forces in its emerging role in cervical cancer screening among hard-to-reach women."

CONCLUSION

- *Many of these barriers exist in across countries in the Caribbean Region*
- *Examine trials and successes of other countries,*
- *Devise local national plans and strategies to reduce the incidence and prevalence of cervical cancer – a vaccine preventable cancer, among our valuable female citizens.*
- *Thank you for your attention.*

Cervical Cancer: Initiatives and Opportunities to Improve Cancer Care and treatment in Jamaica

Dr. Nadine A. Dietrich-Badal

Medical Oncologist

Diploma in Radiotherapy Oncology

Final Yr. Resident in Radiotherapy Oncology

Outline

- Overview of cancer epidemiology
- Risk Factors
- Integrated Comprehensive Care
- Primary prevention
- Screening and early detection
- Diagnosis and treatment
- Palliative Care
- Improvements in cancer care services in Jamaica
- Current Challenges
- The way forward

Disease Estimates - 2018

Indicator	Jamaica	Caribbean	World
Annual # of new cases	486	4200	569,847
Crude incidence rate[a]	33.4	18.8	15.1
Age-standardized incidence rate[a]	28.4	15.5	13.1
Cumulative risk (%) at 75 yrs. old[b]	37	2	1

[a] Rates per 100,000 per yr.

[b] Cumulative risk (incidence); probability or risk of individ
getting the disease (0-74yrs)

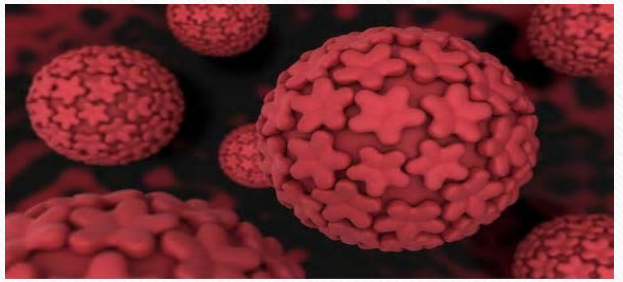
SOURCE: http://gco.iarc.fr/today 05 October 2018

Risk Factors

Risk Factor	Effects on Cervical Cancer
Sexual + Reproductive Health Factors	Persistent HPV infection is the cause of cervical cancer. Risk ↑ with: early of childbirth, high parity, increased no. of lifetime sexual partners, chlamydia + other STDs
Overweight / Obesity	↑ Risk for adenocarcinoma of the cervix
Tobacco use	↑ Risk
Oral contraceptives and hormone drug use	Extended use ↑ risk
HIV/AIDS	Higher risk for HPV infection + pre-invasive lesions may evolve faster into invasive lesion or cancer
Age	↑ with increasing age

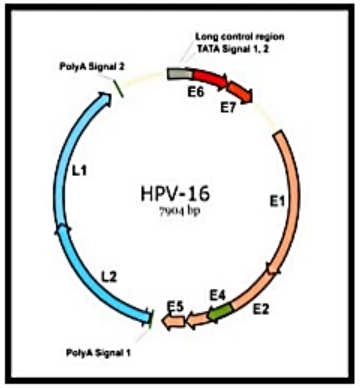
SOURCE: GLOBOCAN 2018

HPV + Oncogenesis



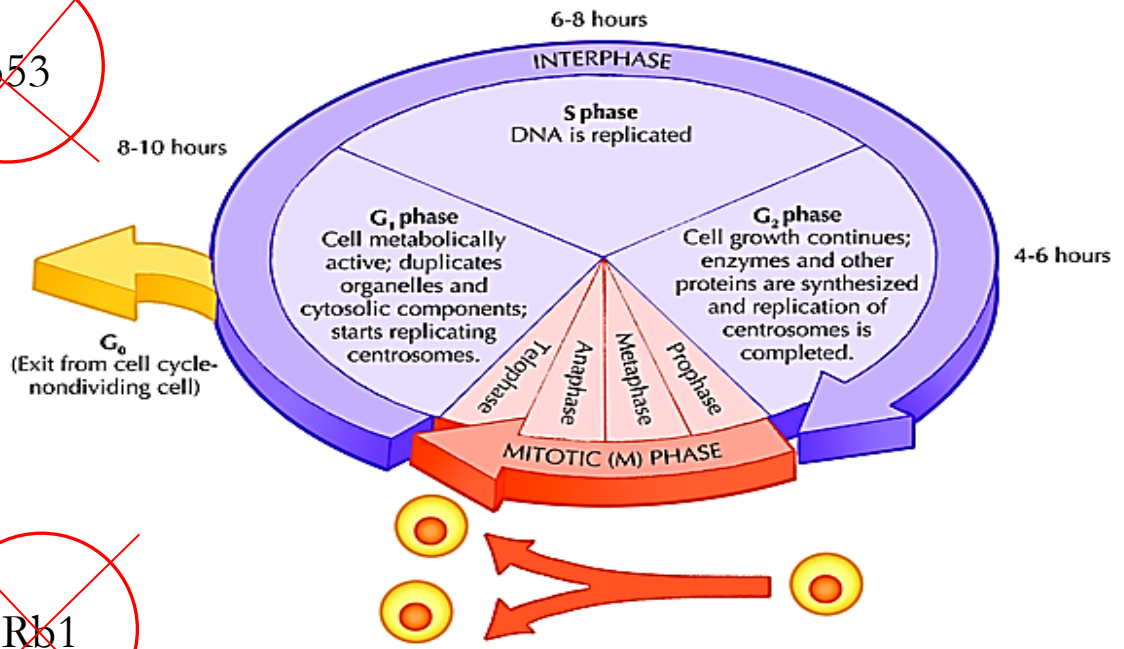
HPV structure

- HPV genome encodes 3 oncoproteins(E5,E6,E7),regula tory genes(E1,E2),capsid proteins(L1,L2).
- Oncogenesis is primarily mediated via the E6 and E7 proteins. HPV E6 complexes promote ubiquitin-mediated destruction of p53.
- Loss of cellular p53 function results in dysregulation of the G1/S and G2/M checkpoints.
- E7 is believed to be the major transforming oncogene during early carcinogenesis, with E6 functioning later.



p53

Rb1



Integrated Comprehensive Care

The 4 Pillars of Oncology

I	**Prevent all cancers that can be prevented**
II	**Treat all cancers that can be treated**
III	**Cure all cancers that can be cured**
IV	**Provide palliative care whenever palliation is required**

Primary Prevention

Prevention / prophylaxis

- **Vaccines: Gardasil® + Cervarix®**
- **Use of Condoms**
- **Abstinence from smoking, sexual intercourse***
- **Routine Screening**
- **Healthy diet and regular exercise**

Screening + Early Detection

- **Papanicolaou Test (pap smear)**
- **HPV-DNA testing**
- **VIA (Visual inspection with acetic acid)**

Co-testing

Diagnosis + Treatment

- History
- Physical Examination
- Biopsy of Cervical Tissue + Pathological review
- Complimentary examinations: +/- Imaging studies

Note: Use of Radiotherapy is critical in treating this disease, with indications ranging from curative to palliative. Consider Fertility sparing surgical techniques as per patient's request when feasible.

Pre-invasive Lesion:

CIN I: Observation + repeat Pap. smear

CINII / III: Colposcopy, Cryotherapy, LEEP or CKC

Invasive Lesion:

Stages I-IIA: Surgical Intervention or chemoradiation

Stages IIB – IVA: Concurrent Chemoradiation

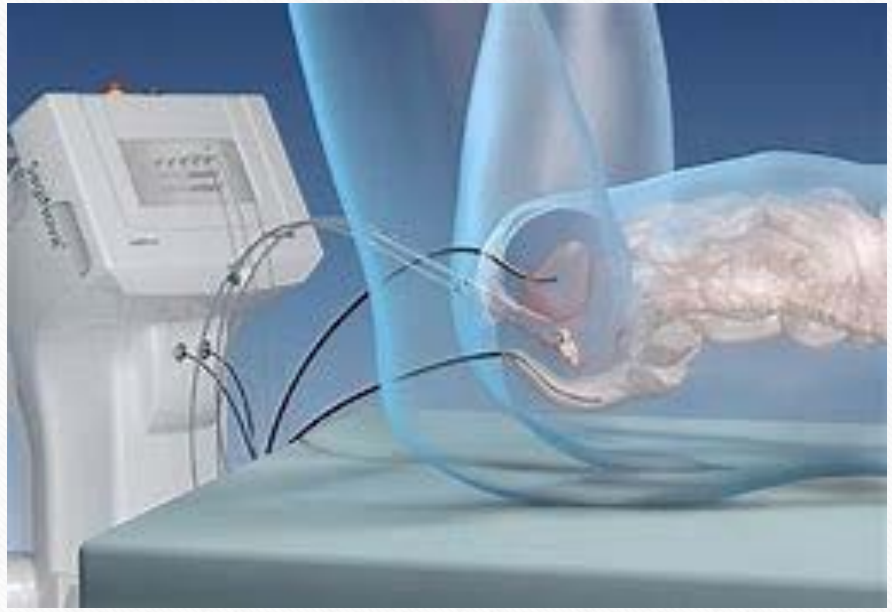
Stage IVB: Systemic therapy +/- Palliative Radiotherapy

- External Beam & Brachytherapy

(Key: LEEP; Loop electrosurgical excision procedure, CKC; cold knife conisation)

Brachytherapy

HDR with remote loading + after loading



Advantages of HDR v/s LDR:

- **↑ Patient turnover**
- **↓ Radiation exposure for pt. and staff**
- **Rigid immobilization**
- **Outpatient treatment**
- **Patient convenience**
- **Individualized treatment with source optimization**

Palliative Care

Covers a broad scope of care that is essential in cancer care as it optimizes the patients QOL and therefore impacts positively on outcome. It includes:

- **Pain management**
- **Symptom control**
- **Emotional, psychological and spiritual support**

Note: Oncospecific treatments can be used with palliative intent, specifically at lower doses for adequate symptom control

Improvements in Cancer Care

- **Screening Guidelines for Cervical Cancer – June 2020**
- **Implementation of a Pilot Program VIA - SRHA**
- **Implementation of HPV vaccination into the national vaccination schedule - 2018**
- **Initiation of a National Cancer Registry - 2018**
- **Incorporation of 2 Linac Machines – 2017 (CRH) + 2018 (NCTC)**
- **Internal formation of MDT (Multidisciplinary Team) for the prioritization + expediting of difficult oncology cases –**
- **Presently undertaking the preparation of protocols + guidelines for oncospecific management**

Current Challenges

- **Insufficient public education**
- **Poor uptake of screening services**

Patient factors: fear, stigma (promiscuity)

System related factors: ease of access, turnaround time for results

- **Lack of funding to assist in:**
  - **Training programs – Oncology Field**
  - **Purchase and incorporation of equipment + maintenance**
- **Long waiting times to access already available services given limitations with # of resources**
- **Unavailability of advanced oncology and surgical services – HDR brachytherapy**
- **Delivery of treatment in inopportune times which impacts negatively on the outcome**
- **Lack of dedication to research due to patient / doctor ratio and lack of computerized database**

Moving Forward

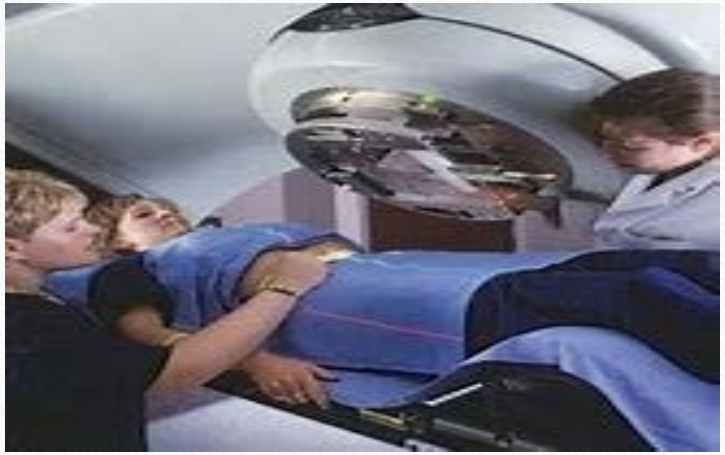
Cervical Cancer elimination plan to be developed in 2021 (PAHO-supported)

- **PAHO/WHO recommends a comprehensive cancer control plan, with leadership and sufficient funding, and strategies for primary prevention, screening and early detection, diagnosis, treatment and palliative care, using a resource-stratified approach.**
- **Increase funding to improve health system barriers and facilitate implementation of effective cervical cancer programs.**
- **Promotion of educational campaigns re importance of HPV vaccines to wipe out stigma and misconceptions that pose as challenges and acceptance at the community level.**

Moving Forward

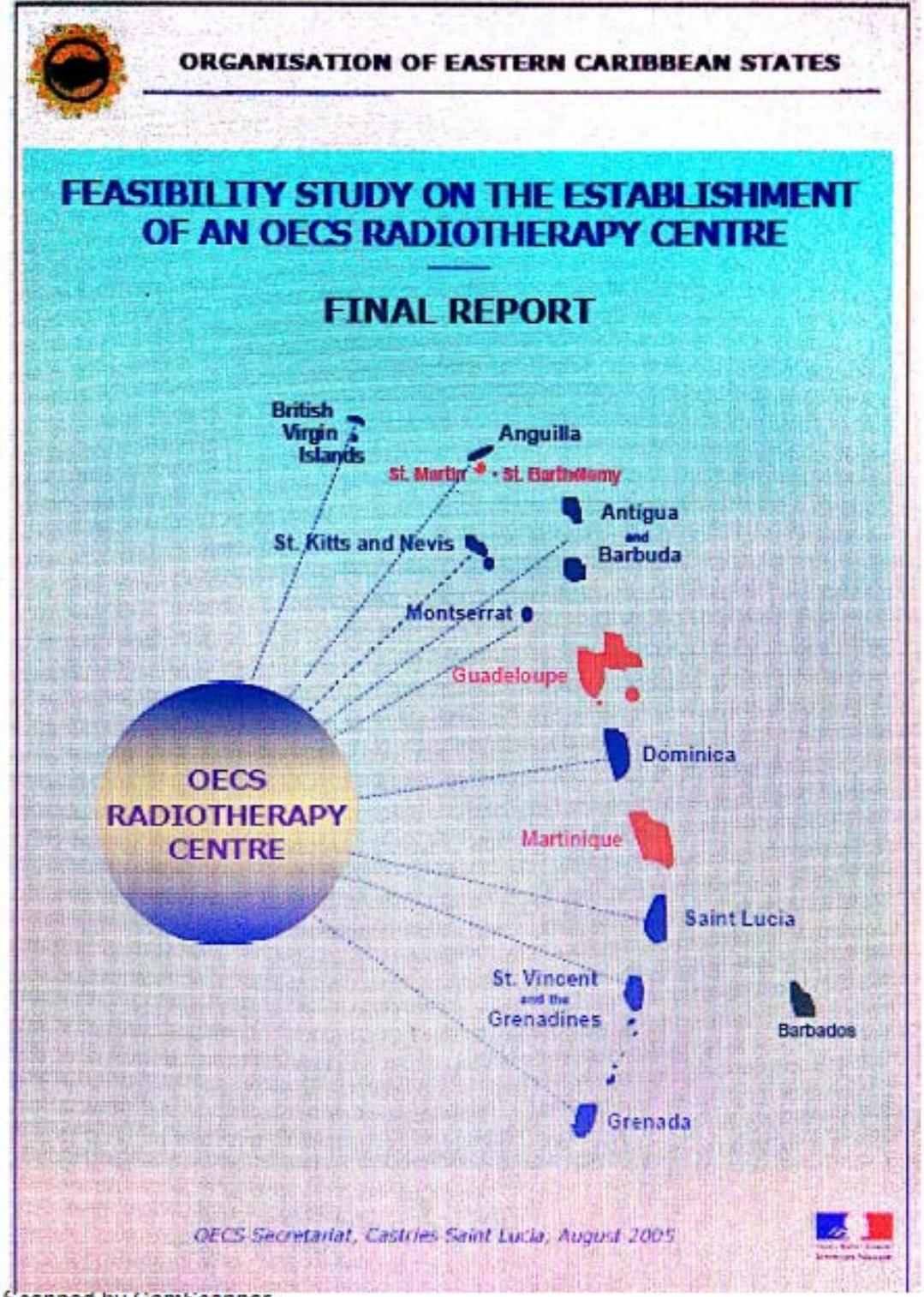
- Improve organized screening programs that achieve a high screening coverage with quality testing, and linked to timely and effective treatment.
- Increase palliative care services and ensure that adequate pain and symptom control, together with emotional, psychological and spiritual support are provided to its citizens.
- Cancer registration needs to be improved to be able to record cancer incidence, mortality and inform cancer programs and policies. Implementation of computerized database collection.
- Participation in clinical trials and contribution to research for the growth towards a better understanding of cancer and improve quality of care.

Thank You



HOW ANTIGUA AND BARBUDA'S CANCER CENTRE IS CREATING SHARED SERVICES IN THE CARIBBEAN

HENRY J HAZEL, CPA, CB, MBA
Chief Operating Officer
The Cancer Centre Eastern Caribbean



The Cancer Centre Eastern Caribbean

- The Brainchild of OECS Ministers of Health, 2003 (Antigua)
- OECS-commissioned Feasibility Study, 2005 (EU-funded)
- OECS mandate to build and operate, 2009 (Anguilla)
- Officially launched June 2015 (OECS event)

THE CANCER CENTRE
Eastern Caribbean

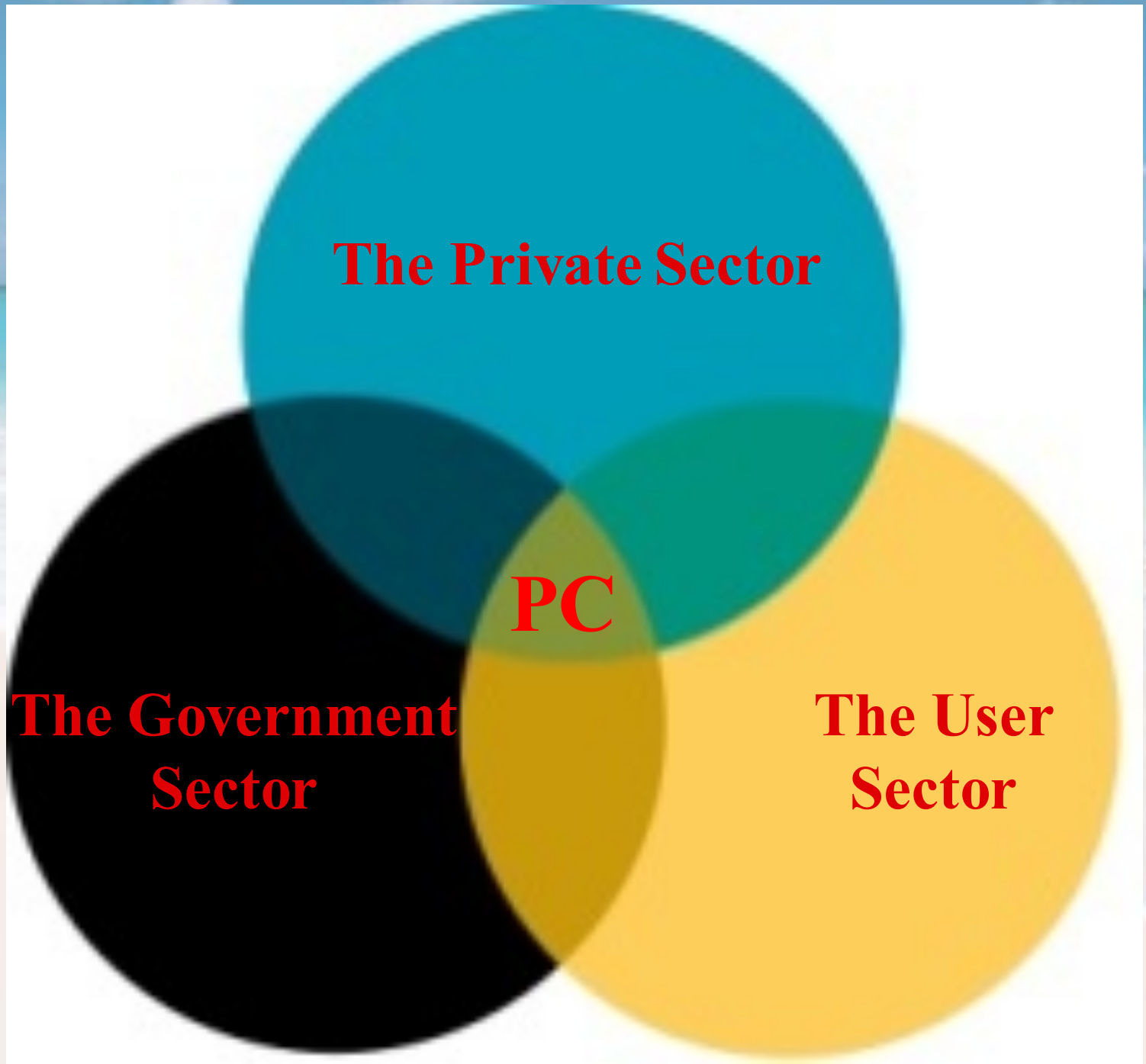
Prime Min. Baldwin Spencer of Antigua and Barbuda invited Dr Conville Brown to develop a Cardiac and Cancer Centre, not only for Antigua and Barbuda, but for the entire OECS, like Dr Brown's The Bahamas Heart Centre and The Cancer Centre Bahamas...

…using Dr Brown's Partnered Care Model

THE CANCER CENTRE EASTERN CARIBBEAN

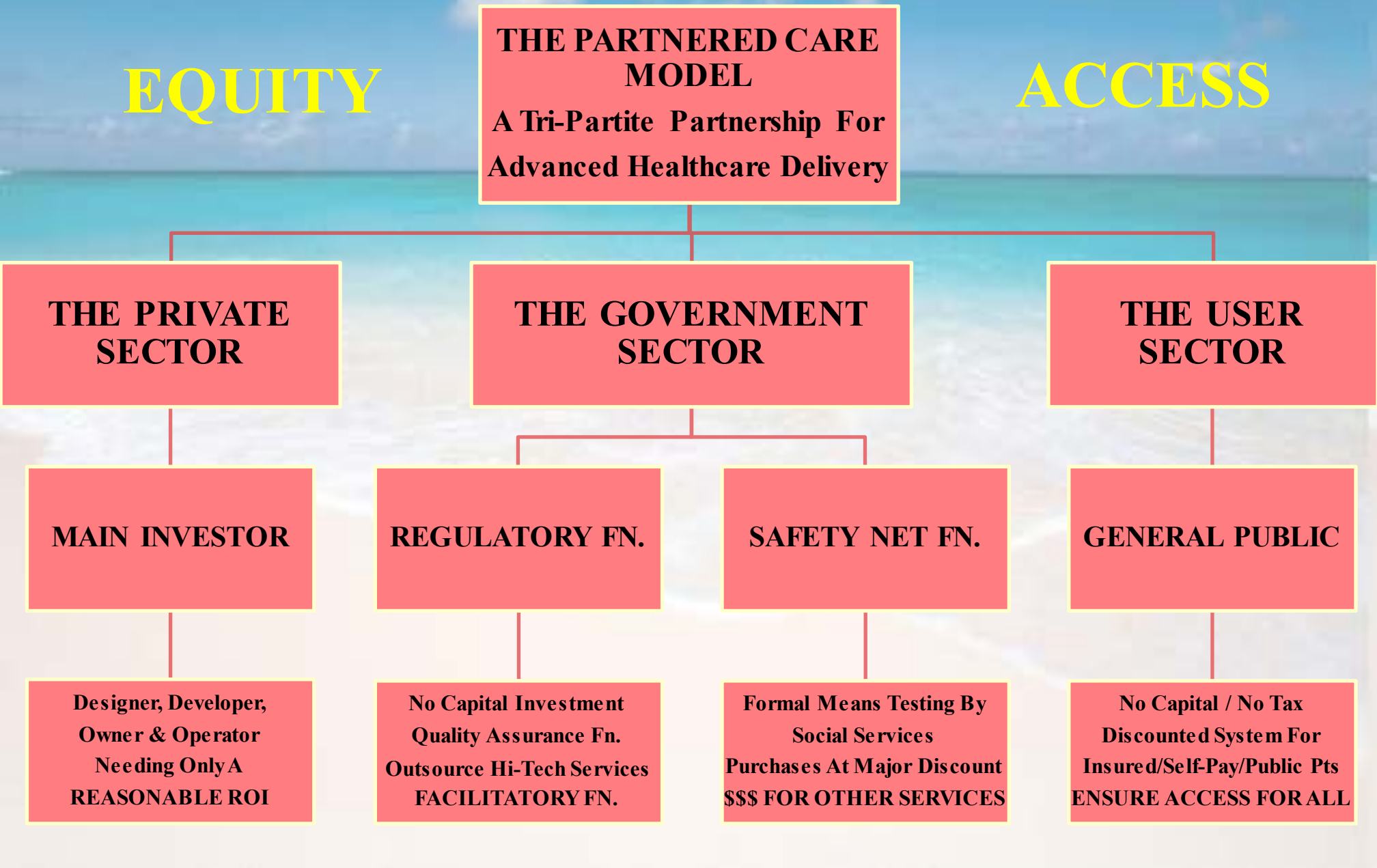

THE BAHAMAS CHEST CENTER
HOME OF
THE BAHAMAS HEART CENTER
72
72
WELCOME
TO
THE

Dr. Conville Brown's Partnered Care Model '90



THE PARTNERED CARE MODEL

By Dr. Conville Brown, 7/1/1990 thru Present, 2016.



The Cancer Centre Eastern Caribbean Complex / The Medical Pavilion Antigua: The 3rd and Final 20,000 SF Version As at JULY, 2013.

For Cancer, Heart and PET-CT Imaging Centres:

CAPITAL: USD15MM + 5MM + 3MM

THE CANCER CENTRE
Eastern Caribbean

THE PHYSICAL PLANT
JUNE, 2015

THE CANCER CENTRE EASTERN CARIBBEAN

THE DAILY Observer
"Let There Be Light"
Vol. 22 | No. 147 | St. John's, Antigua | Saturday June 27, 2015 | Price: $3.00

CANCER CENTRE OPENS

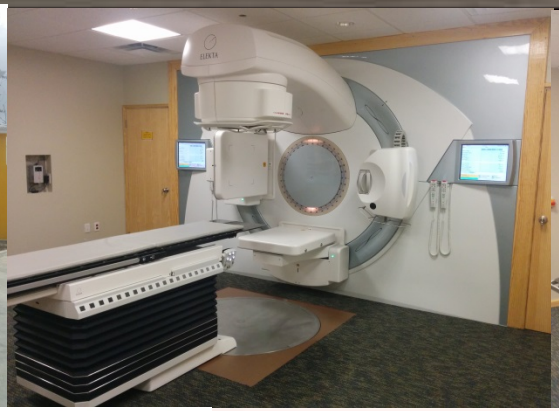
Prime Minister Gaston Browne, Bahamas Prime Minister and sitting Caricom Chair, Perry Christie, Chairman of the Cancer Centre Eastern Caribbean, Dr Conville Brown and Opposition Leader Baldwin Spencer cut the ribbon to mark the opening of the facility. (OBSERVER media photo)

Read story on page 3

State-Of-The-Art CANCER CARE FOR THE OECS, BY THE OECS, AND OF THE OECS!!!

THE CANCER CENTRE EASTERN CARIBBEAN

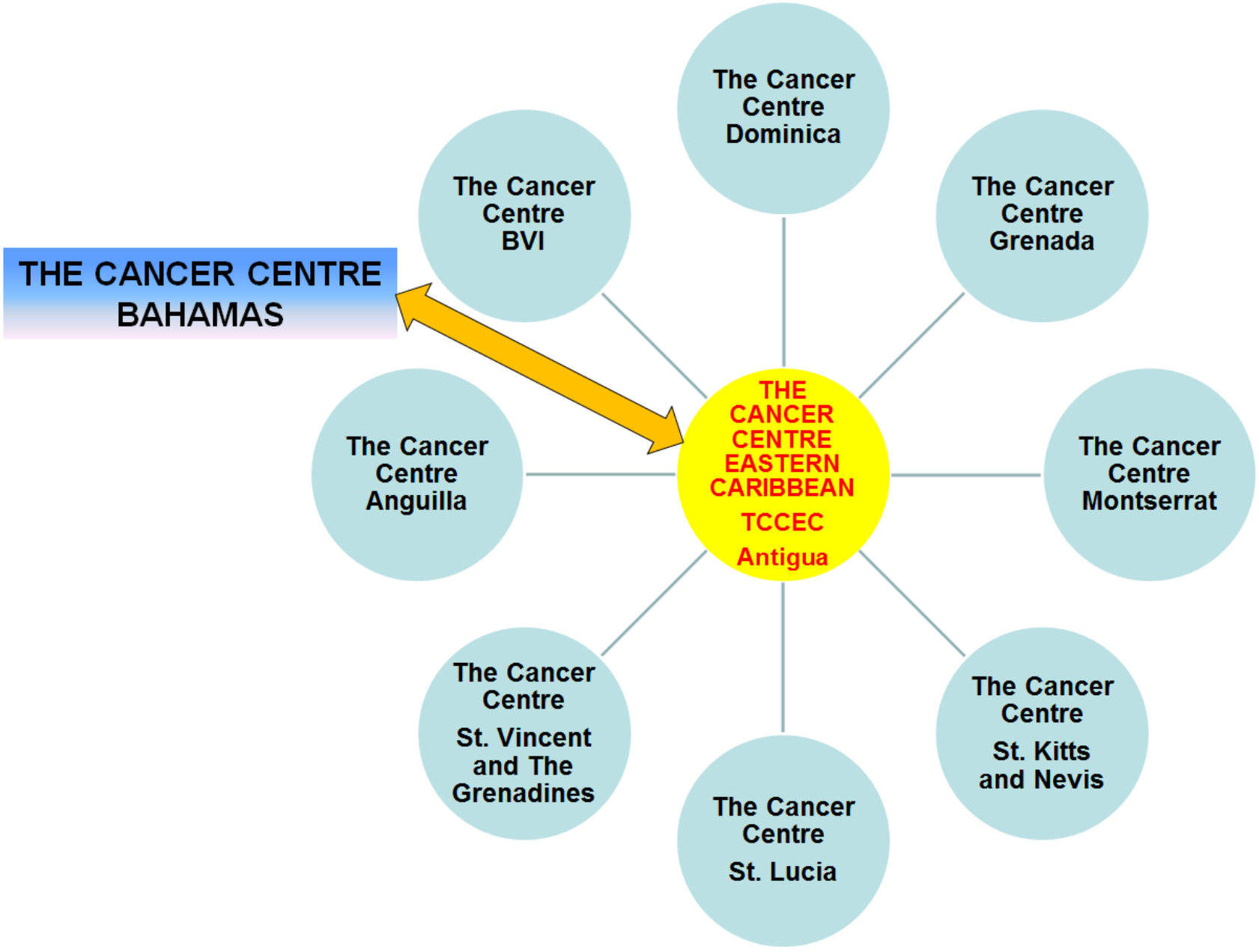
26TH JUNE, 2015.



THE MEDICAL PAVILION
ANTIGUA

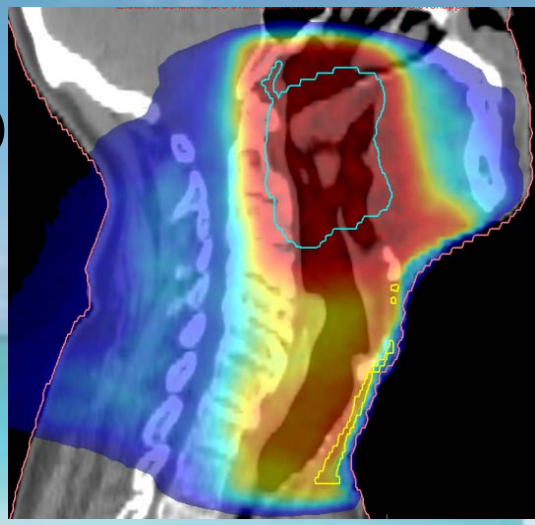
THE CANCER CENTRE EASTERN CARIBBEAN

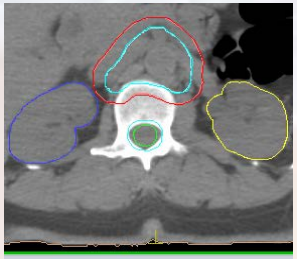
The Caribbean Cancer Centre Network
- TCCCN –
"A Partnered Care Hub & Spoke Model"

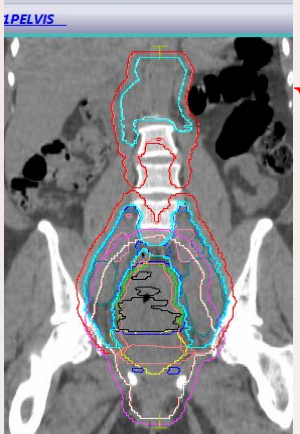


State-Of-The-Art Radiation Therapy Modalities Available

1. 3-D Conformal Radiation Therapy (3-D CRT)
2. Intensity Modulated Radiation Therapy (IMRT)
3. Image-Guided Radiation Therapy (IGRT)
4. Volumetric Modulated Arc Therapy (VMAT)
5. Stereotactic Body Radiation Therapy (SBRT)
6. Stereotactic Radio-Surgery (SRS).







Bringing Only The Best Of The Best

To The OECS!

While PAHO & IAEA-Approved Via Audits!!

THE CANCER CENTRE
Eastern Caribbean

AFFORDABLE RADIATION THERAPY PRICES MADE POSSIBLE BY PARTNERED CARE

1. **STANDARD US PRICING:**
    1. **Can in the range of USD50,000 – 150,000/Course**
    2. **Tremendous cost uncertainty due to CPT Code pricing model with relative values (RV) application**

THE CANCER CENTRE
Eastern Caribbean

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2. **TCCEC INSURED PATIENTS: USD25,000 - 35,000/Course (Aver).**
    1. **Much Lower Than Prevailing Market Prices**
    2. **Packaged Pricing:**
        - **offers 100% predictability on cost**
        - **completely de-mystifies and speeds up Claims Processing**

THE CANCER CENTRE
Eastern Caribbean

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3. **SELF-PAYING PRIVATE PATIENTS:** USD22,500/Course
    1. On Average, 20% Discount off the INSURED's price

THE CANCER CENTRE
Eastern Caribbean

AFFORDABLE RADIATION THERAPY PRICES MADE POSSIBLE BY PARTNERED CARE

1. **STANDARD US PRICING:**
    1. **Can Easily Exceed USD50,000 – 150,000/Course**

2. **TCCEC INSURED PATIENTS: USD25,000 - 35,000/Course (Aver).**
    1. **Much Lower Than Prevailing Market Prices**

3. **TCCEC SELF-PAYING PRIVATE PATIENTS: USD22,500/Course**
    1. **On Average, 20% Discount off INSURED's price.**

4. **OECS GOVERNMENT PATIENTS: FLAT USD10,000/COURSE!!**
    1. **ALL GOVERNMENT-SPONSORED CASES.**
    2. **Price Honoured Since 2009.**

"EQUITY AND ACCESS"

THE CANCER CENTRE
Eastern Caribbean

TCCEC's VALUE PROPOSITION TO OECS RESIDENTS

QUALITY OF CARE at the highest level to be found anywhere in the world

Unrivalled PROFESSIONALISM & COMMITMENT of staff

LATEST PROVEN TECHNOLOGIES in cancer treatment

Meets INTERNATIONAL STANDARDS as attested by PAHO and IAEA

UNBEATABLE LOW PRICES

EASILY ACCESSIBLE from your own country

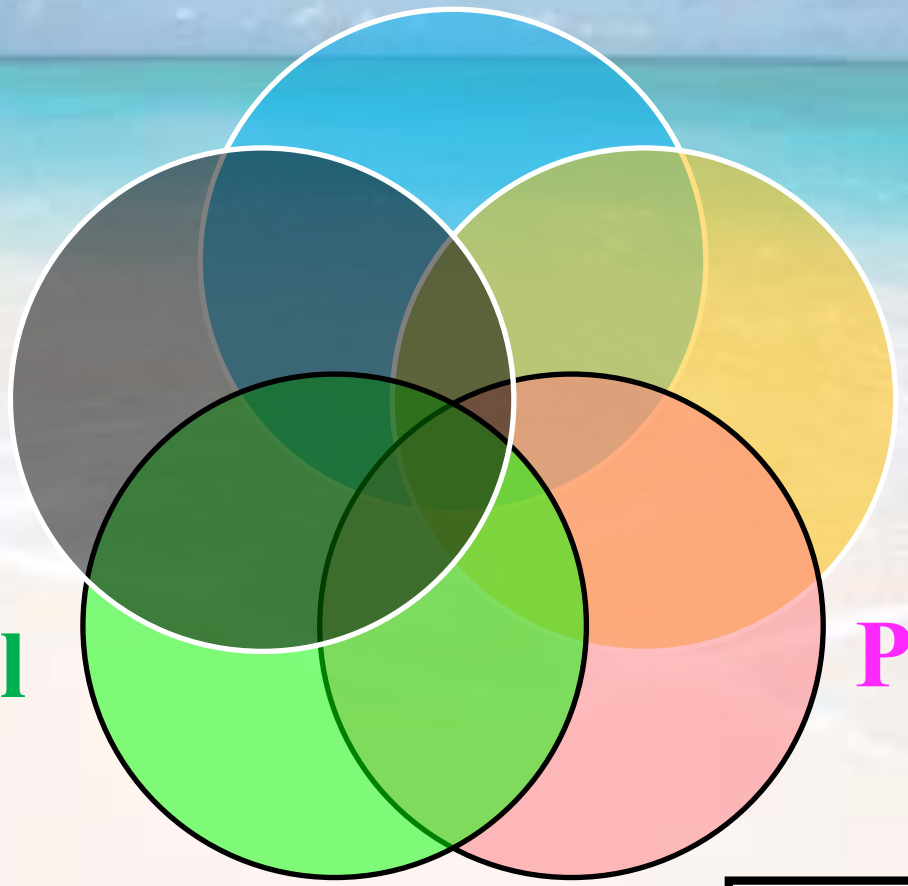
SAVES on the cost, hassle and inconvenience of traveling outside OECS

Makes YOU the FOCAL POINT OF ATTENTION

Treats YOU with COMPASSION

THE CANCER CENTRE
Eastern Caribbean

THE PARTNERED CARE MODEL 5.0
THE PENTA-PARTITE -(5)- PARTNERSHIP



THE CANCER CENTRE
Eastern Caribbean

Summary Of Early TCCEC Impact In The OECS

1. **A Regional Strategic Resource Platform For Cancer Control:** increasingly for **Cancer Control (Care, Training And Research)**, as an OECS-Wide Cancer Centre with a high-value radiation service in Antigua.
2. **Raising Cancer Awareness:** thousands of people (e.g. each patient has 10-20 family members and friends), and many community activities (education, fairs, etc.).
3. **Providing Affordable Access Closer To Home:** less need to leave The OECS, expansion of clinics, with better coordination of care.
4. **Seeing A Good Case-Mix:** appropriate for a major cancer centre.
5. **Caring For The People of The OECS at Many Levels:** Consultations, Inter-disciplinary Decision-Making, Chemotherapy And Radiotherapy, Survivorship.

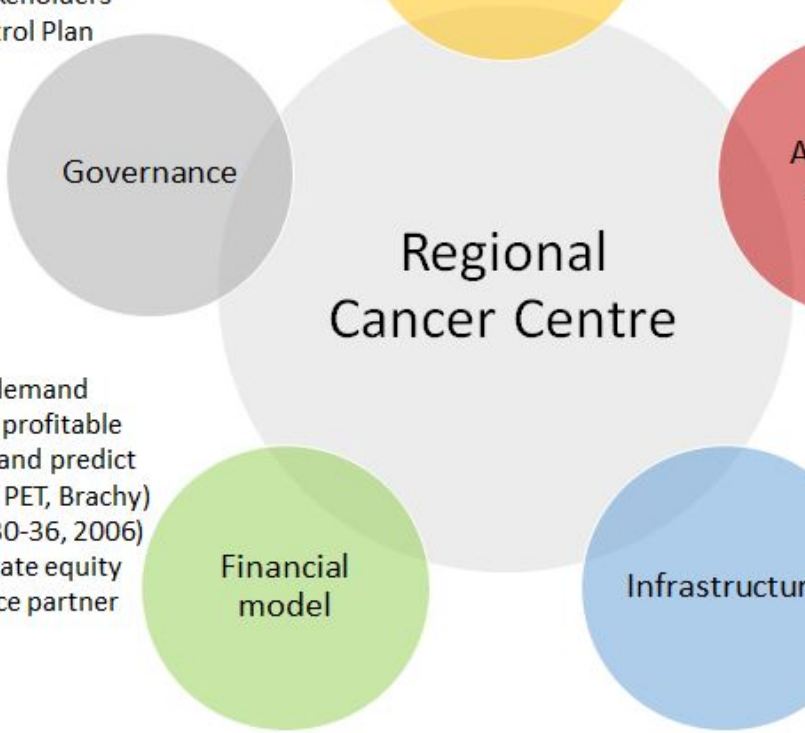
THE CANCER CENTRE
Eastern Caribbean

Summary Of Early TCCEC Impact In The OECS

6. **Ensuring Quality Care:** guidelines, reviewing clinical decisions, radiation QA.
7. **Measuring Outcomes:** evidence for the centre, system and governments.
8. **Improving The Cancer Control System:** analytics to guide optimization of early detection, pace of management, coordination of services.
9. **Providing A Model:** a **Five-Domain Model** to guide TCCEC's evolution; relevant for new centres in other LMIC countries and regions.
10. **Penta-Partite Partnered Care Model:** **A Proven Model Of Advancing Advanced Healthcare Services in Developing Countries, Small Island Developing States (SIDS), or Low-Middle Income Countries (LMICs) and Regions (OECS).**

THE CANCER CENTRE
Eastern Caribbean

THE VISION:
TCCEC As A Comprehensive & Academic Centre



Staff expertise is international and fully capable
Culture of safety, quality assurance and quality control
Networks of island-located consultation and follow-up clinics
Shared clinical policies and developing regional guidelines
Tumour-boards for case-conference clinical discussions
Regional peer-review rounds for radiation plan quality
Holding oncology conferences (2016, 2018)
Eventual training up of local staff

Biostatistics expertise
Routine Data assembly
Regular analytics and clinical audits
Medical physics program with research
University teaching roles with affiliations
Hospital, Consortia and University partners
Evidence-based clinical and management priorities
Loco-regional studies (from screening to survivorship)
Look to Clinical trials (e.g. international, randomized)
Technology 'platform' initiatives (PET, Nano)

Project management
Stability of power and water supply
Disaster plans (hurricane, fire, flood)
Facility design (efficiency, sustainability)
Clinical plan if single radiation machine fails

Estimation of multi-year demand
Some underutilization is still profitable
Banking costs are reasonable and predict
Progressive services (RTX, CTX, PET, Brachy)
Partnership model (WIMJ 55:30-36, 2006)
40% government & 60% private equity
Industry supplier is a resource partner

National membership in IAEA
Commitment to UN SDG's for 2030
Sustained state-level commitments to MOU
Government champions & engaged ministers
National legislation for nuclear applications
Establishing a national cancer registry
Balanced board of stakeholders
National Cancer Control Plan

1. **Five Main Interacting Domains**
2. **Many Items Within Domains Require Further Attention**
3. **Some Of The Steeper Challenges Are Highlighted**
4. **Model Is Highly Relevant To Non-Serviced SIDS And Sparsely Populated Regions, And Small Nations**

THE CANCER CENTRE
Eastern Caribbean

DAY 3

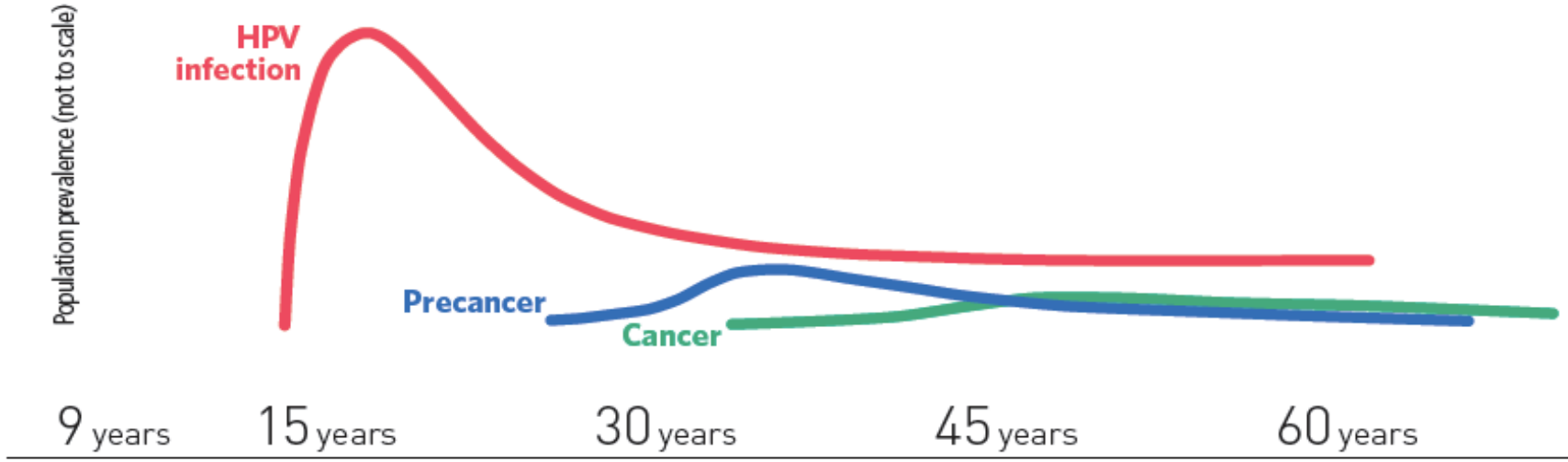
October 29- Day 3 Session 3: HPV vaccination Moderator: Martha Velandia		
10:00 – 10:15	Challenges of the HPV vaccination program	Belize
10:15 – 10:30	Challenges of the HPV vaccination program	Dominica
10:30 – 11:00	Discussion	
11:00 – 11:20	Global Analysis of HPV Vaccination Coverage	Paul Bloem - WHO
11:20-12:40	Guidelines for the Calculation of HPV Vaccination Coverage	Martha Velandia - PAHO Laia Bruni - Institut Català d'Oncologia
12:40- 1:00	Discussion	

Challenges of the HPV Vaccination Program, Belize

HPV Vaccination
Towards the Elimination of Cervical Cancer in the Caribbean Countries
22,23,29 & 30 October 2020

Lilia Middleton
EPI Manager
October 29, 2020

LIFE COURSE APPROACH TO PREVENT HPV INFECTION AND CERVICAL CANCER

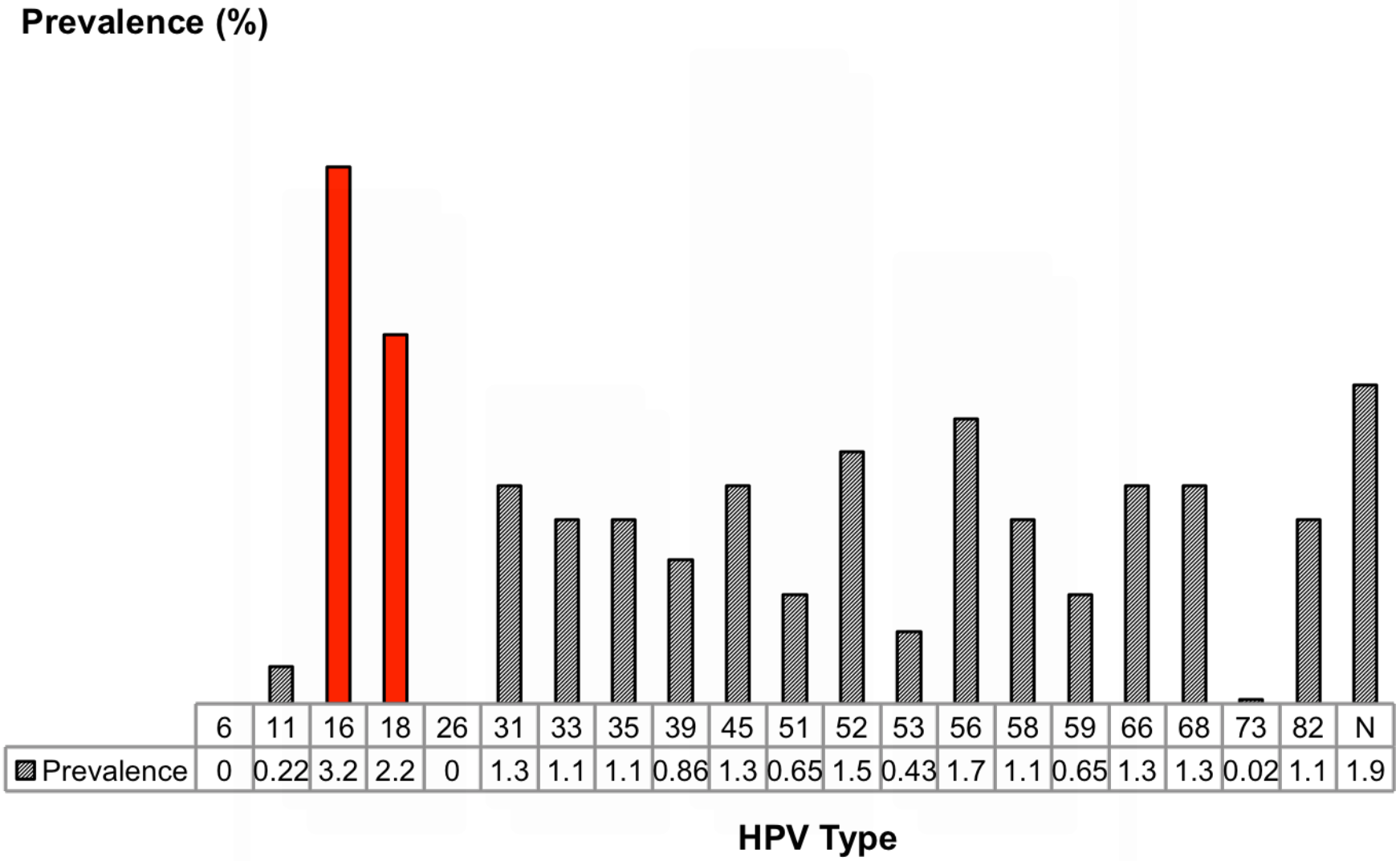


PRIMARY PREVENTION	SECONDARY PREVENTION	TERCIARY CARE
HPV Vaccination **Health education** **Adolescent health services**	**Screening and treatment of precancerous lesions** HPV testing, Pap, VIA cryotherapy colposcopy LEEP, etc	**Diagnosis and treatment** **Pathology** surgery radiotherapy chemotherapy Palliative care

COMMUNITY → PRIMARY HEALTH CARE → SECONDARY HEALTH CARE → TERTIARY HEALTH CARE

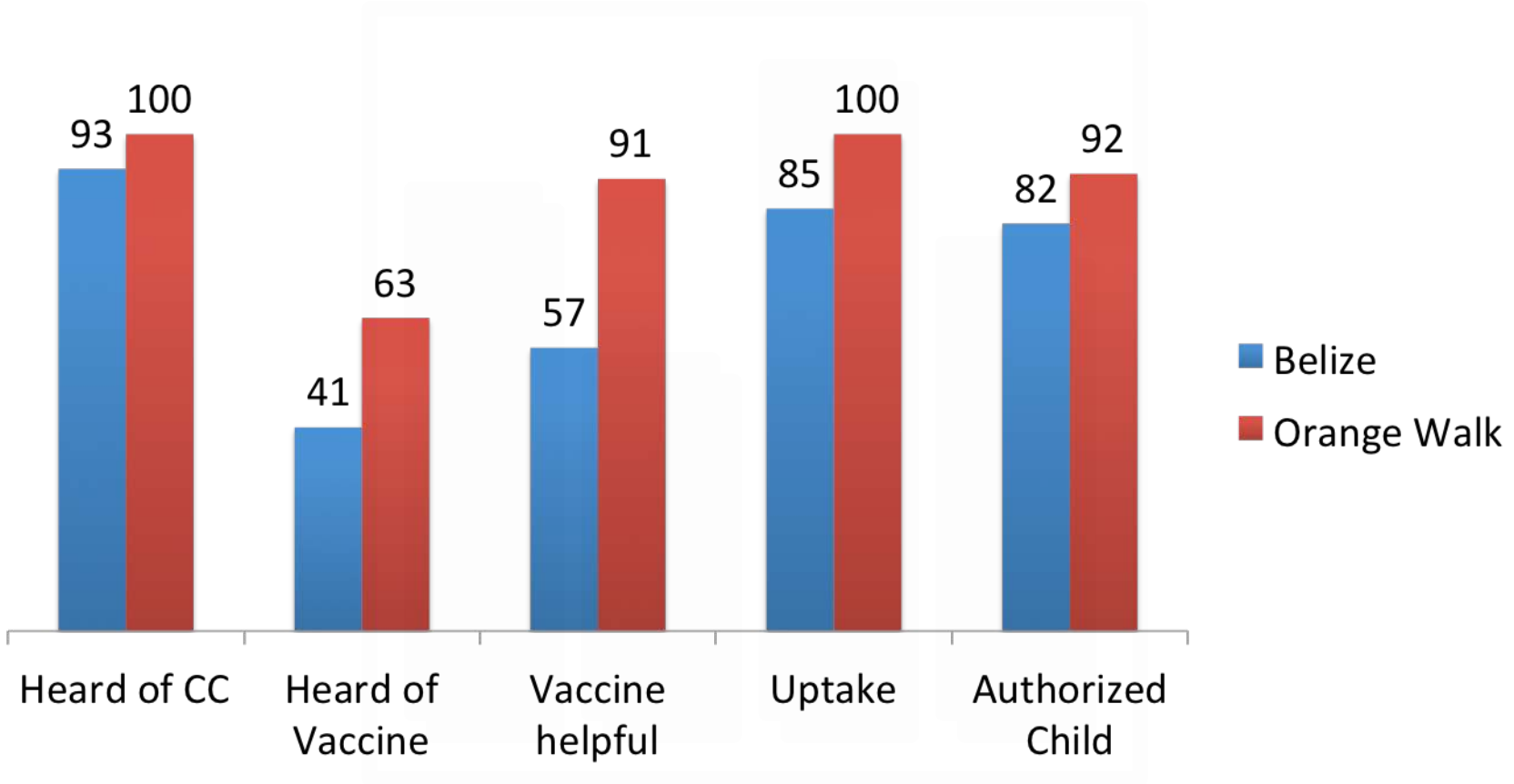
Source: WHO Guidance Note. Comprehensive Cervical Cancer Prevention and Control. 2012

Figure 2. Prevalence of HPV types in the entire study group of Belizean women, Belize City, 2007.



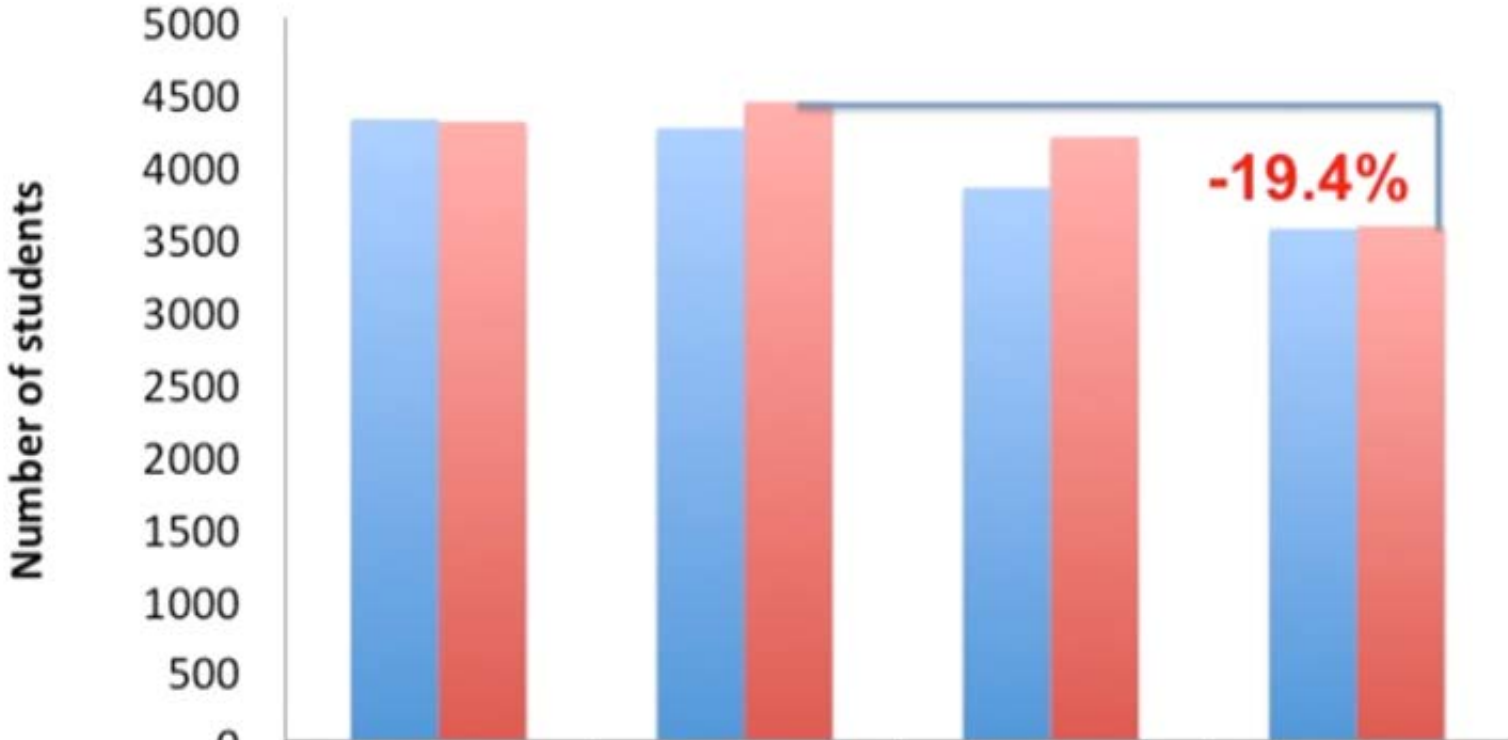
	6	11	16	18	26	31	33	35	39	45	51	52	53	56	58	59	66	68	73	82	N
Prevalence	0	0.22	3.2	2.2	0	1.3	1.1	1.1	0.86	1.3	0.65	1.5	0.43	1.7	1.1	0.65	1.3	1.3	0.02	1.1	1.9

HPV vaccine acceptance 2016 among women access EPI Program



Number of female students in Standard 3-6

Belize 2010-2011 and 2011-2012



	Standard 3	Standard 4	Standard 5	Standard 6
2010-2011	4296	4234	3823	3540
2011-2012	4278	4415	4174	3558

Source: MOEYS. Education Statistical Digest of Belize 2011/2012

Strategy: Introduction of HPV Vaccine in the National Schedule to prevent and control cervical cancer.

- Year of introduction : November 2016
- HPV4 = 6, 11, 16,&18.(Gardasil) One dose of 0.5ml on day 0 and the 2nd dose 6 months after the first dose IM (deltoid area of upper arm)
- 15 years and older = 0 day (first contact), 2nd dose 2 months after the first dose, 3rd dose 6 months after the 1st dose IM
- Target population – Std 4 Class – Boys and girls
- Delivery:
  - ÇSchool based (during mobile clinics, drive thru)
  - ÇHealth facility
  - ÇCampaign

Training: Health and Education Professionals

- Health professionals have received training about HPV vaccine:
  - ÇYear of introduction
  - ÇAnnually
  - ÇNever
  - ÇOther - describe
- Education professionals have received information about HPV vaccine:
  - ÇYear of introduction
  - ÇAnnually
  - ÇNever
  - ÇOther - describe

Communication plan:

Introduction – preparatory phase

- Religious leaders
- Minister and senior management of the Ministry of Education
- Type of vaccine agreed by local experts from public and private sector
- Talk shows through radio and T.V were conducted from national and local media.
- Rapid acceptance survey done
- Cost effectiveness analysis of the introduction of HPV vaccine
- Prevalence of HPV among 500 women

- National and district training sessions were done for public and private health care personnel, district education officers, principals, parents/ caregivers, CSO's.
- Meetings with Alcaldes/ local village leaders were held to assist with dissemination of the information.
- Media breakfast at national and local level
- No funds were available for communication
- Priority given to face to face sensitization sessions

Communication plan:

Routine

- Academia UB – lecturer to Nursing scholars
- Nurses and doctors employed
- Parents, teachers and students
- CHW

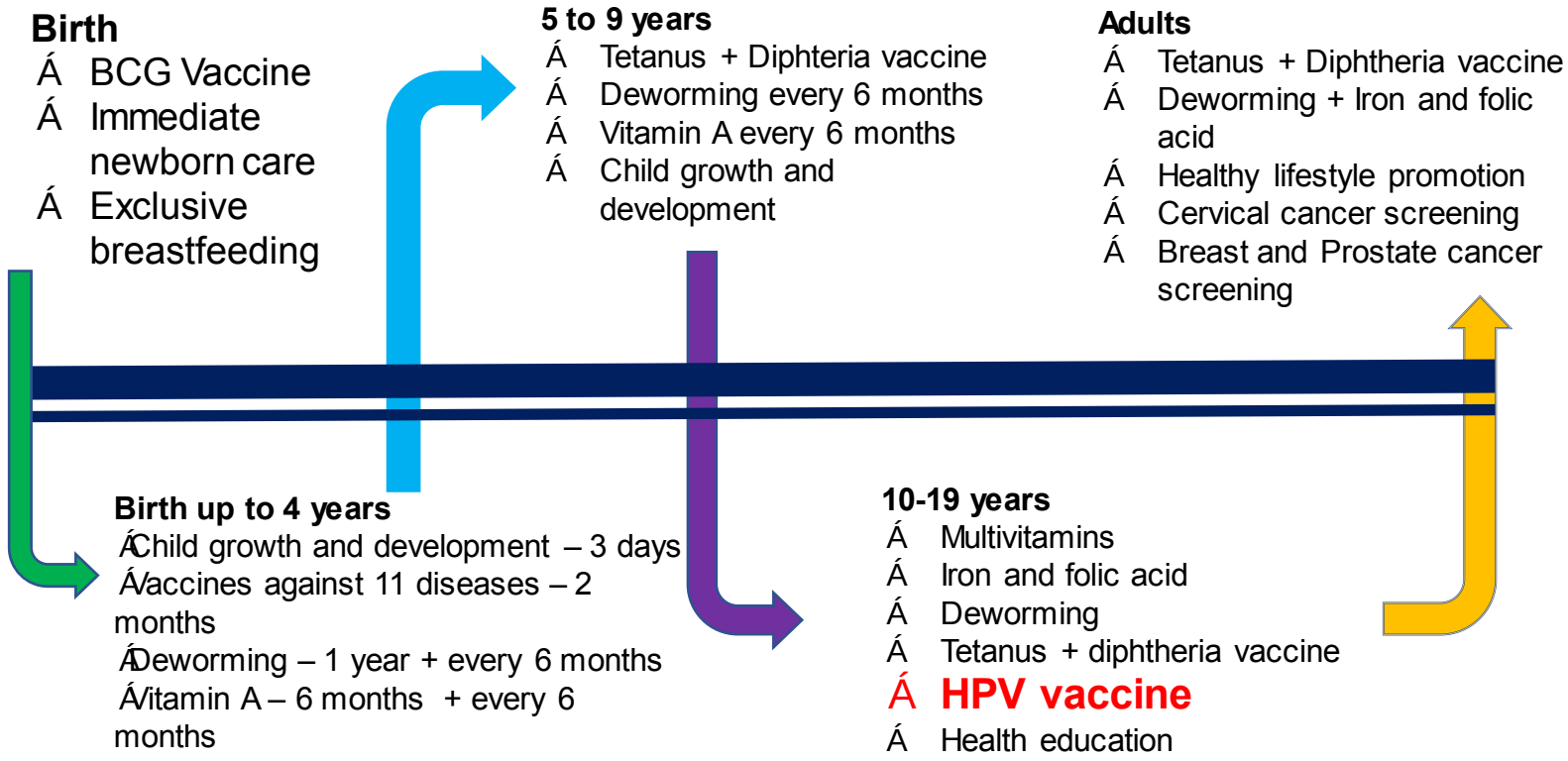
- National and district training sessions were done for public and health care personnel, district education officers, principals, parents/ caregivers.
- Meetings with Alcaldes/ local village leaders were held to assist with dissemination of the information.
- The country does not have a specific budget for communication it is projected as part of the general budget.

Communication plan:

- **Crisis Plan**
- The Public Health Nurse of each District is responsible for coordinating the vaccination at the schools and the EPI manager at the National level.
- In crisis situation, the PHN will inform the EPI manager, through telephone, who in turn will consult with key persons from the MOH HQ.
- Crisis related to vaccination is dealt with immediately by the national and local team (including on weekends)
- Antivax groups were vocal for 2 weeks after the launch, we used the opportunity to provide the public with evidence based data and information

Life Course Preventive Interventions

Crosscutting: Screening and management of acute and chronic illnesses



What is Human Papilloma Virus or HPV?

It's a virus that cause infections in nearly all persons at some point in their lives.

There are many different types of HPV virus. Some types can cause health problems including genital warts and cancers. And there are vaccines that can **STOP** these health problems from happening.

Life Course Preventive Interventions

Crosscutting: Screening and management of acute and chronic illnesses

Birth
- BCG Vaccine
- Immediate newborn care
- Exclusive breastfeeding

Birth up to 4 years
- Child growth and development – 3 days
- Vaccines against 11 diseases – 2 months
- Deworming – 1 year + every 6 months
- Vitamin A – 6 months + every 6 months

5 to 9 years
- Tetanus + Diphtheria vaccine
- Deworming every 6 months
- Vitamin A every 6 months
- Child growth and development

10-19 years
- Multivitamins
- Iron and folic acid
- Deworming
- Tetanus + diphtheria vaccine
- **HPV vaccine**
- Health education

Adults
- Tetanus + Diphtheria vaccine
- Deworming + Iron and folic acid
- Healthy lifestyle promotion
- Cervical cancer screening
- Breast and Prostate cancer screening

What is Human Papilloma Virus or HPV?

It's a virus that cause infections in nearly all persons at some point in their lives.

There are many different types of HPV virus. Some types can cause health problems including genital warts and cancers. And there are vaccines that can **STOP** these health problems from happening.

Belize National Vaccination Schedule

Vaccine	Recommended age	Dose	Site and Route
BCG	At Birth	0.05 ml for below < 2mths 0.1 ml for infants >2 mths and all others	Mid-Upper right arm – intradermal
Hepatitis B – birth dose	At birth		
Inactivated Polio Vaccine (IPV) Oral Polio Vaccine (OPV)	1st dose at 2 mths 2nd dose at 4 mths 3rd dose at 6 mths 1st Booster at 18 mths 2nd Booster dose at 4.5 years	0.5 ml injectable (IPV) 2 drops 2 drops 2 drops 2 drops	Intramuscular Oral Oral Oral Oral
Pentavalent - DPT/Hib/Hep-B	1st dose at 2 mths 2nd dose at 4 mths 3rd dose at 6 mths	0.5 ml 0.5 ml 0.5 ml	Antero-lateral thigh – intramuscular
Measles Mumps Rubella (MMR)	1st dose at 12 mths 2nd dose at 18 mths	0.5 ml 0.5 ml	Left arm – subcutaneous
Diphtheria Pertussis Tetanus (DPT)	Booster dose at 4 -5 years	0.5 ml	Deltoid region - intramuscular
DT Pediatric	Given to children with contraindication to Pertussis in Pentavalent vaccine	0.5 ml	Antero-lateral thigh – intramuscular
Human Papilloma Virus (HPV) Vaccine	Given to females in Standard Four Class. Two doses with 6 months interval between 1st and 2nd dose	0.5	Intramuscular injection in the Deltoid muscle – right or left arm
Td or Adult DT	1st dose at first antenatal visit 2nd dose at least 4 weeks after the 1st dose if required	0.5 ml 0.5 ml	Right or left arm on deltoid muscle - intramuscular

How is HPV spread?

HPV can be passed even when an infected person has no signs or symptoms.

It spreads through direct contact with an infected person and through sexual contact.

Does HPV cause health problems?

In most cases, HPV goes away on its own and does not cause any health problems.

But when HPV does not go away, it can cause health problems like genital warts and cancer.

Genital warts usually appear as a small bump or group of bumps in the genital area. They can be small or large, raised or flat, or shaped like a cauliflower.

A healthcare provider can usually diagnose warts by looking at the genital area.

Almost 1 out of every 4 cancers diagnosed in Belize is a woman with Cervical Cancer

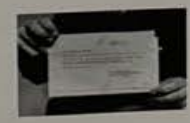
How to stop HPV infections

Get vaccinated

HPV vaccines are safe and effective.

They can protect males and females against diseases (including cancers)

The vaccine is more effective if given before commencing sexual contact



How many doses of HPV vaccines are required?

2 doses total: 1st dose, 6 months, 2nd dose

Second dose 6 months after first dose

Is there any payment for the vaccine?

No out of pocket payment is required for girls in Standard IV class.

Most common side effects

Redness, swelling and pain in the injection site

Parent authorization is required

The Ministry of Education will send a written request to parents for their authorization for girls in Standard IV class to be vaccinated.

100% of girls Vaccinated before exposure will not suffer from cervical cancer caused by HPV 16 and 18

www.health.gov.bz

/Ministry of Health
Belize

Vaccination consent form

The HPV vaccine that protects against cervical cancer, is being offered to your daughter at her school. To get the best protection, it is important that she receives the full course of two doses. The second dose is administered six months after the first dose. I have received a leaflet, accompanying this consent form, with further information on the HPV vaccine. YES ☐ NO ☐

I have read the information contained within this leaflet. YES ☐ NO ☐

I hereby confirm that I was given information on the HPV vaccine, including the most common side effects; which I shall report to the nearest health care provider or health facility. Please fill the data requested below:

Daughter's name

School's name

Consent for full course HPV vaccine

I WANT my daughter to receive the full course of two doses of HPV vaccine
Name of parent or caregiver, relationship and phone number
Signature and date

I DO NOT want my daughter to receive the HPV vaccine
Name of parent or caregiver, relationship and phone number
Signature and date

Ministry of Health

Belize

Fact Sheet on Human Papillomavirus Vaccine (HPV) for Parents/Public

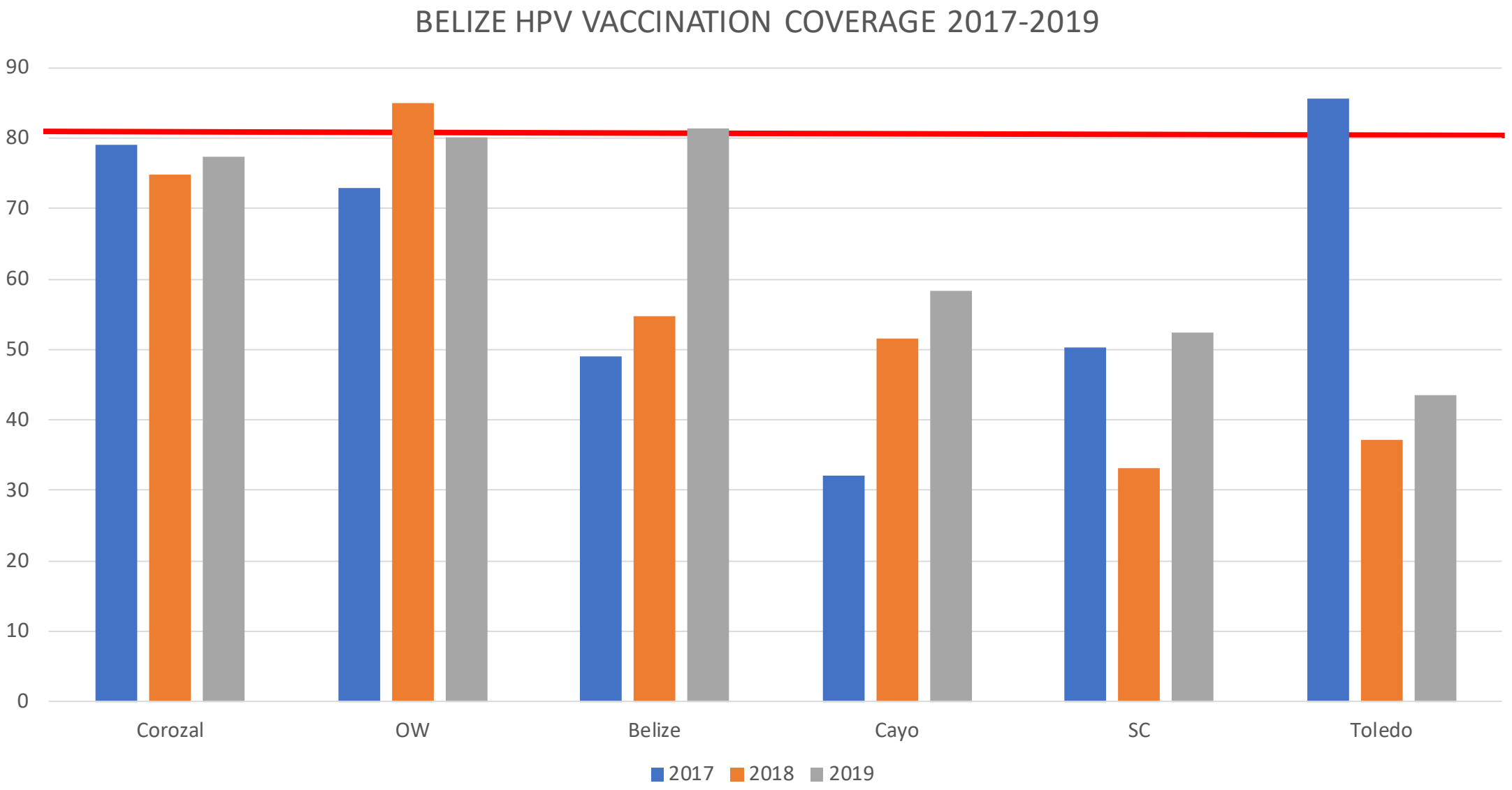
The Human Papillomavirus (HPV) infection is responsible for causing cancer of the cervix known as 'Cervical Cancer' which is the second leading cause of cancer deaths among women, vaginal and vulvar cancers and penile cancer in men.

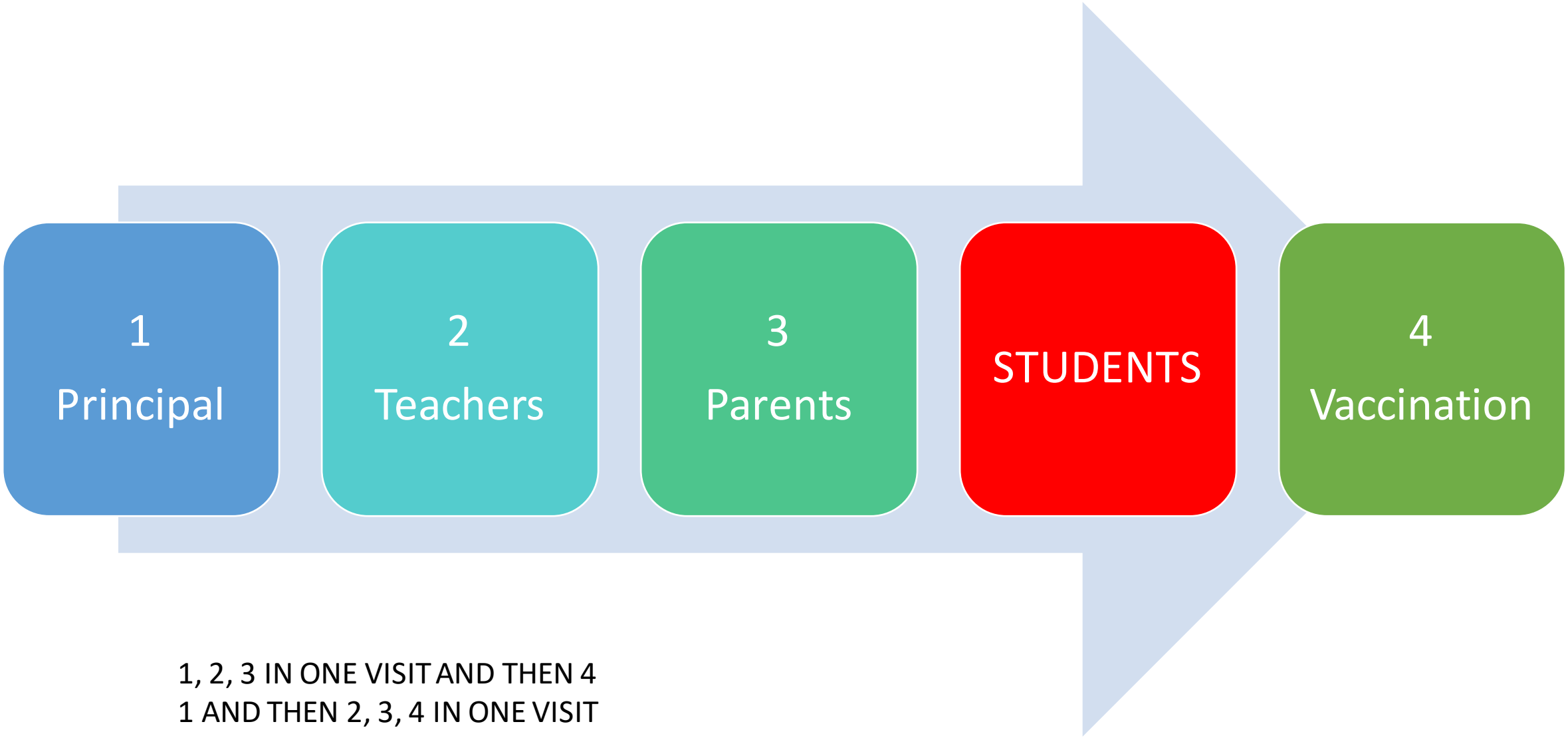
HPV can also cause other types of anal, throat, head and neck cancers, and genital warts in both men and women. Vaccination with HPV vaccine means prevention of these cancers and genital warts.

1. *Why HPV Vaccine?*
   The HPV vaccine protects against 4 major types of Human papilloma viruses (types 6, 11, 16, 18) of Human Papillomaviruses preventing most genital warts and cervical cancer.

2. *Who should get HPV vaccine?*
   HPV vaccine is recommended for both males and females from age 9 to 26 years. It is highly effective and can provide 100% protection before exposure to HPV infection.

3. *Who should NOT get HPV vaccine?*
   Anyone who has had a severe reaction to yeast or the components of the vaccine or to a previous dose of the vaccine should not be vaccinated.


BELIZE HPV VACCINATION COVERAGE 2017-2019
90
80
70
60
50
40
30
20
10
0
Corozal
OW
Belize
Cayo
SC
Toledo
2017
2018
2019



1, 2, 3 IN ONE VISIT AND THEN 4
1 AND THEN 2, 3, 4 IN ONE VISIT
1, 2 IN ONE VISIT AND THEN 3, 4
SHOW LOWEST COVERAGE

Main challenges to reach 80% coverage for girls at 13 years old:

- Myths – HPV: girls will be sterilized, lead to increased sexual activity and early sexual debut. Question frequently asked was “Why only girls?”
- We took for granted that principals and teachers would readily accept to support the program.
- Poor coordination with some schools, poor attendance of parents to scheduled meetings.
- Consent form not being signed, therefore vaccine not given.

Main challenges Cont'd

- There were some social resistance due to the fear of a new vaccine and rumours being circulated by Anti-vax groups.
- Increase work load on already limited MCH staff and insufficient access to transportation.
- Vaccine was not given to Private facilities and some parent preferred for it to be administered by their family physician.
- Closure of schools due to COVID 19, unable to complete the 2nd dose , scheduled for May 2020

Main strengths of the HPV vaccination program :

- Full support by religious leaders, Ministry of Education, Belize Cancer Society and other CSO, NGO (transparency of presentations)
- Integrated into existing school health program
- Training done annually to Principals. Some schools have taken the initiative to educate the parents and have consent form signed .
- Vaccines administered are placed in a google document which is shared with the PHN's and they are better able to update their reports at their facilities.
- Stock out of vaccine in one occasion
- Fully funded by the GOB

Thank You!

Challenges of the HPV Vaccination Program

Country: Dominica

HPV Vaccination
Towards the Elimination of Cervical Cancer in the Caribbean Countries
22,23,29, and 30 October 2020

Strategy: Combined with Cervical Cancer Awareness

- Year of introduction :2019
- HPV vaccine used :Quadrivalent
- Target population :849 Students Grade 6 of Primary schools
- Gender:
  - Both male and female
- Delivery:
  - School based
  - Health facility(For those students who were absent on day of vaccination or whose parents had not submitted the consent form and so could not be done at school.)

Training:

- Health professionals have received training about HPV vaccine:
  - ÇYear of introduction
  - ÇOther – Prior to introduction in 2019 a sensitization session was conducted for all health staff during VWA 2018 as part of training sessions in EPI held to observe VWA.
- Education professionals have received information about HPV vaccine:
  - ÇYear of introduction

Communication Plan

- A comprehensive communication plan was developed.
- This came from a decision to sell the HPV Vaccine as a cervical Cancer prevention method same advocated during development of Cervical cancer guidelines.
-
- First thing that was done was that a steering Committee was established and a Communication Plan developed
- A technical committee to work on the Cervical Cancer Guidelines and HPV Vaccine implementation was also established.

Communication Plan

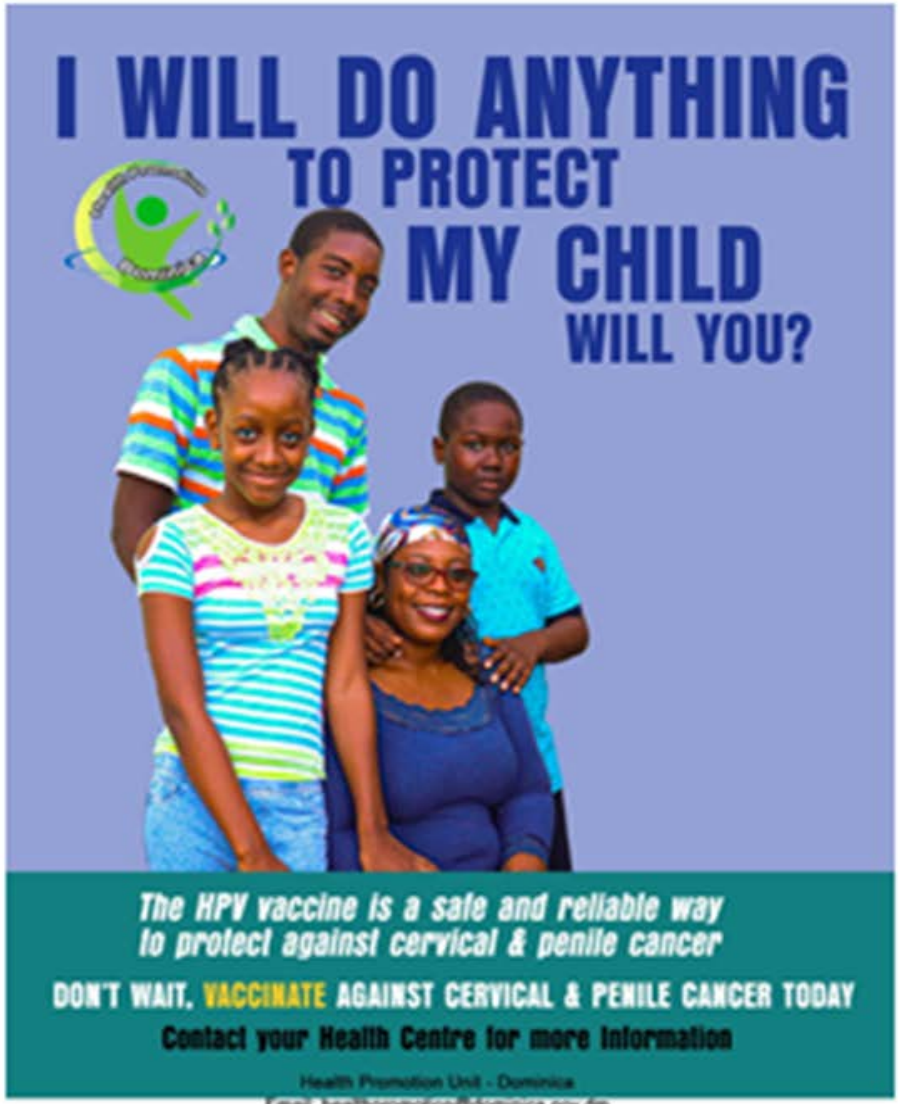
- The plan included the convening of a National Stakeholder Consultation with evidence of strong political will. There the Health Minister made the declaration for the implementation of the Vaccine.
- This was followed by a series of retraining of HCW and advocacy sessions with Educators of all schools and media island wide.
- A total of 130 HCWs from both the public and private sector was trained.
- 68 Educators and 10 media house staff was also trained.

Communication Plan

- Following these training sessions, there was an 8 week none stop media campaign, Face to Face School and Community Campaigns.
- Radio programs including live call in sessions were conducted on all stations .
- Information was also given on HP Face book page , Dominica News on line , Emo News and Newspaper.
- It included the development of posters, PSA and other IECs and meeting with all PTAs on Island and Faith Based Organizations.
- The actual administration of the vaccines commence only when we were satisfied that all stakeholders had been reached.

Communication Plan

- Schedule dates of administration was provided via media and schools so as to sensitize parents , guardians and teachers when it would begin.
- Dominica does have a specific budget for communication. However financial support for the introduction of the HPV vaccine was provided by PAHO.
- There is also a plan specific for crisis management. This would include the management of adverse events if it happened .


I WILL DO ANYTHING
TO PROTECT
MY CHILD
WILL YOU?
The HPV vaccine is a safe and reliable way
to protect against cervical & penile cancer
DON'T WAIT, VACCINATE AGAINST CERVICAL & PENILE CANCER TODAY
Contact your Health Centre for more information
Health Promotion Unit - Dominica
Email: healthpromotion@dominica.gov.dm
Phone: (767) 266 3469/3470

Access and Annual Coverage:

(Graphic the first and second dose annually since introduction to the target population)

- Calculating the **first dose** over the target population has the function of **measuring access**.

Access = $\frac{\text{Number of first doses administered to a given cohort in a determined year}}{\text{Target population of a given cohort}} \times 100$

798x100/849=93.9%

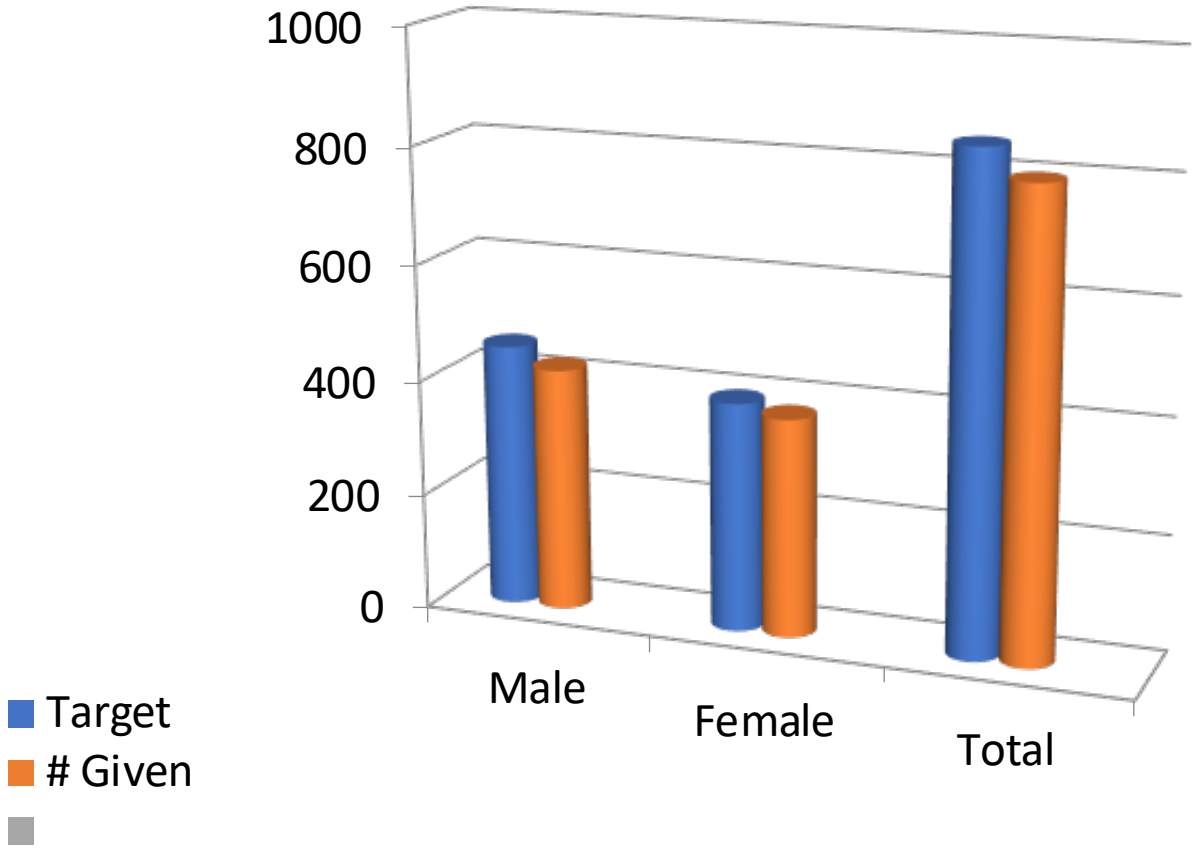
Annual coverage of the HPV vaccine should be calculated with the second dose.

Annual coverage = $\frac{\text{Number of second doses administered to a given cohort in a determined year}}{\text{Target population of a given cohort}} \times 100$

701/849 =82.56%

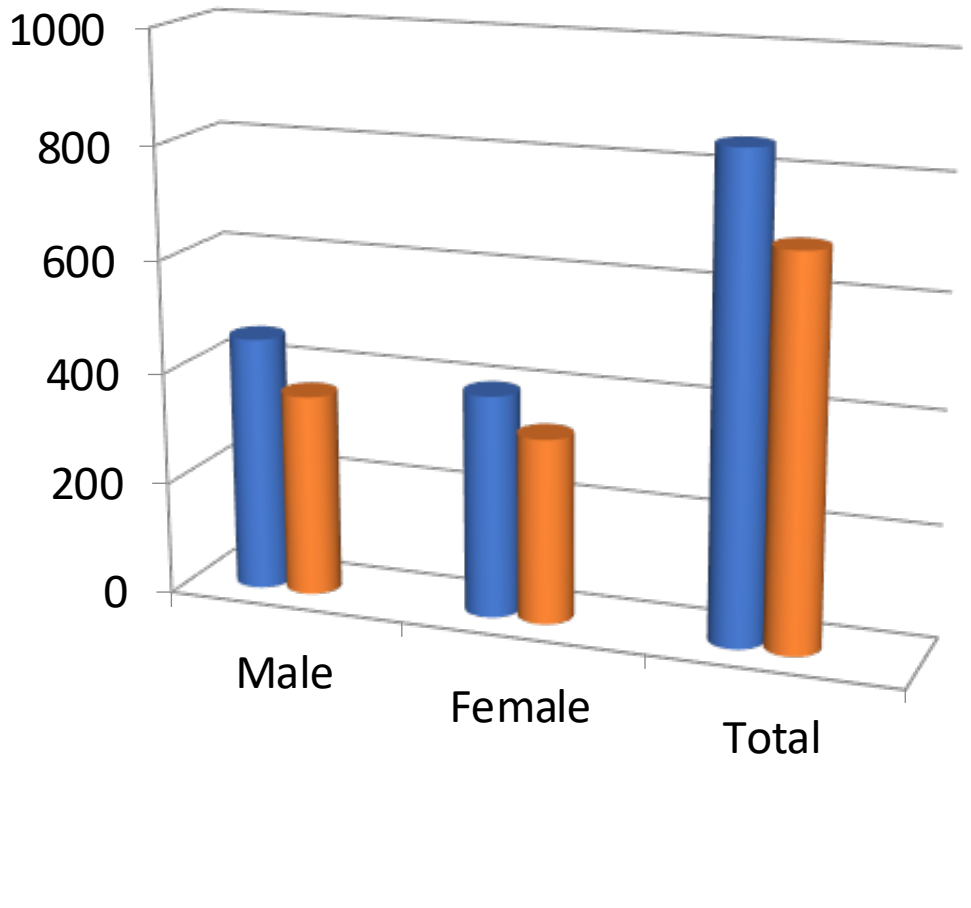
HPV COVERAGE 1st DOSE

	Target	Number Given	Coverage
Male	454	421	92.7
Female	395	377	95.4
Total	849	798	93.9



HPV COVERAGE 2nd DOSE

	Target	Number Given	Coverage
Male	454	360	79
Female	395	329	83.3
Total	849	689	81.1



Main challenges to reach 90% coverage for girls at 15 years old:

- Opposition from some parents of children
- Some teachers of schools not supportive of the programme
- Absent students on day of vaccination
- Refusal of vaccine from more affluent parents
- The COVID -19 Pandemic
- Issue of consent form

Solutions to those challenges

- Opposition from some parents of children
  - We got buy in from health care workers , media and teachers very early
  - Conducted numerous education sessions with all stakeholders including the Media, Ministry of Education, Cancer Society, Medical and Nursing School, Health staff from both Primary and Secondary care and private institutions.
  - Conducted training for Principals/Teachers of Schools and Media workshops were also conducted. Individual schools were also targeted for education .

Solutions to those challenges

- PTA meetings was held with all schools island wide.
- Training sessions were conducted for all staff at district and national level whether they would be involved in administration of the vaccine or not. Aim was to get everybody on board , to provide accurate information and correct any misinformation.

Solutions to those challenges

2. A few cases of absenteeism of children at school

Solution

- Students who were absent was asked to visit the health center near their homes with their parents. Most were subsequently immunized.

3. The impact of COVID-19 delayed the administration of the second dose since the country was on total and partial lock down and all schools were closed.

Solutions to those challenges

- The EPI staff was very committed and communicated with principals of various schools who arranged a specific date when all students of the grade would come to school and be immunized. They turned up and so we were able to commence the second round of vaccinations. Even then not all the students came to school and have not been vaccinated.

- The negative publicity circulating on social media re the COVID -19 vaccine has also caused persons to lose interest in the HPV vaccine and so some parents refused the second dose.

Solutions to those challenges

4. Issue of consent form

In some parts of the island e.g. the city it is customary to give consent forms to parents of students in Grade Six prior to immunizing the children . There is always the possibility that some of these forms would not be returned or no consent would be given.

Solution

- Those students whose parents had not returned the forms were called via the telephone and verbal consent was given.
- Other teachers felt that since the education act mandated that every child at school be vaccinated stood in proxy for the students whose parents had not returned the form .
- Still others came to the health center and was immunized . A small percentage bluntly refused the vaccine.

Solutions to those challenges

- In one case a child was vaccinated whose parents had not given consent . We were able to calm and reassure the parent. She finally came back to thank the Team for giving her twin girls the vaccine since she subsequently had gone for her green card and this was one less vaccine she had to pay for.

- No child developed any adverse reactions from the vaccine which helped to boost parents confidence in the vaccine.

Main strengthens of the HPV vaccination program :

- Strategy to combine cervical cancer prevention and the introduction of the vaccine to fight cervical cancer was very effective.
- Political commitment to the programme. The lunching of the vaccine was done by the Minister of Health at a stakeholder consultation which was rebroadcast nationally.
- Combined effort of all stakeholders involved in planning for the introduction e.g. Cancer Society, Ministries of Health and Education and others.
- Media support. Media was involved from the beginning to solicit their support.
- Very committed EPI staff involved in the administration of the vaccine.
- Support from PAHO and the CPO was phenomenal.

Main strengthens of the HPV vaccination program :

- The entire execution went very well.
- We were always one step in front and looked at all possible challenges and had solutions to deal with them.
- Funding for all aspects of the implementation was available thanks to PAHO and MOH Dominica.

THANK YOU FOR YOUR ATTENTION !!!!

Zaimisolmos visual arts

Global analysis of HPV vaccination coverage

Paul Bloem, WHO IVB-EPI

In collaboration with Laia Bruni, ICO, Barcelona

PAHO Regional meeting on Cervical Cancer Elimination, 29 Oct 2020

HPV vaccine coverage indicators in the Global Health context

WHO Global STI Strategy

- ü 70% of countries to introduce HPV vaccination in the national vaccine schedule by 2020
- ü Reach 90% national coverage and 80% in every district or administrative unit with HVP vaccination by 2030 (GVAP)

NCD Global Monitoring Framework resolution WHA66 10.22 (2030)

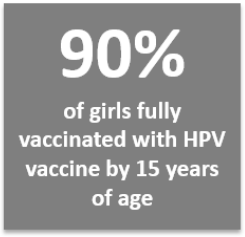
- ü Availability of HPV vaccines as part of a national immunization schedule

Sustainable Development Goals - SDG 2030 indicator 3.b.1

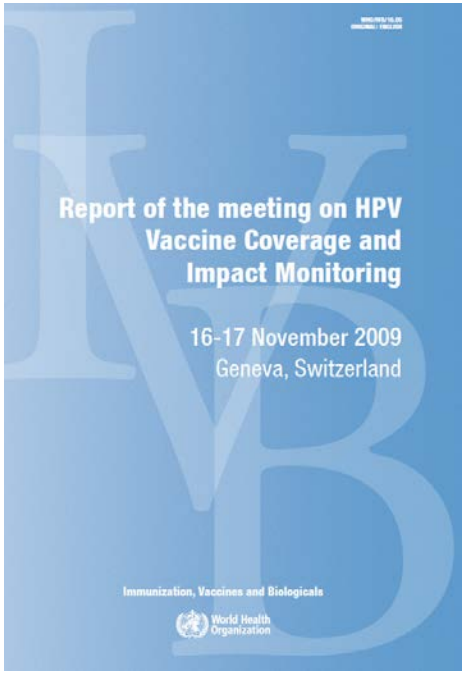
- ü Population protected by all vaccines in schedule (Composite indicator: coverages of DTP3, MCV2, PCVc and HPVc)

Global Cervical Cancer Elimination Strategy (draft)

- ü Target: 90% of girls fully vaccination with HPV vaccine by 15 years of age



History of HPV coverage monitoring



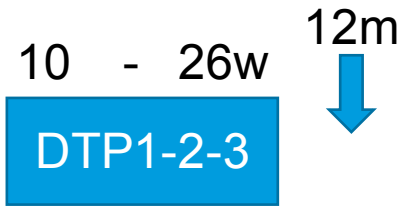
2009

The primary objectives for this November meeting were to:

1) agree on the architecture of guidance on monitoring HPV biologic endpoints (i.e., endpoints that measure HPV or subsequent changes caused by HPV)
2) outline an approach to HPV vaccine coverage monitoring.
3) identify any special studies which might be needed to provide more complete country guidance on monitoring.
4) identify partners and resources for HPV surveillance and monitoring.

"A useful summary indicator to compare vaccine coverage trends over time and across geographical regions will be the proportion of girls vaccinated with 3 doses of HPV vaccine by age 15 years."

Why is measuring HPV vaccine coverage different from other vaccines?



Minimal variations in timing/schedule
Single cohort - birth cohort <12m

JRF HPV vaccine data collection

	Vaccine, Supplement, or Injection Equipment			Recommended age of administration (B=birth; D=days; W=weeks; M=months; Y=years) (instructions)						G-H. Planned introduction		I. Geographic area (instructions)	J. Specific target group (instructions)
				A. 1st dose	B. 2nd dose	C. 3rd dose	D. 4th dose	E. 5th dose	F. 6th dose	Month	Year		
2510	HPV	Human papillomavirus vaccine	No. of valents:									<pick one>	Include target age or school class and specifiy if this applies to females only, males as well and any special groups

HPV Vaccine Doses administered: 2018

(Table instructions)

New 2019

	Females				Males		
	Vaccine administered (age in years)	A. 1st dose	B. 2d dose	C. 3d dose*	A. 1st dose	B. 2d dose	C. 3d dose
4440	9			NR	NR	NR	NR
4450	10			NR	NR	NR	NR
4460	11			NR	NR	NR	NR
4470	12			NR	NR	NR	NR
4480	13			NR	NR	NR	NR
4490	14			NR	NR	NR	NR
4500	15+			NR	NR	NR	NR
4510	unknown age			NR	NR	NR	NR

World Health Organization

JRF - as from 2019

World Health Organization

Admin

	Vaccine/Supplement *Please complete separately for each vaccine, even if they are given in combination (e.g., if Pentavalent vaccine DTP-HepB-Hib is used, fill in the data for DTP3, HepB3 and Hib3 separately)*		A. Description of the denominator used in coverage calculation (instructions)	B. Number in target group *(denominator)* (instructions)	C. Number of doses administered through routine services *(numerator)*	D. Percent coverage (=C/B*100)
4330	HPV Female (final dose)	(instructions)	<Please enter target population>	428025	237739	56
4340	HPV Male (final dose)		<Please enter target population>			
4350	Typhoid		<Please enter target population>			

Official estimate

	Vaccine/Supplement		Official coverage estimates (percent coverage)
5320	HPV Female, final dose	(instructions)	56
5330	HPV Male, final dose		

eJRF - as from 2021

Two changes:

1. Allow reporting for <u>age 15</u> (separately)
2. Allow reporting by <u>Age in years</u> or <u>Year of Birth</u>

	Vaccine administered	
	Age in Years	Year of birth
4440	9	2011
4450	10	2010
4460	11	2009
4470	12	2008
4480	13	2007
4490	14	2006
4500	15	2005
4510	16+	2004+
4520	unknown age	

New 2021

Source: WHO Human Papilloma Virus vaccine coverage monitoring manual (2020) https://apps.who.int/iris/bitstream/handle/10665/331807/9789240002746-eng.pdf?ua=1

HPV coverage estimates:
why only now, why not part of WUENIC?

- **Why only now?** Needed to wait for sufficient countries to introduce HPV, to start reporting data to JRF and cohort to mature to calculate coverage by 15 years of age
- **Why "outside" WUENIC?** Data sources more restricted
  - Specific challenges with estimating HPV coverage, methodology being refined.
  - Use UN Denominators for estimates (*comparability*)
  - Few countries have HPV vaccine coverage survey data to calibrate administrative data
    - *HPV not yet part of multi indicator surveys (MICS, DHS (pilot))*
- **Delay**: Concern about coverage estimate reflecting program performance up to 5 years earlier

  ü Second indicator developed to measure last years performance

WHO estimates of HPV vaccine coverage

two indicators

1) "HPV vaccination protection by 15 years"

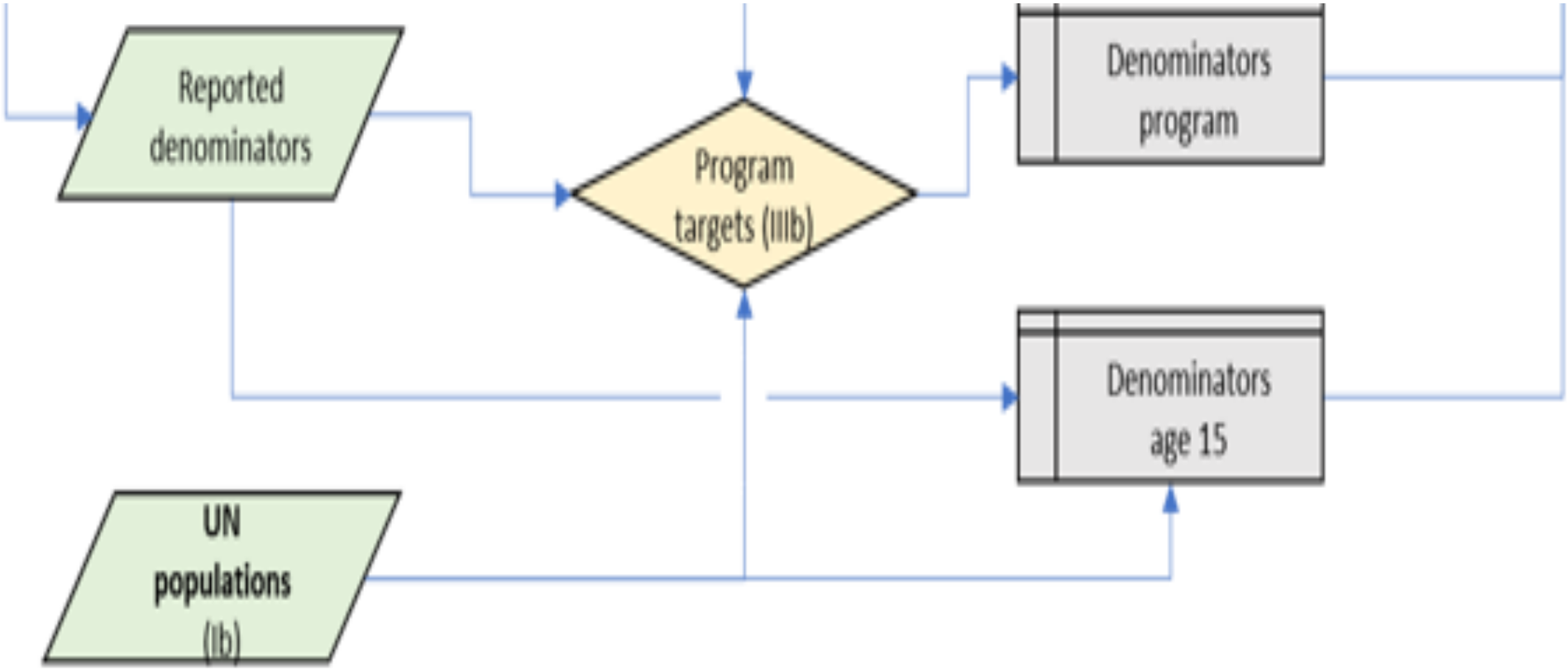
- Coverage in 15 years old cohort, *vaccinated any time between 9-14 years of age*
  - Numerator: Doses of HPV1 & HPVc in girls 15 yr in calendar year
  - Denominator: 15 year old cohort of girls

2) "HPV vaccination programme coverage"

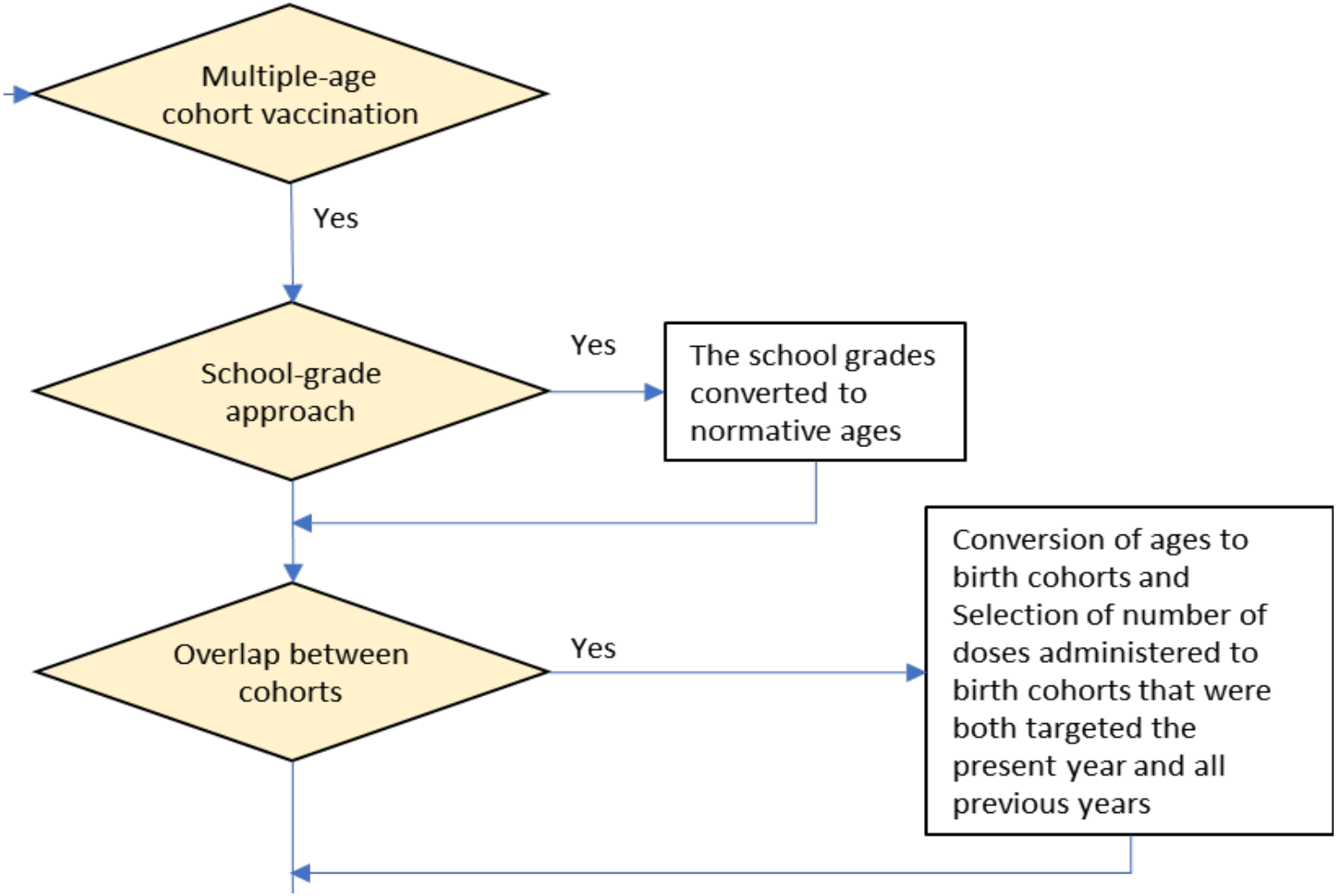
- Vaccination coverage according to national schedule *in calendar year*
  - Numerator: Doses of HPV1 & HPVc in girls in calendar year
  - Denominator: girls in eligible age group

Review of Methodology IVIR-AC (2019)

FLOW CHART OF HPV VACCINE COVERAGE ESTIMATION OPERATIONAL PROCEDURES AND SOURCES



DEALING WITH MAC - MAC CORRECTIONS



CALCULATIONS OF TWO INDICATORS

EXAMPLE COUNTRY 2014 DEMO, 2015 INTRODUCTION

INTRO

ONE DOSE						
JRF		Year				
		2014	2015	2016	2017	2018
Age	9	241	3,627	3,291	4,424	0
	10	1,057	12,372	8,851	8,740	0
	11	1,764	16,645	5,694	4,683	0
	12	1,819	15,397	1,470	1,230	0
	13	1,120	8,466	392	265	0
	14	489	2,624	106	2,351	0
	15	224	1,199	3,005	309	0
		@	@	@	@	@
15HPV1 -F	Birth cohort turning 15	1999	2000	2001	2002	2003
	Aged 15 vaccinated at 9-14	0	489	3,744	10,391	19,904
	Population age 15	21,355	21,309	21,276	21,269	21,346
	Coverage by age 15 (15HPV1)		2%	18%	49%	93%

PrHPV1 -F	Total vaccinated	6,490	59,131	19,804	21,693	
	Population		64,733	22,427	22,779	
	Program uptake (HPV1)	-	91%	88%	95%	
Program Info		DEMO	Mac Grade 5-6-7	Grade 5	Grade 5	

CALCULATIONS OF TWO INDICATORS

BOTSWANA EXAMPLE (JRF 2010-2017)

INTRO

ONE DOSE							
JRF		Year					
		2014	2015	2016	2017	2018	
Age	9	241	3,627	3,291	4,424	0	
	10	1,057	12,372	8,851	8,740	0	
	11	1,764	16,645	5,694	4,683	0	
	12	1,819	15,397	1,470	1,230	0	
	13	1,120	8,466	392	265	0	
	14	489	2,624	106	2,351	0	
	15	224	1,199	3,005	309	0	
		@	@	@	@	@	
15HPV1 -F	Birth cohort turning 15	1999	2000	2001	2002	2003	
	Aged 15 vaccinated at 9-14	0	489	3,744	10,391	19,904	
	Population age 15	21,355	21,309	21,276	21,269	21,346	
	Coverage by age 15 (15HPV1)		2%	18%	49%	93%	

PrHPV1 -F	Total vaccinated	6,490	59,131	19,804	21,693	
	Population		64,733	22,427	22,779	
	Program uptake (HPV1)	-	91%	88%	95%	
Program Info		DEMO	Mac Grade 5-6-7	Grade 5	Grade 5	

CHALLENGES WITH QUALITY AND COMPLETENESS OF DATA

WHO JRF-HPV VACCINATION COVERAGE DATA (2010-2017)

Among NIPs with coverage data:	Global	AMRO
Problems/issues with the data reported (one or more)	**62 (**	
2nd/3rd doses higher than 1st doses (direct calculation)		
Difficulties to assign 2nd doses (age/yea		(40%)
Data incomplete (missing	1%)	3 (15%)
Data incon	15 (22%)	7 (35%)
	22 (32%)	3 (15%)
	21 (31%)	9 (45%)
ber of doses)	5 (7%)	(0%)
ther both sexes	6 (9%)	4 (20%)
erages >100% (direct calculation)	16 (24%)	7 (35%)

Situation markedly increased in 2020 after 2019 data and historical was received from PAHO countries

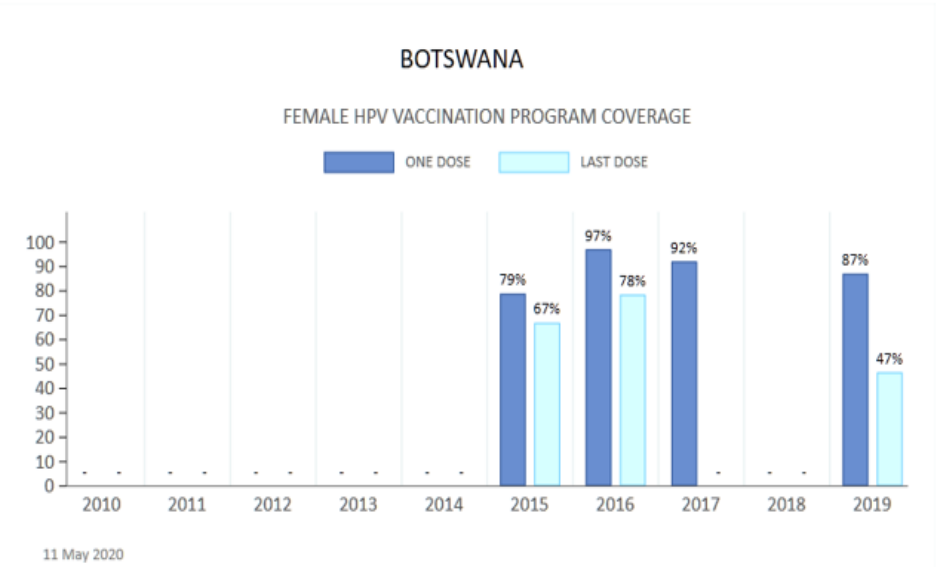
HPV Coverage Country profile (May) : Botswana

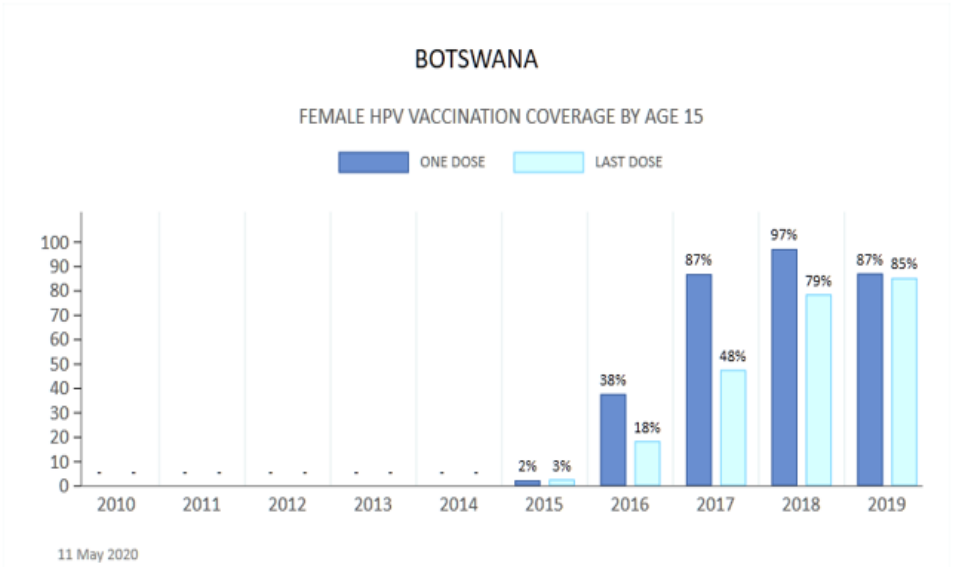
History of the HPV vaccination program

		sex	age	schedule	approach	delivery (main)	school grade	delivery (other)
NATIONAL - GIRLS ONLY FEB 2015	PRIMARY TARGET:	FEMALES	9-13	2 DOSES (0 - 6M)	MULTI SCHOOL-GRADE VACCINATION	BOTH SCHOOL AND FACILITY-BASED	5-7	
2016	PRIMARY TARGET:	FEMALES	9-13	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	BOTH SCHOOL AND FACILITY-BASED	5	

QUERY TO THE COUNTRY
1) IS THE PROGRAM INFORMATION CORRECT?
□ YES
□ NO
IF NO, PLEASE COMMENT:

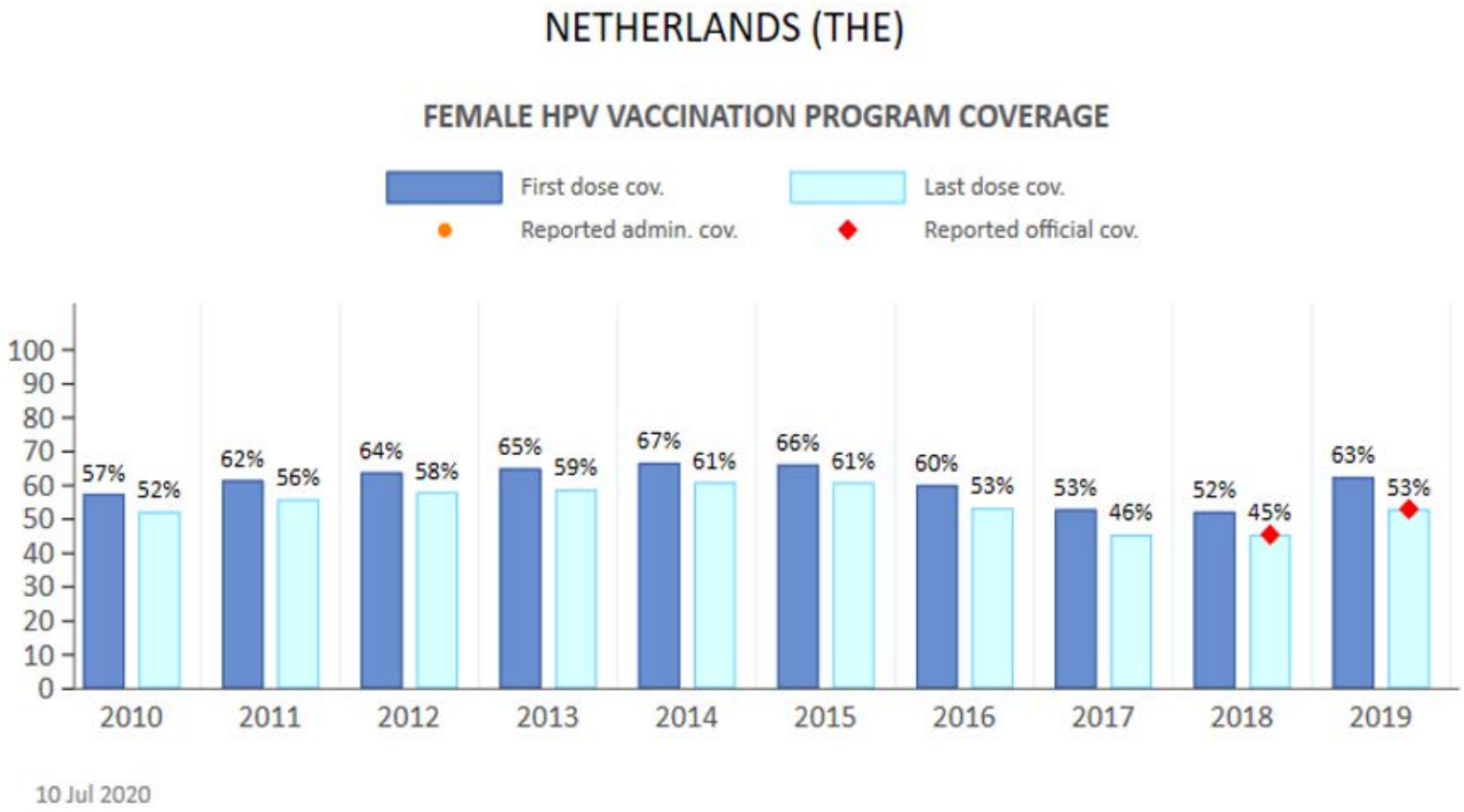
RESULTS: WHO HPV VACCINATION COVERAGE ESTIMATES





World Health Organization

When survey or registry data are available data points

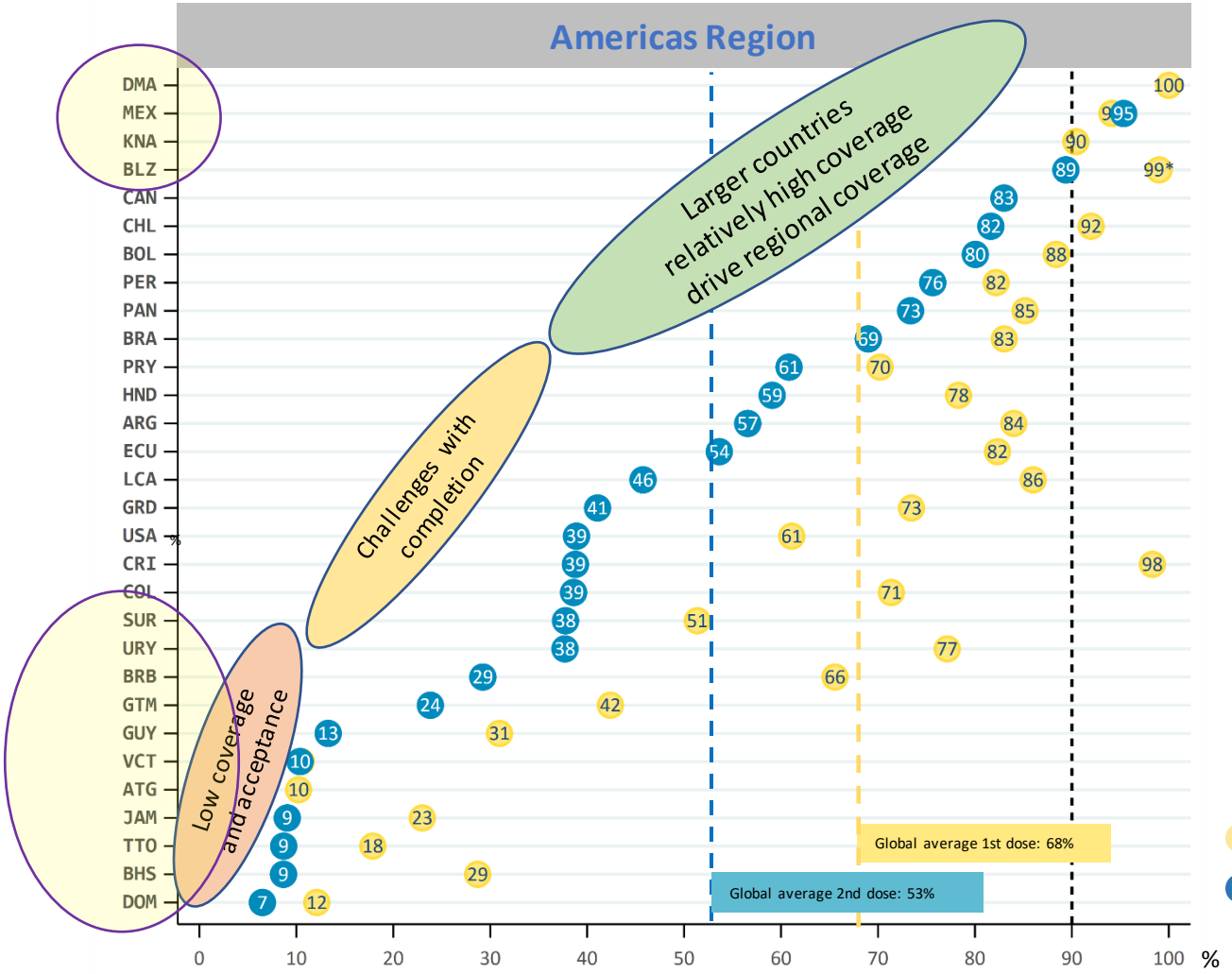


"NOTE: Proxy estimate based on reported coverage by age 13 (registry)"

World Health Organization

Americas Region HPV vaccine coverage estimates 2019

Program indicator

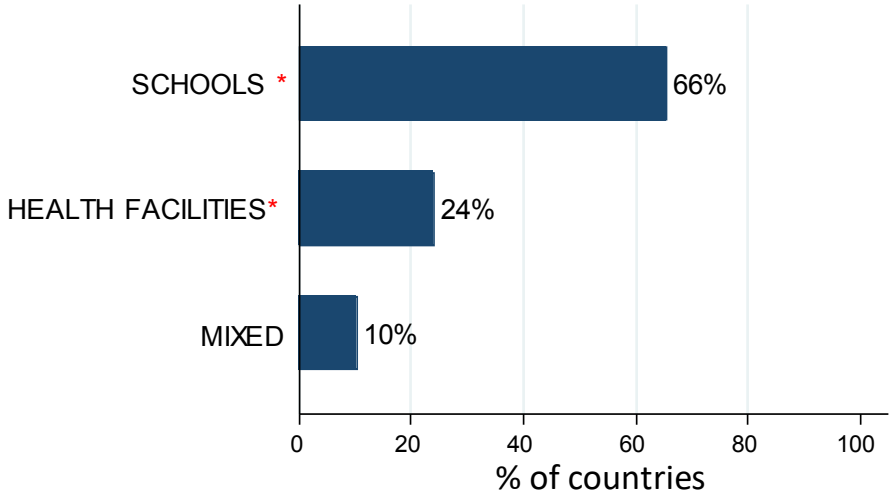


Note: * coverage over 100%, truncated

Source: IVB Database, July 2020.

ANALYSIS BY STRATEGY

PRIMARY DELIVERY STRATEGIES (2018)



* Note: These strategies are not always "exclusive"

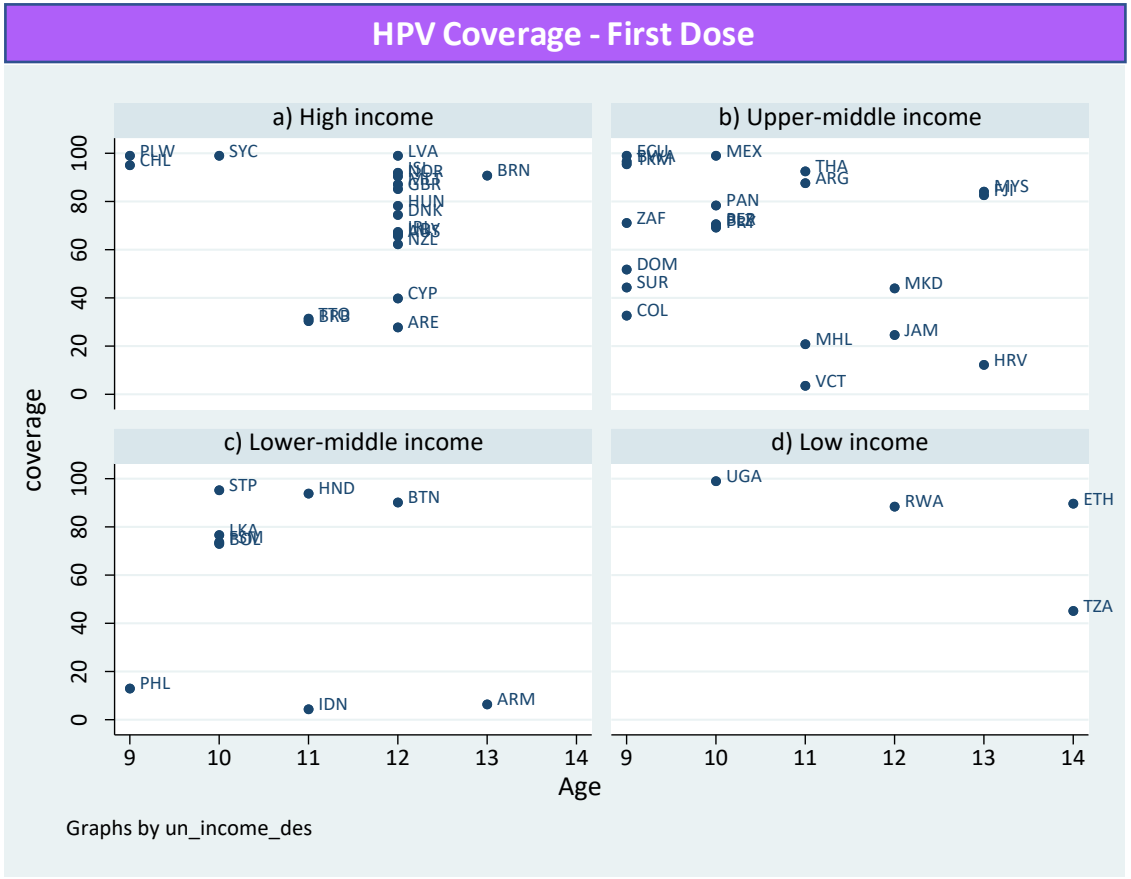
Source: IVB Database, 1 June 2019. Preliminary data

World Health Organization

ANALYSIS BY STRATEGY - AGE

HPV vaccine coverage in countries with single cohort strategies, 2018

females, by target cohort (age), income group and dose



Source: IVB Database, 15 July 2019

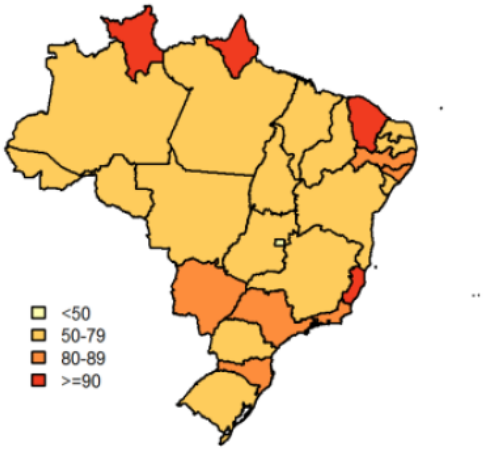
World Health Organization

Analysis of subnational data

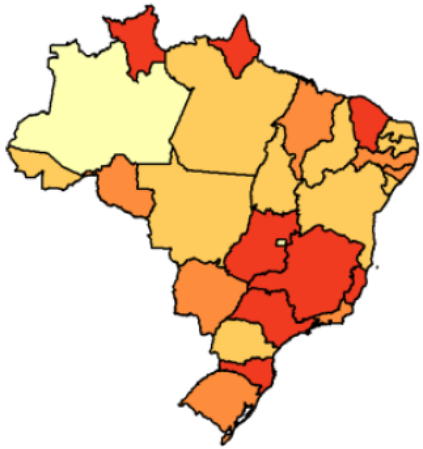
Figura 11 - Cobertura vacinal contra HPV (segunda dose), segundo coorte no ano de 2017.

Segunda dose

Girls 14 yr



Girls 15 yr



Girls 16 yr

Source: Lima Moura, Fiocruz /ENSP, 2019 (Thesis)

World Health Organization

Analysis of data - equity

Human papillomavirus (HPV) vaccination coverage among adolescents 13-17 years by State, HHS Region, and the United States, National Immunization Survey-Teen (NIS-Teen), 2019

Vaccination Coverage for Selected Area(s)

Vaccinations/Groups	State/Region/U.S.	n	%	CI	Progress Toward Healthy People 2020 (red line)
Principal City					
≥1 dose HPV Vaccination, Female					
Age					
13-17 Years	United States	8,916	73.2	(±1.9)	0 — 100
Poverty					
Living At or Above Poverty	United States	7,266	72.6	(±2.0)	0 — 100
Living Below Poverty	United States	1,323	75.9	(±5.3)	0 — 100
Unknown poverty	United States	327	73.4	(±7.7)	0 — 100
Race/Ethnicity					
American Indian or Alaska Native only, non-Hispanic	United States	114	66.3	(±19.1)	0 — 100
Asian only, non-Hispanic	United States	350	75.4	(±8.6)	0 — 100
Black only, non-Hispanic	United States	639	72.4	(±5.3)	0 — 100
Hispanic	United States	1,616	78.9	(±4.4)	0 — 100
White only, non-Hispanic	United States	5,603	70.5	(±2.3)	0 — 100
Urbanicity					

World Health Organization

Key messages

- HPV data collection by age and dose key
- Importance of quality and consistency of (JRF) reporting
- HPV coverage data continuously updated and improved based on feedback from countries
- Use of coverage data and analysis to improve programme performance
  - Strategies
  - Subnational data
  - Equity analysis

World Health Organization

Guidelines for the calculation of HPV vaccination coverage

Martha Velandia MD MSc.

Regional Advisor Immunization

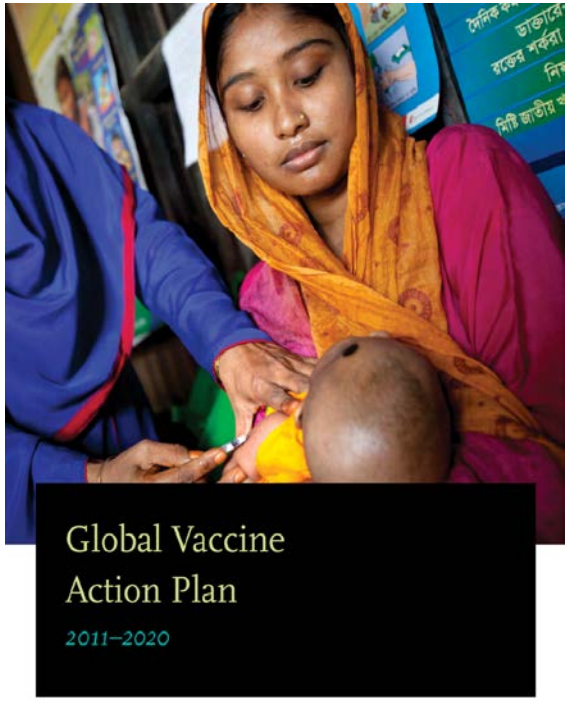
Organización Panamericana de la Salud
Organización Mundial de la Salud
Américas

OPS

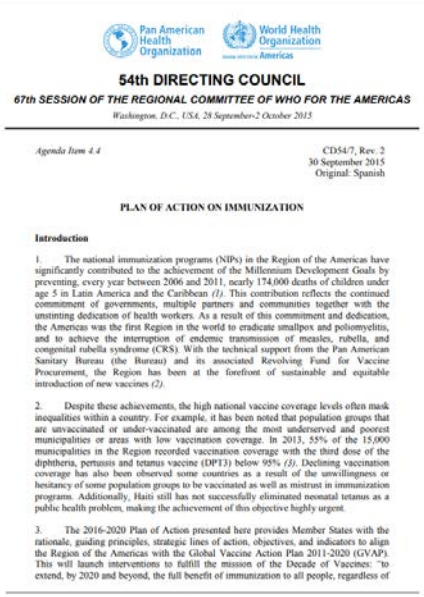
Content

1. Background
2. Data collection
3. Challenges for monitoring vaccination coverage
4. Methodology
5. Considerations

Background



RIAP



Pan American Health Organization | World Health Organization Americas

54th DIRECTING COUNCIL

67th SESSION OF THE REGIONAL COMMITTEE OF WHO FOR THE AMERICAS

Washington, D.C., USA, 28 September-2 October 2015

Agenda Item 4.4

CD54/7, Rev. 2
30 September 2015
Original: Spanish

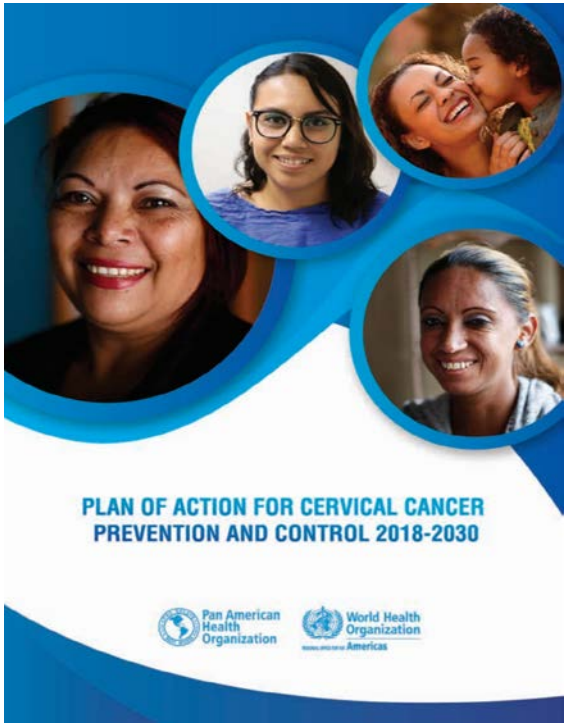
PLAN OF ACTION ON IMMUNIZATION

Introduction

1. The national immunization programs (NIPs) in the Region of the Americas have significantly contributed to the achievement of the Millennium Development Goals by preventing, every year between 2006 and 2011, nearly 174,000 deaths of children under age 5 in Latin America and the Caribbean *(1)*. This contribution reflects the continued commitment of governments, multiple partners and communities together with the unstinting dedication of health workers. As a result of this commitment and dedication, the Americas was the first Region in the world to eradicate smallpox and poliomyelitis, and to achieve the interruption of endemic transmission of measles, rubella, and congenital rubella syndrome (CRS). With the technical support from the Pan American Sanitary Bureau (the Bureau) and its associated Revolving Fund for Vaccine Procurement, the Region has been at the forefront of sustainable and equitable introduction of new vaccines *(2)*.

2. Despite these achievements, the high national vaccine coverage levels often mask inequalities within a country. For example, it has been noted that population groups that are unvaccinated or under-vaccinated are among the most underserved and poorest municipalities or areas with low vaccination coverage. In 2013, 55% of the 15,000 municipalities in the Region recorded vaccination coverage with the third dose of the diphtheria, pertussis and tetanus vaccine (DPT3) below 95% *(3)*. Declining vaccination coverage has also been observed some countries as a result of the unwillingness or hesitancy of some population groups to be vaccinated as well as mistrust in immunization programs. Additionally, Haiti still has not successfully eliminated neonatal tetanus as a public health problem, making the achievement of this objective highly urgent.

3. The 2016-2020 Plan of Action presented here provides Member States with the rationale, guiding principles, strategic lines of action, objectives, and indicators to align the Region of the Americas with the Global Vaccine Action Plan 2011-2020 (GVAP). This will launch interventions to fulfill the mission of the Decade of Vaccines: "to extend, by 2020 and beyond, the full benefit of immunization to all people, regardless of



Pan American Health Organization | World Health Organization Americas | PAHO

Background


SUSTAINABLE DEVELOPMENT GOALS
1 NO POVERTY
2 ZERO HUNGER
3 GOOD HEALTH AND WELL-BEING
4 QUALITY EDUCATION
5 GENDER EQUALITY
6 CLEAN WATER AND SANITATION
7 AFFORDABLE AND CLEAN ENERGY
8 DECENT WORK AND ECONOMIC GROWTH
9 INDUSTRY, INNOVATION AND INFRASTRUCTURE
10 REDUCED INEQUALITIES
11 SUSTAINABLE CITIES AND COMMUNITIES
12 RESPONSIBLE CONSUMPTION AND PRODUCTION
13 CLIMATE ACTION
14 LIFE BELOW WATER
15 LIFE ON LAND
16 PEACE, JUSTICE AND STRONG INSTITUTIONS
17 PARTNERSHIPS FOR THE GOALS
SUSTAINABLE DEVELOPMENT GOALS

Indicator 3. B. 1 is the proportion of the target population covered by all vaccines included in their national programme

Goal: By 2030 provide access to affordable essential medicines and vaccines for all

- Coverage of DTP containing vaccine (3rd dose): Percentage of surviving infants who received the 3 doses of diphtheria and tetanus toxoid with pertussis containing vaccine in a given year.
- Coverage of Measles containing vaccine (2nd dose): Percentage of children who received two dose of measles containing vaccine in a given year.
- Coverage of Pneumococcal conjugate vaccine (last dose in the schedule): Percentage of surviving infants who received the last dose of pneumococcal conjugate vaccine in a given year.
- **Coverage of HPV vaccine (last dose in the schedule)**: Percentage of 15 years old girls received the recommended doses of HPV vaccine. Currently performance of the programme in the previous calendar year based on target age group is used.

  Based on UN population estimates for consistency across countries

JRF: source of information

Data collection: JRF

HPV Vaccine Doses administered: 2019

(Table instructions)

		FEMALES				MALES			
	Vaccine administered (age in years)	A. 1st dose	B. 2nd dose	C. 3d dose*	D. Target Population	A. 1st dose	B. 2nd dose	C. 3d dose	D. Target Population
4440	9								
4450	10								
4460	11								
4470	12								
4480	13								
4490	14								
4500	15+								
4510	unknown age								

* WHO recommends a 2-dose schedule for girls < 15 years of age (Position Paper published in October 2014). If 2-dose schedule was used please leave Column C blank.

Accuracy of reported HPV Vaccine Doses

	Describe any factors limiting the accuracy of the administered doses :
4520	<describe>

2021 eJRF process

Reunión Regional en GUATEMALA

OCTUBRE 2017

Para compartir experiencias

DOSES			POPULATION			
1	2	3	1	2	3	
211	191		539	211	0	35%
292852.5	195943		346110	346110	0	57%
369	345		707	369	0	47%
1852	405	82	3500	1531	0	12%
2504	NA		NR		0	NA
316	251	210	700	700	700	30%
1180357	1033628		10170060	10170060	0	10%
NR	NR	NR	NR		0	73%
69	183	23	0	0	0	NR
90056	89999		115445	113924	0	78%
50577	51867	930	50577	50577	0	NR
166038	142792	0	164225	164225	0	86%
3216	1829	0	NR	NR	0	NR
77622	54182	0	98227	98227	0	55%
1206620	1199167	0	1245090	1180941	0	96%
73497	38079	0	68002	68002	0	56%
44142	43057	40519	67385	67385	67385	60%
819883	0	0	552836	0	0	NR
1472	1472	0	4677	4677	0	32%
213	0	0	434	434	0	NR
14441	5213	3949	18000	18000	18000	22%
16510	12998	10402	25413	25413	25413	41%
NR	NR	NR	NR	NR	NR	63% Girls 50% boys

do not report the target population.

Girls/boys enrolled for the first dose as the target population to receive the second dose

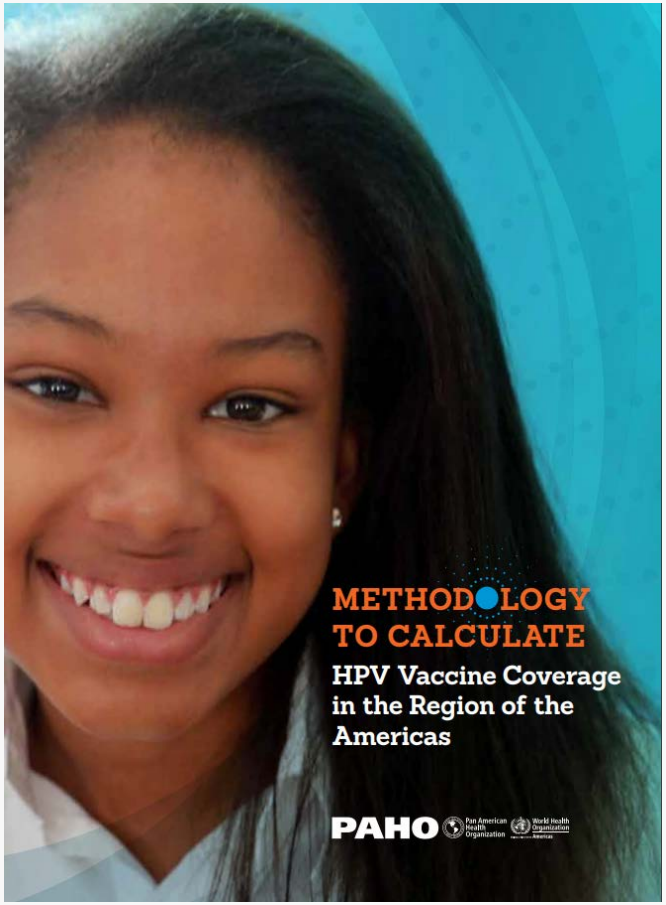
Not report the doses administered, but rather only coverage

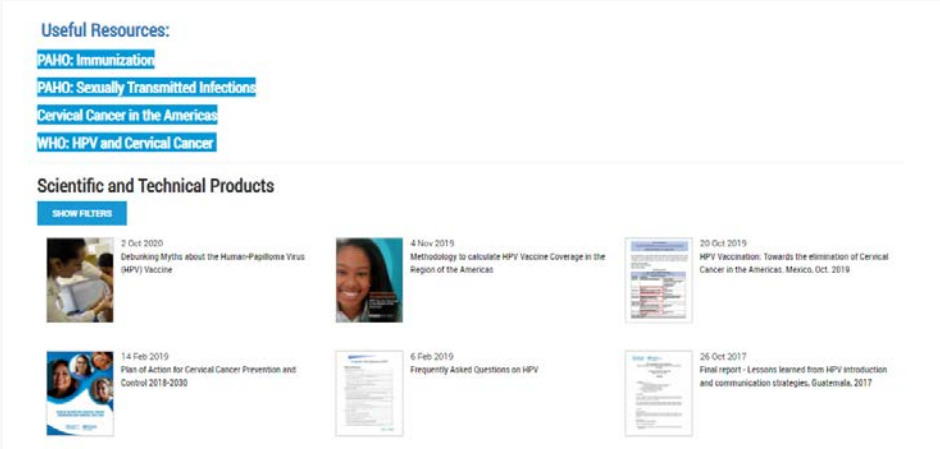
considered the girls/boys enrolled for vaccination as the target population

vaccinated more children than the reported population

Service delivery platform	Problem
School based:	year/grade/class vs age
	Girls/boys that are not enrolled in school
	High rates of absenteeism
Health care facility based	Difficulties for girls/boy to attend – access

https://www.paho.org/en/tag/human-papillomavirus-hpv-vaccine



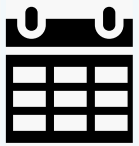


Objectives

Establish a standard methodology to follow up on vaccine recipients and calculate HPV vaccine coverage in the Americas, allowing to:

- Measure progress on vaccination of the target population selected by country, as well as define strategies to reach pertinent and equitable coverage.
- Compare coverage levels obtained by different countries in the Region and from countries in other regions.
- Compare regional coverage with that of other regions in the world.

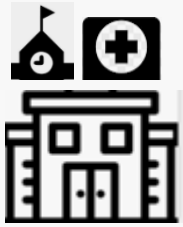
Variables



The **month and year vaccination started**

Changes in Schedule/dose /age

The **target population** in the same year (a single cohort or different cohorts, that is, people with different birth years).

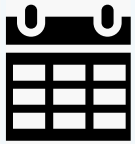


Strategy: school and or health care facility

Age in years at vaccination with a given dose (birth cohort), even if vaccination takes place during a specific grade in school.

Dose administered It is important to ensure that every dose is recorded and consolidated, regardless of the strategy used (intramural or extramural) or the provider (public, private or other).

Sex of the person vaccinated, stating whether the person is a boy o a girl .



Vaccination dates

Indicators
Access

$$\text{Access} = \frac{\text{Number of first doses administered to a given cohort in a determined year}}{\text{Target population of a given cohort}} \times 100$$

Example: In a country, 880 girls born in 2008 and who turned 9 in 2017 were vaccinated with the first dose of the HPV vaccine. According to population data, 1500 is the number of girls who turned 9 in 2017.

Indicators
Access

$$\text{Access} = \frac{\text{Number of first doses administered to a given cohort in a determined year}}{\text{Target population of a given cohort}} \times 100$$

Example: In a country, 880 girls born in 2008 and who turned 9 in 2017 were vaccinated with the first dose of the HPV vaccine. According to population data, 1500 is the number of girls who turned 9 in 2017.

$$\text{Access} = \frac{880}{1500} \times 100 = 58.7\%$$

Indicators
Annual Coverage

$$\text{Annual coverage} = \frac{\text{Number of second doses administered to a selected cohort in a determined year}}{\text{Target population of the selected cohort}} \times 100$$

Example: Continuing with the same example, 550 girls out of a cohort of 1500 received the second dose of the HPV vaccine in 2017.

Indicators
Annual Coverage

$$\text{Annual coverage} = \frac{\text{Number of second doses administered to a selected cohort in a determined year}}{\text{Target population of the selected cohort}} \times 100$$

Example: Continuing with the same example, 550 girls out of a cohort of 1500 received the second dose of the HPV vaccine in 2017.

$$\text{Annual coverage} = \frac{550}{1500} \times 100$$

=36.7%

Indicators: Annual dropout

$$\text{Annual dropouts} = \frac{(\Sigma \text{ of first doses administered to one or more cohorts during a calendar year} - \Sigma \text{ of second doses administered to one or more cohorts during a calendar year})}{\Sigma \text{ of first doses administered to a cohort during a calendar year}} \times 100$$

$$\text{Access} = \frac{880}{1500} \times 100 = 58.7\%$$

$$\text{Annual coverage} = \frac{550}{1500} \times 100 = 36.7\%$$

Indicators: Annual dropout

$$\text{Annual dropouts} = \frac{(\Sigma \text{ of first doses administered to one or more cohorts during a calendar year} - \Sigma \text{ of second doses administered to one or more cohorts during a calendar year})}{\Sigma \text{ of first doses administered to a cohort during a calendar year}} \times 100$$

$$\text{Access} = \frac{880}{1500} \times 100 = 58.7\%$$

$$\text{Annual coverage} = \frac{550}{1500} \times 100 = 36.7\%$$

[(880-550)/880]*100=37.5

Indicators

HPV coverage for girls at 15 years old

$$\text{HPV coverage for girls at 15 years old} = \frac{\sum \text{of second doses administered to girls 9-14 years old from the first year of vaccination until the year prior to year of analysis}}{\text{Population of the cohort of 15 year-old girls in the year of analysis}} \times 100$$

Year of birth	2008	2007	2006	2005	2004	2003	2002
Year	9	10	11	12	13	14	15
2017	350,327	379,435	182,990	161,206	138,637	72,186	9,940
2016	255,401	288,204	224,516	177,346	87,924	38,371	
2015	300,787	622,206	737,635	343,225	196,754		
2014	14,301	23,886	589,065	967,862			
2013	480	18,415	109,378				

How many girls that were born in 2008 were vaccinated in 2017?

Year of birth	2008	2007	2006	2005	2004	2003	2002
Year	9	10	11	12	13	14	15
2017	350,327	379,435	182,990	161,206	138,637	72,186	9,940
2016	255,401	288,204	224,516	177,346	87,924	38,371	
2015	300,787	622,206	737,635	343,225	196,754		
2014	14,301	23,886	589,065	967,862			
2013	480	18,415	109,378				

How many girls that were born in 2008 have been vaccinated?

- 9 years old in 2017: 350 327

How many girls that were born in 2007 have been vaccinated?

Year of birth	2008	2007	2006	2005	2004	2003	2002
Year	9	10	11	12	13	14	15
2017	350,327	379,435	182,990	161,206	138,637	72,186	9,940
2016	255,401	288,204	224,516	177,346	87,924	38,371	
2015	300,787	622,206	737,635	343,225	196,754		
2014	14,301	23,886	589,065	967,862			
2013	480	18,415	109,378				

How many girls that were born in 2008 have been vaccinated?

- 9 years old in 2017: 350 327

How many girls that were born in 2007 have been vaccinated?

- **10 years old in 2017: 379 435 +**
- **9 years old in 2016: 255 401 = 634 836**

How many girls that were born in 2006 have been vaccinated?

Year of birth	2008	2007	2006	2005	2004	2003	2002
Year	9	10	11	12	13	14	15
2017	350,327	379,435	182,990	161,206	138,637	72,186	9,940
2016	255,401	288,204	224,516	177,346	87,924	38,371	
2015	300,787	622,206	737,635	343,225	196,754		
2014	14,301	23,886	589,065	967,862			
2013	480	18,415	109,378				

How many girls that were born in 2008 have been vaccinated?

- 9 years old in 2017: 350 327

How many girls that were born in 2007 have been vaccinated?

- **10 years old in 2017: 379 435 +**
- **9 years old in 2016: 255 401 = 634 836**

How many girls that were born in 2006 have been vaccinated?

- **11 years old in 2017: 182 990 +**
- **10 years old in 2016: 288 204 +**
- **9 years old in 2015: 300 787 = 771 981**

How many girls that were born in 2005 have been vaccinated?

Year of birth	2008	2007	2006	2005	2004	2003	2002
Year	9	10	11	12	13	14	15
2017	350,327	379,435	182,990	161,206	138,637	72,186	9,940
2016	255,401	288,204	224,516	177,346	87,924	38,371	
2015	300,787	622,206	737,635	343,225	196,754		
2014	14,301	23,886	589,065	967,862			
2013	480	18,415	109,378				

How many girls that were born in 2008 have been vaccinated?

- 9 years old in 2017: 350 327

How many girls that were born in 2007 have been vaccinated?

- **10 years old in 2017: 379 435 +**
- **9 years old in 2016: 255 401 = 634 836**

How many girls that were born in 2006 have been vaccinated?

- **11 years old in 2017: 182 990 +**
- **10 years old in 2016: 288 204 +**
- **9 years old in 2015: 300 787 = 771 981**

How many girls that were born in 2005 have been vaccinated?

- **12 years old in 2017: 161 206 +**
- **11 years old in 2016: 224 516 +**
- **10 years old in 2015: 622 206 +**
- **9 years old in 2014: 14 301 = 1 022 229**

Year of birth	2008	2007	2006	2005	2004	2003	2002
Year	9	10	11	12	13	14	15
2017	350,327	379,435	182,990	161,206	138,637	72,186	9,940
2016	255,401	288,204	224,516	177,346	87,924	38,371	
2015	300,787	622,206	737,635	343,225	196,754		
2014	14,301	23,886	589,065	967,862			
2013	480	18,415	109,378				

How many girls that were born in 2004 have been vaccinated?

- **13 years old in 2017: 138 637+**
- **12 years old in 2016: 177 346 +**
- **11 years old in 2015: 737 635 +**
- **10 years old in 2015: 23 886 +**
- **9 years old in 2014: 480 = 1 077 984**

How many girls that were born in 2003 have been vaccinated?

- **14 years old in 2017: 72 186 +**
- **13 years old in 2016: 87 924 +**
- **12 years old in 2015: 343 225+**
- **11 years old in 2014: 589 065 +**
- **10 years old in 2013: 18 415 = 1 110 815**

How many girls that were born in 2002 have been vaccinated?

- **15 years old in 2017: 9 940 +**
- **14 years old in 2016: 38 371 +**
- **13 years old in 2015: 196 754 +**
- **12 years old in 2014: 967 862 +**
- **11 years old in 2013: 109 378 = 1 322 305**

Indicators

HPV coverage for girls at 15 years old

Year	Age (Years)						
	9	10	11	12	13	14	15
2017	350,327	379,435	182,990	161,206	138,637	72,186	9,940
2016	255,401	288,204	224,516	177,346	87,924	38,371	
2015	300,787	622,206	737,635	343,225	196,754		
2014	14,301	23,886	589,065	967,862			
2013	480	18,415	109,378				
Total doses administered	350,327	634,836	771,981	1,022,229	1,077,984	1,110,815	1,322,305
Year of birth	2008	2007	2006	2005	2004	2003	2002
Population	1,590,611	1,645,204	1,705,705	1,745,525	1,752,494	1738,274	1,726,191
Coverage (%)	22.0	38.6	45.3	58.6	61.5	63.9	76.0
Population not vaccinated	1,240,284	1,010,368	933,724	723,296	674,510	627,459	403,886

WHO/UNICEF estimates of Human papillomavirus immunization coverage

WHO/UNICEF estimates of Human papillomavirus immunization coverage

This year, the United Nations Children's Fund (UNICEF) and the World Health Organization (WHO) start to develop estimates of HPV coverage for the period 2010 through 2019 for all countries that introduced HPV vaccination in national immunization schedule and at least one data point was available. The estimates are based on information from the WHO/UNICEF Joint Reporting Form (JRF) on Immunization received between April 2011 and 08 May 2020

WHO recommends HPV vaccination for girls between 9 and 14 years of age. The exact ages targeted for HPV vaccines vary between countries with vaccination strategies differ from single ages, school classes to multiple cohorts. As a result, defining meaningful and comparable coverage indicators for this vaccine is relatively complex. Therefore, the methodology uses two complementary indicators, one for **programme performance** in the last calendar year for all vaccination started in girls below 15 years of age and a complementary summary indicator on the resulting **coverage in the cohort of 15-year old girls regardless of the year of vaccination**. This latter indicator uses a cohort approach tracking as numerator the cumulative doses the same cohort of girls that is 15-year old in the reporting year has received over the previous period as per the data reported to WHO and UNICEF since 2011 (eg doses administered to girls 10 years old in 2013, 11 in 2014, 12 in 2015, 13 in 2016 and 14 in 2017).Both indicators aim to measure coverage among all girls in target population regardless of strategy implemented.

To establish the historical coverage series since 2010 and ensure comparability between countries the UN Population Division estimates are used as denominator for each country. In case you have more accurate target population estimates please provide to us in the attached excel sheet.

We would appreciate your review of these estimates (See HPV_ESTIMATES_TO REVIEW worksheet) and would be grateful for validation on input data, comments and any additional information or data that would further inform not only the most recent year's coverage estimates but also the historical time series.

Worksheets ANNEX_DATA_REPORTED_JRF and ANNEX_UN POPULATION serve as supplementary material

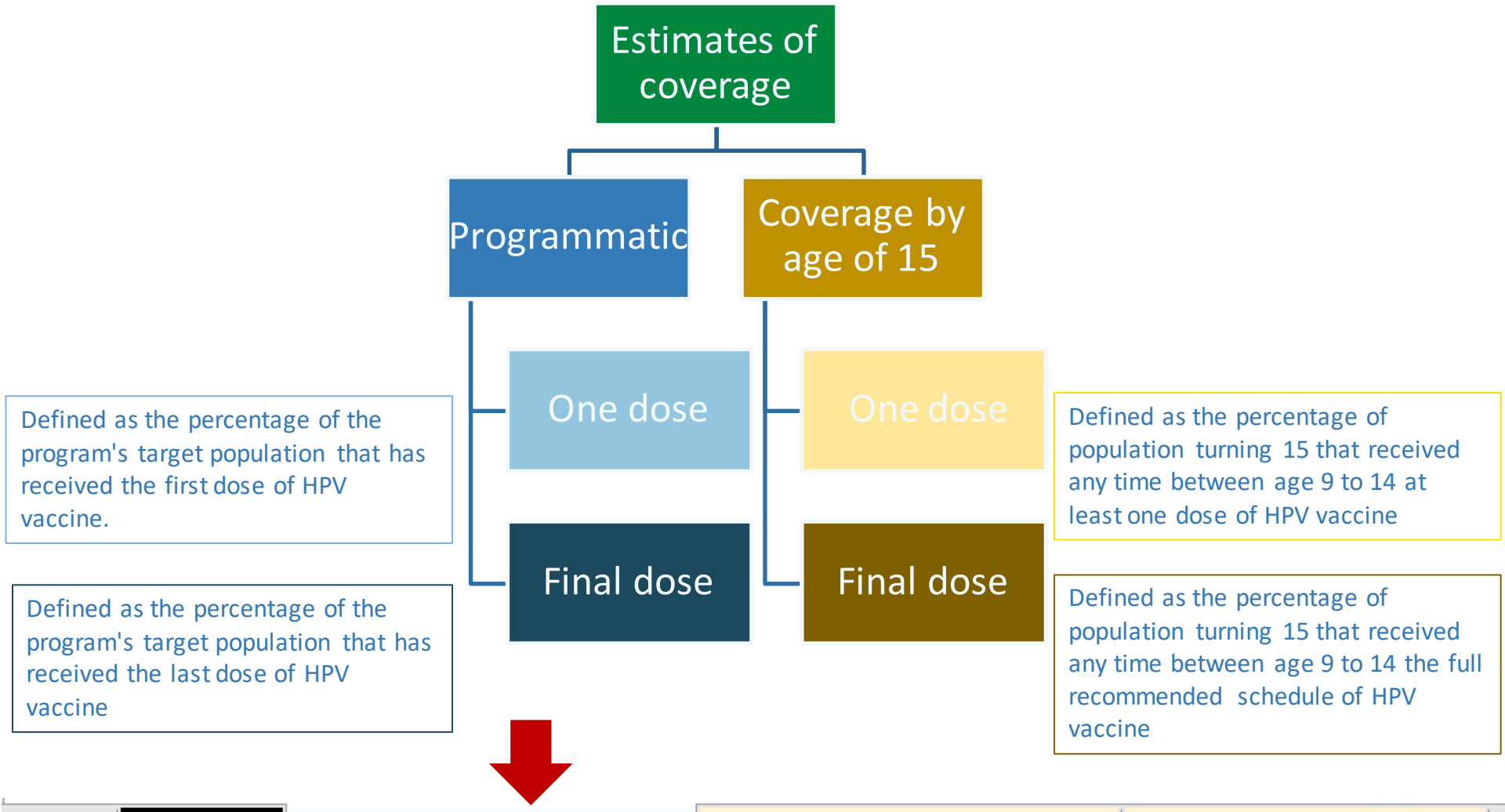
Indicators

prHPV1 (HPV VACCINATION PROGRAM COVERAGE - ONE DOSE):
Defined as the percentage of the program's target population that has received the first dose of HPV vaccine. **For this indicator is imperative to define the age targets groups each year.**

prHPVc (HPV VACCINATION PROGRAM COVERAGE - FINAL DOSE):
Defined as the percentage of the program's target population that has received the last dose of HPV vaccine. **For this indicator is imperative to define the age targets groups each year.**

15HPV1 (HPV VACCINATION COVERAGE BY AGE 15 - ONE DOSE):
Defined as the percentage of population turning 15 that received any time between age 9 to 14 at least one dose of HPV vaccine. **These coverage figures are highly dependant on the consistency and quality of reporting from the previous 5 years**, since it accumulates the number of doses administered to a specific birth cohort over time.

15HPVc (HPV VACCINATION COVERAGE BY AGE 15- COMPLETE SCHEDULE):
Defined as the percentage of population turning 15 that received any time between age 9 to 14 the full recommended schedule of HPV vaccine. **These coverage figures are highly dependant on the consistency and quality of reporting from the previous 5 years**, since it accumulates the number of doses administered to a specific birth cohort over time.



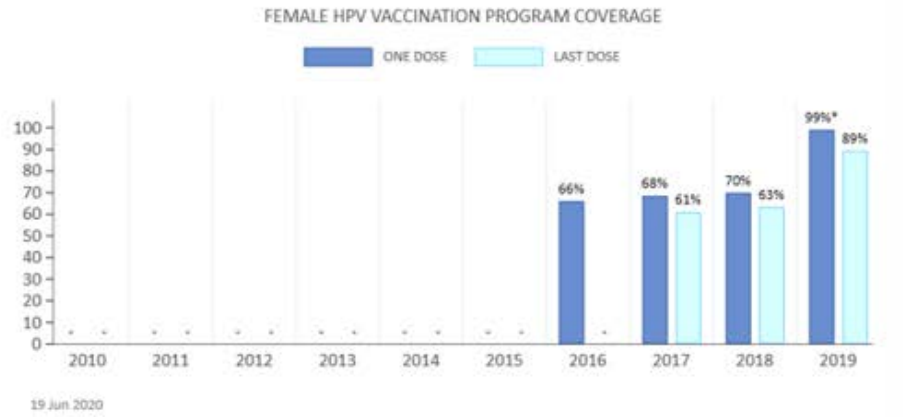
CURRENT PROGRAM

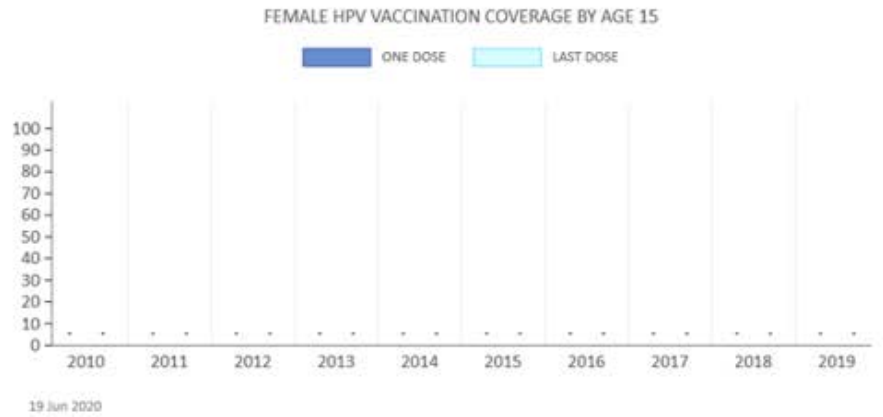
		sex	age	schedule	approach	delivery (main)	school grade	delivery (other)
	PRIMARY TARGET:	FEMALES	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	
	PRIMARY TARGET:	MALES	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	

History of the HPV vaccination program

		sex	age	schedule	approach	delivery (main)	school grade	delivery (other)
NATIONAL - GIRLS ONLY NOV 2016	PRIMARY TARGET:	FEMALES	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	
NATIONAL - INCLUSION MALES? 2019	PRIMARY TARGET:	BOTH	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	

RESULTS: WHO HPV VACCINATION COVERAGE ESTIMATES





SEE DETAILS ON THE ESTIMATES BELOW, PLEASE REVIEW:

FEMALES

A) PRHPV1: HPV VACCINATION PROGRAM COVERAGE - ONE DOSE - FEMALES

COVERAGE ESTIMATES	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
ESTIMATE							66%	68%	70%	99%*
ESTIMATE - NUMERATOR							2504	2561	2583	4062
ESTIMATE - DENOMINATOR							3791	3740	3698	3693
NOTES										
DEFINITION OF AGE TARGET GROUPS FOR DENOMINATOR							Population 10 yo	Population 10 yo	Population 10 yo	Population 10 yo

NUMBER OF HPV VACCINE DOSES ADMINISTERED BY AGE AT VACCINATION

Source: [1] (Annual reports from the Ministry of Health to WHO/UNICEF Joint Reporting Form on Immunization)

a) FEMALES

JRF DATA: HPV vaccine doses administered - 1st dose - FEMALES

		Year													
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Age	9											267	280	373	420
	10											1,253	1,232	1,244	1,482
	11											572	591	584	946
	12											315	332	240	731
	13											84	103	94	286
	14											13	12	48	197
	15+												11	0	
	Missing												0	0	

JRF DATA: HPV vaccine doses administered - 2nd dose - FEMALES

		Year													
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Age	9												291	297	342
	10												1,110	1,149	1,219
	11												510	549	762
	12												284	229	565
	13												75	89	229
	14												11	29	184
	15+												0	0	
	Missing												0	0	

b) MALES

JRF DATA: HPV vaccine doses administered - 1st dose - MALES

		Year													
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Age	9														150
	10														528

POPULATION BY SINGLE AGE AND YEAR

Source: United Nations, Department of Economic and Social Affairs, Population Division (2019). World Population Prospects 2019, Online Edition. Rev. 1.

a) FEMALES

UN DATA: Population estimates - FEMALES

		Year													
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Age	9	3,724	3,784	3,830	3,862	3,885	3,916	3,924	3,901	3,848	3,789	3,742	3,701	3,692	3,721
	10	3,650	3,724	3,783	3,827	3,858	3,899	3,923	3,927	3,898	3,839	3,791	3,740	3,698	3,693
	11	3,567	3,653	3,724	3,781	3,821	3,873	3,906	3,928	3,929	3,896	3,844	3,795	3,739	3,694
	12	3,475	3,574	3,656	3,723	3,775	3,840	3,883	3,911	3,933	3,933	3,903	3,851	3,800	3,736
	13	3,384	3,486	3,580	3,658	3,720	3,797	3,853	3,890	3,916	3,939	3,943	3,913	3,860	3,803
	14	3,301	3,400	3,497	3,585	3,657	3,745	3,814	3,864	3,897	3,922	3,951	3,955	3,923	3,867
	15	3,223	3,321	3,415	3,506	3,588	3,684	3,764	3,827	3,874	3,906	3,936	3,965	3,968	3,932

b) MALES

UN DATA: Population estimates - MALES

		Year													
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Age	9	3,787	3,837	3,873	3,900	3,923	3,959	3,979	3,974	3,944	3,908	3,882	3,856	3,847	3,861
	10	3,711	3,775	3,822	3,856	3,886	3,932	3,965	3,981	3,971	3,936	3,911	3,881	3,853	3,847
	11	3,625	3,703	3,762	3,805	3,839	3,897	3,938	3,969	3,983	3,968	3,943	3,915	3,880	3,850
	12	3,529	3,622	3,694	3,747	3,788	3,853	3,905	3,943	3,973	3,985	3,977	3,949	3,919	3,878
	13	3,435	3,533	3,618	3,684	3,733	3,804	3,864	3,911	3,947	3,977	3,995	3,985	3,955	3,921
	14	3,347	3,443	3,536	3,614	3,674	3,751	3,817	3,873	3,917	3,951	3,989	4,006	3,994	3,960
	15	3,264	3,356	3,451	3,538	3,609	3,694	3,767	3,829	3,882	3,923	3,964	4,001	4,016	4,000

NUMBER OF HPV VACCINE DOSES ADMINISTERED BY AGE AT VACCINATION

Source: [1] (Annual reports from the Ministry of Health to WHO/UNICEF Joint Reporting Form on Immunization)

a) FEMALES

		Año													
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Edad	9									96,868	94,867	90,056	97,498	107,866	114,286
	10												8,775	8,308	8,414
	11														252
	12														168
	13														145
	14														
	15+														
	Missing														

Datos de Naciones Unidas (UN): Estimaciones poblacionales - MUJERES

		Año													
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Edad	9	133,068	129,828	126,942	124,597	122,555	120,418	118,708	[illegible]	118,601	119,758	120,708	121,980	123,272	124,241
	10	136,326	133,101	129,879	127,073	124,829	122,540	120,323	[illegible]	118,266	119,225	120,126	121,273	122,563	123,623
	11	139,577	136,405	133,149	129,926	127,189	124,838	122,533	120,272	118,735	118,651	119,584	120,667	121,828	122,897
	12	142,926	139,670	136,498	133,192	129,958	127,188	124,855	122,572	120,330	118,947	119,002	120,115	121,198	122,135
	13	144,992	143,017	139,778	136,588	133,220	129,965	127,197	124,919	122,722	120,535	119,359	119,524	120,635	121,482
	14	145,122	145,090	143,124	139,882	136,662	133,259	129,981	127,253	125,097	123,021	121,111	119,944	120,035	120,910
	15	143,901	145,240	145,204	143,225	139,970	136,750	133,308	130,046	127,424	125,427	123,827	121,861	120,518	120,303

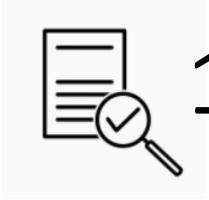
ESTIMACIÓN DE COBERTURA	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
ESTIMACIÓN					82%	79%	75%	80%	88%	92%
ESTIMACIÓN - NUMERADOR					96868	94867	90056	97498	107866	114286
ESTIMACIÓN - DENOMINADOR					118601	119758	120708	121980	123272	124241
NOTAS										

DEFINICION DE GRUPO OBJETIVO POR EDAD PARA EL DENOMINADOR					Población 9 años	Población 9 años	Población 9 años	Población 9 años	Población 9 años	Población 9 años

Coverage at 15 years

	women population	AGE	2013	2014	2015	2016	2017	2018	2019	Σ	Coverage at 15 y
2008	3,901	9	291	297	342	267	280	373	420	420	
2009	3,927	10	1,110	1,149	1,219	1,253	1,232	1,244	1,482	1,855	
2008	3,928	11	510	549	542	572	591	584	546	2,070	
2007	3,911	12	284	229	565	315	332	240	731	2,814	
2006	3,890	13	75	89	229	84	103	94	286	2,712	
2005	3,864	14	11	29	184	13	12	48	197	2,711	
2004	3,827	15+	0		0		11	0	0		0

What to do?



1. Check

CURRENT PROGRAM

		sex	age	schedule	approach	delivery (main)	school grade	delivery (other)
	PRIMARY TARGET:	FEMALES	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	
	PRIMARY TARGET:	MALES	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	

History of the HPV vaccination program

		sex	age	schedule	approach	delivery (main)	school grade	delivery (other)
NATIONAL - GIRLS ONLY NOV 2016	PRIMARY TARGET:	FEMALES	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	
NATIONAL - INCLUSION MALES? 2019	PRIMARY TARGET:	BOTH	10	2 DOSES (0 - 6M)	SINGLE SCHOOL-GRADE VACCINATION	SCHOOL-BASED	6	

2. Answer the questions

QUERY TO THE COUNTRY
1) IS THE PROGRAM INFORMATION CORRECT?
□ YES
□ NO
IF NO, PLEASE COMMENT
2) PLEASE CONFIRM THAT BOYS VACCIANTIONS WAS OFFICIALLY INTRODUCED IN 201. THE SHEDULE FORM ONLY STATES FEMALE VACCINATION.
□ YES
□ NO
IF NO, PLEASE COMMENT

NUMBER OF HPV VACCINE DOSES ADMINISTERED BY AGE AT VACCINATION

Source: [1] (Annual reports from the Ministry of Health to WHO/UNICEF Joint Reporting Form on Immunization)

a) FEMALES

JRF DATA: HPV vaccine doses administered - 1st dose - FEMALES

		Year												
		2006										2017	2018	2019
Age	9											280	373	420
	10											1,232	1,244	1,482
	11											591	584	946
	12											332	240	731
	13											103	94	286
	14											12	48	197
	15+											11	0	
	Missing											0	0	

3. Check if the doses correspond to what is reported

- **Missing doses**
- **Wrong reported**

POPULATION BY SINGLE AGE AND YEAR

Source: United Nations, Department of Economic and Social Affairs, Population Division (2019). World Population Prospects 2019, Online Edition. Rev. 1.

a) FEMALES

UN DATA: Population estimates - FEMALES

		Year												
		2006	200								5	2016	2017	2018	2019
Age	9	3,724	3,78								9	3,742	3,701	3,692	3,721
	10	3,650	3,72								9	3,791	3,740	3,698	3,693
	11	3,567	3,65								6	3,844	3,795	3,739	3,694
	12	3,475	3,57								3	3,903	3,851	3,800	3,736
	13	3,384	3,48								9	3,943	3,913	3,860	3,803
	14	3,301	3,400	3,497	3,585	3,657	3,745	3,814	3,864	3,897	3,922	3,951	3,955	3,923	3,867
	15	3,223	3,321	3,415	3,506	3,588	3,684	3,764	3,827	3,874	3,906	3,936	3,965	3,968	3,932

4. Check the denominators

FEMALES

A) PRHPV1: HPV VACCINATION PROGRAM COVERAGE - ONE DOSE - FEMALES

COVERAGE ESTIMATES	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
ESTIMATE								3%	70%	99%*
ESTIMATE - NUMERATOR								561	2583	4062
ESTIMATE - DENOMINATOR								740	3698	3693
NOTES										

5. Check the calculations

6. Answer the questions

QUERY TO THE COUNTRY
3) ANY COMMENT ON THE DATA ABOVE?
□ YES
□ NO
IF YES, PLEASE COMMENT
4) PLEASE CAN YOU CONFIRM IF THERE WAS ANY KIND OF EXTENDED VACCINATION THAT EXPLAIN THE HIGHER NUMBER OF DOSES ADMINISTERED TO GIRLS IN 2019? ALSO THE DENOMINATOR YOU REPORT IN THE ADMINITRATIVE COVER
□ YES
□ NO
IF YES, PLEASE COMMENT

COMPLEMENTARY INFORMATION	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
OFFICIAL COVERAGE REPORTED										
ADMINISTRATIVE COVERAGE REPORTED										

QUERY TO THE COUNTRY
5) ANY COMMENT ON THE DATA ABOVE?
□ YES
□ NO
IF YES, PLEASE COMMENT

Considerations

- Use of the vaccination coverage calculation methodology
  - Monitoring coverage
  - SDG
- Quality and completeness of the data
  - Identify entire target population
    - Not just enrolled for the first dose
    - Not just the first doses as denominator for second doses
  - Ages
  - Gender
  - Consistency in data reporting

THANK YOU!

DAY 4

October 30- Day 4 Session 4: Impact of the HPV vaccine Moderator: Maria Tereza da Costa		
10:00 – 10:20	HPV ESAVI and impact of Sociogenic Events on HPV Vaccination	Maria Tereza da Costa - PAHO
10:20 - 10:40	Impact of Vaccination against Human Papillomavirus in Argentina	Alejandra Picconi - National Institute of Infectious Diseases- ANLIS "Dr. Malbrán"-Argentina
10:40 – 11:00	PAHO Proposal to Evaluate the Impact of HPV Vaccines in Latin America and the Caribbean	Laia Bruni - Institut Català d'Oncologia-Spain
11:00– 12:00	Discussion	
	Conclusion and next steps: building national elimination plans	Silvana Luciani - PAHO Lúcia Helena de Oliveira - PAHO Cuauhtémoc Ruiz Matus - PAHO Paul Bloem – WHO

HPV ESAVI and Impact of Sociogenic Events on HPV Vaccination

Maria Tereza da Costa Oliveira
Consultant on New Vaccines
IM/FPL/PAHO-WHO – WDC

Lucia Helena De Oliveira
Regional Advisor on New Vaccines
IM/FPL/PAHO-WHO – WDC

Pan American Health Organization
World Health Organization
Americas

PAHO

CONTENTS

- HPV Vaccines Safety
- ESAVI*
  - Events Related with the HPV Vaccines
  - Myths attributed to HPV Vaccines
- Sociogenic events in Latin America and their impact
- Steps to Respond a Crisis due to an ESAVI
- Conclusions

*ESAVI= Event allegedly attributed to vaccination or immunization, for the initials in Spanish.

HPV Vaccines Safety

Doses of HPV vaccines have been distributed since licensure in 2006, globally (2020 data).

The WHO Global Advisory Committee on Vaccine Safety (GACVS, reiterated that the HPV vaccine is extremely safe, and vaccine-associated events are mild and moderate, resolving quickly on their own.

Doses of HPV vaccines have been applied.
LAC 2015 -2019
(Source: JRF)

Local Reactions:

- Injection site pain is very common (up to 80%). Pain is more commonly reported at the time of injection than in the hours and days following vaccination.
- Severe pain (spontaneous pain or pain that prevented normal activity) was reported for approximately 6% of vaccinees.

Other injection site reactions consist of erythema and swelling (25% for both).

HPV vaccine-associated local events are mild and moderate, resolving quickly on their own.

Systemic Reactions

Headache (33%); Pyrexia (10%)
Other possibly related with the vaccination: dizziness, myalgia, arthralgia, and gastrointestinal symptoms (nausea, vomiting, abdominal pain).

Systemic reactions reported were generally mild and self-limiting

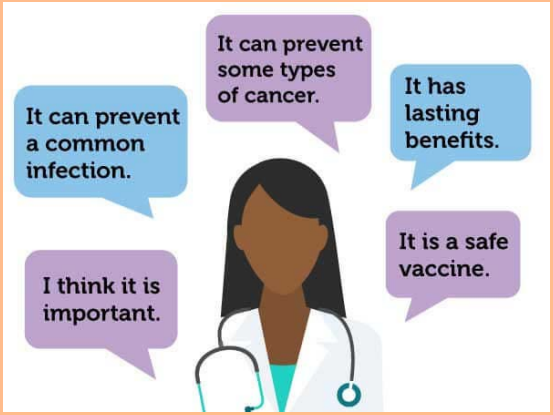
Anaphylaxis: the risk has been characterized as approximately 1.7 cases per million doses. No other adverse reactions have been identified.

Syncope was established as a common anxiety or stress related reaction to the injection.

Source: WHO. Safety update of HPV vaccines. Meeting of the Global Advisory Committee on Vaccine Safety, 7–8 June 2017. WER 2017; 92(28): 393–404.

Measures to Prevent Syncope

- Inform the girl/boy about the vaccine (without scaring her/him)
- Avoid the following:
  - Fasting,
  - Low fluid intake,
  - Very hot environment,
  - Waiting standing in a line for a long time.



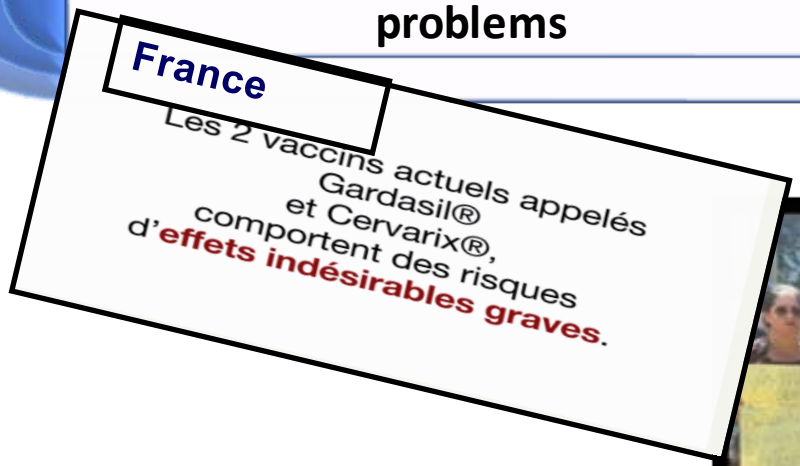
- Whenever possible, the vaccine should be applied in a private well-ventilated place and the person should be seated.
- **Although most of the episodes are stress-related (vasovagal syncope), all patients should have a physical examination to exclude any existing health condition.**

Myths attributed to HPV Vaccines

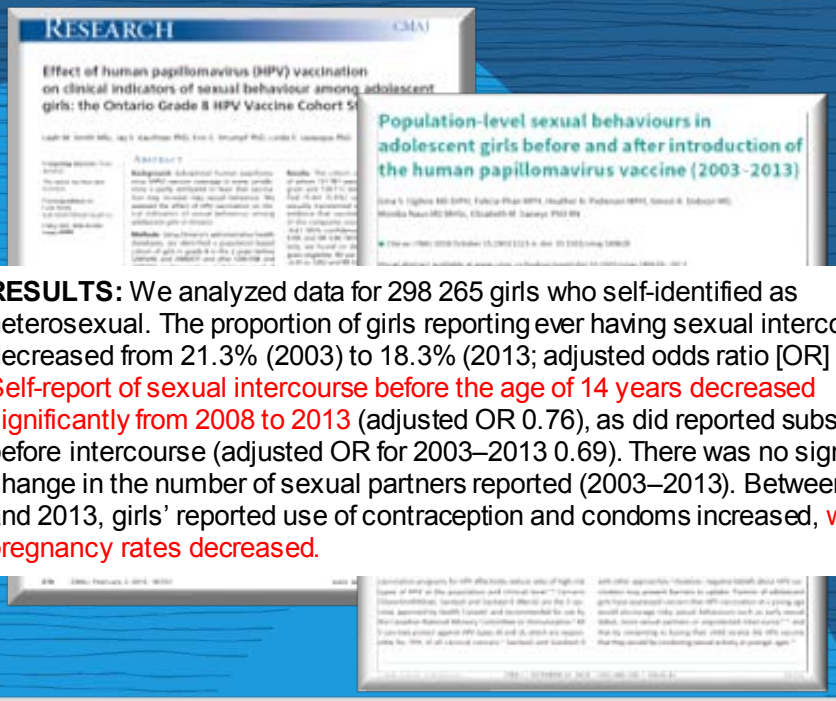
The vaccine stimulate early sexual activity

The vaccine causes infertility

The vaccine causes serious health problems



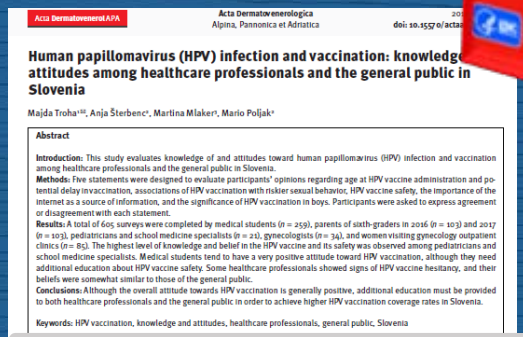
Myth: HPV Vaccination and Sexual Behavior


RESEARCH

Effect of human papillomavirus (HPV) vaccination on clinical indicators of sexual behaviour among adolescent girls: the Ontario Grade 8 HPV Vaccine Cohort S

Population-level sexual behaviours in adolescent girls before and after introduction of the human papillomavirus vaccine (2003-2013)

RESULTS: We analyzed data for 298 265 girls who self-identified as heterosexual. The proportion of girls reporting ever having sexual intercourse decreased from 21.3% (2003) to 18.3% (2013; adjusted odds ratio [OR] 0.79). Self-report of sexual intercourse before the age of 14 years decreased significantly from 2008 to 2013 (adjusted OR 0.76), as did reported substance use before intercourse (adjusted OR for 2003–2013 0.69). There was no significant change in the number of sexual partners reported (2003–2013). Between 2003 and 2013, girls' reported use of contraception and condoms increased, while pregnancy rates decreased.


Acta Dermatovenerol APA

Acta Dermatovenerologica Alpina, Pannonica et Adriatica

Human papillomavirus (HPV) infection and vaccination: knowledge attitudes among healthcare professionals and the general public in Slovenia

Majda Troha[1,2], Anja Šterbenc[3], Martina Mlaker[3], Mario Poljak[3]

Abstract

Introduction: This study evaluates knowledge of and attitudes toward human papillomavirus (HPV) infection and vaccination among healthcare professionals and the general public in Slovenia.

Methods: Five statements were designed to evaluate participants' opinions regarding age at HPV vaccine administration and potential delay in vaccination, associations of HPV vaccination with riskier sexual behavior, HPV vaccine safety, the importance of the internet as a source of information, and the significance of HPV vaccination in boys. Participants were asked to express agreement or disagreement with each statement.

Results: A total of 605 surveys were completed by medical students ($n = 259$), parents of sixth-graders in 2016 ($n = 103$) and 2017 ($n = 103$), pediatricians and school medicine specialists ($n = 21$), gynecologists ($n = 34$), and women visiting gynecology outpatient clinics ($n = 85$). The highest level of knowledge and belief in the HPV vaccine and its safety was observed among pediatricians and school medicine specialists. Medical students tend to have a very positive attitude toward HPV vaccination, although they need additional education about HPV vaccine safety. Some healthcare professionals showed signs of HPV vaccine hesitancy, and their beliefs were somewhat similar to those of the general public.

Conclusions: Although the overall attitude towards HPV vaccination is generally positive, additional education must be provided to both healthcare professionals and the general public in order to achieve higher HPV vaccination coverage rates in Slovenia.

Keywords: HPV vaccination, knowledge and attitudes, healthcare professionals, general public, Slovenia

"Since the implementation of school-based HPV vaccination program in British Columbia, sexual risk behaviors reported by adolescent girls either reduced or stayed the same. These findings contribute **evidence against any association between HPV vaccination and risky sexual behaviors.**"

People have misbeliefs, including health professionals:

Results of a research from Slovenia: Medical Students (11,2%), Gynecologists (14,7%) and Parents (17,5 to 27,2%) believe its true.

Myth: HPV vaccines cause infertility

Since 2012, individual case reports have linked vaccination against HPV with primary ovarian insufficiency (POI), defined as dysfunction or depletion of ovarian follicles, menopausal symptoms and reduced fertility before the age of 40.

...

GACVS concluded that the available data do not support an association between HPV vaccination and infertility or POI. The current safety profile continues to be extremely favourable, as discussed at 7 previous GACVS meetings, and consistent with the pre-licensure safety profile.[21] HPV vaccine safety will continue to be monitored and will be reviewed by GACVS as appropriate. GACVS recommends that communications strategies about vaccine safety ensure appropriate understanding of the safety profile.

"Although the safety of HPV vaccine has received considerable media attention, the evidence does not suggest a causal relationship between HPV vaccination and infertility."

Source: WHO. Safety update of HPV vaccines. Meetings of the Global Advisory Committee on Vaccine Safety, 4–5 December 2019 . WER 2020; 95 (4): 30-33.

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Myth: HPV vaccines cause autoimmune conditions

- Although case reports have identified a range of new onset chronic conditions occurring post-vaccination, including autoimmune diseases, a well-conducted population-based study on post-licensure safety surveillance showed **no association between HPV vaccine and such conditions.** Data are reassuring that **HPV vaccine does not increase the risk of Guillain- Barré syndrome.**
- A review of post-licensure safety surveillance during >4 years of routine use of the bivalent vaccine found no patterns or trends for potential immune-mediated diseases after vaccination and observed incidences of **Bell's palsy** and confirmed Guillain-Barré syndrome were within the expected range in the general population.
- Concerns have been raised about **complex regional pain syndrome (CRPS) and postural orthostatic tachycardia syndrome (POTS)** following HPV vaccination. Despite the difficulties in diagnosing both disorders, reviews of pre- and post-licensure **data provide no evidence that these syndromes are a direct effect of the HPV vaccines.**

Source: WHO position paper, May 2017 available at http://www.who.int/wer 2017, 92, 241–268

Sociogenic Events on HPV Vaccination

Crises can result from clusters of "adverse events following immunization", reports of new studies or data on the safety of a vaccine, media reports and rumors about vaccine safety or regulatory action such as recall of a vaccine. These events can result in a negative perception of a vaccine's safety and adversely affect its acceptance. Strategies for communication about vaccine safety are necessary.

PAHO

Colombia:

Decreasing HPV vaccination coverage: mapping roles of different stakeholders and societal-historical factors.

Alex Vorsters[1], Nubia Muñoz[2], Raul Murillo[3], Pierre Van Damme[1], Emilie Karafillakis[4], Silvia de SanJosé[5], Laia Bruni[5], Heidi Larson[4].
1Center for the Evaluation of Vaccination, University of Antwerp, Belgium; 2 Emeritus Professor, National Cancer Institute of Colombia; 3 Cancer Center, Javeriana University, Bogota, Colombia; 4 Vaccine confidence project, London School of Hygiene and Tropical Medicine, UK; 5 Cancer Epidemiology Research Programme at the Catalan Institute of Oncology (ICO), Barcelona, Spain;

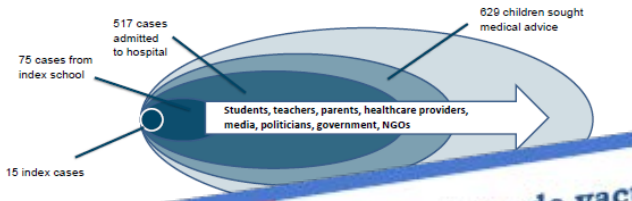
Introduction:

Vaccination coverage is the result of a complex interplay between different stakeholders with a specific societal and cultural background. The goal of this poster is to provide a brief overview of major events/aspects that may have contributed to the current situation in Colombia. By listing the role or potential role of different stake holders or cultural-historical factors we may be able to compare different countries and find common denominators.

Possible event(s) leading to crisis:

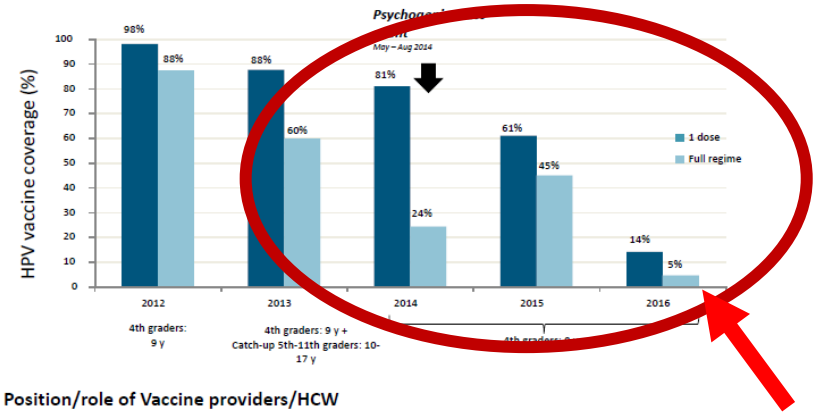
- In 2014, a mass psychogenic event in Carmen de Bolivar, a small city in the north of Colombia, was used and continues being used by the media to shake public confidence in HPV immunization despite strong support from the government.

Ripple effect of the outbreak (1)



*No-associated with HPV vaccines as defined by the National Programme after their analyses

Coverage rate HPV vaccination (4)



Position/role of Vaccine providers/HCW

- HPV vaccination programme is school based.
- Some HCW are also fueling the distrust on the HPV vaccine by publishing case reports that suggest that the HPV vaccine is responsible for some autoimmune diseases diagnosed after vaccination. E.g. (Dr. Juan M Anaya) a Colombian immunologist proposes screening for autoimmune diseases before HPV vaccination. (3)

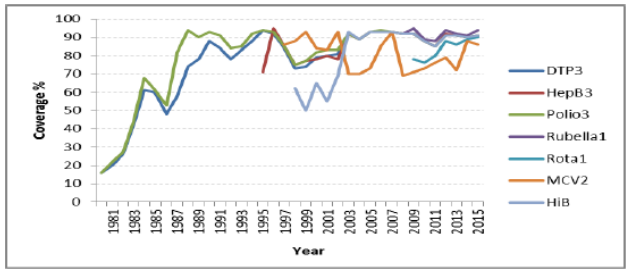
Organized "anti-vaccine" activities

- Girls experiencing alleged adverse effects (50 are represented by Monica Lion Del Rio, attorney and mother of a girl with symptoms of side effects)

Societal-historical factors related to adherence to universal prevention progams

- Cervical cancer screening coverage, % (age and screening interval, reference): 69.9% (All women aged 18-69 screened every 1y. (6)
- Screening ages (years) 25-69 (cytology), 30-50 (VIA), 30-69 (HPV test)
- Good coverage of EPI vaccines

Coverage of the Expanded Immunization Programme in Colombia(7)



6.
7. _monitoring/globalsummary/timeseries/tswucoveragepol3.html

Poster at HPV symposium: Building Trust, Managing Risk: Vaccine Confidence and Human Papillomavirus Vaccination
7-8 June 2017 at the London school of hygiene & tropical medicine.

HPV Immunization Stress-related Response (ISRR) in Brazil

Results: "No biological association was found between HPV vaccine and the clinical problems presented by the patients."

- The psychogenic nature of patients' convulsive seizures in a suspected outbreak of an ISRR cluster following HPV vaccination in Rio Branco, Brazil were explored **to confirm the suspected diagnosis of psychogenic non-epileptic seizures (PNES), and to avoid hesitancy to vaccinate.**
- Twelve patients with convulsive seizures were submitted to prolonged intensive video electroencephalography monitoring, brain magnetic resonance imaging, cerebrospinal fluid diagnostic testing, laboratory subsidiary examinations, and complete neurological and psychiatric evaluations.
- Ten patients received the positive diagnosis of PNES, and two patients (brother and sister) received the diagnosis of idiopathic generalized epilepsy.

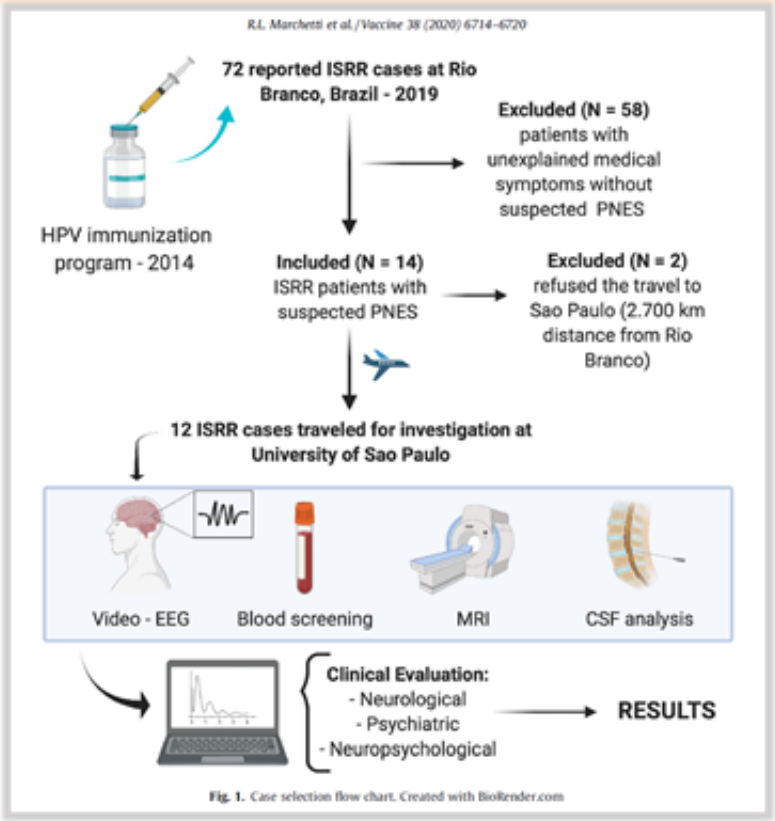


Fig. 1. Case selection flow chart. Created with BioRender.com

Source: Immunization stress-related responses presenting as psychogenic non-epileptic seizures following HPV vaccination in Rio Branco, Brazil. Marchetti, RL et al. Vaccine 38 (2020) 6714-6720.
Available at: https://doi.org/10.1016/j.vaccine.2020.08.044

PAHO

Health Professionals Play an Important Role in Promoting HPV Vaccination and Avoiding Rumors and Myths

reported reasons for not receiving HPV vaccination in the school programme were parental concerns about vaccine safety and parental perceptions that their child was at low risk of HPV infection [93].

Provider recommendation is very influential in the decision to vaccinate. A US study found that parents who had received a high-quality provider recommendation to vaccinate (strong endorsement, offer same day vaccination, discuss cancer prevention) were 9 times more likely to have vaccinated their child against HPV than parents who received no recommendation [94]. In Denmark, each girl reaching a certain age is invited through a letter from the national vaccination programme to get vaccinated by the family doctor. This has enabled the programme to reach high coverage (>80%) in the first years after introduction [3]. A study from Austria, where males and females are vaccinated, found that information on the vaccine from physicians has a strong influence on uptake even in a school-based programme. It also found that higher paternal educational status significantly increased the chances of a male child being HPV vaccinated but did not influence girl's vaccination, which indicates that sex-specific strategies may be required [95].

PAHO/WHO

"Four Immediate Steps When Responding to an Event that May Erode Trust"

1 Gather your inner circle

Coordination is critical during all phases of crisis response. If it is believed that the event may damage trust in vaccines and cause a negative media response, your inner circle of allies should be gathered immediately.

Consider the following

- Establish a coordination and working group (if not already established).
- Engage relevant partners across institutions, e.g. ministries of health, education and social affairs; regulatory authorities; centers for disease control, health promotion, communication, press and emergency response; vaccine experts; professional associations.
- Agree how you will continue to coordinate, communicate and share information within the group.
- Agree on roles and responsibilities.

2 Understand the problem

Not all events that may potentially erode confidence in vaccines and vaccination require a communications response. Not responding may impair trust in vaccines and health authorities. Over-communicating may cause unnecessary public concern. Thus, it is important – throughout the process – to analyse events and plan the communications response accordingly.

Consider the following

- Obtain as much information as possible about the event(s) that took place.
- Analyse the situation: what is the potential level of impact on trust in vaccines and the immunization programme?
- Shape your communications response according to your conclusions.

3 Liase with key stakeholders

A critical first step in such events is to liaise with key stakeholders. Good stakeholder relations are critical to ensuring trust during a crisis.

Consider the following

- Consult your list of key stakeholders.
- Liaise with stakeholders to benefit from the support of advocates.
- Share information with stakeholders to avoid confusion and distrust and to avoid any negative interference from adversaries.

4 Communicate externally

The right response may limit the negative consequences of the crisis or even prevent the situation from escalating into a crisis. Honest and open communication is crucial for maintaining and building trust.

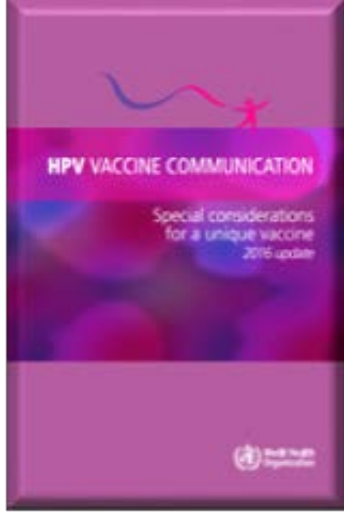
Consider the following

- Decide whether the event warrants external communication and plan your response based on your analysis of the event.
- Revisit your crisis communication plan and prepare a plan for external communication.
- Communicate broadly and to selected target groups; communicate often using consistent messages through many channels.
- Communicate where there are uncertainties and what you are doing to reduce them.

World Health Organization Europe

PAHO

PAHO Technical Advisory Group on Vaccine-preventable Diseases (TAG) - Recommendations on HPV Vaccines



- TAG congratulates PAHO Member States that have recently decided to introduce HPV vaccine into their routine immunization programs. TAG reiterates the importance of [redacted] against HPV among girls and induce herd immunity among boy populations. Curre[redacted] prote[redacted]
- Given [redacted] State[redacted] sched[redacted] for decisi[redacted] the routin[redacted]
- TAG r[redacted] vaccin[redacted] to target[redacted] vaccination series.
- Whenever possible, Member States should monitor the impact of HPV vaccination.

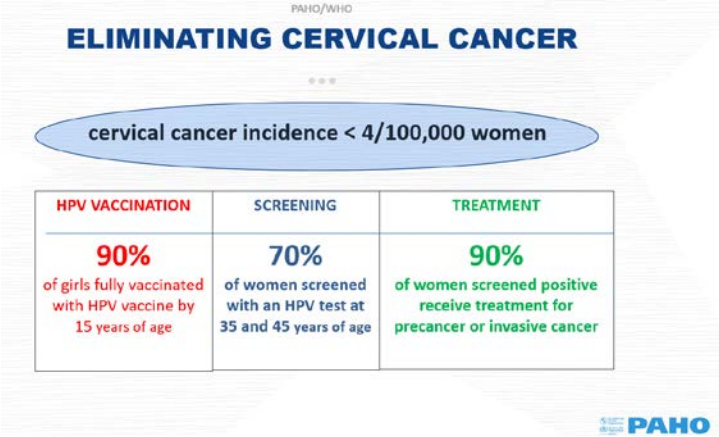
TAG urges PAHO Member States to carefully consider their approaches to communication around the HPV vaccine, making sure to generate audience-specific messages. Additionally, TAG calls on PAHO to support intercountry exchanges on lessons learned regarding communication on the safety of HPV vaccine and crisis management.

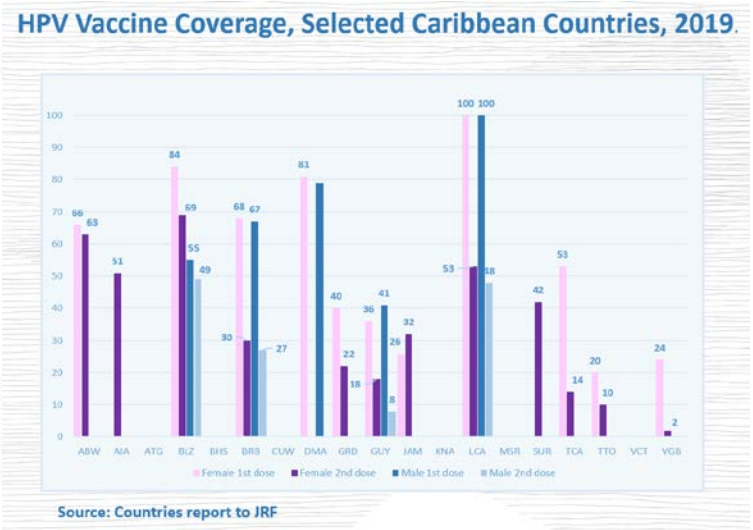
TAG Meeting on July 2017, Panama City, Panama

PAHO

Conclusions

- **WHO/GACVS considers HPV vaccines to be extremely safe. HPV vaccine-associated events are mild and moderate, resolving quickly on their own.**
- **HPV vaccines prevent a deadly cancer, that kills 34000 women yearly in the Region of the Americas.**
- **Most countries have introduced the vaccine; the challenge is to achieve 90% 2nd dose coverage in girls in order to eliminate cervical cancer.**





PAHO

Conclusions

- **Despite the safety of HPV vaccines, they have received considerable media attention. Sociogenic events have impacted negatively the HPV coverage in the Region and worldwide.**
- **Health professionals play an important role in promoting HPV vaccination and avoiding rumors and myths; they must be updated very often about the safety of the vaccines.**
- **Countries must be prepared to respond to any event that may damage trust in vaccines and cause a negative media response.**
- **If it happens, countries must revisit the crisis communication plan. The right response may limit the consequences of a crisis or even prevent it.**

Acknowledgment

John Fitzsimmons

THANK YOU!

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

HPV Vaccination
Towards the Elimination of Cervical Cancer in the Caribbean Countries. 30 October 2020

IMPACT OF VACCINATION AGAINST HUMAN PAPILLOMAVIRUS (HPV) IN ARGENTINA

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GLOBAL HPV LABNET

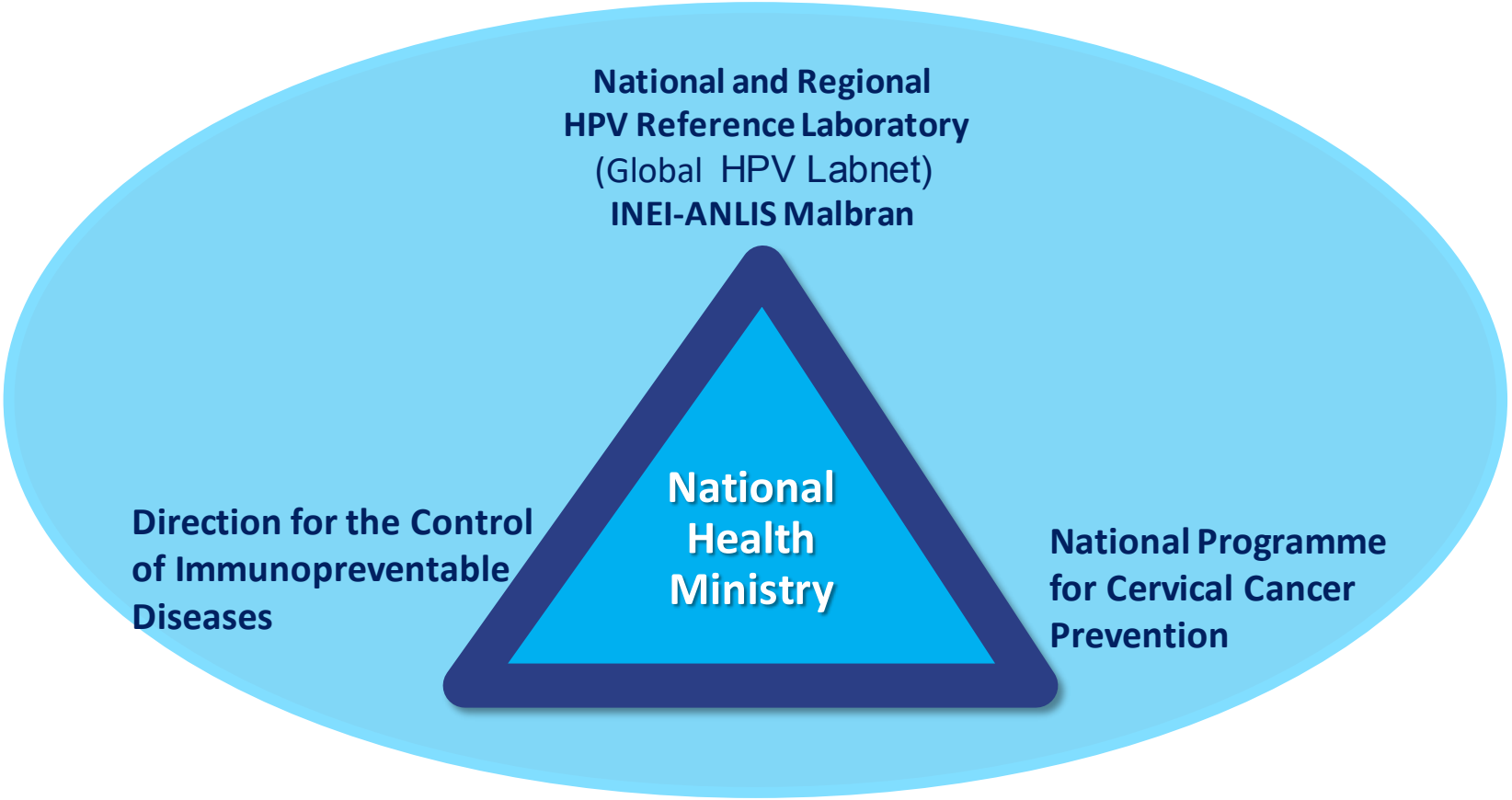
- I have no conflict of interest to declare

Outline

- Scenario on HPV vaccination in Argentina.

- Local HPV surveillance and first data on evaluation of the impact of HPV vaccination in Argentina.

Comprehensive government-funded national HPV and cervical cancer prevention approach of Argentina, since 2011.



National Vaccination Calendar of Argentina - 2011

Edad	BCG (1)	Hepatitis B (HB) (2)	Neumococo Conjugada	Pentavalente (DPT-Hib-HB) (3)	Cuádruple (DPT-Hib) (4)	Sabin (OPV) (5)	Triple Viral (SRP) (6)	Gripe	Hepatitis A (HA) (7)	Triple bacteriana Celular (DPT) (8)	Triple bacteriana Acelular (dTap) (9)	Doble bacteriana (dT) (10)	VPH (11)	Doble viral (SR) (12)	Fiebre Amarilla (FA) (13)	Fiebre Hemorrágica Argentina (FHA) (14)
Recién nacido	Única dosis [A]	1ª dosis [B]														
2 meses			1ª dosis	1ª dosis		1ª dosis										
4 meses			2ª dosis	2ª dosis		2ª dosis										
6 meses				3ª dosis		3ª dosis										
12 meses			3ª dosis [D]				1ª dosis	Dosis Anual [F]	Única dosis						Única dosis	
18 meses					1° Refuerzo	4ª dosis										
24 meses																
5-6 años (Ingreso escolar)						Refuerzo	2ª dosis			2° Refuerzo						
11 años		Iniciar o completar esquema [C]					Iniciar o completar esquema [E]				Refuerzo		3 dosis (sólo niñas) [J]			
A partir de los 15 años																Única dosis
16 años												Refuerzo [I]				
Cada 10 años												Refuerzo			Refuerzo	
Embarazadas								Dosis Anual								
Puerperio								Dosis Anual [G]						Única dosis [E]		
Personal de Salud		3ª dosis						Dosis Anual			1 dosis [H]					

(Consultar al médico acerca de las vacunas que deben recibir los niños que comenzaron su vacunación según el calendario anterior)

[A] Antes de egresar de la maternidad.
[B] En las primeras 12 horas de vida.
[C] Si no hubiera recibido el esquema completo. Aplicar 1° dosis, 2° dosis al mes de la primera y 3° dosis a los 6 meses de la primera.
[D] Previene la meningitis, neumonia y sepsis por neumococo.
[E] Si no hubiera recibido dos dosis de Triple viral o una de Triple viral más una dosis de Doble viral.
[F] Deberán recibir en la primovacunación 2 dosis de vacuna separadas al menos por cuatro semanas.
[G] Madres de niños menores a 6 meses deberán recibir vacuna antigripal si no la hubiesen recibido durante el embarazo.
[H] Se indica a personal de Salud que atiende niños menores de 1 año.
[I] Los que comenzaron el plan dTap les corresponderá este refuerzo a los 21 años.
[J] La vacuna contra el VPH está indicada solamente para niñas de 11 años. Aplicar 1° dosis, 2° dosis al mes de la primera y 3° dosis a los 6 meses de la primera.

(1) BCG Tuberculosis (formas invasivas)
(2) HB Hepatitis B
(3) DPT-HB-Hib: (Pentavalente) difteria, tétanos, Tos convulsa, Hep B, Haemophilus influezae b.
(4) DPT-Hib: (Cuádruple) difteria, tétanos, Tos convulsa, Haemophilus influezae b.
(5) OPV: (Sabin) vacuna para poliomielitis oral.
(6) SRP: (Triple viral) sarampión, rubéola, paperas.
(7) HA (Hepatitis A).
(8) DPT: (Triple bacteriana) difteria, tétanos, Tos convulsa.
(9) dTap (Triple bacteriana acelular).
(10) dT (Doble bacteriana) difteria, tétanos.
(11) VPH: vacuna contra el virus del papiloma humano.
(12) SR: (Doble viral) sarampión, rubéola.
(13) FA: (Fiebre amarilla) una dosis para residentes o viajeros a zonas de riesgo.
(14) FHA: (Fiebre hemorrágica argentina) una dosis para residentes o viajeros a zonas de riesgo.

VACUNARSE ES SER SOLIDARIO:
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a vos y a quienes te rodean.

ARGENTINA Con vos, siempre.

Ministerio de Salud
Presidencia de la Nación

- **Bivalent vaccine**
- **Girls 11 y**
- **0-1-6-month schedule**

Más información
www.msal.gov.ar
vacunas@msal.gov.ar
0800-222-1002

Vaccination against HPV in Argentina (mandatory and free)

2011

Incorporation to the National Vaccination Calendar for 11-y-old girls born from 2000

(0- 1- 6 months)

2014

Transition to quadrivalent vaccine

2015

Reduction to

two doses for girls 11 y

2017

Extension to 11-year-old boys born as of 2006

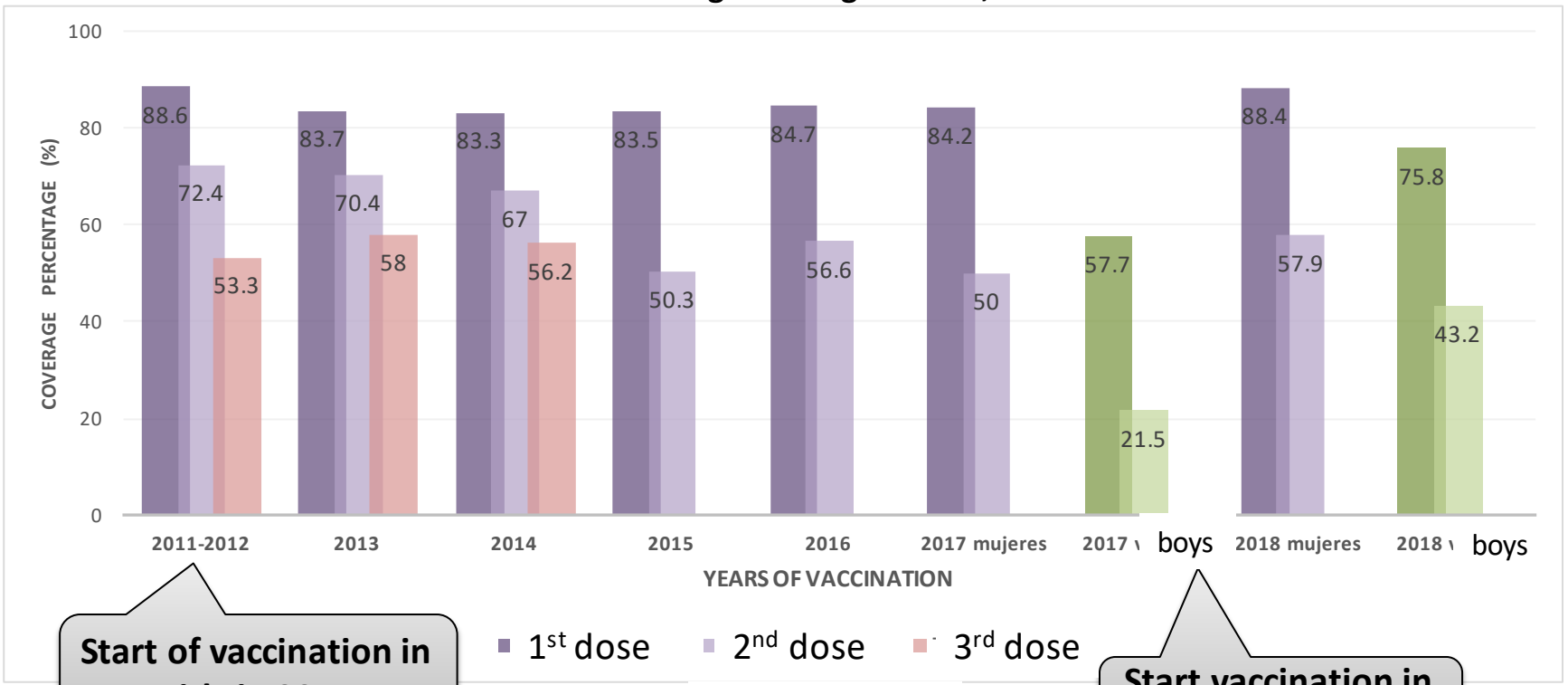
Men and women aged 11 to 26 years with HIV and transplanted individuals

Two-dose scheme

HPV vaccination coverage in Argentina- Data from 2011-2018

Average coverage: 85.2%, 69.9%, 55.8%

Average coverage: 83.3% , 51.1%



Start of vaccination in girls in 2011

Start vaccination in boys in 2017

Source: DiCEI

Outline

- Scenario on HPV vaccination in Argentina.

- Local HPV surveillance and first data on evaluation of the impact of HPV vaccination in Argentina.

Establishment of the HPV Regional Reference Laboratory (WHO HPV LabNet) in Buenos Aires (Argentina): on site-visit for evaluation, August 2008

Reviewers: A. Bispo (PAHO, WDC); E. de Villiers (DKFZ); E. Unger (CDC); T. Zhou (WHO)

During the detailed technical review of protocols and performance practices, reviewers also have provided suggestions, advice and technical tips to the laboratory to improve testing quality control and throughput

MEETING FOR THE DEVELOPMENT OF A REGIONAL FRAMEWORK FOR THE EVALUATION OF HPV VACCINE

Instituto Malbran, Buenos Aires, Argentina

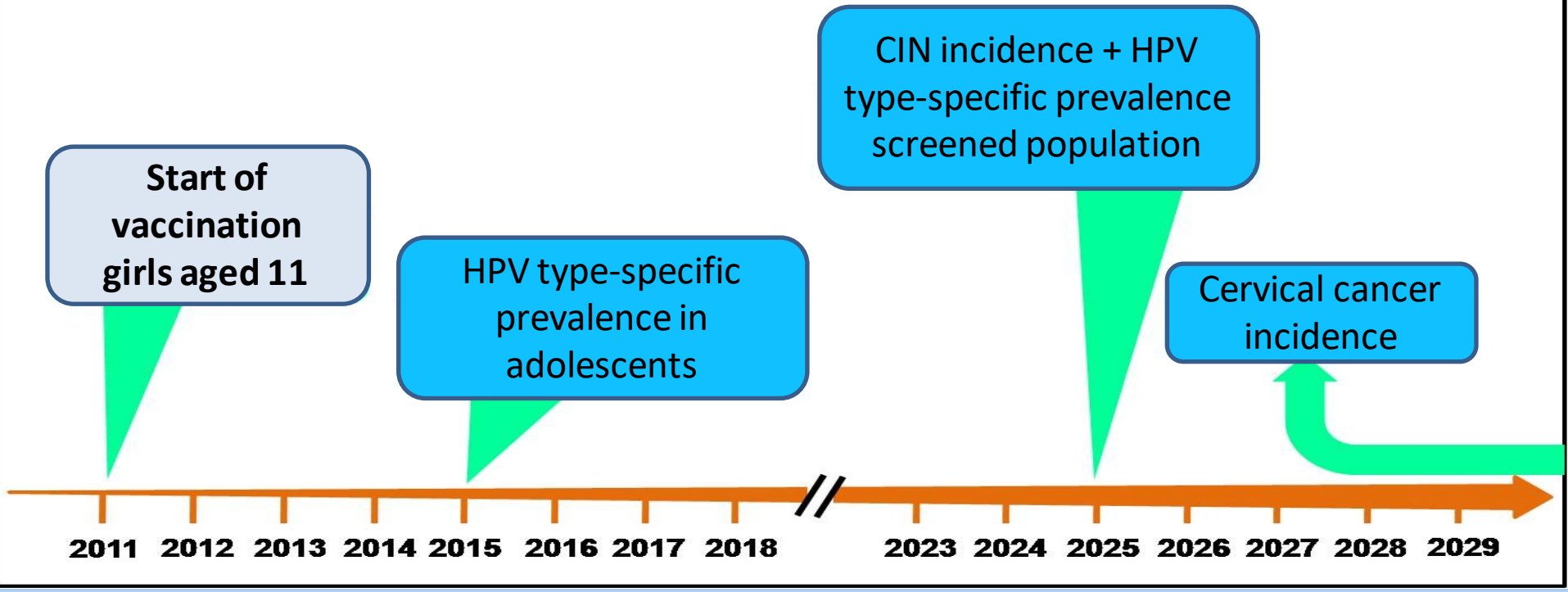
8 y 9 de noviembre de 2012

Organización Panamericana de la Salud

Oficina Regional de la Organización Mundial de la Salud

110 1902 - 2012

Evaluation of the impact of vaccination against HPV: short, medium and long term



(*HPV Surveillance and Monitoring Meeting, 6-7 MAY 2009, OMS, Ginebra; Wilkinson D, Int J Cancer. 2010; Dillner J. et al, Clin Exp Immunol 2010; Hariri et al. VPD Surveillance Manual, CDC, 5th Edition, 2011)*

Objectives

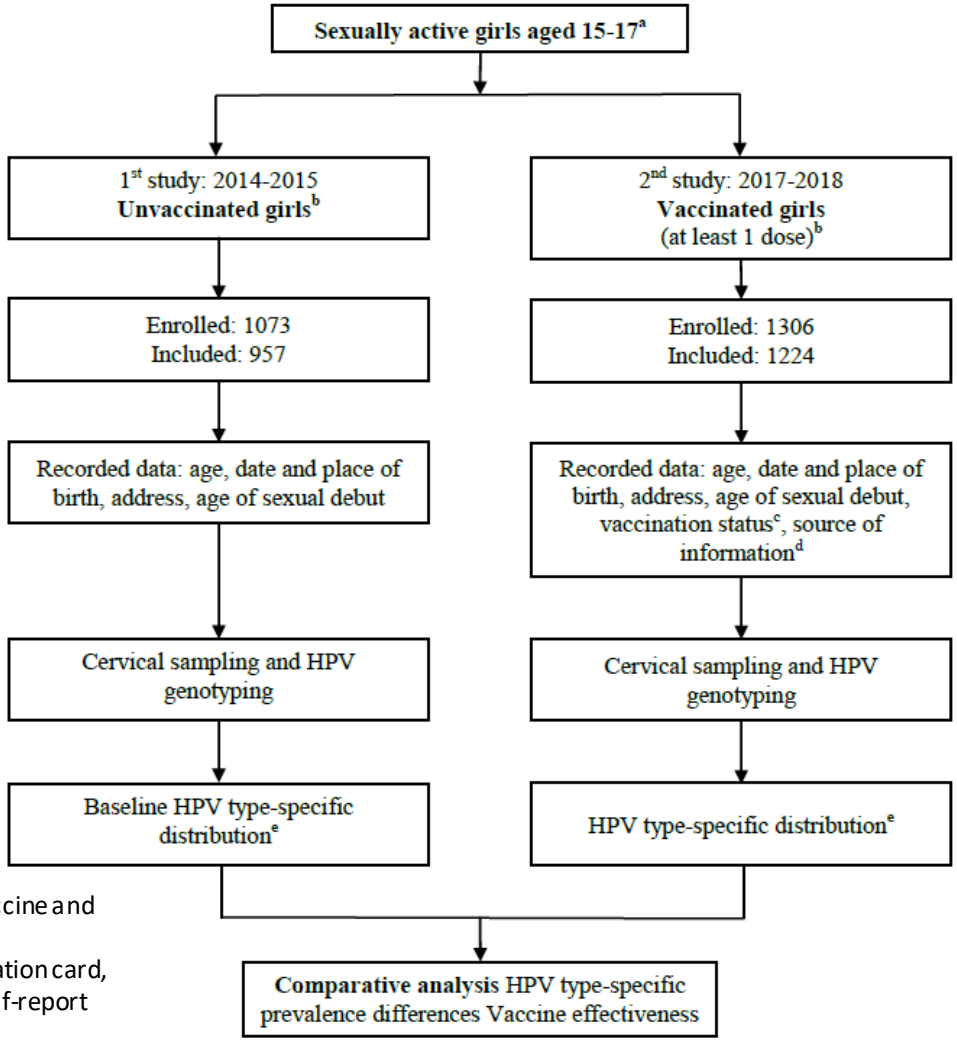
- To assess the impact of vaccination against HPV in the short term, by comparing the type-specific prevalence of HPV in sexually active adolescents aged 15 to 17, UNVACCINATED vs VACCINATED, from Argentina.

- To estimate vaccine efficacy for vaccine genotypes and potential cross-protection against related HPV types.

Materials and Methods I: Work flow

Two consecutive cross-sectional studies were performed

Identical procedures in both studies (SOPs and audits)



Vaccination status: type of vaccine and number of received doses
Source of information: vaccination card, electronic clinical history or self-report

Materials and Methods II

Sexually active girls
(aged 15-17)

First study: 2014 -2015
Unvaccinated girls (UV)

Second study: 2017 - 2018
Vaccinated girls (VA) (at least 1 dose)

DNA extraction and purification
(QIAcube system, *Qiagen*)

HPV DNA Detection: Generic PCR BSGP5+/6+bio* (140 pb)
(van den Brule et al, 2002; Schmitt et al., 2008)

HPV Genotyping: Reverse Line Blot (RLB)* Č **36 genotypes (**[illegible] **genera):**
(HPVs 6, 11, 16, 18, 26, 31, 33, 34, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 55, 56, 57, 58, 59, 61, 66, 68, 70, 71, 72, 73, 81, 82, 83, 84, y 89) .

***In house* methodology validated by WHO HPV LabNet and controlled with proficiency panels from the Int. HPV Ref. Center**

Materials y Methods III

Statistics analysis

- IBM® SPSS® Statistics 23.0.0.3 statistical software. Logistic regression analysis

- The 95% Confidence Interval was established with an $p < 0.05$ in all cases for testing statistical significance.

- Vaccine effectiveness (VE) was calculated as (1 – Odds Ratio) x100.

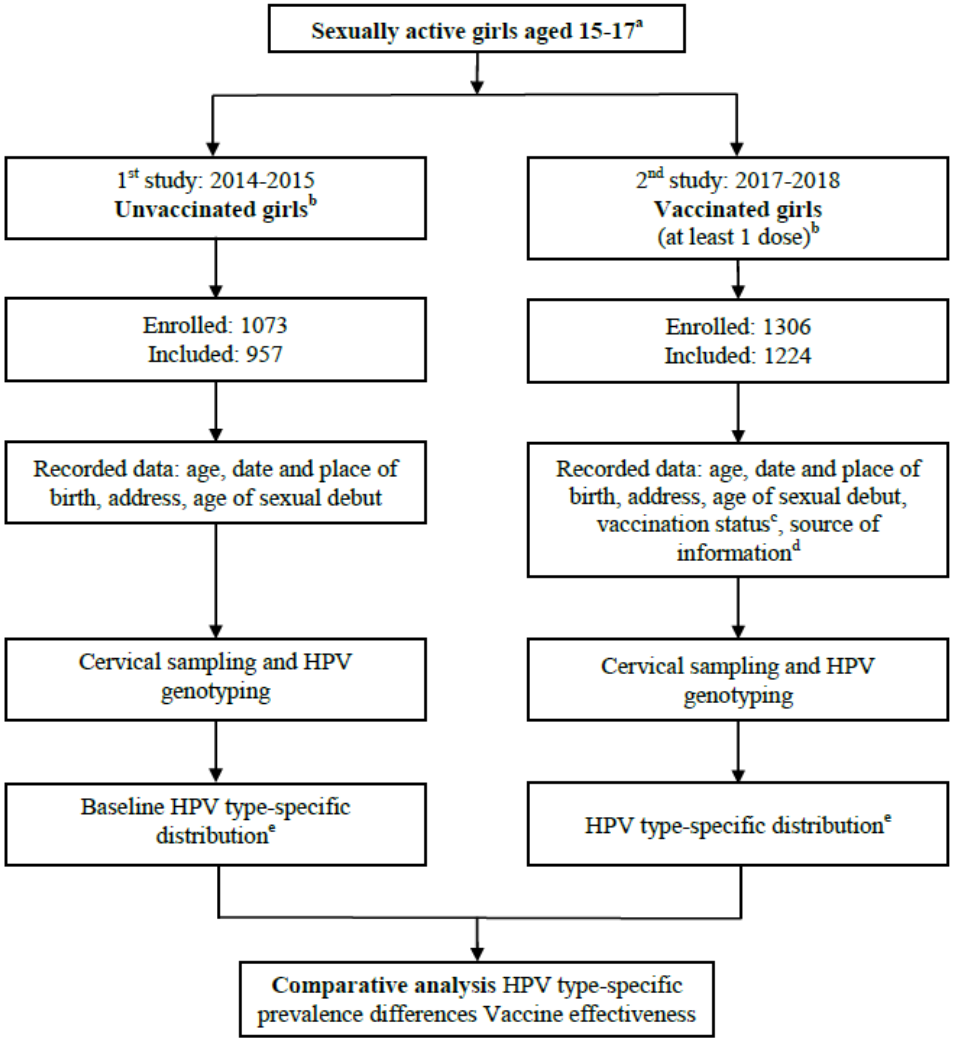
Results I

Included samples:

- **957 UV** : mean age 15.6 y
  mean age of sexual debut 13.8 y
- **1224 VA**: mean age 16.8 y
  mean age of sexual debut 14.9 y

Source of information in relation to the vaccine status: 70.8% self-reported, 27.7% Cards and 1.7% medical history.

Address georeferencing : vast majority of girls from both groups lived in the same neighbourhoods, close to the hospitals [redacted] -economic level.



Results II: What vaccine and how many doses did VA girls receive?

Vaccine	1 Dose (%)	2 Doses (%)	3 Doses (%)	Unknown** (%)	Total (%)
Bivalent	75 (6.1)	235 (19.2)	622 (50.8)	38 (3.1)	970 (79.2)
Quadrivalent	3 (0.2)	43 (3.5)	46 (3.7)	6 (0.5)	98 (8.0)
Unknown*	22 (1.8)	19 (1.5)	77 (6.3)	38 (3.1)	156 (12.7)
Total	100 (8.2)	297 (24.3)	745 (60.9)	82 (6.6)	1224 (100)

* Girls who stated having been vaccinated but did not remember which vaccine they had received.
** Girls who stated having been vaccinated but did not remember the number of doses received.

These results are reasonable and consistent with the real setting, considering that:

- Most of VA received the vaccine in 2011- 2014 when the Program had the bivalent vaccine available
- The national average for the 3-dose coverage was 70.4% for girls vaccinated between 2011 and 2014.

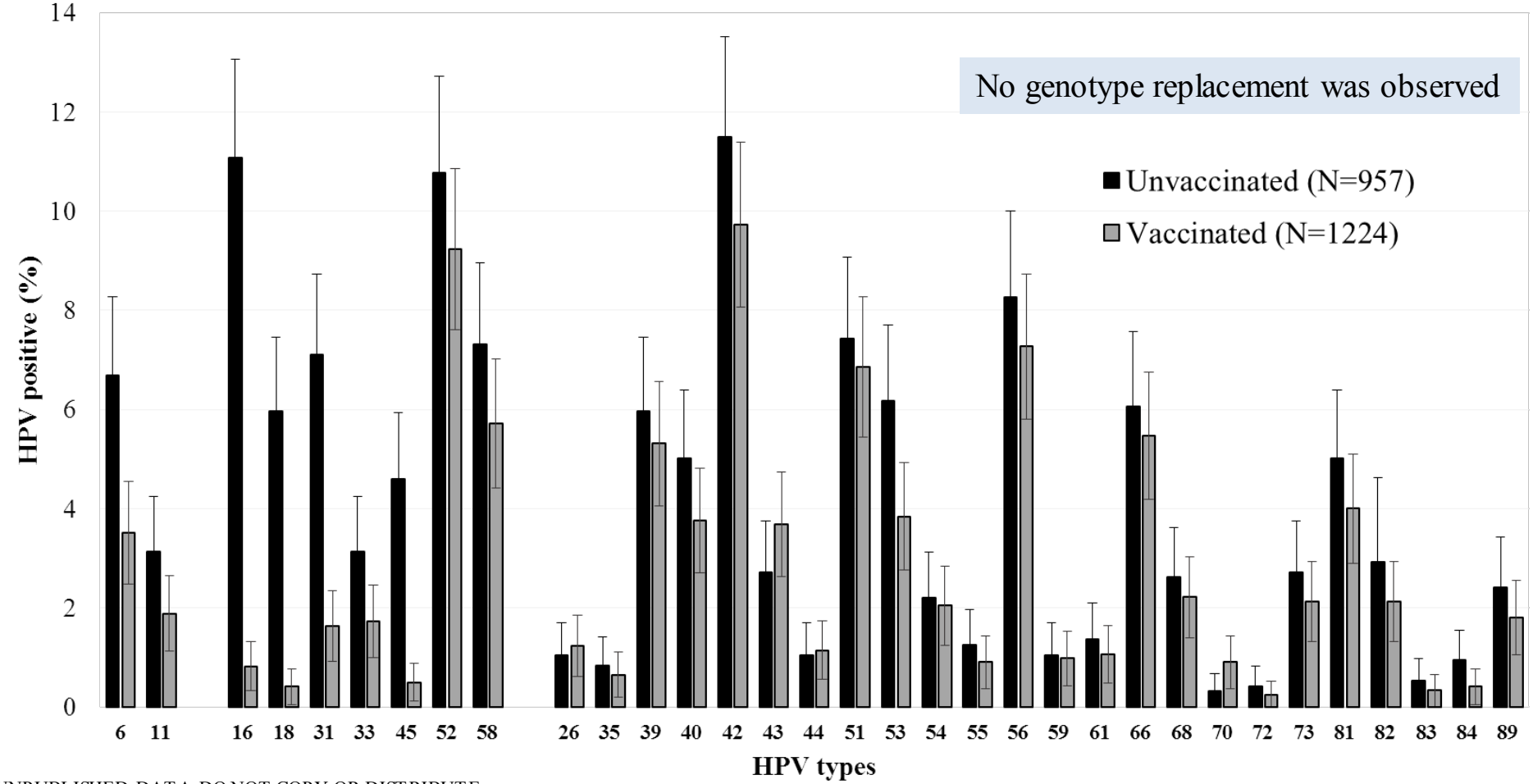
Results reflec[redacted]

Results III: Overall HPV prevalence in vaccinated girls declined slightly but significantly in relation to the unvaccinated ones

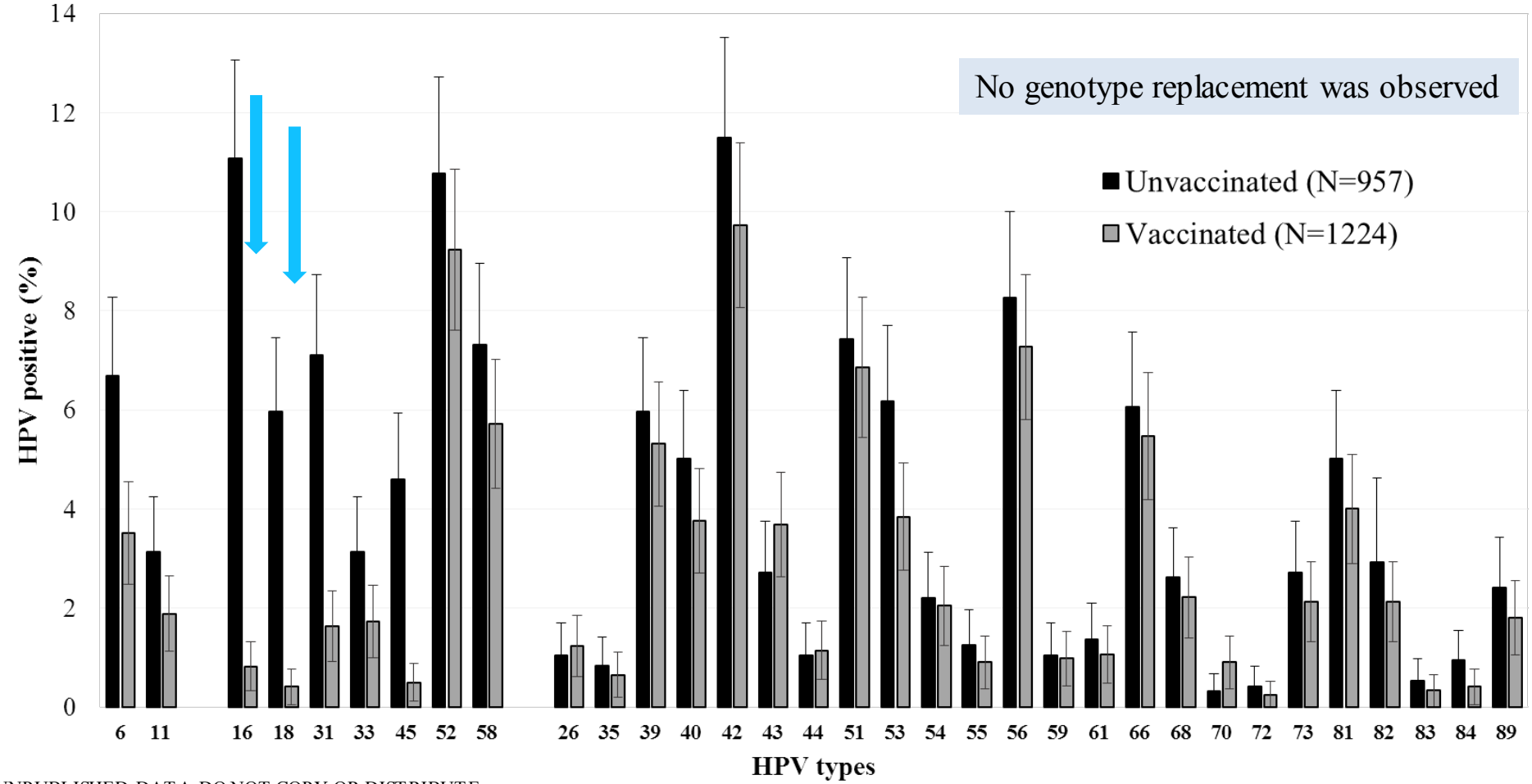
HPV	Unvaccinated (n=957)		Vaccinated (n=1224)		
	n (%)	95%CI	n (%)	95%CI	
Positive	**539 (56.3)**	53.2 - 59.5	**609 (49.8)**	46.9 - 52.6	**p=0.002**
Negative	418 (43.7)	40.5 - 46.8	615 (50.3)	47.5 - 53.1	

Abbreviation: CI= Confidence interval.

Distribution of HPV genotypes identified in unvaccinated and vaccinated adolescent girls from Argentina.



Distribution of HPV genotypes identified in unvaccinated and vaccinated adolescent girls from Argentina.



Prevalence of vaccine and selected non- vaccine HPV types for UV and VA

HPV types	Unvaccinated girls (N=957)		Vaccinated girls (N=1224)		OR (95% CI)	P value
	N (%)	(95%CI)	N (%)	(95%CI)		
2vHPV/ 4vHPV vaccine						
HPV 16	106 (11.1)	(9.1-13.1)	10 (0.8)	(0.3-1.3)	0.066 (0.034-0.127)	< 0.001
HPV 18	57 (6.0)	(4.5-7.5)	5 (0.4)	(0.1-0.8)	0.065 (0.026-0.162)	< 0.001
HPV 16,18	145 (15.2)	(12.9-17.4)	15 (1.2)	(0.6-1.8)	0.069 (0.041-0.119)	< 0.001
HPV 6	64 (6.7)	(5.1-8.3)	43 (3.5)	(2.5-4.5)	0.508 (0.343-0.755)	0.001
HPV 11	30 (3.1)	(2.0-4.2)	23 (1.9)	(1.1-2.6)	0.592 (0.341-1.026)	0.061
HPV 6,11	91 (9.5)	(7.7-11.4)	63 (5.2)	(3.9-6.4)	0.516 (0.370-0.721)	< 0.001
HPV 6,11,16,18	215 (22.5)	(19.8-25.1)	78 (6.4)	(5.0-7.7)	0.235 (0.178-0.309)	< 0.001
HR-HPV 16/18 related types*						
HPV31	68 (7.1)	(5.5-8.7)	20 (1.6)	(0.9-2.4)	0.217 (0.131-0.260)	< 0.001
HPV33	30 (3.1)	(2.0-4.2)	21 (1.7)	(1.0-2.4)	0.539 (0.307-0.948)	0.032
HPV45	44 (4.6)	(3.3-5.9)	6 (0.5)	(0.1-0.9)	0.102 (0.043-0.241)	< 0.001
HPV52	103 (10.8)	(8.8-12.7)	113 (9.3)	(7.6-10.9)	0.843 (0.636-1.117)	0.235
HPV58	70 (7.3)	(5.7-9.0)	70 (5.7)	(4.4-7.0)	0.769 (0.546-1.083)	0.132

Results VI: Estimated vaccine effectiveness in sexually active adolescent girls from Argentina.

HPV	Vaccine effectiveness (95 % CI)
HPV16	93.4 (87.3- 96.6)
HPV18	93.5 (89.7- 95.9)
HPV16/18	93.1 (88.0- 95.9)
HPV16/18/31/45	89.3 (84.7- 92.5)

Conclusions

- First study to monitor HPV vaccination in Latin America; the available data so far came from high-income countries where there may be different epidemiology of HPV, sexual behavior, and disease cofactors; so that information cannot be directly and accurately extrapolated to LMIC. This information is of value to make the best public policy decisions for sustaining and optimizing immunization.

- During the first 7 years post HPV vaccine introduction in Argentina, the prevalence of vaccine-type HPV16/18 decreased by >93% in vaccinated sexually active girls, demonstrating high effectiveness.

- The significant drop in non-vaccine genotypes related to HPV 16/18 (HPV31 and 45) would indicate cross protection, which could increase the success of vaccination.

- Continued surveillance for HPV infection in 4vHPV-vaccinated cohorts will be critical to deepen knowledge and support actions.

Strong reduction in prevalence of HPV16/18 and closely related HPV types in sexually active adolescent women following the introduction of HPV vaccination in Argentina.

(Presented in Oral Session, IPVC 2020; accepted for publication in Papillomavirus Research)

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[S Salud Investiga ("Carrillo-Oñativia" and "A. Sonis" fellowships), Dirección de Control de Enfermedades and Instituto Nacional de Enfermedades Infecciosas- ANLIS , Ministerio de Salud de Argentina].

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Thanks for your attention!

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

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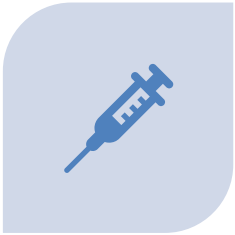
Pan American Health Organization
World Health Organization
Americas

PAHO

CONTENTS

BACKGROUND

BROAD BODY OF EVIDENCE AT THE GLOBAL LEVEL IS TAKEN INTO ACCOUNT IN INTRODUCING THE HPV VACCINE IN NATIONAL PROGRAMS



POST- INTRODUCTION: USING OWN EVIDENCE TO DEMONSTRATE THE VALUE OF THE HPV VACCINE CAN HELP TO **SUPPORT INVESTMENT IN THE VACCINE**

ACTIVITIES ARE AIMED AT **PROMOTING THE BENEFITS OF THE VACCINE**, INCREASING ITS **RECOMMENDATION** BY HEALTH PROFESSIONALS, AND IMPROVING ITS **ACCEPTABILITY** BY THE POPULATION

PROGRESS IS MADE TOWARD THE ELIMINATION OF **CERVICAL CANCER**

AS A PUBLIC HEALTH PROBLEM

BACKGROUND

- **Regional Meeting on Lessons Learned from Introduction of the HPV Vaccine, Guatemala, October 2017**

- Collaboration with multidisciplinary experts to develop a **guidance document on assessing the impact of HPV vaccination**

OBJECTIVES

Provide **conceptual and methodological guidance** on measuring the **impact of HPV vaccination** in the Region

Present an overview of possible designs that may be used to assess the impact of HPV vaccination

Prioritize outcomes by importance for vaccination programs

Propose study designs for each outcome and note considerations

TARGET AUDIENCE

- IM program managers and professionals
- MoH epidemiologists or institutions involved in impact assessment studies
- Professionals in the area of cervical cancer prevention
- HPV reference laboratory professionals
- Others (adolescent health, reproductive, STIs…)

Useful resource for conceiving new studies and for interpreting or using the findings of impact assessments

Special Aspects of Assessing the Impact of HPV Vaccination

Long latency period between infection and development of cancer

Multiple biological outcomes

Coexistence with a cervical cancer screening program

Scarcity of surveillance systems or registries for monitoring outcomes related to HPV infection

Availability of information on vaccination

Aspects to Consider in Designing a Study to Assess the Impact of HPV Vaccination

Regardless of the outcome being considered, the following points should be considered:

- Vaccination coverage
- Sources of information/data
  - Existing data (availability, access, format, quality)
  - New data
- External factors
  - Changes in the screening program
  - Tests
  - Changes in behavior sexual
- Sample size
- Time required to conduct the study
- Available human and financial resources

OUTCOMES FOR MEASURING THE IMPACT OF HPV VACCINATION

OUTCOMES FOR MEASURING THE IMPACT OF HPV VACCINATION

The correct time to measure the impact will depend on:

- ü The **age** at which is the **vaccine** is administered in the program
- ü The age group being **screened**
- ü The **age at initiation of sexual relations**
- ü The time typically elapsed between **HPV infection and the development of each outcome**

BIOLOGICAL OUTCOMES FOR ASSESSING THE IMPACT OF HPV VACCINATION

	Impact measurement	Approx. interval following vaccination in preadolescence	Indicators
HPV infection	Short-term	5 years or more	Prevalence of HPV infection
Genital warts	Short-term	5 years or more	Incidence of genital warts
Precancerous cervical lesions	Medium-term	10 years or more	1) Incidence of precancerous cervical lesions 2) Proportion of precancerous cervical lesions attributable to the HPV genotypes included in the vaccines
Cervical cancer	Long-term	20 years or more	1) Incidence of cervical cancer 2) Mortality from cervical cancer 3) Proportion of cervical cancer attributable to the HPV genotypes included in the vaccines

IMPACT ON CERVICAL CANCER

Impact on Cervical Cancer

= Main outcome to be assessed

- Several decades will have to pass
- The incidence of cervical cancer will be affected by a combination of **HPV vaccination and cervical screening**
- Although the incidence of **other HPV-related cancers** can be monitored, the degree to which they are attributable to HPV can vary and their incidence is very low

Overall reduction in the incidence and number of cervical cancer cases attributable to the HPV types included in the vaccine **when the vaccinated cohorts reach the age at which cervical cancer begins to occur more frequently**

Impact on Cervical Cancer - INDICATORS

Incidence of cervical cancer

Mortality from cervical cancer

- PBCR – Population Based Cancer Registry
  - Prioritize the establishment of a PBCR/strengthen existing registries and assess cervical cancer mortality
- Vital statistics
  - Prioritize improving the coverage and quality of the mortality registry

Impact on Cervical Cancer - INDICATORS

Incidence of cervical cancer

Mortality from cervical cancer

Proportion of cervical cancer **attributable to vaccine genotypes**

Detection of VPH16 or VPH18 in a cancer, regardless of the co-detection of other types

HIGH-GRADE PRECANCEROUS CERVICAL LESIONS

IMPACT ON HIGH-GRADE PRECANCEROUS CERVICAL LESIONS

ÁCervical intraepithelial neoplasia (CIN), grade 2, CIN2/3, CIN3, and AIS, defined as CIN2+

- Cervical cancer precursors
- Cases detected in cervical screening

Reduction in the **incidence** and **number of cases** of **CIN2/3+ attributable to HPV vaccine genotypes**

- Incidence of lesions is directly affected by **changes in screening recommendations, program practices, and/or participation** in the program

- Is there an established population or opportunistic screening, with a record of the screening results or mandatory reporting of CIN2+ lesions to a registry?
- Alternative: sentinel sites

Impact on high-grade precancerous cervical lesions - INDICATORS

Incidence of CIN2+

Proportion of CIN2+ attributable to HPV vaccine genotypes

It is indispensable for the screening program to have information based on cytology and/or biopsy

IMPACT ON HPV INFECTION

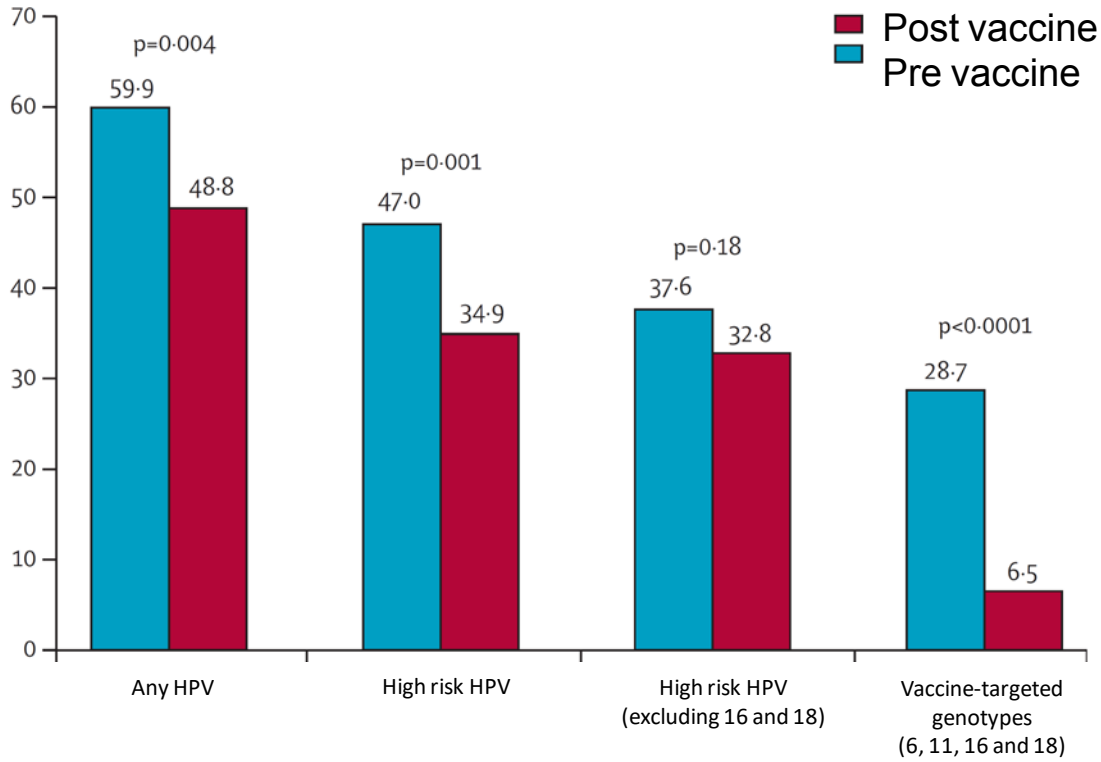
IMPACT ON HPV INFECTION

- First biological outcome for assessing impact

- A **progressive reduction in prevalence of infection due to the HPV types included in the vaccines** can be seen in the adult population under study as the proportion of vaccinated women increases

- **A reduction in HPV infection due to the types included in the vaccines can be observed even if no changes are seen in the overall prevalence of HPV** (*unless the genotypes have been replaced)*

Example of a before/after study. HPV prevalence before (2005-2007) and after (2010-2012) the introduction of the quadrivalent HPV vaccine in Australia (Tabrizi et al., 2014).



IMPACT ON HPV INFECTION INDICATOR

- **Prevalence of HPV16/18 infection in sexually active women**

- A 4-valent or 9-valent vaccine may be considered for assessing the **prevalence of infection due to other genotypes** included in the vaccine (HPV6/11 or HPV31/33/35/52/58)

- The study may assess either the prevalence of infection due to high-risk HPV or the prevalence of genotype-specific infection

IMPACT ON HPV INFECTION

- **Considerable resources** are needed over several years
  - Infrastructure for taking, processing, and analyzing samples; performing molecular techniques to detect the presence of HPV DNA; and genotyping
- **Identical procedures** (recruitment, sampling, sample processing, HPV detection/genotyping, and data collection during the assessment period)
- **Selection of the study population** (representative population surveys, family planning clinics, sexual health programs, prenatal visits, STI clinics, primary health care facilities, hospitals, education centers)
- **Pilot study** (feasibility and baseline prevalence)

IMPACT ON GENITAL WARTS

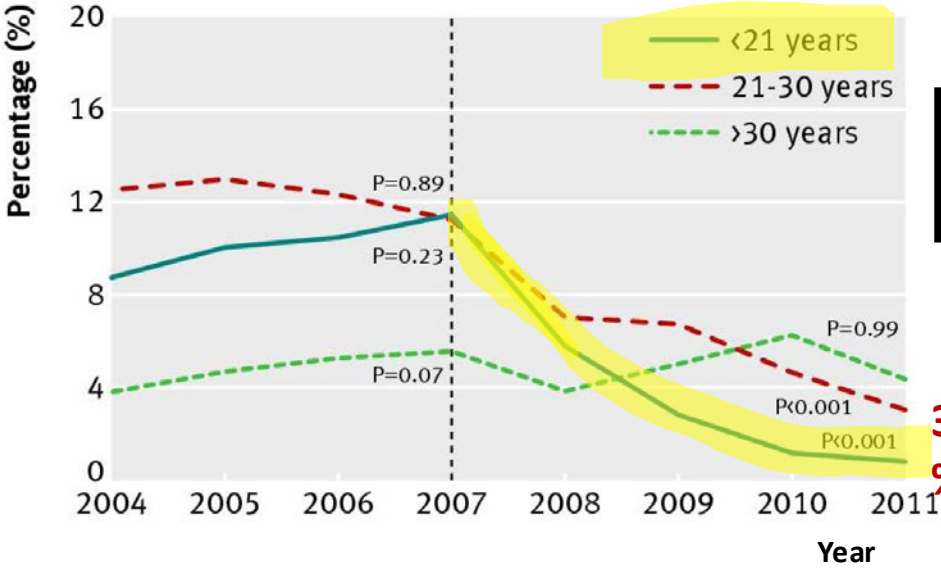
IMPACT ON GENITAL WARTS

- Genital warts are mainly caused by VPH6/11 infection, which is a low oncogenic-risk type
- First clinical outcome for which impact can be assessed in countries that administer a 4-valent or 9-valent vaccine
- **INDICATOR**: Incidence of genital warts per 100,000 population in a given period, stratified by age group, in women and men
  - Expected **reduction in the incidence of genital warts in women and men**

The magnitude of the observed impact on genital warts does not necessarily correspond to the magnitude of the impact on cervical cancer

IMPACT ON ANOGENITAL WARTS IN AUSTRALIA

Proportion of Australian-born women diagnosed with genital warts at the 1st visit



years

-30 years

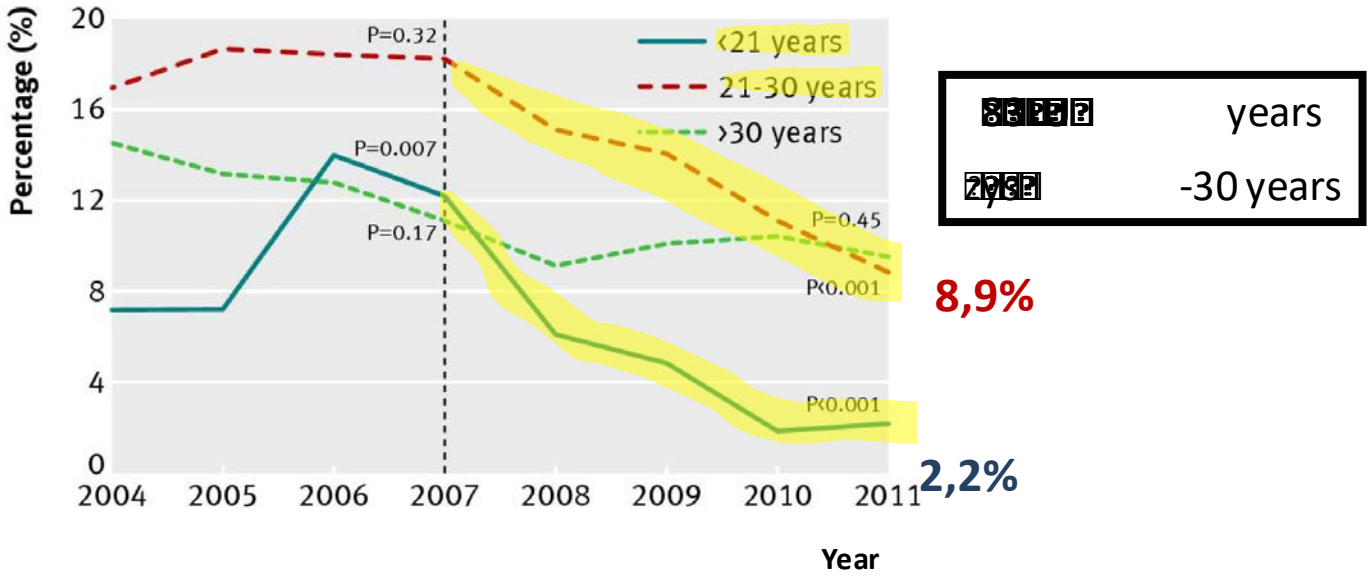
3,1 %

0,85 %

Ali et al. 2013 BMJ

IMPACTO EN VERRUGAS ANOGENITALES EN AUSTRALIA

Proportion of heterosexual men diagnosed with genital warts at the 1st visit



Ali et al. 2013 BMJ

IMPACT ON GENITAL WARTS

- Pathology for clinical diagnosis **does not require the use of specific tests** or any particular infrastructure
- In most countries, genital warts **are not a notifiable disease and are not reported at the national level**, which means that a valid information source will be a need to be found to monitor this outcome

Consider the indicators and prioritize according to:

- Available infrastructure in the country
- Available information sources
- Budgetary impact of the different options, depending on whether it is an initial or ongoing investment
- Capacity to continue monitoring the indicator over time
- Networks/strategies that might be used for recruitment
- When the impact will be assessed

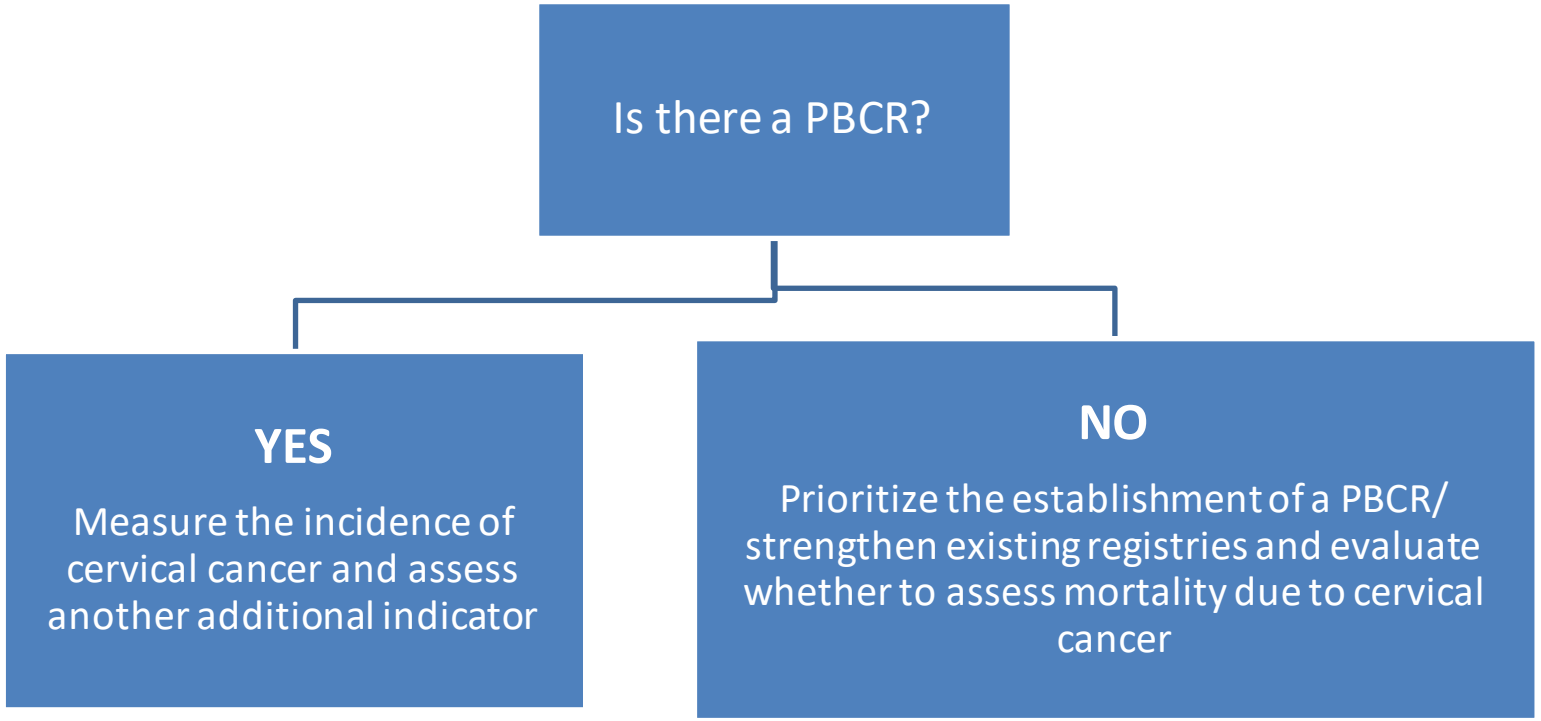
ALGORITHM FOR SELECTING OUTCOMES TO ASSESS THE IMPACT

ü*Importance in terms of cervical cancer, which is the main target of the vaccination program*

1a. Cervical cancer

Although this is the most important outcome to be measured, several decades will pass before it can be assessed!

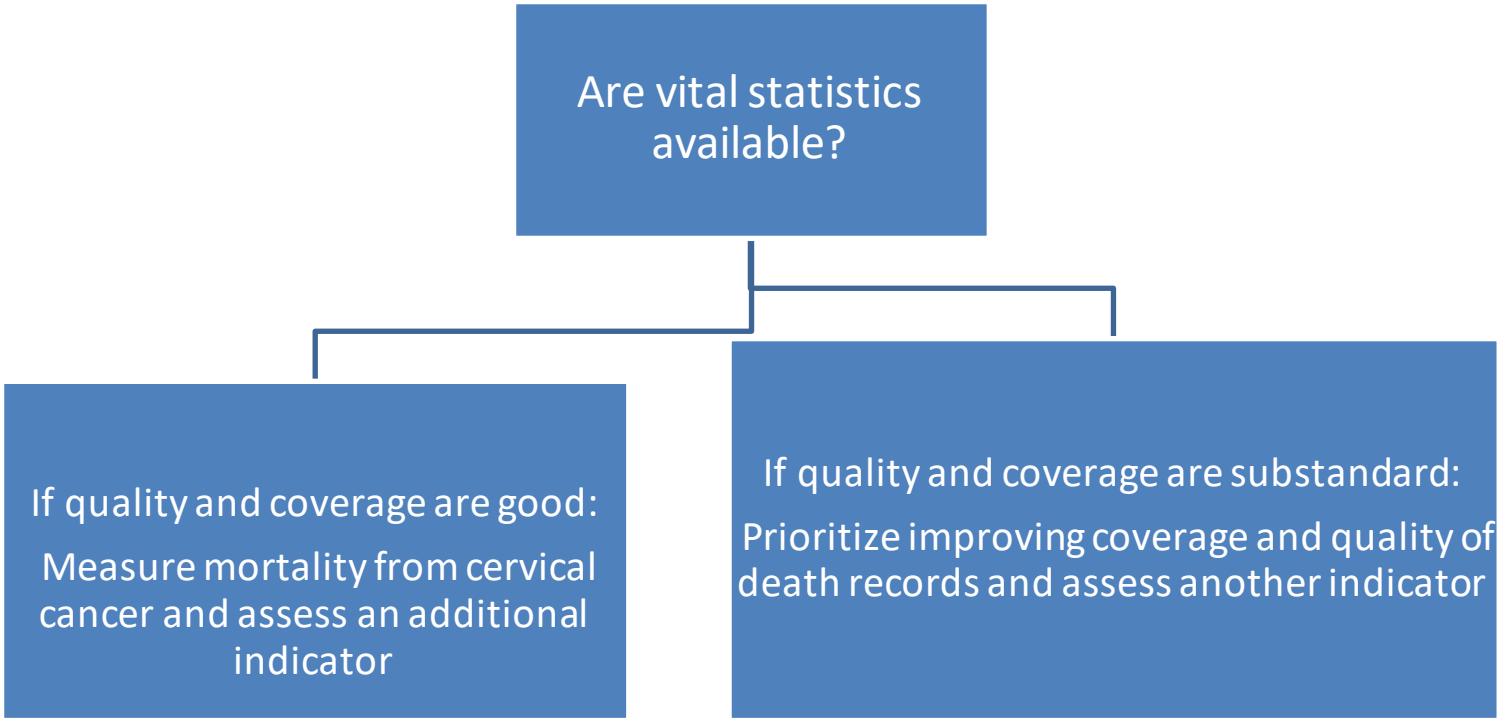
1.1. Incidence of cervical cancer



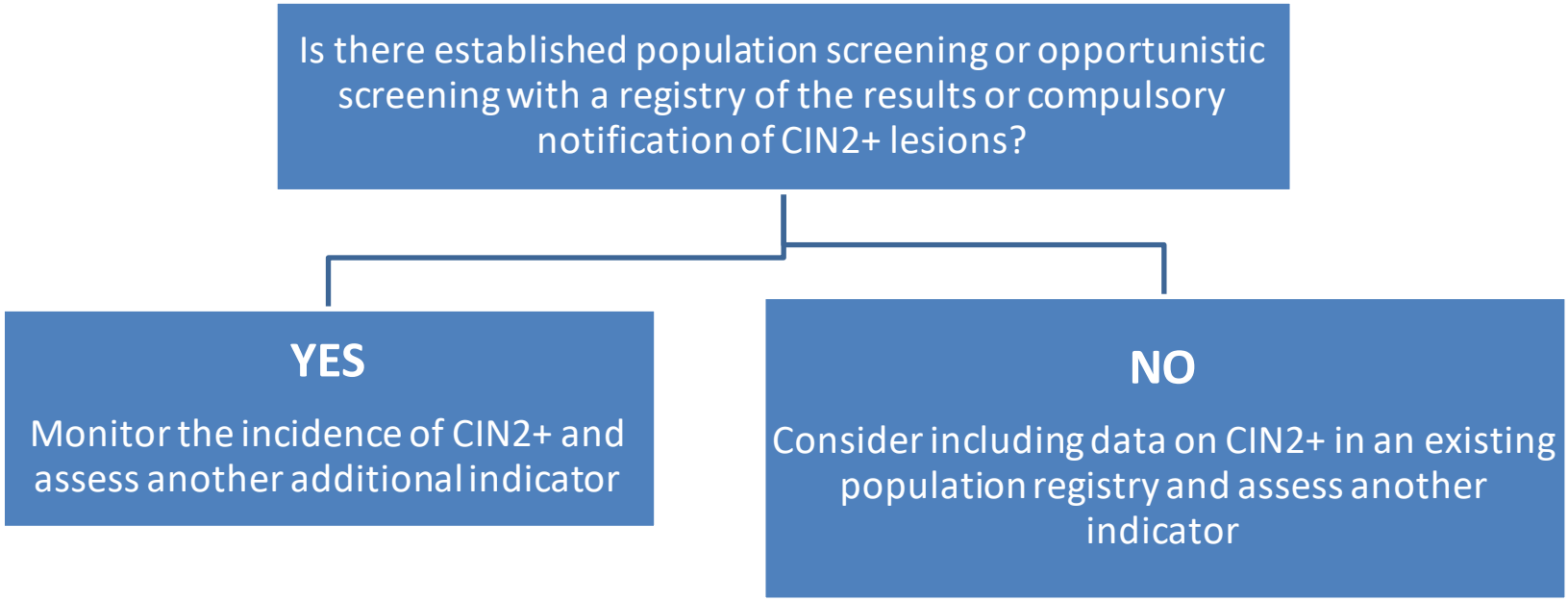
1b. Cervical cancer

- Note: Occurrence is a delayed outcome!
- First, the quality and coverage of vital statistics should be assessed

1.2. Mortality from cervical cancer



2. High-grade precancerous cervical lesions



3. HPV infection

1) Sampling of the general population

A representative sample taken from the general population or from opportunistic recruitment at health care facilities

2) Sampling of women who participate in the cervical cancer screening program

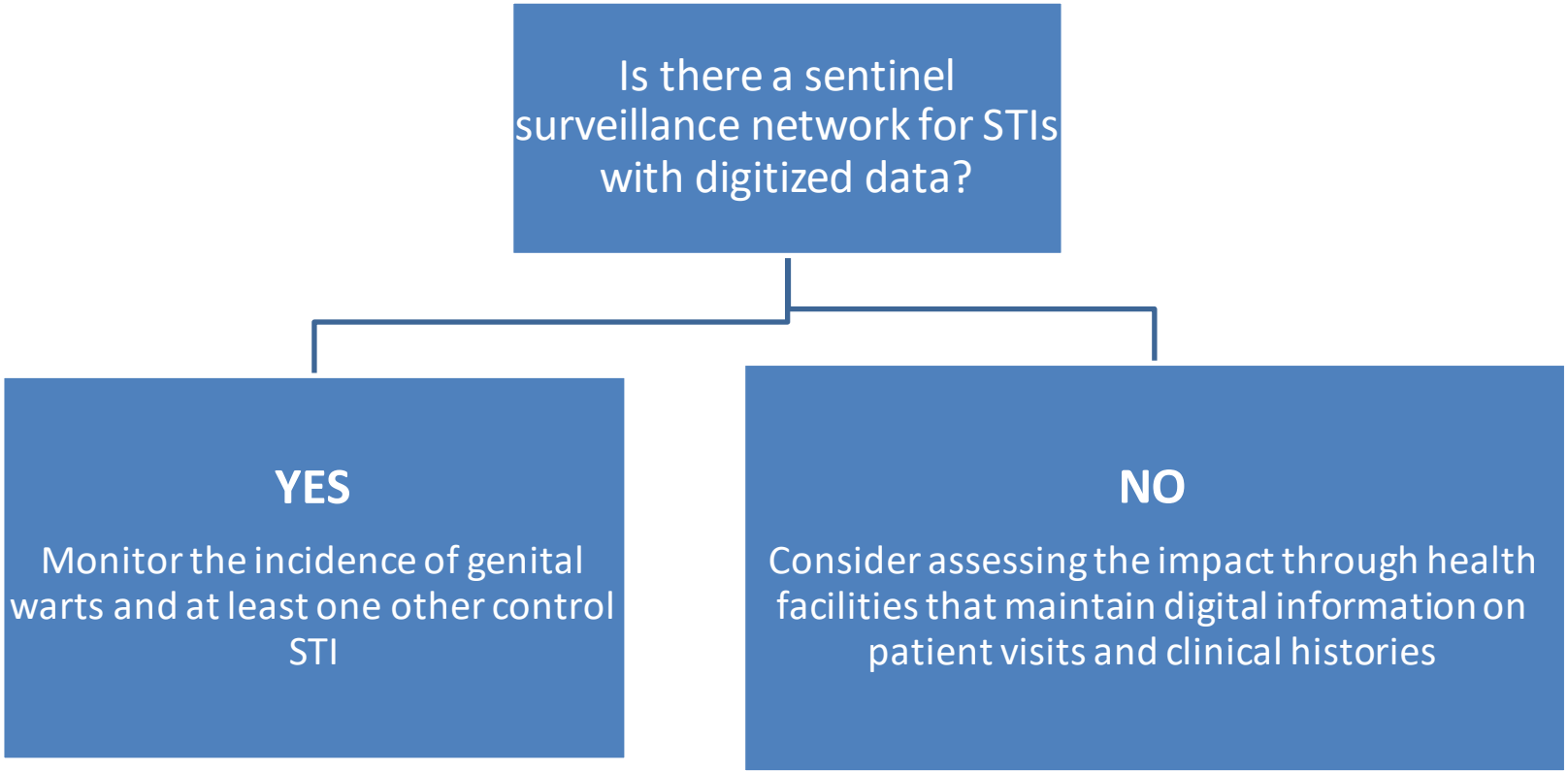
This approach is highly feasible if:

- there is an organized or opportunistic screening program that is stable over time
- an HPV detection/genotyping test is used for primary screening or triage
- the same HPV test is used consistently

3) Sampling of women who participate in the screening program for Chlamydia trachomatis

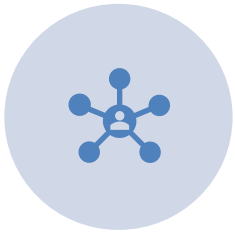
4. Genital warts

(In countries with 4-valent or 9-valent vaccine)



CONCLUSIONS

CHALLENGES INHERENT IN IMPACT ASSESSMENTS OF HPV VACCINE



NEED FOR **COLLABORATION NETWORKS** AND COORDINATION WITH OTHER **TEAMS/PROGRAMS**

NEED FOR **METHODOLOGICAL, STATISTICAL, AND TECHNICAL** ADVICE ON DESIGNNG STUDIES

LABORATORIES, SAMPLES, AND QUALITY TESTING

INFRASTRUCTURE AND EXISTING **RESOURCES**

PRIORITIZATION OF INDICATORS

WHEN RESOURCES ARE LIMITED , NEED TO FOCUS EFFORTS ON **INCREASING VACCINATION COVERAGE, SCREENING, AND TREATMENT**

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Gracias
Thank you
Obrigada
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BACK-UP SLIDES

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SAMPLE SIZE

The following table shows the required sample sizes according to the prevalence of

	HPV vaccination coverage				
Prevalence of HPV16/18 infection in the reference group					
0.5%	4,350	5,900	8,200	11,800	18,000
1%	2,150	3,000	4,100	5,900	8,950
2%	1,100	1,500	2,100	3,050	4,650
5%	450	600	850	1,200	1,800
10%	200	300	400	550	850
20%	100	130	180	250	400
30%	60	80	110	160	250

IMPACT ON THE PROPORTION OF NIC2+ ATTRIBUTABLE TO HPV16/18 GENOTYPES

- The attribute can be defined as **detection of VPH16 or VPH18 in NIC2+** regardless of co-detection of other types
- It will be necessary to have sufficient infrastructure + resources to determine the HPV genotype or else send the samples to another laboratory
  - Clinics that perform **colposcopy and biopsy**
  - A **pathology** laboratory that meets quality standards
  - A laboratory that performs **genotyping** and tests to detect **HPV DNA**
- ++ Feasible strategy is to choose colposcopy clinics or sentinel pathology laboratories (consecutive selection of cases)
- Proportion of NIC2+ attributable to VPH16/18 is estimated for both the pre- and post-vaccine periods or based on analysis of trends over time