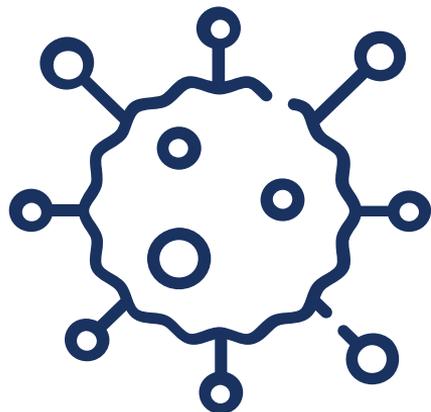


# HUMAN PAPILLOMAVIRUS (HPV)

THE CURRENT LANDSCAPE OF HPV VACCINES  
GLOBALLY AND THE CHIC PROJECT

# OVERVIEW

- What is Human Papillomavirus (HPV)?
- What are the main causes of HPV?
- How can we diagnose HPV?
- What is the global burden of HPV?
- How can we prevent HPV?
- What vaccines are available for HPV?
- What is the CHIC project?

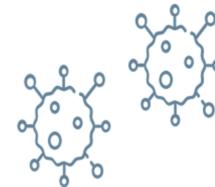


# What is HPV?

# WHAT IS HPV?

- Human Papillomavirus (HPV) is the most common sexually transmitted infection that causes skin or mucous membrane growths (warts)
- There are currently over 100 strains of HPV
  - HPV 16 and 18: most common strains to cervical cancer
- Infections are commonly transmitted sexually or through skin-skin contact

HPV infections are so common that nearly all men and women **will get HPV at some point in their lives**



# 43,000,000

People were affected by HPV in 2018

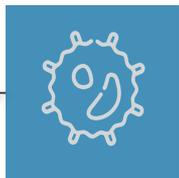
4 out of 5 people will get an HPV infection on their lifetime.



HPV infection is most common among people in their teens and early 20s.

# HPV SYMPTOMS

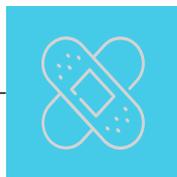
Updated: May 2021



## 01

### WARTS

Vary in appearance depending on which HPV strain is involved



## 02

### GENITAL ITCHING

Usually in the same spot as genital warts



## 03

### ASYMPTOMATIC

Your body clears the infection without you knowing it

# HPV DIAGNOSIS

Updated: May 2021

## ACETIC ACID SOLUTION TEST



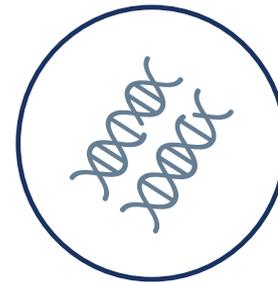
Acetic acid is applied to the HPV-infected areas and helps identify difficult-to-see lesions

## PAP TEST



Samples of cervix or vagina cells are analyzed for abnormalities that can lead to cancer

## DNA TEST



Conducted on cervix cells to recognize the DNA of HPV strains linked to genital cancers

# HPV TREATMENT

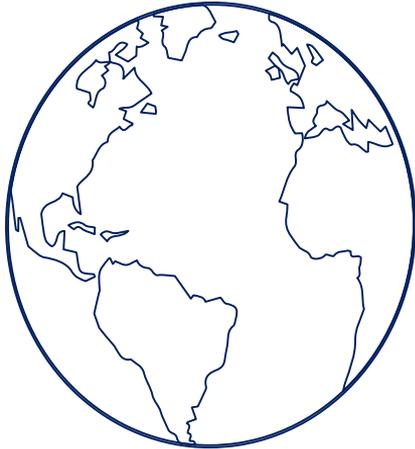
- There is no **direct** treatment for HPV infection.
- There are only treatments for the health problems that HPV can cause:

## MEDICATIONS

- Used to eliminate warts through direct application on the lesions and require multiple uses.
  - Salicylic acid
  - Imiquimod
  - Podofilox
  - Trichloroacetic acid

## SURGERY

- If medications do not work, doctors may suggest surgery or other procedures
  - Freezing with liquid nitrogen (cryotherapy)
  - Loop electrosurgical excision procedure (LEEP)
  - Surgical removal
  - Laser surgery

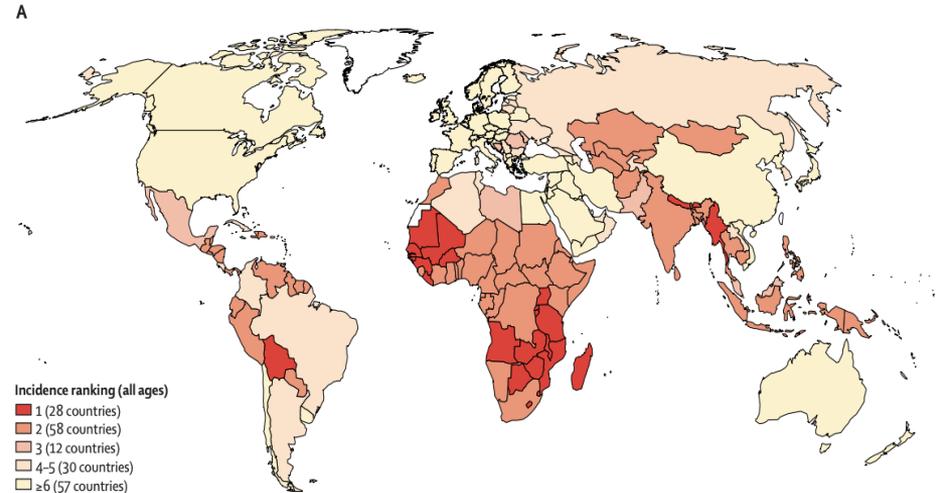


# Global Burden of HPV

# GLOBAL BURDEN OF HPV

Updated: May 2021

- Long-lasting HPV infections pose the risk of developing cervical cancer, the fourth most common cancer among women.
- Over 85% of the global burden of HPV-related cervical cancers falls among women in low and middle-income countries (LMICs).
  - In 2018, 51% new cervical cancer cases worldwide occurred in women living in LMICs.
- The current gaps in cervical cancer morbidity and mortality are linked to the global distribution of treatment resources as LMICs face limited health resources.

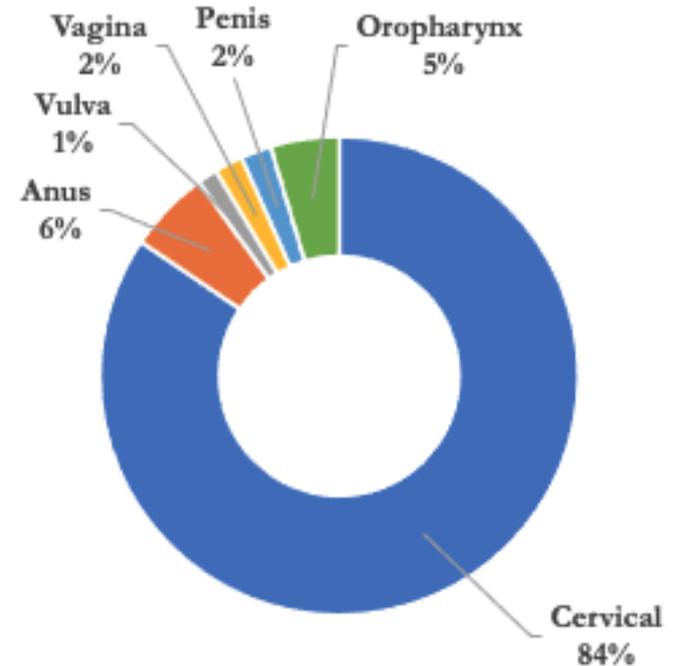


Ranking of cervical cancer incidence burden in 2018 relative to all other cancer sites in women of all ages

# GLOBAL BURDEN OF HPV (2017)

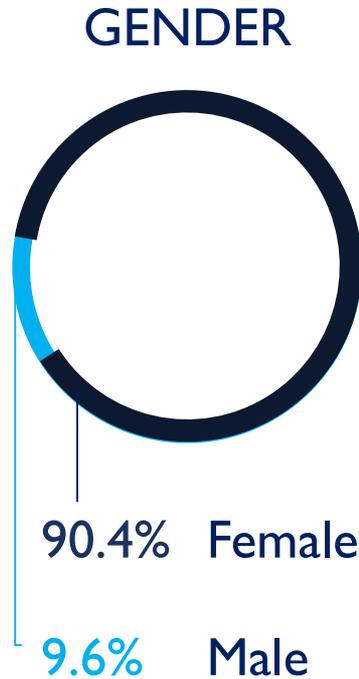
Updated: May 2021

HPV-related cancer site	Number of Incident Cases	Number Attributable to HPV
Cervix	530,000	530,000
Anus	40,000	35,000
Vulva	34,000	8,500
Vagina	15,000	12,000
Penis	26,000	13,000
Oropharynx-related	534,000	37,200
Total HPV-related sites	1,200,000	630,000



# CANCER CASES ATTRIBUTABLE TO HPV

Updated: May 2021



**630,000**  
Overall cancer  
cases worldwide



**4.5%**  
of all cancer cases  
worldwide

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HPV is linked to  
an estimated

99%

of all cervical  
cancer cases

# CERVICAL CANCER IS THE 4TH MOST COMMON CANCER IN WOMEN

An estimated **11 million women** from LMICs will be diagnosed with cervical cancer in the next **10-20 years**

# CERVICAL CANCER WORLDWIDE

Updated: May 2021

- In 2018, an estimated 570,000 women were diagnosed with cervical cancer.
- 311,000 women died from the disease, with nearly 90% of deaths occurring in LMICs.
- Almost all cervical cancer cases (99%) are linked to HPV infection.

When diagnosed, cervical cancer is one of the most **successfully** treatable forms of cancer



# GLOBAL STRATEGY TOWARD ELIMINATION

The WHO has developed target goals to eliminate cervical cancer by 2030

**90%**

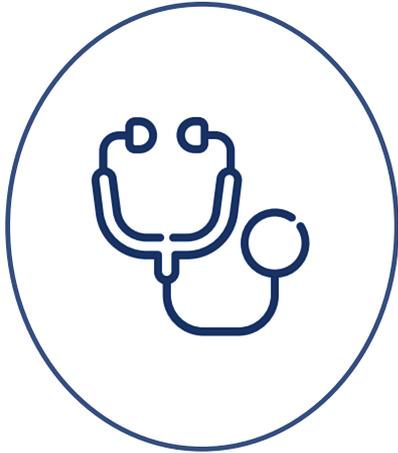
of girls fully vaccinated  
with the HPV vaccine  
by 15 years of age

**70%**

of women screening  
using a high-  
performance test by  
age 35 and again by  
age 45

**90%**

of women identified  
with cervical disease  
receive treatment



# HPV Prevention

# HPV PREVENTION

## HPV VACCINE

Prevents over 90% of HPV-related cancers



## SCREENING

Pap smears and HPV tests look for cell changes that can be caused by HPV

## PRACTICE SAFE SEX

Use latex condoms during sex. HPV is the most common STI.



## LIMIT SEXUAL PARTNERS

Significantly reduce the risk of contracting HPV

# HPV SCREENING

Two screening tests can help prevent cervical cancer:

## Pap Test

- Looks for *precancers*, cell changes on the cervix that might become cervical cancer if they are not treated appropriately.
- Cells will be checked to see if they look normal.

## HPV test

- Looks for the virus (HPV) that can cause cell changes.
- Cells will be tested for HPV.

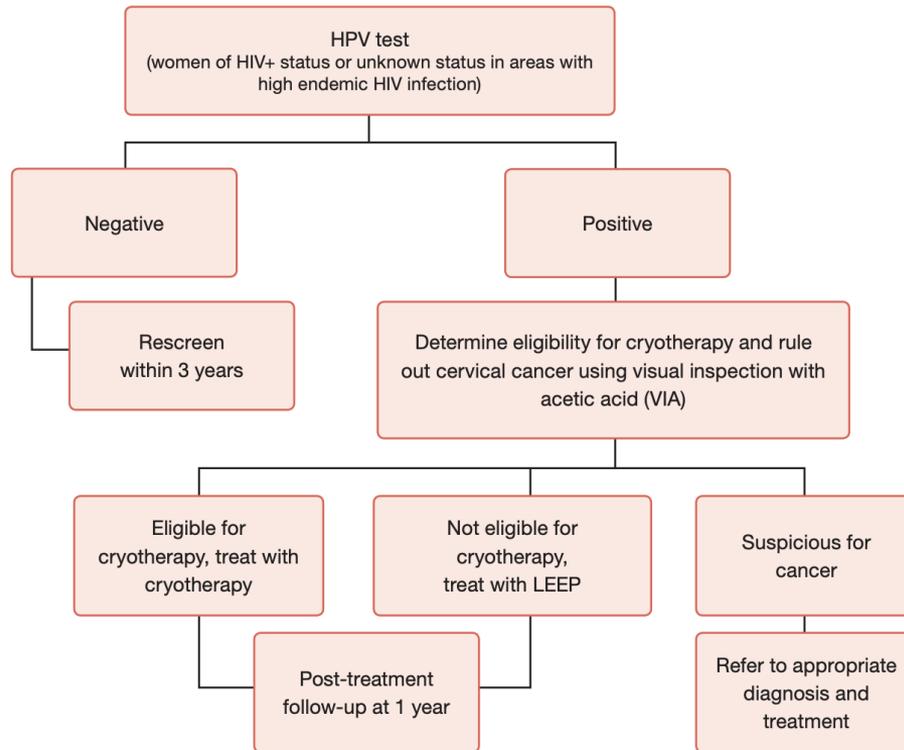
# WHEN TO GET SCREENED

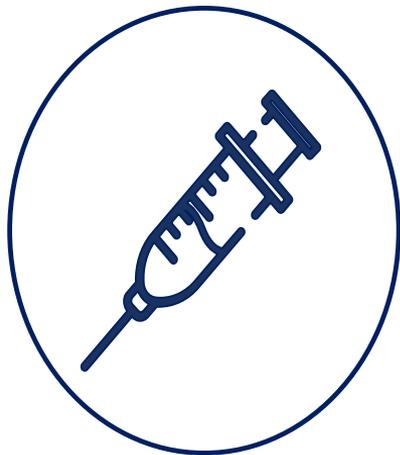
## RECOMMENDED AGE TO START SCREENING: 30 YEARS OF AGE

- The WHO recommends women 30 years of age and over to start screening because of their higher risk of cervical cancer.
- Priority should be given to screening women aged 30-49 years, rather than maximizing the number of screening tests in a woman's lifetime.
- Screening even once in a lifetime is beneficial.

## Screen with an HPV test and treat with cryotherapy, or LEEP when not eligible for cryotherapy

When an HPV test is positive, treatment is provided. With this strategy, visual inspection with acetic acid (VIA) is used to determine **eligibility** for cryotherapy.





# HPV Vaccination

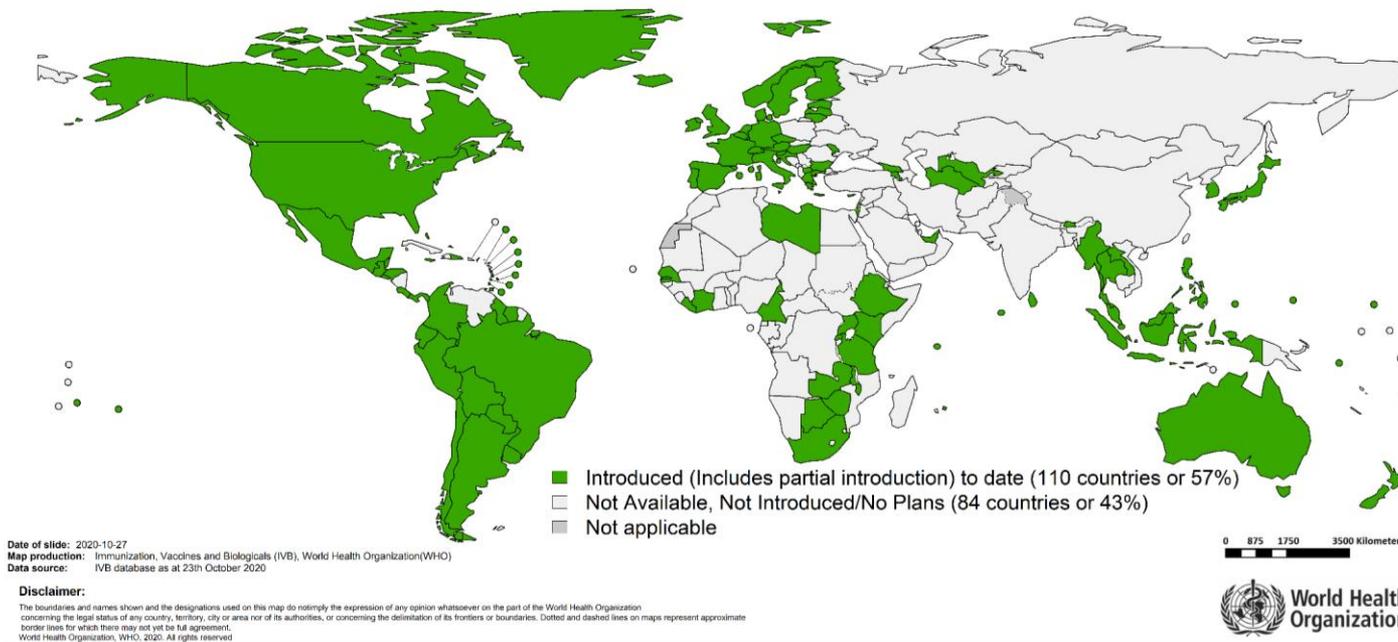
# HPV VACCINATION COVERAGE

- ✗ The WHO monitors HPV vaccination coverage at the country level to assess the performance of implemented vaccine programs, track vaccine uptake, and ensure that coverage is maximized and maintained.
- ✗ Effective regional monitoring provides information to estimate the long-term impact of HPV vaccination on morbidity and mortality, vaccine efficacy, and disease patterns.
- ✗ Currently, there are 110 countries that have introduced HPV vaccines in their national immunization program.
- ✗ However, 84 countries have yet to introduce HPV vaccine programs.



**World Health  
Organization**

## Countries that have introduced HPV vaccines in their national immunization program



World Health Organization



INTERNATIONAL  
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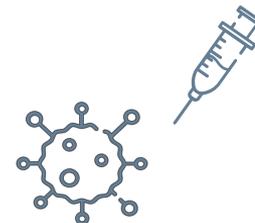


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# HPV VACCINATION

- To date, three safe and efficacious HPV vaccines have been licensed by the U.S. Food and Drug Administration (FDA) that protect against **70%** of cancer-causing HPV infections.
- HPV vaccination is the most cost-effective intervention for the prevention of cervical cancer.
- The Center for Disease Control and Prevention (CDC) reported the percentage of all HPV-related cervical precancers declined from 53% in 2008 to 44% in 2014.

More than **270 million** doses of the HPV vaccine have been distributed worldwide



# HPV VACCINE SAFETY

- Over 12 years of monitoring and research have revealed that HPV vaccination is safe.
  - Clinical trials with more than **75,000** men and women were studied before the vaccines were licensed by the FDA.
- Any safety concerns detected will be reported to health officials, healthcare professionals, and the public.
- Studies suggest that protection from HPV vaccine is long-lasting and does not decrease over time.
  - Studies have followed people who received HPV vaccine for nearly **10 years** and the effectiveness remains high among those individuals.



# HPV VACCINE SIDE EFFECTS



Pain, redness, or swelling in the arm where the shot was given



Nausea



Fever



Headache or feeling tired



Dizziness or fainting



Muscle or joint pain

# HPV vaccination in girls is predicted to avert **61 million** cases in the next century

# FDA-APPROVED HPV VACCINES

Vaccine Protects against:

**CERVARIX**  
(bivalent HPV vaccine)

HPV 16, 18

**GARDASIL 4**  
(quadrivalent HPV vaccine)

HPV 6, 11, 16, 18

**GARDASIL 9**  
(9-valent HPV vaccine)

HPV 6, 11, 16, 18, 31, 33, 45, 52, 58

# CERVARIX

- **Manufacturer:** GlaxoSmithKline Biologicals
- **Efficacy:** 91.4 %
- **Efficacy Endpoints:**
  - Incident infection with HPV-16 and/or HPV-18.
  - Persistent infection with HPV-16 and HPV-18 that lasts for 12 months.
- **Mechanism of Action:**
  - Non-infectious recombinant vaccine prepared from the virus- like particles (VLPs) of HPV types 16 and 18.
- **Common Side Effects:**
  - Joint pain, headache, nausea, low energy



# GARDASIL 4

- **Manufacturer:** Merck Sharp & Dohme
- **Efficacy:** 100%
- **Efficacy Endpoints:**
  - Protection against overall cervical and genital disease related to HPV 6, 11, 16, and 18.
- **Mechanism of Action:**
  - Non-infectious recombinant vaccine prepared from the virus-like particles (VLPs) of HPV types 6, 11, 16, 18
- **Common Side Effects:**
  - Fever, headache, nausea, diarrhea, abdominal pain, fainting



# GARDASIL 9

- **Manufacturer:** Merck Sharp & Dohme
- **Efficacy:** 100%
- **Efficacy Endpoints:**
  - Protection against persistent cervical infections with HPV types 16 and 18.
  - Preventing cervical, vulvar, and vaginal disease caused by the five additional HPV types (31, 33, 45, 52, and 58).
- **Mechanism of Action:**
  - Non-infectious recombinant vaccine prepared from the virus-like particles (VLPs) of HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58.
- **Common Side Effects:**
  - Injection site reactions (swelling, redness, pain), headache, fever



# COST-EFFECTIVE PREVENTATIVE MEASURES

- The WHO estimates that every **US\$ 1** invested through 2050 to meet the 90-70-90 targets, **US\$ 3.20** will be returned to the economy.
  - This value rises to **US\$ 26.00** when accounting for societal benefits.
- About 250,000 women will remain productive members of the workforce, adding an estimated **US\$ 28 billion** to the world's economy.
  - Of that, US\$ 700 million will be due to increased workforce participation.
  - The greatest averted costs amount to **US\$ 27.3 billion** through the indirect socioeconomic benefits of good health.

# HPV VACCINE DOSING SCHEDULES BASED ON AGE

## Who gets 2 doses?

### 9-14 YEARS OLD

Recommend prior to initiation of sexual activity

- Dose 1: 0 months
- Dose 2: Up to 15 months after first dose



## Who gets 3 doses?

### 15 YEARS AND OLDER

Recommended for those with immunocompromising conditions, including those known to be HIV positive

- Dose 1: 0 months
- Dose 2: 1-2 months after first dose
- Dose 3: 6 months after first dose



# EMERGENCE OF SINGLE-DOSE VACCINATION

- There have been three randomized control trials conducted to evaluate the efficacy and immunology of single-dose HPV vaccines.
  - Costa Rica HPV Vaccine Trial (CVT)
  - IARC India HPV Vaccine Trial
  - PApilloma TRIal against Cancer In young Adults (PATRICIA)
- The Single-Dose HPV Vaccine Evaluation Consortium conducted systematic reviews on six observational studies based on data from the three clinical trials.
  - Evidence-based data continue to show that single-dose HPV vaccination could substantially reduce the incidence of HPV attributable cervical precancer and cancer and would likely be a high-value public health intervention.

# COSTA RICA HPV VACCINE TRIALS (CVT)

- CVT was a blinded, randomized clinical trial of the Cervarix vaccine.
  - 7,466 women were enrolled from seven study clinics between June 2004 and December 2005.
- Three observational studies have been based on CVT for single-dose HPV vaccination.
  - Two studies have compared the **HPV infection and vaccine-induced immunogenicity** in participants of single-dose and multidose vaccine schedules.
  - An ongoing study extends the data of the previous studies to seven years following the first vaccine dose in participants following the same dosing schedules.
- Researchers have found that a single dose vaccine provides cross-protection as it protects against three other cancer-causes HPV strains not targeted by the vaccine.

# IARC INDIA HPV VACCINE TRIAL

- The study was originally designed to compare two versus three doses of Gardasil 4 among healthy unmarried females aged 10–18 years in India.
  - However, the Indian government suspended all HPV vaccine trials in April 2010.
  - The clinical trial became a prospective observational cohort study of single-dose versus multidose vaccine schedules.
- Two observational studies were based on the IARC trial of two versus three doses of HPV vaccine in India.
  - A study compared **HPV infection and immunogenicity data** in participants of single-dose and multidose vaccine schedules.
  - An ongoing study extends the previous data of previous studies to seven years following the first vaccine dose in participants following the same dosing schedules.

# PAPILLOMA TRIAL AGAINST CANCER IN YOUNG ADULTS (PATRICIA)

- PATRICIA conducted double-blinded randomized control trials in 14 countries to evaluate the efficacy of a three-dose regimen.
  - 18,729 women were enrolled between May 2004 and June 2005.
- One observational study combined these findings with CVT data.
  - The observational study assessed the **HPV infection and immunogenicity data** in participants of single-dose and multidose vaccine schedules.

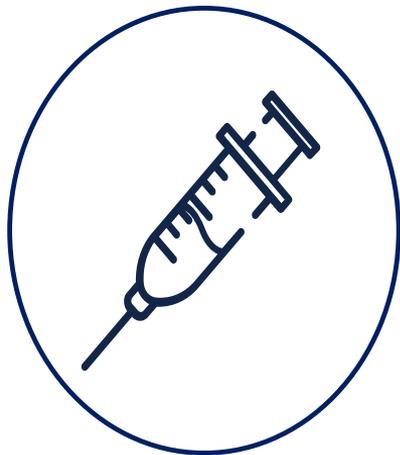
# BENEFITS OF SINGLE-DOSE HPV VACCINATION

Accelerate the introduction of HPV vaccines into low- and middle-income countries.

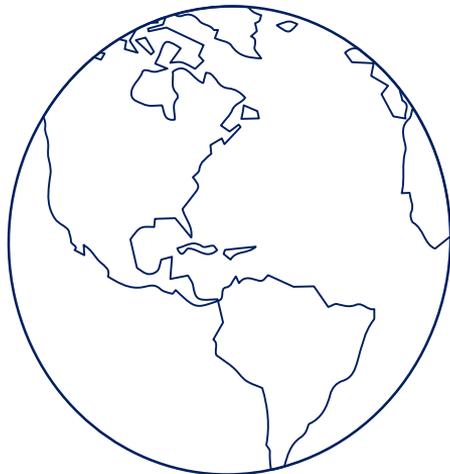
- Alleviation of financial and logistical barriers to vaccination services can lead to higher vaccine uptake.

Contribute to the global HPV vaccine supply

- The WHO targets for cervical cancer elimination has increased vaccine demand that has resulted in HPV vaccine shortages predicted to last another 3–5 years (Updated: June 2020).
- Administration of a single-dose vaccine can reduce the infrastructure required to administer multiple doses, potentially leading to widespread vaccination.



In 2011, Gavi gave low-income countries access to HPV vaccines for as little as **\$4.50** per dose



As of 2019, **100 countries** have introduced HPV vaccine into their national immunization program

However, this only covers **30%** of the global target population

# GLOBAL BARRIERS TO HPV VACCINATION

Despite the proven safety, efficacy, and cost-effectiveness of HPV vaccines, there are significant barriers in global implementation.

## VACCINE INTRODUCTION

Less than 30% of LMICs have introduced HPV vaccination compared to 85% of high-income countries

## FINANCIAL CAPACITY

Limited sustainable financing methods compromise the ability of LMICs to effectively implement HPV vaccine programs

# COVID-19 CHALLENGES



## GLOBAL RECESSION

Reduced national incomes have restricted vaccine delivery to many LMICs



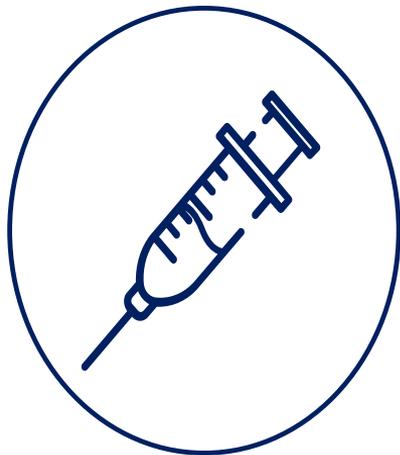
## MITIGATION MEASURES

Stay-at-home orders and social distancing measures increase the risk of under-immunization in LMICs.



## HEALTHCARE SHORTAGES

Numerous LMICs have reported of shortages in providers and PPE, limiting health services



# Coalition to Strengthen the HPV Immunization Community (CHIC) Project

# PRIMARY GOAL

The **Coalition to Strengthen the HPV Immunization Community (CHIC)** HPV Council provides a platform dedicated to accelerating progress in HPV vaccine introduction, access, and program optimization in Gavi-eligible countries.

**CHIC** prioritizes efficient translation of implementation research findings to guide practice and more equitable access to immunization ideally within the context of a stable HPV vaccine market.

# CHIC COUNCIL PARTNERS

THE INTERNATIONAL  
VACCINE ACCESS CENTER  
(IVAC)



JHPIEGO

UNIVERSITY OF  
ANTWERP



LONDON SCHOOL OF  
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MEDICINE



# DOMAINS

## SECRETARIAT

Led by JHSPH IVAC

- Guide the overall strategy for an initiative that fosters inclusive, cross-disciplinary and diverse HPV community and practice.

## COUNCIL

Led by Jhpiego

- Review available evidence and generate scientific consensus for HPV policy, programs, and research.

## SYMPOSIA

Led by University of Antwerp/LSHTM

- Design and host symposia for HPV stakeholders, including implementers, policy makers, and researchers.

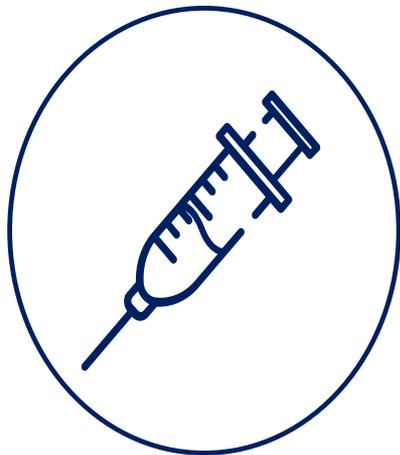
# KEY PRIORITIES

## Priority 1

To build strengthened leadership of a robust community of practice around HPV vaccines that connects scientists, decision makers and decision-influencers in a country and global vaccine markets

## Priority 2

To create and manage a strengthened platform to amplify voices of the global south in shaping HPV vaccination science, policy, and program dialogues



# HPV COUNCIL

# TERMS OF REFERENCE

- The Secretariat will develop **terms of reference (ToRs)** for Council members and for a Chair or two Co-Chairs
- ToRs will outline **numbers of events, outputs, and activities** that a member will be expected to engage in each year, in addition to **setting term limits and creating a governance approach** to the Council that ensures that institutional memory is balanced against regular refreshment of membership expertise.

## COUNCIL MEMBER CANDIDATES

- Candidates will be considered for **representation across regions and countries considered to be high-priority and strategic.**
- Candidates will have a **strong track record** in technical advocacy, research or science, policy, programs, or translation of science into practice.
- We will seek a **balance of candidates** with HPV-specific expertise (e.g. HPV vaccine scientists) against discipline-specific expertise (e.g. immunization program experts or cervical cancer program experts).