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.
Your body clears the infection without you knowing it

WARTS
Vary in appearance depending on which HPV strain is involved

GENITAL ITCHING
Usually in the same spot as genital warts

ASYMPTOMATIC
Your body clears the infection without you knowing it

**HPV DIAGNOSIS**

**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

• 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)**

<table>
<thead>
<tr>
<th>HPV-related cancer site</th>
<th>Number of Incident Cases</th>
<th>Number Attributable to HPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>530,000</td>
<td>530,000</td>
</tr>
<tr>
<td>Anus</td>
<td>40,000</td>
<td>35,000</td>
</tr>
<tr>
<td>Vulva</td>
<td>34,000</td>
<td>8,500</td>
</tr>
<tr>
<td>Vagina</td>
<td>15,000</td>
<td>12,000</td>
</tr>
<tr>
<td>Penis</td>
<td>26,000</td>
<td>13,000</td>
</tr>
<tr>
<td>Oropharynx-related</td>
<td>534,000</td>
<td>37,200</td>
</tr>
<tr>
<td><strong>Total HPV-related sites</strong></td>
<td><strong>1,200,000</strong></td>
<td><strong>630,000</strong></td>
</tr>
</tbody>
</table>

CANCER CASES ATTRIBUTABLE TO HPV

GENDER

90.4% Female
9.6% Male

630,000
Overall cancer cases worldwide

4.5%
of all cancer cases worldwide

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.
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.
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

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## HPV SCREENING

Two screening tests can help prevent cervical cancer:

<table>
<thead>
<tr>
<th>Pap Test</th>
<th>HPV test</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Looks for <em>precancers</em>, cell changes on the cervix that might become cervical cancer if they are not treated appropriately.</td>
<td></td>
</tr>
<tr>
<td>• Cells will be checked to see if they look normal.</td>
<td>• Looks for the virus (HPV) that can cause cell changes.</td>
</tr>
<tr>
<td></td>
<td>• Cells will be tested for HPV.</td>
</tr>
</tbody>
</table>

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 test**
(women of HIV+ status or unknown status in areas with high endemic HIV infection)

- **Negative**
  - Rescreen within 3 years

- **Positive**
  - Determine eligibility for cryotherapy and rule out cervical cancer using visual inspection with acetic acid (VIA)
    - Eligible for cryotherapy, treat with cryotherapy
    - Not eligible for cryotherapy, treat with LEEP
    - Suspicious for cancer
      - Refer to appropriate diagnosis and treatment

Post-treatment follow-up at 1 year
HPV Vaccination
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.
Countries that have introduced HPV vaccines in their national immunization program
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


Updated: May 2021
HPV vaccination in girls is predicted to avert 61 million cases in the next century

FDA-APPROVED HPV VACCINES

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Protects against:</th>
</tr>
</thead>
<tbody>
<tr>
<td>CERVARIX</td>
<td>HPV 16, 18</td>
</tr>
<tr>
<td>(bivalent HPV vaccine)</td>
<td></td>
</tr>
<tr>
<td>GARDASIL 4</td>
<td>HPV 6, 11, 16, 18</td>
</tr>
<tr>
<td>(quadrivalent HPV vaccine)</td>
<td></td>
</tr>
<tr>
<td>GARDASIL 9</td>
<td>HPV 6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>(9-valent HPV vaccine)</td>
<td></td>
</tr>
</tbody>
</table>

Updated: May 2021
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
- **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

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.
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.
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.


Updated: May 2021
Numerous LMICs have reported shortages in providers and PPE, limiting health services. Stay-at-home orders and social distancing measures increase the risk of under-immunization in LMICs. Reduced national incomes have restricted vaccine delivery to many LMICs.

Coalition to Strengthen the HPV Immunization Community (CHIC) Project
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 HYGIENE AND TROPICAL 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
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.
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).