HPV Vaccination: An Underused Strategy for the Prevention of Cancer

Gilla K. Shapiro

Journal: Current Oncology 2022

PRESENTER: GHAZALEH BAGHAEI

ATTENDING: DR. A. ESHGHINEZHAD

Case in the office

A 35 year old woman with AUB

abnormal pap smear screening showing ASCUS + positive HPV DNA test, referred for colposcopy of the cervical lesion.

The final diagnosis was CIN II

Abstract

- This paper synthesizes the impact of HPV on the global burden of cancer and the potential benefit of HPV vaccination.
- Approximately 5% of the world's cancers are specifically attributed to HPV
- cervical cancers in low- and middle-income countries
- head and neck cancers in high-income countries
- gender-neutral HPV vaccination
- the barriers and facilitators of global HPV vaccination.

The Burden of HPV

- an important proportion of the global cancer burden is associated with infectious agents including viruses, bacteria, and parasites
- HPV is the most common sexually transmitted infection worldwide. The majority of sexually active people will contract HPV during their lifetime (approximately 75–80%)
- While most HPV infections (70–90%) are asymptomatic and will resolve on their own within 1–2 years, persistent infection (or multiple reinfections) can cause morbidity and Mortality
- 200 different genotypes , more than 20 carcinogen
- 16/18, so-called “high-risk” strains cause almost all cervical cancers
- However, the burden of HPV extends beyond cervical cancers. HPV also causes oropharyngeal (mouth, throat, tongue, and tonsils), vaginal, vulvar, penile, and anal cancers
- rare but serious: recurrent respiratory papillomatosis (maternal HPV infection as well as individual sexual behaviours)
- higher risk of HIV acquisition

The Burden of HPV

- HPV 6/11, i.e., so-called “low risk” strains : 96–100% of anogenital warts…impact one’s quality of life
- 4.5–5.2% of global cancers attributed specifically to HPV : 630,000 new cancer cases annually
- prevalence and persistence of HPV infection varies by geographical region, sex, age, ethnicity, anatomical location of the infection, having a weakened immune system, and health behaviours (such as number of sexual partners, sexual practices, or tobacco use)
- **8.6%** of all cancers in females and **0.8%** of all cancers in males
- **The greatest global burden** of HPV-associated cancers is cervical cancer in low- and middle-income countries (LMIC)
- However, in high-income countries (HIC), HPV infection is a major and increasing cause of head and neck cancers in both males and females
- In HIC, **oropharyngeal** cancers are the most common HPV-associated cancer : vaccination and screening programs for cervical cancer, a higher frequency of oral sex, a greater number of sexual partners, a reduction in tobacco use, and the improvement in HPV detection
- **psychosocial impacts of HPV-associated cancers**: physical and psychological concerns associated with their diagnosis AND distress related to the cause and transmission of HPV….. body image issues, concerns about increased cancer risk for their sexual partners, or not engage in sexual intimacy for fear of transmitting HPV
- given the benefit of some preventative measures, individuals may experience self-blame, guilt, or shame if they did not engage in these health behaviours, or confusion or anger if they took preventative measures and nevertheless developed cancer.

Vaccination as a Tool to Prevent Cancer

- primary and secondary prevention
- pap screening and HPV DNA testing to detect cervical cancers in early stages **BUT no** comparable screening measure other HPV cancers, including head and neck cancers. **(Secondary prevention)**
- However**, primary prevention** through HPV vaccination is available(vaccine) and is estimated to have the potential to prevent 70% to 90% of **all** HPV-related cancers.
- Therefore, not all HPV-related malignancies can be prevented through these available vaccines.

Table 1. Available vaccines to prevent HPV-associated cancers.

Brand Name	Gardasil®	Cervarix®	Gardasil®9	Cecolin®
Developer	Merck	Glaxo SmithKline	Merck	Xiamen Innovax Biotech
Date licensed	2006	2007	2014	2020 *
Type of vaccine	Quadrivalent	Bivalent	Nonavalent	Bivalent
HPV strains targeted	6/11/16/18	16/18	6/11/16/18/31/33/45/52/58	16/18

* Licensed in China in 2020 and currently under review by the World Health Organization [41].

Vaccination as a Tool to Prevent Cancer

- vaccines are recommended primarily for younger individuals before potential exposure to HPV.
- Until April 2022, the World Health Organization (WHO) recommended **two** doses of the HPV vaccine **for girls** aged 9–14. Given increasing evidence that single-dose schedules provide comparable efficacy to two or three doses, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) recently recommended a **one- or two-dose** schedule for **girls** and young women who are 9–20 years old.
- compromised immune system, including those living with HIV, continue to be recommended to receive **three doses** of the HPV vaccine if feasible, and if not, at least two doses.
- some countries with the resources have chosen to offer **gender-neutral** vaccination programs. However, debate persists regarding whether HPV vaccination programs should also target boys.
- whether the prevalence of HPV infection in boys merits intervention
- that through herd protection effects, HPV vaccination programs that target girls will also benefit many boys and be a more cost-effective option .

Vaccination as a Tool to Prevent Cancer

- However, a female-only approach to vaccination relies on **herd protection** and does not consider low or a sudden drop in female HPV vaccine uptake rates (preventing herd effects).
- Furthermore, female-only vaccination does not protect MSM, who experience a high burden of anal cancer and anogenital warts [45], or heterosexual men with sexual partners who chose to not be vaccinated or came from a country that did not have an HPV immunization program.

Vaccination as a Tool to Prevent Cancer

- HPV vaccines are safe and effective in reducing HPV-related infections, genital warts, and pre-cancers.
- Clinically effective protection and sustained antibody titers….. at least 10 years after vaccination.
- HPV vaccine's **real-world impact** : significant reductions in HPV-related infections: a decrease of HPV 16/18 infections (by 68%) and anogenital warts (by 61%) in countries with **female vaccine coverage of at least 50%**
- A recent study that examined 1.67 million Swedish girls and women from 2006 to 2017 found a substantially reduced risk of invasive cervical cancer at the population level
- more time is needed to investigate the full benefit of HPV vaccines for **head and neck cancers** ,particularly given the **long interval** between HPV infection and the development of oropharyngeal cancers. Nevertheless, burgeoning evidence has found a significant decrease in **vaccine-type oral or oropharyngeal HPV infections** in study participants who were immunized with HPV vaccines, which is suggestive of the potential of HPV vaccines for the prevention of these cancers.

Vaccination as a Tool to Prevent Cancer

- The safety of the HPV vaccines is endorsed by the World Health Organization, the Centers for Disease Control and Prevention, the National Advisory Committee on Immunization, and other international immunization advisory committees.
- rare serious adverse events . Mostly just pain and/or swelling in the site of injection.
- HPV vaccination….a cost-effective public health strategy; esp. among **girls** and in settings **where cervical cancer screening is low.**
- Models of HPV vaccination that **included both boys and girls …..** Also **cost-effective** when they took into consideration **all** HPV-related diseases, such as the burden of HPV-associated **head and neck** cancers, and the **suboptimal coverage of vaccination in females** . A recent systematic review of the cost-effectiveness of HPV vaccines, which also included **non-cervical** HPV-associated disease, found that female-only vaccination strategies were 2.85 times more cost-effective, while gender-neutral vaccination was 3.89 times cost effective.

The Underuse of HPV Vaccination

- global vaccine coverage is not reaching the targets required to provide herd immunity.
- Models predict that elimination of HPV infections requires global vaccination rates of 80%
- WHO Cervical Cancer Elimination strategy…HPV vaccination 90% of all adolescent girls by 2030
- BUT in 2020, the average completion rates across WHO regions ranged from 29% to 60%
- Rates vary by country: in some HIC, such as Australia and the United Kingdom, school-based programs have reached 70% to 80% of girls for the final dose ;however, in other HIC, such as France, coverage has not reached 50%.
- HPV vaccine coverage lower than other routine vaccines in younger children.
- In some countries where gender-neutral vaccination is available, fewer boys than girls have received the HPV vaccine >>>> potential consequences for the prevention of HPV-associated head and neck cancers.
- **United States**, **increased** HPV vaccine coverage over time. other countries instability or unexpecteddeclines in HPV vaccine coverage (unrelated to the COVID-19 pandemic). in 2013, **Japan**'s government removed a proactive recommendation for HPV vaccines due to unconfirmed reports of safety concerns that appeared in Japanese media HPV vaccine coverage plummeted from approximately 70% to less than 1%! **Colombia**, **Denmark**, and **Ireland**, have experienced **sudden drops** in HPV vaccine coverage

Drivers for Achieving High Global HPV Vaccine Coverage

- in 2018 WHO established the “Measuring Behavioural and Social Drivers of Vaccination” (BeSD) to identify key drivers for achieving high global HPV vaccine coverage
- **four domains** that are modifiable contributors to vaccine uptake:

1.practical issues,

2.motivation,

3.social processes,

4. and thinking and feeling

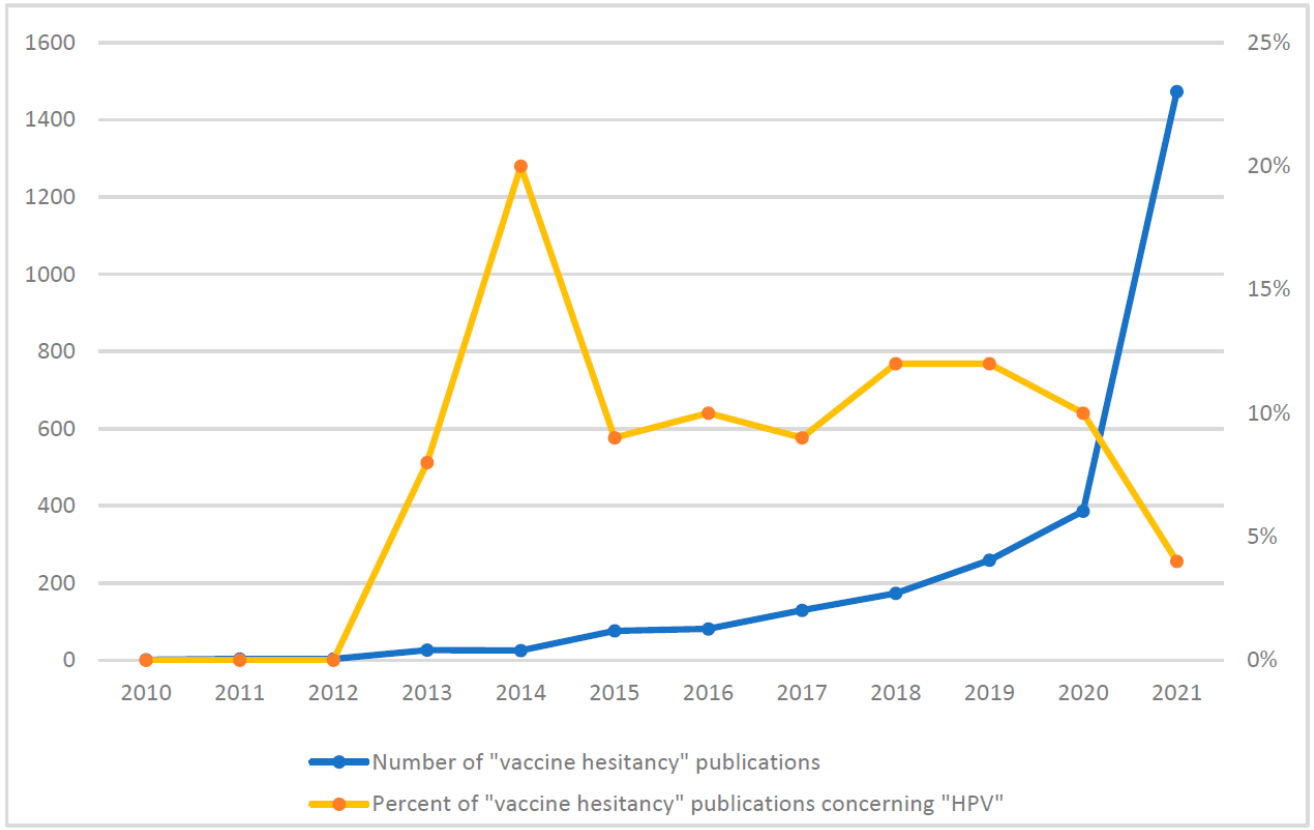
Drivers for Achieving High Global HPV Vaccine Coverage: Practical Issues

- **availability and accessibility**
- As of March 2022, only 117 countries of 194 WHO Member States (i.e., 60%) had introduced HPV vaccination for girls in their national immunization schedules, and since 2013, only 38 countries had included boys (20%)
- LMIC introduced HPV vaccination in national programs at much **slower rates** than HIC>>> global disparities in HPV-related cancer incidence and mortality
- limitations in the **affordability** of the HPV vaccines, particularly in LMIC
- **Worldwide shortages of HPV vaccines**
- HPV vaccination program disruptions due to the COVID-19 pandemic : For example, in England, HPV vaccination in 2020–2021 had increased from 2019–2020, but were not yet consistently reaching pre-pandemic rates, and those who have missed HPV vaccinations had not caught up by 2021 >>>> **rapid recovery is crucial to prevent future excess cancer burden**
- **School-aged children** and adolescents are often more difficult for immunization programs to reach (compared to the vaccination of younger children) >>>> **school-based** HPV vaccine programs have demonstrated benefits in increasing vaccine uptake and equity BUT >>>> **many LMIC do not have funded school health programs**, and providing HPV vaccination in schools can be expensive and unfeasible
- **A simpler vaccine schedule with fewer doses** can improve ease of access and HPV vaccination, particularly in LMIC.

Drivers for Achieving High Global HPV Vaccine Coverage: Motivation

- Although individuals have been conflicted or opposed to receiving vaccinations since modern inoculation was introduced 200 years ago, the use of the term **"vaccine hesitancy"** to describe this phenomenon is relatively new
- Being conflicted about, or opposed to, getting the HPV vaccine.
- Intention to receive the HPV vaccine has been found to be a predictor of vaccine uptake.
- While the literature base on "vaccine hesitancy" increased from 2010–2021, it exploded in association with the COVID-19 pandemic. Not surprisingly, most (77%) of the published literature on vaccine hesitancy focused on COVID-19 in 2021
- The percent of publications on vaccine hesitancy that focused specifically on HPV peaked in 2014 (at 20%)

Drivers for Achieving High Global HPV Vaccine Coverage: Motivation



Drivers for Achieving High Global HPV Vaccine Coverage: Social processes

- Social norms and influence—including by **one's family, friends, healthcare provider, and religious or community leaders**—impact motivation to receive the HPV vaccine.
- healthcare provider's recommendation …. a critical factor for HPV vaccination
- physician-focused interventions (education and training, audit and feedback and/or electronic decision support or alerts) increase HPV vaccine uptake.
- For example, a systematic review of 59 eligible studies from the United States (of 265,083 patients) found that receiving a healthcare provider's recommendation was associated with HPV vaccine initiation (with a pooled **odds ratio of over 10**)
- **the impact of online social networks and media** on HPV vaccine intentions and uptake. One study found that as little as 5 to 10 min of access to vaccine-critical websites influenced participants' risk perception and vaccine intentions
- a study of **over 250,000 tweets** related to the HPV vaccines in the United States **(between 2013 and 2015)** found that vaccine coverage was lower in states where there was a higher proportion of exposure to **safety concerns**, **misinformation**, and **conspiracies**
- A recent population-based retrospective cohort study of all girls born in Denmark from 1997 to 2006 had similar findings; where periods of extensive negative media coverage were associated with substantially reduced HPV vaccination
- **a quick and proactive response to managing public concerns is critical and may include tracking public sentiment and social media, having a social media presence, providing accurate information, and using evidence-based communication methods.**

Drivers for Achieving High Global HPV Vaccine Coverage: Thinking and Feeling

- Psychological factors—including **knowledge**, **values**, **attitudes**, and **beliefs**—also influence individuals' motivation to receive the HPV vaccine.
- **Changing policies regarding HPV vaccines** (e.g., the administered vaccine, number of recommended doses, and groups targeted for vaccination) can make it a challenge to establish **consistent population-level knowledge** about the HPV vaccines.
- Overall, knowledge of HPV-related diseases and the HPV vaccine is often found to be **variable or low**
- the perceived benefit of HPV vaccination for preventing cancer and other diseases has been consistently related to HPV vaccine acceptability and uptake
- Like other vaccines: notable attitudes and beliefs that contribute to **HPV vaccine hesitancy** include **lack of confidence**, **lack of trust in vaccination programs and providers**, **concerns about vaccine safety**, **and concerns about vaccine side effects.**
- unique aspects of the HPV vaccine that impact attitudes and beliefs, including **it being a vaccine for school aged children**, **a relatively newer vaccine**, **a vaccine for a sexually transmitted infection**, and **a vaccine that is used to prevent cancer.**
- **For example:** a **delay** in HPV vaccination related to parents and providers waiting until a child is "about to be sexually active"
- **For example:** Despite a lack of evidence concerns raised by religious leaders and parents that vaccinating children against HPV could provide children with **permission to engage in risky sexual behaviors.**
- **Individuals can also hold multiple and incongruent beliefs at one time such as thinking a child is at risk for an HPV-associated cancer and thinking that the HPV vaccine is not safe.**

Conclusion

- HPV vaccination stands out as having **unrealized potential** to prevent cancers, financial cost, and psychological distress.
- HPV causes cervical cancer and is a substantial burden for LMIC, while HPV-associated head and neck cancers are also a leading and increasing priority for HIC.
- substantial research about HPV vaccine's effectiveness, safety, and cost-effectiveness ☆
- global HPV vaccine coverage is **not** consistently reaching targets and has been further impacted by program disruptions caused by the COVID-19 pandemic.
- **the BeSD framework** to understand modifiable drivers of HPV vaccine acceptance and uptake ⇨ regularly measure these factors, develop interventions to promote vaccine acceptance, and improve global HPV vaccine coverage.
- Future research in diverse populations with comparative measurement of these factors across countries and over time is needed to comprehensively evaluate these aspects

THE END