The influence of expanding sex-specific HPV vaccination efforts on HPV prevalence in the southeastern US, a mathematical SIS-V model

Bevin Manuelpillai, Lexi Guyah, Simone Anderson,
Gayathri Dhurjati, Kirsten Wade, Thomas Hess

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Introduction

Infection with human papillomavirus (HPV) is a relatively common condition that can lead to health consequences with a wide range of severity. In the United States, the lifetime probability of HPV infection is 85% for females and 91% for males (Chesson, et al. 2014). The annual burden of HPV-associated diseases in the United States was estimated to be about $8 billion dollars per year in 2010 (Chesson, et al. 2012). There are many different strains of HPV, some of which cause genital warts and others which cause cancer. HPV is a primary cause of most cases of cervical cancer in females as well as some cases of anal and oropharyngeal cancer in both sexes and penile cancer in males (Schiffman, et al. 2007). Co-infection with different HPV strains is common, and evidence of cyclical positive and negative HPV tests for the same viral strain over the lifetime has led some to suggest a latent phase of HPV infection (Gravitt & Winer, 2017). Most infections with HPV are asymptomatic and are often cleared without clinical intervention in 12-24 months; Persistent infection with HPV can lead to precancerous and/or cancerous conditions later in life (Schiffman, et al. 2007). The most prevalent strains are those that tend to cause persistent infection.

Vaccines protecting against a variety of HPV strains have been available for about two decades, but vaccine uptake remains variable both geographically and demographically. The most used vaccine in the United States since 2016 is the Gardasil-9 vaccine, which protects against the 9 most common strains of HPV, including those responsible for most cases of cervical cancer, genital warts, and oropharyngeal cancer (NCI, 2021). In the United States, HPV vaccination is currently recommended for both females and males starting in early adolescence and requires two doses to be complete (CDC 2024). Vaccination can occur in older adolescents and young adults, but it is recommended to occur before commencement of sexual activity, so vaccine protection is conferred before exposure. Studies investigating catch-up vaccination suggest that a very small proportion (3-4%) of people are vaccinated between the ages of 18-21 (Chen, et al. 2021), and those vaccinated at a later age (21+) may not see equivalent levels of vaccine protection (Silverberg, et al. 2018; Cuoto, et al. 2014).

HPV vaccination rates are lower and cervical cancer rates higher in the southern US compared to the national average (Hirth 2019), indicating a regional disparity in both the public health and economic burden of HPV infection and HPV-associated diseases. Average vaccination rates in the southeastern U.S. (56%) are lower than the national average (63%) (St. Jude Children's Research Hospital, 2023). Vaccination also varies widely by sex, with about 40% of females but only 10% of males reporting receipt of the vaccine among adults in the United States (McElfish, et al. 2020; Williams, et al. 2017).

In the present study, we aim to understand which approaches to increasing levels of vaccine coverage in the southeastern U.S. have the largest impact on overall HPV prevalence. Specifically, we will answer the following questions:

1) How does expanding levels of full pre-adolescence HPV vaccination for both males and females influence the overall prevalence of HPV among sexually active individuals in the southeastern United States?

a) How does increasing male vaccination levels to current female levels (equal vaccination between sexes) impact overall HPV prevalence?

b) How does increasing female vaccination alone impact prevalence?

c) What is the relationship between increasing both male and female vaccination levels and overall HPV prevalence?

2) How does expanding rates of catch-up vaccination impact overall prevalence?

3) What is the comparative effectiveness of increasing i) pre-adolescent vaccination rates or ii) catch-up vaccination rates on reducing the overall prevalence of HPV in the southeast?

Methods

Target population The present study focuses on contiguous US states in the southeastern region (Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Virginia, and West Virginia), as defined by the HPV Vaccination Roundtable of the Southeast, a collaboration between St. Jude Children's Research Hospital (2023) and representatives from this more highly burdened region. The age range of our target population is based on the assumption that age of legal adulthood in the United States (18 years of age) approximates sexual maturity and activity, thus initiating a period of potential high risk of exposure to HPV, and the average age of marriage for US adults (29 years of age; US Census Bureau 2023) as a proxy for entering a lower exposure period of life.

note to edit the age range??

Model structure **Equations** *Males*

$dS_m = -\lambda_m N_{sm} + (1-\omega_m)N_m + \delta N_{im} - \mu N_{sm}$

$dI_m = \lambda_m N_{vm}(1-\psi) + (\lambda_m N_{sm})N_m - \delta N_{im} - \mu N_{im}$

$dV_m = -\lambda_m N_{vm}(1-\psi) + (\omega_m \mu N_m) - \mu N_{vm}$

Females

$dS_f = -\lambda_f N_{sf} + (1-\omega_f)N_f + \delta N_{if} - \mu N_{sf}$

$dI_f = \lambda_f N_{vf}(1-\psi) + (\lambda_f N_{sf})N_f - \delta N_{if} - \mu N_{if}$

$dV_f = -\lambda_f N_{vf}(1-\psi) + (\omega_f \mu N_f) - \mu N_{vf}$

Parameters

Analysis methods

\ ### Results