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Cost-effectiveness of nonavalent HPV vaccination among males aged 22 through 26 years in the United States ☆

Harrell W. Chesson [a,*], Elissa Meites [b], Donatus U. Ekwueme [c], Mona Saraiya [c], Lauri E. Markowitz [b]

[a] Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA
[b] Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA
[c] Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA, USA

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ABSTRACT

Introduction: In the United States, routine human papillomavirus (HPV) vaccination is recommended for females and males at age 11 or 12 years; the series can be started at age 9 years. Vaccination is also recommended for females through age 26 years and males through age 21 years. The objective of this study was to assess the health impact and cost-effectiveness of harmonizing female and male vaccination recommendations by increasing the upper recommended catch-up age of HPV vaccination for males from age 21 to age 26 years.

Methods: We updated a published model of the health impact and cost-effectiveness of 9-valent human papillomavirus vaccine (9vHPV). We examined the cost-effectiveness of (1) 9vHPV for females aged 12 through 26 years and males aged 12 through 21 years, and (2) an expanded program including males through age 26 years.

Results: Compared to no vaccination, providing 9vHPV for females aged 12 through 26 years and males aged 12 through 21 years cost an estimated $16,600 (in 2016 U.S. dollars) per quality-adjusted life year (QALY) gained. The estimated cost per QALY gained by expanding male vaccination through age 26 years was $228,800 and ranged from $137,900 to $367,300 in multi-way sensitivity analyses.

Conclusions: The cost-effectiveness ratios we estimated are not so favorable as to make a strong economic case for recommending expanding male vaccination, yet are not so unfavorable as to preclude consideration of expanding male vaccination. The wide range of plausible results we obtained may underestimate the true degree of uncertainty, due to model limitations. For example, the cost per QALY might be less than our lower bound estimate of $137,900 had our model allowed for vaccine protection against re-infection. Models that specifically incorporate men who have sex with men (MSM) are needed to provide a more comprehensive assessment of male HPV vaccination strategies.

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1. Introduction

Human papillomavirus (HPV) infection can cause a range of adverse health outcomes in females and males, including anogenital cancers, oropharyngeal cancer, genital warts, and recurrent respiratory papillomatosis (RRP) [1]. The HPV vaccination program in the United States has been in place for over a decade [2]. The Advisory Committee on Immunization Practices (ACIP) has recommended routine HPV vaccination since 2006 for females and 2011 for males [1–3]. Current ACIP guidance calls for routine HPV vaccination of females and males at age 11 or 12 years (or can be started at age 9 years) [1,3]. ACIP also recommends catch-up vaccination through age 26 years for females and through age 21 years for males [1,3]. Further, ACIP provides additional recommendations through age 26 years for people with immunocompromising conditions, transgender people, and for men who have sex with men [MSM], including men who identify as gay or bisexual [3]. MSM bear a disproportionate burden of HPV-associated genital warts and cancers, particularly anal cancer [4,5].

In 2011, the United States was the first country to include males in the routine HPV vaccination program [6,7]. This decision was based on vaccine clinical trial data, burden of infection and disease, programmatic issues and cost effectiveness, and used the newly implemented ACIP Grading of Recommendations, Assessment,

☆ The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

* Corresponding author at: Centers for Disease Control and Prevention, Mail-stop E-80, 1600 Clifton Road, Atlanta, GA 30329-4027, USA.
E-mail address: HChesson@cdc.gov (H.W. Chesson).

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Development, and Evaluation (GRADE) process [8,9]. Since that time, additional data have been collected about HPV vaccination coverage in the United States, the percentage of HPV-associated cancers attributable to HPV, and the prevalence of HPV and HPV-associated diseases in males. Although the initial recommendation for males was for a quadrivalent HPV vaccine (4vHPV), a 9-valent vaccine (9vHPV) was licensed in the United States in 2015 and is now the only HPV vaccine available in this country.

ACIP continuously reviews data relevant to vaccination policy as they become available and also considers revisions to existing recommendations based on such data [10]. One common question about existing HPV vaccine recommendations is whether the upper age limit for males should be changed to 26 years [11]. This modification would harmonize the age recommendations for males and females and might facilitate implementation of HPV vaccination recommendations. In addition, expanding catch-up vaccination through age 26 years for all males might help increase the likelihood that men in special risk groups would be offered HPV vaccination even if they are unaware of or choose not to disclose their risk status in health care settings [12].

The objective of this study was to assess the health impact and cost-effectiveness of expanding male HPV vaccination recommendations to include all males through age 26 years instead of age 21 years. Specifically, we examined the incremental costs and benefits of a 9vHPV program for females and males aged 12 through 26 years compared to a 9vHPV program for females aged 12 through 26 years and males aged 12 through 21 years.

2. Methods

2.1. Study questions addressed

We examined the incremental cost-effectiveness of 9vHPV of males aged 22 through 26 years in the United States, in the context of current vaccination policy. The specific study question we addressed was: What would be the cost-effectiveness of a 9vHPV program for ages 12 through 26 years for all sexes (“expanded scenario”), compared to a 9vHPV program for females aged 12 through 26 years and males aged 12 through 21 years (“comparison scenario”)? In addressing this issue, we also examined the cost-effectiveness of the “comparison scenario” compared to a “no vaccination” scenario. To clarify, the cost-effectiveness of the comparison scenario was calculated versus no vaccination, and the cost-effectiveness of the expanded scenario was calculated versus the comparison scenario.

2.2. Cost-effectiveness ratios

To address the study question, we calculated the incremental cost per quality-adjusted life year (QALY) gained by the expanded scenario (vs. the comparison scenario). The numerator of the incremental cost per QALY ratio was calculated as the projected increase in vaccination costs (costs of vaccination in the expanded scenario minus the costs of vaccination in the comparison scenario) minus the projected increase in averted HPV-associated direct medical costs (medical costs averted in the expanded scenario minus the medical costs averted in the comparison scenario). The denominator of the incremental cost per QALY ratio was the projected gain in the number of QALYs saved by the expanded scenario, and was calculated as the number of QALYs gained in the expanded scenario minus the number of QALYs gained in the comparison scenario. Formally, the calculation of the incremental cost-effectiveness ratio (ICER) can be expressed as:

$$ICER = \frac{(V_e - V_c) - (A_e - A_c)}{(Q_e - Q_c)},$$

where V denotes vaccination costs, A denotes averted direct medical costs, Q denotes QALYs gained, and the subscripts e and c refer to the expanded scenario and the comparison scenario, respectively [13].

2.3. Perspective, scope, time frame, and analytic horizon

We assessed costs from the healthcare system perspective and included all direct medical costs averted by vaccination, without regard to the payer of these costs (e.g., health insurance, government program, individual patient or family, etc.). Medical costs averted and QALYs gained were accrued by prevention of the following HPV-related health outcomes: anogenital cancers (cervical, vaginal, vulvar, anal, and/or penile), oropharyngeal cancer, cervical intraepithelial neoplasia (CIN), genital warts, and juvenile-onset RRP. We applied a 100-year time horizon. Specifically, the vaccine program was assumed to be in place for 100 years, vaccination costs were incurred in each of the 100 years, and we assessed lifetime costs averted and lifetime QALYs gained for HPV-associated health outcomes that were prevented over the 100-year period. Future costs and QALYs were discounted to present value using a 3% annual discount rate as is commonly recommended for cost-effectiveness studies in the United States [13,14].

2.4. Model description

We applied a deterministic, dynamic, population-based model that has been used previously to examine a range of HPV vaccination strategies in the United States [15,16] and was recently expanded to include the additional five HPV types prevented by 9vHPV [17,18]. For this application of the model, we have updated vaccination coverage and cost assumptions to reflect recent data, and have updated the medical treatment costs to 2016 U.S. dollars using the health care component of the Personal Consumption Expenditures price index (https://www.bea.gov/) [19]. In this section, we provide a brief description of the current model we applied. The technical appendix contains a full description of this model and a complete listing of all model parameter values and sources.

Our model employs three important simplifying features that distinguish it from other, more complex HPV models in the literature. First, our model does not explicitly account for the pathologic transition from HPV acquisition to HPV-associated disease. Without modeling the natural history of HPV infections in individuals, our model approximates the percentage reduction in HPV-associated outcomes based on the percentage reduction in cumulative HPV acquisition at the population level. For example, suppose that as a result of the HPV vaccination program, cumulative lifetime acquisition of HPV 16 among 45-year-old women in year 25 of the HPV vaccination program was 50% lower than it would have been in the absence of vaccination. In this example, the incidence of HPV 16-associated cervical cancer among this birth cohort of 45-year-old women would be calculated by the model to be approximately 50% lower than it would have been in the absence of vaccination.

The second simplifying feature is the approach used to model HPV transmission dynamics. In our model, all people who have not yet acquired a given HPV type are subject each year to a sex- and age-specific probability of acquiring the given HPV type, and each year these probabilities are adjusted in accordance with sex- and age-specific reductions in HPV in the population due to HPV vaccination.

The third simplifying feature of our model is that we do not explicitly account for cervical cancer screening, and therefore cannot assess the impact of potential changes in cervical cancer screening strategies. Instead, cervical cancer screening was