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Health and economic benefits of single-dose HPV vaccination in a Gavi-eligible country

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ABSTRACT

Background: Although guidelines for prophylactic human papillomavirus (HPV) vaccination recommend two doses for girls ages 9–14 years, several studies have demonstrated similar protection with one dose. Our objective was to evaluate the long-term health and economic impacts of routine one-dose HPV vaccination compared to (1) no vaccination and (2) two-dose HPV vaccination in a low-income country.
Methods: We used a three-tiered hybrid modeling approach that captured HPV transmission, cervical carcinogenesis, and population demographics to project long-term health and economic outcomes associated with one-dose HPV vaccination (assuming 80% efficacy against HPV-16/18 infections under three waning scenarios) and two-dose HPV vaccination (assuming 100% efficacy over the lifetime) in Uganda. Costs included the vaccine program (dosage and delivery) costs over a 10-year period and cervical cancer costs over the lifetimes of the current population of Ugandan women. Health outcomes included number of cervical cancer cases and disability-adjusted life years (DALYs). Incremental cost-effectiveness ratios (i.e., cost per DALY averted) were calculated and compared against the Ugandan per-capita gross domestic product.
Results: Routine one-dose HPV vaccination of 9-year-old girls required substantial upfront investment but was cost-saving compared to no vaccination when accounting for the cost-offsets from future cancers averted. Forty years after initiating routine vaccination and depending on assumptions of vaccine waning, one-dose HPV vaccination with equivalent coverage (70%) averted 15–16% of cervical cancer cases versus 21% with two-dose vaccination but required only half the upfront economic investment. Vaccination with two doses had an attractive cost-effectiveness profile except if one-dose vaccination enabled higher coverage (90% vs. 70%) and did not wane.
Conclusions: One-dose HPV vaccination resulted in cost-savings compared to no vaccination and could be cost-effective compared to two-dose vaccination if protection is longstanding and higher coverage can be achieved.

1. Introduction

Cervical cancer is caused by persistent infection with one of 13 sexually transmitted high-risk human papillomavirus (HPV) genotypes [1]. Globally, approximately 70% of cervical cancers are attributable to HPV genotypes 16 and 18 [2]. The World Health Organization recommends two-dose prophylactic HPV vaccination for young girls aged 9–14 years, with a 6-month interval between doses and completion prior to initiation of sexual activity [3].

Several studies—including the Costa Rica Vaccine Trial [4], a multicenter cohort study in India [5], and the industry-sponsored PATRICIA trial [6]—have indicated similar vaccine protection among those receiving one or two doses of HPV vaccine. Compared with a two-dose HPV vaccination schedule, one-dose HPV vaccination could potentially reduce programs costs, ease administration, enable the delivery of multi-cohort vaccination, and increase HPV vaccine program adoption in populations with limited access to healthcare and a high burden of cervical cancer. Yet many uncertainties remain, including the efficacy, duration of vaccine protection and value of a single HPV vaccine dose. Several vaccine trials are underway to evaluate the properties of a one-dose vaccine schedule, but it will be several years before those data become available.

As we await additional empirical data, mathematical models that integrate available evidence on sexual behavior and cervical

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cancer natural history can project epidemiological, health, and economic outcomes over the considerable time horizon between intervention and prevention of cancer. Such analyses can help inform stakeholder decision-making in light of data gaps and uncertainties. In particular, countries eligible for funding from Gavi, the Vaccine Alliance face severe resource constraints, prompting decision makers to consider the value – or cost-effectiveness – of reduced HPV vaccine dosing schedules prior to policy adoption or augmentation. Our objective was to evaluate the long-term health and economic impacts of routine one-dose HPV vaccination, compared to (1) no vaccination and (2) two-dose HPV vaccination in the context of a low-income Gavi-eligible country.

2. Methods

2.1. Analytic overview

We used a three-tiered hybrid modeling approach (Fig. 1) to capture important behavioral, epidemiological and demographic information in order to estimate the health and economic outcomes associated with alternative one-dose HPV vaccination scenarios in Uganda. We linked a dynamic agent-based model of HPV transmission ("Harvard-HPV") to a static individual-based model of cervical carcinogenesis ("Harvard-CC") in order to capture both the direct and indirect "herd immunity" benefits of HPV vaccination, as well as the complex natural history of HPV-induced cervical cancer. Finally, we used a companion population-based model ("Harvard-Scale Up") to project the health and economic consequences for the population of Ugandan women over time.

2.2. Simulation models

Harvard-HPV is an agent-based dynamic model of partnership acquisition and HPV transmission that was based on a previous compartmental model of HPV-16/18 transmission [7]. The model allows the interaction of heterosexual men and women guided by individual-level attributes such as HPV infection duration, natural immunity, partner concurrency, number of lifetime partners, and duration of partnership(s) in order to capture both the direct and indirect benefits under alternative HPV vaccination scenarios. In contrast to the previous HPV-16/18 transmission model [7], Harvard-HPV is an individual (i.e., agent-based) model and includes additional stratified HPV genotypes (HPV-16, -18, -31, -33, -45, -52, and -58). As Harvard-HPV requires highly-detailed data on sexual behavior that are limited in the setting of Uganda, we used a version of the model that reflects sexual mixing patterns in the U.S. population (see Technical Appendix). We used Harvard-HPV to generate HPV incidence reductions (including herd immunity) by genotype and age over time associated with alternative HPV vaccination scenarios that served as inputs into Harvard-CC.

Harvard-CC is a static, individual-based (i.e., microsimulation) model that tracks women from age 9 years as they transition through HPV-related health states (i.e., no HPV infection, HPV infection, cervical intraepithelial neoplasia grades 2 and 3, and cervical cancer) until death, either from all causes or cervical cancer

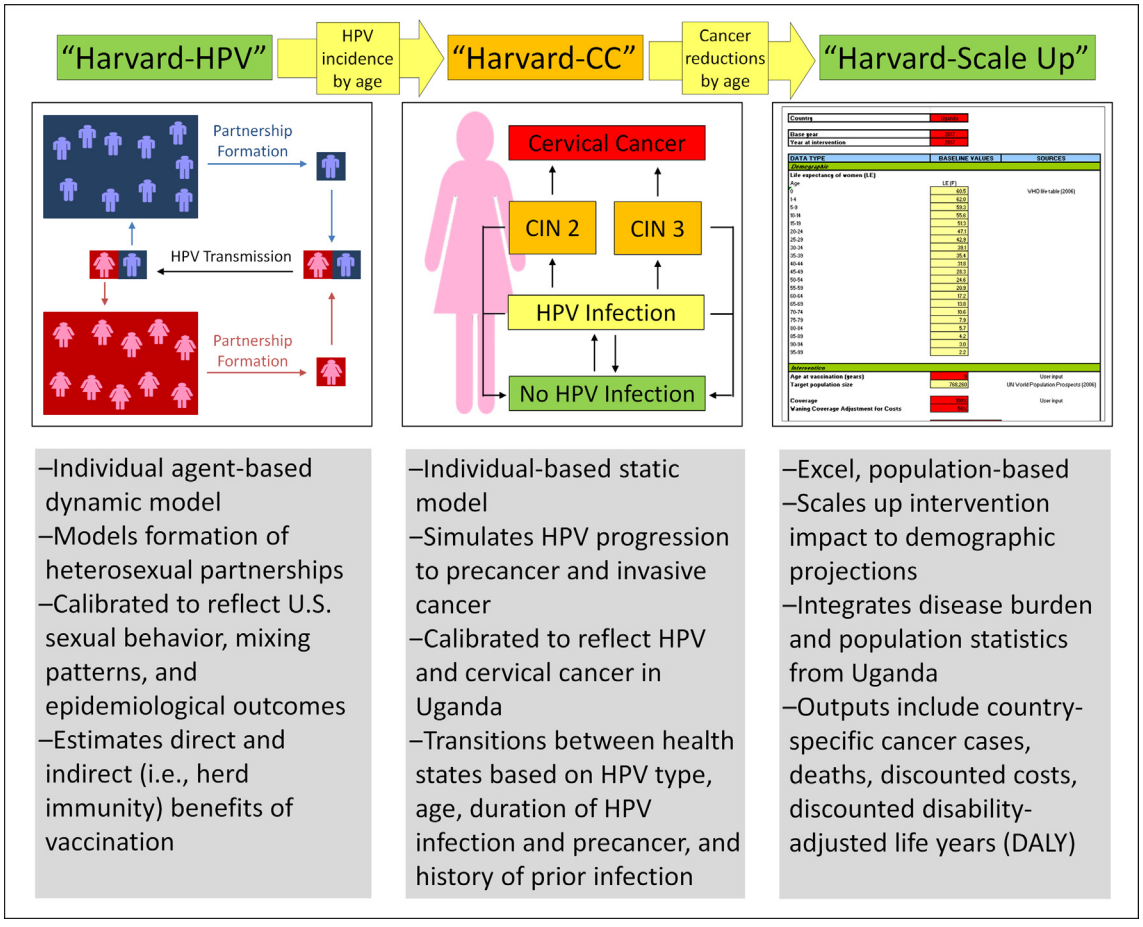

Fig. 1. Overview of three-tiered model-based approach. Abbreviations. CC: cervical cancer, CIN: Cervical intraepithelial neoplasia, HPV: Human papillomavirus.

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