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The newsletter on Human Papillomavirus because we can envisage cervical cancer elimination

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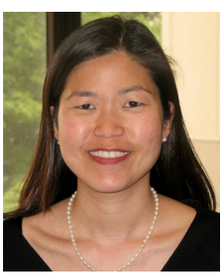
Could 1 dose be less efficacious than 2 doses but still be a great public health intervention?



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Single-dose HPV vaccination has the potential to enhance the feasibility and affordability of primary prevention against HPV-related cancers worldwide. Evidence to date suggests that the efficacy of one-dose HPV vaccination is high [1,2], but even if demonstrated to be statistically inferior to that of two doses, the population-level effectiveness may still be great and worth the investment. The magnitude of effect – both absolute and relative to two doses – hinges on several key factors, including vaccine efficacy, duration of vaccine-induced protection, and achievable coverage. While clinical trials and studies are underway to resolve these uncertainties, decisions regarding the adoption of HPV vaccination – either with one or two doses – are being considered globally.

As we await more robust empirical data, mathematical models can be used to capture the burden of disease in a population and assess the impact and cost-effectiveness of HPV prevention strategies to inform decision-making. "Dynamic" models simulate the transmission of infectious diseases and the corresponding herd immunity benefits from interventions, such as vaccination. Using a previous dynamic model of HPV16 and 18 infections [3]– recently expanded to reflect sexual partnerships at the individual-level and include additional HPV types – we conducted preliminary explorations of one-dose HPV vaccination, varying key parameters expected to have the greatest impact on health outcomes.

Mathematical models can be used to capture the burden of disease in a population and assess the impact and cost-effectiveness of HPV prevention strategies to inform decision-making

Scenarios were restricted to routine vaccination of 12-year-old girls, assuming efficacy for one-dose vaccination of 80% against incident HPV16 and 18 infections, based on the lower-bound target efficacy for single-dose regimens of HPV vaccines in a new, formal randomized control trial [4] (ClinicalTrials.gov Identifier: NCT 03180034). Given the unknown longevity of one-dose protection, we explored simplified waning assumptions, including no waning (i.e., lifetime protection), and 15 or 10 years of full protection followed by linear waning of vaccine protection over an additional 20 years. The effect of vaccination coverage was also explored. Vaccination with two doses was included as a baseline comparator, assuming 100% lifetime protection against HPV16/18 infections with achievable coverage of 70%. Model-projected outcomes included prevalence of HPV16 and 18 infections in a population of women over time.

Figure 1 shows the projected HPV16 prevalence in females over a 35-year period since initiation of routine HPV vaccination with either one dose or two doses, assuming protection is lifelong (i.e., no waning) with either dosage. At 70% coverage, both one-dose and two-dose vaccination scenarios are shown to greatly reduce HPV16 prevalence over time compared to no vaccination. For example, 30 years after routine vaccine implementation, two doses at 100% efficacy achieves 85% reduction in HPV16 prevalence compared to no vaccination, whereas one dose at 80% efficacy achieves 70% reduction. While it is not surprising that, assuming all else is equal, prevalence reduction is lower with one dose given its assumed lower efficacy (80%). We found that increasing one-dose vaccination coverage (from 70% to 90%) can almost completely offset this lower prevalence reduction. This relationship held true even when baseline vaccination coverage was assumed to be lower at 50%.

Figure 2 displays these projections under assumptions of waning vaccine protection with one dose, assuming 80% protection against HPV16/18 for 15 years, followed

by a linear reduction to 0% protection over an additional 20 years. Here, HPV16 prevalence again drops considerably over time with one-dose vaccination even if protection is not lifelong. In this scenario, increasing one-dose vaccination coverage from 70% to 90% is able to achieve similar reductions in HPV16 prevalence compared to two-dose vaccination until roughly 20 years post vaccine initiation, after which the effects of one-dose waning begin to diminish the population effect. The gap between one-dose and two-dose vaccination is even more pronounced and occurs sooner when one-dose vaccination begins to wane earlier (e.g., at 10 years; data not shown). At a lower baseline coverage of 50%, an increase in one-dose coverage up to 90% is required to offset lower prevalence reduction associated with lower and waning one-dose efficacy (data not shown). Under all scenarios, a similar trend can be observed for HPV18, although absolute prevalence is lower.

These projections must be interpreted with caution given the uncertainty and limitations in the model itself. This particular model was calibrated to the US population in order to leverage available data on sexual behaviors; to the extent that sexual behaviors vary across populations, especially in low and middle income countries where questions regarding one-dose vaccination are most pressing, results may not be generalizable. The analyses projected only the short-term outcomes of HPV infection over a relatively short time horizon; however, the model can be used to project longer-term outcomes of cancers averted, life expectancy gains, and cost-effectiveness, which will be included in ongoing work. Finally, only a limited number of coverage and efficacy values were explored and simplified vaccine waning scenarios were included. For example, vaccination coverage under both dosage regimens was assumed to be immediate without a more realistic period of scale-up, and no other (non-linear) specifications of waning were tested. We chose 15 years for waning to begin given new seven-year protection data for the bivalent HPV vaccine [5] but acknowledge that a shorter duration of protection would result in more modest HPV reductions.

First, the absolute population-level benefit associated with one-dose HPV vaccination stands to be great, even at lower efficacy and durability than two-dose vaccination.

Despite these limitations, this preliminary analysis offers several important insights. First, the absolute population-level benefit associated with one-dose HPV vaccination stands to be great, even at lower efficacy and durability than two-dose vaccination. Second, a one-dose vaccination program may be able to compensate for lower vaccine efficacy and durability if it can achieve higher coverage, depending on if and how vaccine efficacy wanes. Given the high number of countries that have yet to adopt an HPV vaccination program – and paired with its inherently lower cost and greater feasibility – one-dose HPV vaccination has the potential to boost HPV vaccine impact globally. ■

References

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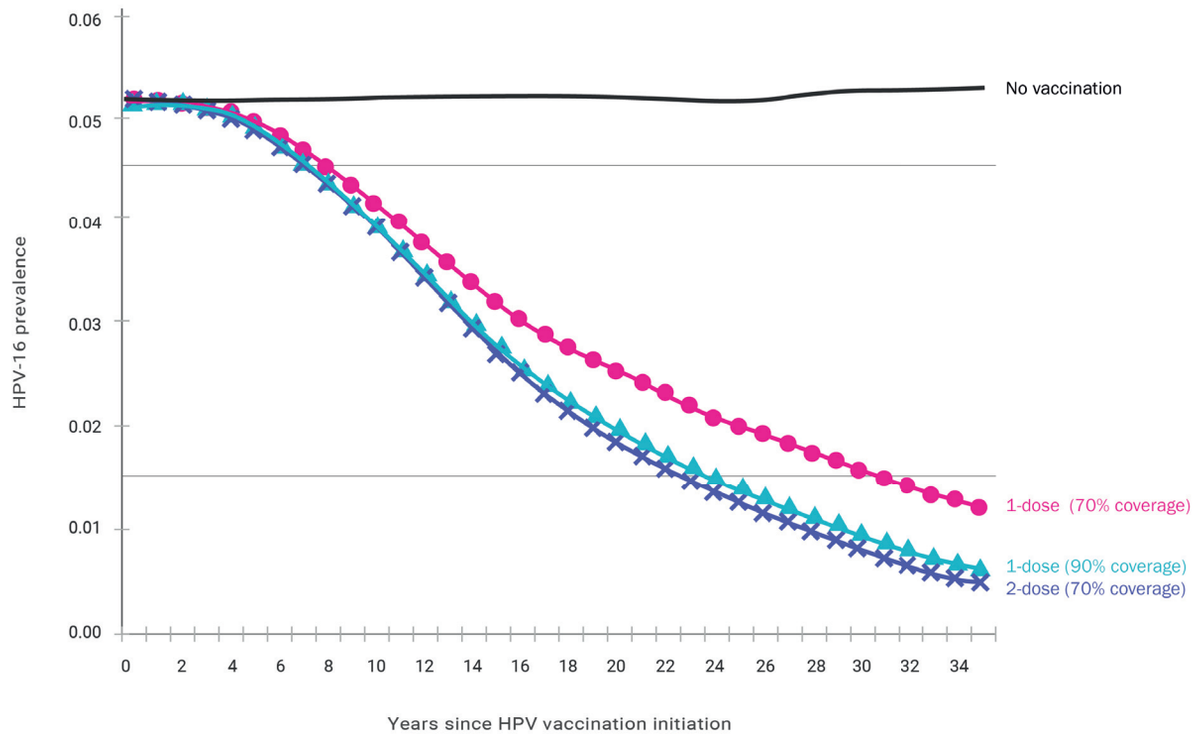
Figure 1

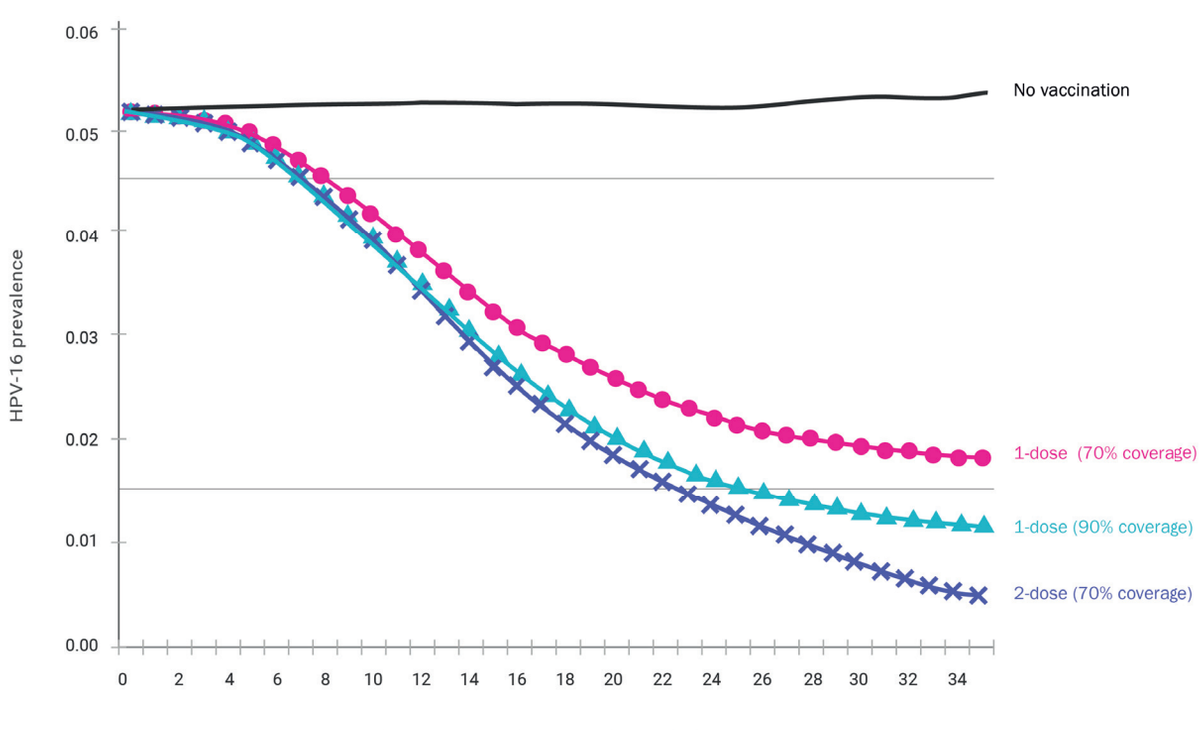
Model-projected HPV16 prevalence in females over time, no waning



Vaccine efficacy against HPV16/18 infections was assumed to be 100% for two doses, and 80% for one dose over the lifetime. HPV16 prevalence was among females aged 12 to 60 years.

Figure 2

Model-projected HPV16 prevalence in females over time, waning after 15 years



Vaccine efficacy against HPV16/18 infections was assumed to be 100% for two doses over the lifetime, and 80% for one dose for 15 years, after which vaccine protection waned linearly to 0% over an additional 20 years. HPV16 prevalence was among females aged 12 to 60 years.