The Journal of Infectious Diseases
MAJOR ARTICLE

Human Papillomavirus Vaccination of Boys and Extended Catch-up Vaccination: Effects on the Resilience of Programs

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Background. Decreasing human papillomavirus (HPV) vaccine prices makes scaling up of vaccination programs attractive for countries that initially targeted 1 or a few birth cohorts of girls and/or achieved low coverage. This article aims to compare the impact of alternative HPV vaccination strategies, using data from Sweden, a high-income country that has experienced vaccine price changes.

Methods. Using an HPV transmission model, we compared the existing vaccination program to alternatives, accounting for a 1-time catch-up vaccination of 22–26-year-old women, with or without routine vaccination of school-age boys, and for a 1-time catch-up vaccination of males aged 13–26 years. We also assessed the resilience of vaccination alternatives to coverage reduction.

Results. On the basis of an HPV16/18 prevalence of 12% before the HPV vaccine era, extended catch-up vaccination for females and males yielded relative reductions in the HPV prevalence of 49.4% and 55.6%, respectively, during the first 10 years after the start of each vaccination strategy, whereas the existing program yielded a relative reduction of 38.6% during the same period. The increased prevalence reduction due to catch-up vaccination continued for about 30 years. As compared to female-only routine and extended catch-up vaccination, routine vaccination of males with or without catch-up was, respectively, 12.6-fold and 7.2-fold more resilient to coverage reduction.

Conclusions. Vaccination strategies based on catch-up vaccination of females and males are effective for accelerating HPV prevalence reduction. Inclusion of routine male vaccination improves the resilience of vaccination programs.

Keywords. human papillomavirus vaccination; gender neutral; catch-up; resilience; coverage reduction.

The target population of human papillomavirus (HPV) vaccination programs in high-income countries varies between countries, with vaccination of both sexes implemented in Australia, Austria, Canada, and the United States [1, 2]. A key issue is whether an extension of existing vaccination programs should primarily aim for increased vaccination of girls and young women (improving coverage and/or extending the target age ranges) and/or whether programs should be extended to boys [2]. The steady decrease in HPV vaccine prices makes scaling up attractive for high-income countries that initially targeted only 1 or a few birth cohorts of girls and/or achieved low coverage.

The success of a vaccination program is closely linked to the sustainability of the program, public opinion of health interventions, and resilience (ie, the propensity to maintain high effectiveness) to conditions that might undermine vaccination coverage. Mathematical models are convenient to investigate counterfactually the potential for mitigation strategies devised to improve the resilience of vaccination programs [3, 4]. By using real-life input data from Sweden and focusing on viral end points (ie, detection of HPV types directly targeted by the vaccines), which are the earliest indicators of the impact of an effective program, characteristics of different vaccination strategies, including their resilience, can be examined.

Decreases in vaccination coverage or performances of infection prevention programs have repeatedly occurred as a result of targeted antivaccination campaigns [5, 6], trends in social preferences toward vaccination [7], or reduced public health efforts for infection prevention programs [8, 9], despite robust program funding. Reversing the effects of impaired infection prevention can take several years and can cost significantly more than initially allocated to the prevention program. For example, New York City spent more than $1 billion to curb a tuberculosis epidemic in the 1990s that was largely attributable to reduced public health efforts to prevent tuberculosis [10]. Mitigation strategies have been proposed as effective and cost-saving measures to prevent infections with pandemic potential, such as influenza [3, 4, 11].

The bivalent and quadrivalent HPV vaccines were made commercially available in 2007 for girls aged 13–17 years at a

Received 24 March 2015; accepted 25 June 2015; published online 3 July 2015.
Presented in part: EUROGIN International Multidisciplinary Congress, Seville, Spain, February 2015.

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The Journal of Infectious Diseases® 2016;213:199–205

DOI: 10.1093/infdis/jiv368

subsidized price in Sweden. Until 2012, vaccination was opportunistic, meaning that individuals had to seek and request vaccination from their primary care physician or a vaccination center [12]. Toward the end of the opportunistic vaccination period, coverage with ≥1 dose was 31.9% among women aged 18–19 years and 24.7% among females aged 13–17 years [13]. In 2012, organized school-based vaccination on a 3-dose schedule began targeting girls aged 10–12 years, with catch-up vaccination of females aged 13–18 years. By 2014, coverage with ≥1 dose was 82.14% for the first cohort of girls in the school-based program and 58.52% for females targeted in the catch-up program [14]. The vaccine price obtained in the tender of the organized program was <20% of the price when the vaccine was first introduced.

The aim of this article is to compare the impact of different HPV vaccination strategies, using real-life input data from Sweden, a high-income country that comprehensively registers data relevant for HPV infection prevention and has experienced vaccine price changes. A particular focus is given to exploring whether extended vaccination strategies would result in an increased resilience of programs.

METHODS

HPV Transmission Model and Study Population

The transmission dynamic model of HPV infection used in the present article has been already described [15, 16]. Briefly, it is a population-based single-type model, which accounts for the presence of males and females susceptible to, infected with, and immune to HPV infection. The model's output was fitted to the age group–specific (range, 15–19 to 40–44 years) prevalence curves of cervical HPV16, HPV18, HPV31, HPV33, HPV45, HPV52, and HPV58 infections (Supplementary Figure 1), which were obtained from a large series of women tested within the Swedish *Chlamydia trachomatis* screening program between March and November 2008 [17]. HPV types were identified using polymerase chain reaction, followed by matrix-assisted laser desorption ionization–time of flight mass spectrometry. Detailed analytical methods have been previously reported [17]. Type-specific HPV infections were modeled separately as independent infections [18–20]. A total of 100 000 sets of parameter values were generated by independently sampling a uniform distribution for each parameter within a prespecified range of values [15]. Each set of values was used to generate a model-based type- and age-specific prevalence curve. Finally, for each HPV type, we calculated the binomial log-likelihood to assess the fit of each model's output to the above-mentioned age-specific prevalence [15, 16]. For the present article, we selected, for each HPV type, the 10 model-generated curves that fitted the observed data best, projected the consequences of introducing different vaccination strategies, and reported the median values across each set of 10 projections as a summary measure of vaccination influence.

Vaccine Efficacy (VE)

We report the impact of vaccination for bivalent and quadrivalent vaccines, with 95% and 92% VE against persistent infection due to HPV16 and HPV18, respectively [21]. VE against HPV16 persistent infection among boys was assumed to be 79% for all vaccines [22]. Owing to the lack of accurate estimates among males, for all other types, VE was assumed to be the same for both sexes. The duration of prophylactic HPV VE against HPV16 and HPV18 is approaching 10 years, but whether cross-protection will be equally long lasting is unclear [21]. Therefore, we did not consider cross-protection in our estimates. In the Supplementary Materials, we report the estimated impact of nonavalent vaccine against HPV16/18/31/33/45/52/58 infection, with 95%, 92%, and 96% VE against HPV16, HPV18, and HPV31/33/45/52/58, respectively [23].

Vaccination Strategies: Base Case and Alternative Options

The base case, strategy 1, represents the current Swedish organized vaccination program initiated in 2012 and serves as the reference strategy when comparing extensions of the program (Figure 1*A*). The current vaccination program targets girls only. Specifically, organized school-based vaccination covers girls aged 11–12 years, with an estimated 2-dose coverage in 2014 of 80.5%, and a catch-up effort aimed at vaccinating females aged 13–18 years achieved a 2-dose coverage of 53.2% in 2014 (which is a slight decrease from ≥1 dose coverage [P. Sparén, personal communication]) [14]. Therefore, strategy 1 was modeled as routine vaccination of 11-year-old girls, with coverage of 80.5% among 12-year-old girls and 53.2% among 13–18-year-old females during the first year. Coverage for a 2-dose schedule was chosen for the model because this is in line with upcoming changes to the Swedish vaccination program and updated guidance from the World Health Organization [24, 25].

We assessed the effectiveness of 3 alternative vaccination options and compared them to that in the base case (Table 1 and Figure 1). In the first alternative option (strategy 2), routine vaccination of school-age girls and catch-up vaccination of females aged 13–18 years was combined with extended 1-time catch-up vaccination of women aged 22–26 years in 2015 (Figure 1*B*). Routine vaccination of school-age boys was added to the routine and extended 1-time catch-up vaccination of females in strategy 3 (Figure 1*C*). Finally, in strategy 4, routine vaccination of school-age boys, as well as 1-time extended catch-up vaccination of males, was added to routine and extended catch-up vaccination of females (Figure 1*D*).

Quantitative Analyses

For each of the 4 simulated vaccination strategies, we present (1) the percentage reduction attributable to vaccination (RAV) in the prevalence of vaccine-specific HPV types among women aged 15–35 years, overall and by birth cohort, relative to the prevalence in the base scenario; (2) the expected HPV16/18

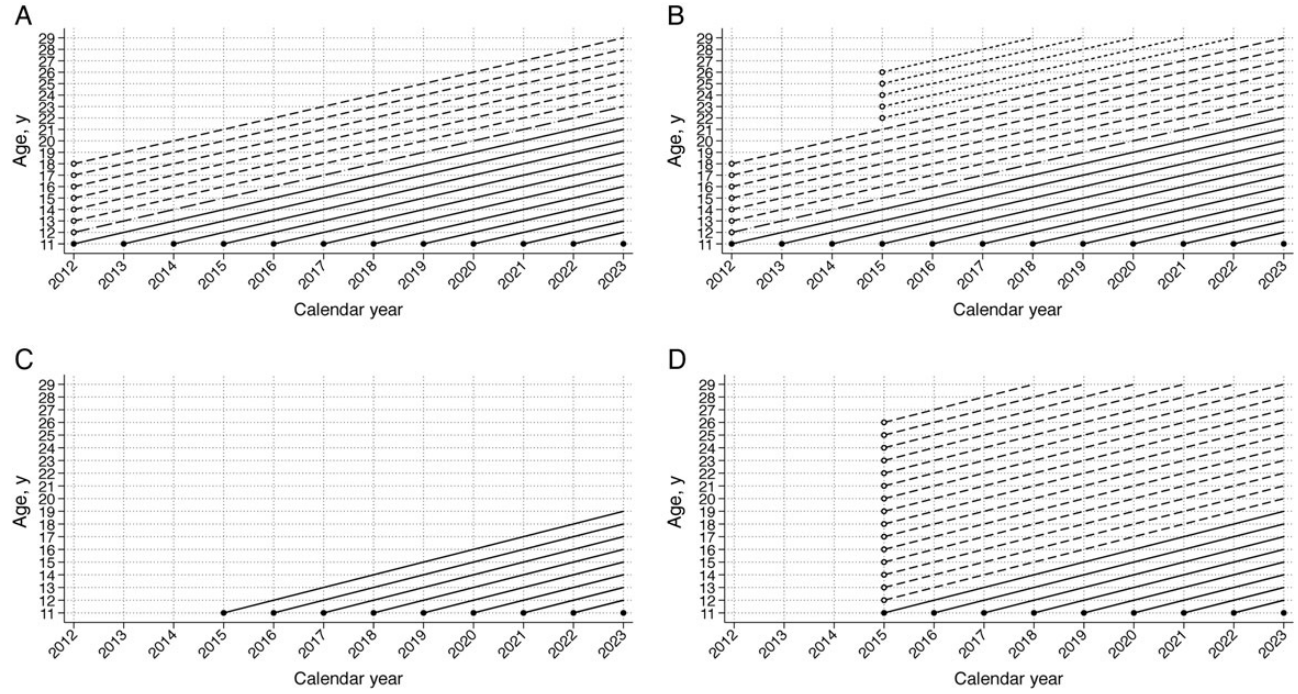

Figure 1. Base case and alternative vaccination strategies, by sex, age and year of vaccination, and birth-cohort immunization status. *A*, Base case among females. Solid lines, routine vaccination program with a 2-dose coverage of 80.50%; dot-dashed line, catch-up vaccination program with a 2-dose coverage of 80.50% (1-time catch-up); dashed lines, catch-up vaccination program with a 2-dose coverage of 53.25% (1-time catch-up); dots, time of vaccination. *B*, Extended catch-up vaccination among females. Solid lines, routine vaccination program with a 2-dose coverage of 80.50%; dot-dashed line, catch-up vaccination with a 2-dose coverage of 80.50% (1-time catch-up); dashed lines, catch-up vaccination program with a 2-dose coverage of 53.25% (1-time catch-up); short dashed lines, extended catch-up vaccination program with a 2-dose coverage of 80.50% (1-time catch-up); dots, time of vaccination. *C*, Routine vaccination among males. Solid lines, routine vaccination program with a 2-dose coverage of 80.50%; dots, time of vaccination. *D*, Routine and extended catch-up vaccination among males. Solid lines, routine vaccination program with a 2-dose coverage of 80.50%; dashed lines, catch-up vaccination program with a 2-dose coverage of 80.50% (1-time catch-up); dots, time of vaccination.

prevalence for each vaccination option and the absolute increase in the reduction of the HPV16/18 prevalence (ie, the percentage RAV difference) among the 3 alternative vaccination strategies as compared to the base case; (3) the relative cumulative number of vaccine doses, compared with the base case, for each alternative vaccination strategy over time since the vaccination program started; and (4) the resilience over time of each vaccination strategy after experiencing a temporary reduction of the vaccination program coverage.

For each vaccination option, resilience was calculated as the difference in percentage RAV estimated with and without temporary coverage reduction. To model a temporary reduction of the coverage within an existing routine vaccination program, we decreased the coverage of routine vaccination by 50% for the 5-year period between 13 and 18 years after the start of the vaccination program (ie, during 2025–2029).

RESULTS

Reduction of HPV Prevalence Attributable to Vaccination

The percentage RAV of the HPV16/18 prevalence, by vaccination strategy, is shown in Figure 2 and can be described as the vaccine effectiveness of each strategy over time. The alternative options involving catch-up vaccination of females only (strategies 2 and 3) speeded up the reduction in prevalence, compared with the base case. By contrast, including extended catch-up vaccination of males (strategy 4), further speeded up the impact of vaccination. The increased effectiveness of alternative options including catch-up vaccination cohorts and males continued 25–30 years after the vaccination program started, but the magnitude of added effectiveness decreased as the strategies converged. For all vaccination strategies, the estimated percentage RAV of HPV16/18 prevalence corresponded to a decrease in the annual age-standardized incidence from the current value of 7.4 cancers/100 000 women [26] to 1.9 cancers/100 000 women, under the assumption that the fraction of cervical cancers attributable to HPV16/18 (ie, 74% [27]) and screening program performance would not change over time. Strategies including extended catch-up vaccination were expected to speed up the cancer incidence reduction attributable to vaccination. Results were similar when evaluating the RAV for nonavalent vaccine types (Supplementary Figure 2).

Absolute Gain in HPV16/18 Prevalence Reduction

The model-based HPV16/18 prevaccination prevalence among women 15–35 years of age was 12% (Supplementary Figure 1).

Table 1. Alternative Human Papillomavirus Vaccination Strategies Explored in This Study

Strategy, Sex	Age Range in Years, Program	Coverage, %[a]	Description
1			
Female	11–12, school based; and 13–18, catch-up	80.50 and 53.25, respectively	Base-case strategy, current practice in Sweden
2			
Female	11–12, school based; 13–18, catch-up; and 22–26, delayed extended catch-up	80.50, 53.25, and 80.50, respectively	Add 1-time delayed extended catch-up of women aged 22–26 y in 2015 with higher coverage, then proceed with routine vaccination of girls only
3			
Female	11–12, school based; 13–18, catch-up, and 22–26, delayed extended catch-up	80.50, 53.25, and 80.50, respectively	Delayed extended catch-up of women, with routine vaccination of boys at same age as girls, starting in 2015
Male	11–12, school based	80.50	
4			
Female	11–12, school based; 13–18, catch-up, and 22–26, delayed extended catch-up	80.50, 53.25, and 80.50, respectively	One-time delayed extended catch-up of boys and women in 2015; continue with routine vaccination of girls and add routine vaccination of boys at the same age as girls, starting in 2015
Male	11–12, school based; and 13–26, delayed extended catch-up	80.50 and 80.50, respectively	

[a] Calculations based on 2-dose completion among girls in the first vaccination cohorts (follow-up through 2014-12-31).

The expected HPV16/18 prevalence for each vaccination option and the absolute gain in percentage RAV of each alternative, compared with the base case, by years after the vaccination program started are reported in Table 2. The largest difference in prevalence (ie, 1.3%) for the options with extended catch-up vaccination of females only (strategies 2 and 3) was observed 10 years after the vaccination program started, while with extended delayed catch-up vaccination of both males and females (strategy 4), the largest difference in prevalence (ie, 2.1%) was observed 15 years after the vaccination program started. Analogously, the absolute gain in percentage RAV of alternative vaccination options, compared with the base case, peaked 10 years after the vaccination program started for the options with extended catch-up vaccination of females only (strategies 2 and 3), whereas with extended delayed catch-up vaccination of both males and females (strategy 4), the gain in percentage RAV peaked 15 years after the vaccination program started. The maximum gain was 10.8% for strategies 2 and 3 and 17.6% for strategy 4. The negligible difference in percentage RAV gain between alternative strategies with and without routine vaccination of boys (strategy 2 and 3 vs strategy 4) indicates that routine vaccination of boys did not contribute to speeding up the impact of vaccination. By contrast, catch-up vaccination of males (strategy 4) could significantly accelerate HPV16/18 infection prevention among females. The gain in nonavalent vaccine type prevalence reduction, compared with the base case, was similar to the results for HPV16/18 (Supplementary Table 1). A cohort analysis of these results showed that the speeding up of vaccination impact was largely attributable to the reduction of HPV prevalence among women 20 and 25 years of age 10 and 15 years after the vaccination program started (Supplementary Tables 2 and 3).

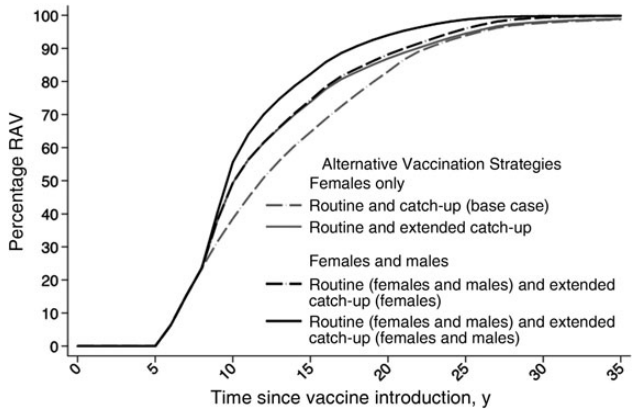

Figure 2. Percentage reduction attributable to vaccination (RAV) of the prevalence of human papillomavirus types 16/18 (HPV16/18) among females aged 15–34 years.

Resilience to Vaccination Coverage Reduction

If coverage were halved during the 5–year period 13–18 years after the vaccination program started, alternative options with routine vaccination of boys and routine vaccination and extended catch-up vaccination of males proved to be 7.2-fold and 12.6-fold more resilient than vaccination of females only (Figure 3*A* and 3*B*, respectively). With female-only routine and extended catch-up vaccination, the effectiveness decreased on average by about 1.42% for 38 years (ie, between 10 and 48 years since coverage reduction), with a peak reduction of about 3.1% 25 years since coverage reduction. In contrast, with routine vaccination of boys and routine and extended catch-up vaccination of males the effectiveness decreased on average by about 0.34% and 0.19% for 22 years (ie, between 10 and 32 years since coverage reduction), respectively, with a peak reduction of about 0.43% and 0.25%, 14 and 19 years since coverage reduction, respectively. To assess the sensitivity of our estimates to the duration of vaccination coverage reduction, we repeated the simulations, assuming a coverage reduction of 2 years; alternative options with routine vaccination of boys and routine and extended catch-up vaccination of males were 6.2-fold and 11.9-fold more resilient than vaccination of females only. The peak reductions of effectiveness were 0.69%, 0.20%, 0.08%, for female only vaccination combined with extended catch-up

Table 2. Human Papillomavirus Types 16/18 Prevalence and Gain in Percentage Reduction Attributable to Vaccination (RAV) Among Alternative Vaccination Strategies, Compared With the Base Case, by Years After Vaccination Program Start

	Strategy 1 (Base Case): Routine and Catch-up (F)		Strategy 2: Routine and Extended Catch-up (F)		Strategy 3: Routine (F and M) and Extended Catch-up (F)		Strategy 4: Routine (F and M) and Extended Catch-up (F and M)	
Years	Prevalence, %	Gain in Percentage RAV	Prevalence, %	Gain in Percentage RAV	Prevalence, %	Gain in Percentage RAV	Prevalence, %	Gain in Percentage RAV
10	7.4	NA	6.1	10.8	6.1	10.8	5.3	17.1
15	4.2	NA	3.1	9.1	3.1	9.7	2.1	17.6
20	2.0	NA	1.6	3.9	1.4	5.1	0.7	11
25	0.7	NA	0.7	0.6	0.5	2.1	0.1	4.8
30	0.3	NA	0.2	0.3	0.1	1.6	0.0	2
35	0.1	NA	0.1	0.2	0.0	1	0.0	1.1

Abbreviations: F, females; M, males; NA, not applicable.

vaccination of women, routine vaccination of boys, and routine and extended catch-up vaccination of males, respectively.

Cumulative Number of Vaccine Doses

Expanding vaccination programs to include additional cohorts and target males as well results in an increased number of vaccine doses used, especially at the start of the program involving extended catch-up vaccination (Table 3). In extended catch-up vaccination of girls (strategy 2), the number of vaccine doses needed in the first 5 years of program was 1.6 times that in the base case (strategy 1). The greatest increase in the number of vaccine doses was found when adding routine and extended catch-up vaccination of males to routine and extended catch-up vaccination of females (strategy 4, 3.5 times the value for the base case strategy in the first 5 years of program). After about 30 years, the ratio of the cumulative number of doses used under each alternative vaccination strategy converged to 1 and 2 times that of the base case strategy for options without and those with routine vaccination of boys (strategies 2 and 3), respectively. By contrast, school-based and extended vaccination of both sexes (strategy 4) required at least 50 years to converge to 2 times the number of vaccine doses needed, compared with the base case (Table 3).

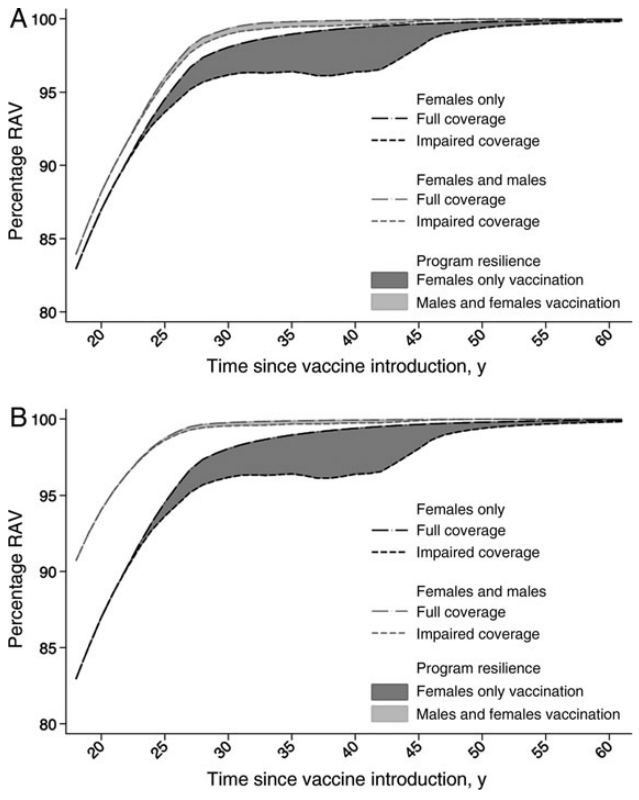

Figure 3. Resilience of vaccination strategies to a 5-year period of impaired coverage. *A*, Routine and extended catch-up vaccination among females, with routine vaccination among males. *B*, Routine and extended catch-up vaccination among males and females. Abbreviation; RAV, reduction attributable to vaccination.

DISCUSSION

Our results show that alternative vaccination strategies based on an intensive catch-up vaccination of individuals up to 26 years of age are effective for accelerating the decrease in the burden of vaccine-preventable HPV cervical infections in women, compared with the current vaccination program efforts. There was

Table 3. Ratio of Cumulative Number of Doses of Vaccine Among Alternative Vaccination Strategies, Compared With the Base Case, by Years After Vaccination Program Start

Years	Strategy 2: Routine and Extended Catch-up (F), Ratio	Strategy 3: Routine (F and M) and Extended Catch-up (F), Ratio	Strategy 4: Routine (F and M) and Extended Catch-up (F and M), Ratio
5	1.6	1.9	3.5
25	1.2	2.0	2.5
45	1.1	2.0	2.3

The base case involves routine and catch-up vaccination of females.

Abbreviations: F, females; M, males.

also clear evidence that increased resilience of vaccination programs would occur with the inclusion of males in the programs. Specifically, the addition of routine vaccination of 11-year-old boys would protect against a loss of effectiveness resulting from temporary coverage reduction. Such loss of effectiveness would take >2 decades to recover from in the absence of male vaccination.

Despite geographical heterogeneity across counties [14], the overall coverage of HPV vaccination in the first cohort of girls in the school-based program was >80%. According to our model, such coverage, combined with the very high VE of bivalent/quadrivalent and nonavalent vaccines, if maintained indefinitely, would approach elimination of HPV types targeted by vaccines. The proposed alternative vaccination strategies would reach elimination faster than the existing base case strategy, and more-intensive coverage of both sexes would result in earlier achievement of the elimination target. However, for elimination to become a realistic option, the vaccine-induced immune protection should last for most of the period during which an individual is sexually active, and there should not be subgroups of the population poorly covered by vaccination, such as immigrants or men having sex with men, that could act as infection reservoirs [28].

The alternative vaccination option envisaging routine coverage of boys (ie, strategy 3) would double the cumulative number of doses of vaccine required, compared with the base case vaccination option. The options envisaging intensive catch-up vaccination of young adults (ie, strategies 2 and 4) would require a larger initial number of doses of vaccine, and, 5 years after the vaccination program started, the ratio of the cumulative number of doses would be 1.6 and 3.5 for catch-up vaccination of young females and males, respectively. On the other hand, vaccination of both sexes also makes HPV infection prevention in females more resilient to temporary drops in vaccination coverage (Figure 3). For simplicity, in the present study we simulated a 50% drop in coverage for 5 years, between 13 and 18 years after the vaccination program started, which is when most of the anticipated effect of catch-up vaccination had already occurred and the RAV was >90%. Therefore, according to our model, the decline in RAV mainly delayed HPV elimination. As expected, a drop in coverage for a shorter interval (ie, 2 years) was associated with a smaller absolute reduction of effectiveness. However, when an earlier and complete interruption of vaccination for 5 years was simulated, a more substantial decrease in vaccine effectiveness was observed in a strategy of girls-only vaccination, while sex-neutral vaccination significantly mitigated the negative effects of this temporary interruption of vaccination (data not shown).

The current Swedish national vaccination program was designed using the results of a mathematical model with input data on HPV seroprevalence and sexual behavior data from Sweden [29, 30]. Despite structural differences, the results of the current model and the results of the previously published model are comparable, and their estimated overall long-term effectiveness options are consistent (ie, 99% vs 96% for girls-only vaccination and 99% vs 99% for sex-neutral vaccination for the current and previous models, respectively). Similarly, according to both models, catch-up vaccination of females in the previous study and of females and males in the present study accelerated the overall impact of vaccination by a few years. The consistency between the projections of the 2 models supports the robustness of our approach to use a mathematical model as a tool to plan the scaling up of an existing national vaccination program. Our projections are also reasonably consistent with recent data from the Swedish *C. trachomatis* screening study, which suggest that, among 13–22-year-old females, the percentage RAV of HPV16/18 prevalence was approximately 43% five years after vaccination introduction [31]. Our model predicted that a similar percentage RAV would occur in the same age group within about 7 years after vaccination introduction (data not shown). The discrepancy between model- and data-based estimates may be attributable to earlier sexual debut among adolescents, compared with the time of debut assumed in the transmission model.

Our study has strengths and limitations. We mainly focused on viral end points, because they represent the earliest and most relevant end points for HPV vaccination programs and the accuracy of model-based projections. For bivalent/quadrivalent vaccine types, we concentrated on HPV16/18 infections, as information about natural history and vaccine cross-protection against other high-risk HPV types is still limited and heterogeneous [21, 32]. Restriction to HPV infections up to the age of 35 years minimizes the potential impact of different cervical screening practices on the interpretation of our findings [33].

Owing to the rapidly changing dosage schedules and declining prices of HPV vaccination, we chose not to study the monetary costs of purchasing and delivering HPV vaccines [34]. Instead, we calculated the ratio of the cumulative number of doses of vaccine for each alternative vaccination strategy versus the number for the base case; this approach is uniquely based on demographic projections [35]. Our study only included estimates of vaccination benefit in females, although the reduction in incidence of HPV infection and HPV-associated cancers in males is an additional benefit of vaccination [36, 37]. However, much fewer studies have addressed the natural history of HPV infections among males than females [38], and existing data are still insufficient to accurately calibrate a dynamic model that will allow reliable projections for males. However, the contribution of HPV to other cancer types and, in particular, the potential for the vaccines to prevent HPV-related cancer of the oropharynx and anus in males (especially men having sex with men) may add value to sex-neutral vaccination [22]. Finally, vaccination of both sexes would be more equitable and less discriminatory [1, 2].

In conclusion, expanding the catch-up vaccination cohorts accelerates the relative reduction in HPV prevalence among women. If vaccination coverage is high, 25–30 years after

vaccination commences, the effectiveness converges. The most salient impact of male vaccination is the mitigation of loss of vaccine effectiveness in the face of an unexpected reduction in coverage. The resilience to temporary changes in vaccination coverage of strategies that include male vaccination is likely to be crucial to the safe adoption of HPV-based cancer prevention programs with robust long-term effectiveness. Ensuring a resilient program will be most important in settings where funding, public opinion, and health priorities are changeable.

Supplementary Data

Supplementary materials are available at http://jid.oxfordjournals.org. Consisting of data provided by the author to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes

Acknowledgments. We thank Pär Sparén, for providing real-time vaccination coverage data and for ongoing discussions regarding the Swedish vaccination program; Raul Murillo (International Agency for Research on Cancer), for information regarding HPV vaccination coverage in Colombia; and Prof Bo Lewin (Department of Sociology, Uppsala University), for data from the Sex in Sweden survey.

K. M. E. collected and prepared the data, wrote a draft of the manuscript, and provided advice on the analysis. F. L. further developed the model machinery and ran the model with Swedish data. S. F. provided advice on the analyses and conceptualization of the project. J. D. conceptualized the study (along with I. B.) and oversaw the analyses and writing. I. B. performed the analyses, prepared the figures and tables, edited the manuscript, and oversaw the project. All authors have seen and approved the content and have contributed significantly to the work.

Disclaimer. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Financial support. This work was supported by the European Community's Seventh Framework program FP7/2007–2013 (grant 603019 [CoheaHr]), Bill and Melinda Gates Foundation (grant OPP1053353) and the Swedish Foundation for Strategic Research.

Potential conflicts of interest. J. D.'s institution has received grants from Merck/SPMSD for other studies on HPV vaccines. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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