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Strong Herd Effects of Human Papillomavirus Vaccination

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Substantial health benefits of human papillomavirus (HPV) vaccination have been observed in many settings around the world and are due to both high direct and indirect vaccine effects.^{1–3} HPV vaccines have high efficacy for those vaccinated and vaccinated persons provide indirect protection to those who remain susceptible to infection, through reductions in exposure to HPV.^{4,5} Indirect protection provided by vaccination has been observed for many vaccines and is referred to as “herd immunity,” “herd protection,” or “herd effects.”^{6–8} Although these terms are frequently used interchangeably, the term “herd immunity” often has a specific meaning: a threshold of immunity in the population that provides complete protection against sustained transmission.^{6–8} Terms like “herd protection” and “herd effects” have been used to refer to the indirect effects of vaccination without a complete cessation of transmission. For example, HPV vaccination with 20% coverage can achieve some degree of herd effects (e.g., reductions in HPV prevalence in unvaccinated persons),⁴ although this level of vaccination coverage is not enough to achieve full herd immunity in which there is no sustained transmission in the population.

Mathematical modeling studies of HPV vaccination worldwide have consistently predicted that vaccination will result in substantial herd effects.⁹ For example, a 2011 modeling study projected that a female-only HPV vaccination program with moderate to high vaccination coverage (e.g., $\geq 50\%$) of 12-year-old girls would result in substantial reductions in prevalence of HPV vaccine types in males within the first 10–15 years of the vaccination program.¹⁰ Since HPV vaccination programs were first introduced almost 20 years ago, studies in real-world settings have demonstrated herd effects of HPV vaccination in numerous countries and for different HPV-attributable outcomes.^{2,4} Mathematical modeling studies have also explored vaccine coverage needed for herd immunity and predict that

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these coverage levels likely differ by HPV type, since HPV types vary in prevalence, transmissibility, and duration of infection; however, at 80% coverage in a program vaccinating both boys and girls, models predicted possible elimination of HPV vaccine types.^{9,11,12}

One of the first studies to show strong herd effects of HPV vaccination was conducted by Ali et al. (2013) in Australia, a country that quickly achieved high vaccination coverage of girls in the routine vaccination age group (12–13 years) and also catch-up vaccination of girls and women through age 26 years.⁵ Ali et al. (2013) documented large declines in genital wart diagnosis rates in unvaccinated young heterosexual men in Australia just five years after introduction of the female-only vaccination program.⁵ A subsequent meta-analysis reported similar findings, with declines of more than 50% in genital wart diagnosis rates in males aged 15–24 years, compared to the pre-vaccination era, in countries with catch-up vaccination of females and vaccination coverage of at least 50%.² A more recent study from Denmark, conducted 10 years after implementation of a female-only HPV vaccination program, found no infection with quadrivalent HPV vaccine types among unvaccinated men aged 18–20 years who had ever had sex, suggesting strong herd effects of the female-only quadrivalent HPV vaccine program for 12-year-olds instituted in 2009 with subsequent catch-up campaigns through age 27 years.¹³

Other herd effects of HPV vaccination also have been demonstrated. For example, within six years of the initiation of Australia's HPV vaccination program, substantial reductions in the prevalence of the quadrivalent HPV vaccine types (6/11/16/18) were observed among unvaccinated women aged 18–24 years attending cervical cancer screening.¹⁴ In the United States, data from the National Health and Nutrition Examination Survey (NHANES) have demonstrated decreases in prevalence of HPV vaccine types consistent with herd effects.^{15,16} Overall decreases in prevalence of quadrivalent HPV vaccine types among women cannot be explained solely by direct effects at observed vaccination coverage levels.¹⁷ Among sexually active females aged 14–26 years, in 2011–2014 compared to the pre-vaccine era, prevalence of quadrivalent HPV vaccine types decreased by 89% among those vaccinated and 34% among those unvaccinated.¹⁶ In another study from the United States, data from a 5-site, population-based surveillance system showed decreases in HPV 16 and HPV 18 positivity in cervical precancer tissue specimens among unvaccinated women in 2014 compared to 2008.¹⁸

Herd effects can influence the potential health impact and cost-effectiveness of changes to HPV vaccination strategies. For example, the cost-effectiveness of expanding an existing female-only vaccination program to include males becomes less favorable as the degree of herd effects achieved by the existing female-only vaccination program increases.¹⁰ Similarly, the cost-effectiveness of expanding the existing U.S. HPV vaccination program for males and females aged 12–26 years to include mid-adults aged 27–45 years depends in part on the degree of herd effects of the existing program.¹⁹

Real-world data showing herd effects of HPV vaccination are important not only to demonstrate vaccine impact, but also to inform mathematical models of HPV transmission, which are useful, if not vital, for considerations of HPV vaccine recommendations.

Documentation of herd effects can be used for model validation, which involves the comparison of model projections against independent data sets.²⁰ HPV models have been validated by showing that the model projections for a female-only vaccination program closely match the observed declines in prevalence of HPV vaccine types in males in Quebec²¹ and in anogenital warts diagnoses in males in Australia.²² Documentation of herd effects can also be used for model calibration, which involves the fitting of model projections to observed data.²⁰ For example, if a model predicts unrealistically small or large herd effects of HPV vaccination, the model's parameters can be adjusted accordingly to increase the robustness of the model to inform future vaccination recommendations.²²

In the current issue of *The Journal of Infectious Diseases*, Wolfe and colleagues provide evidence of herd effects and, in fact, herd immunity from HPV vaccination in Quebec. Specifically, in a convenience sample of 369 unvaccinated men aged 16–20 years, only two infections with quadrivalent HPV vaccine types were detected, both of which occurred in men with male sex partners. The only apparent explanation for the low prevalence of quadrivalent HPV types (0.5%) in unvaccinated men in 2020–2022 is herd effects following onset of quadrivalent HPV vaccination of girls in 2008 with a transition to a mixed schedule (nonavalent + bivalent) for girls and boys in 2018. Unlike the studies of HPV prevalence in Australia and Denmark,^{13,14} the Wolfe study did not include a comparison of HPV prevalence in unvaccinated men in the vaccination era to that of an otherwise similar group of men in the pre-vaccination era. However, a high prevalence of quadrivalent HPV types in men in the pre-vaccination era had been established worldwide and in Canadian settings specifically.²³ Thus, it would have been unlikely in the pre-vaccination era to find prevalence of quadrivalent HPV vaccine types as low as 0.5% in a convenience sample of 369 young Canadian men with a median number of 3 lifetime sex partners.

Men who have sex with men (MSM) do not benefit from herd effects of female-only HPV vaccination programs to the same extent as men who have sex with women only.^{24,25} Thus, it was not surprising that MSM accounted for the only two infections with quadrivalent HPV vaccine types in the Wolfe study. Still, prevalence of quadrivalent HPV vaccine types was low (2/60, or 3.3%) among MSM, suggesting the possibility of a limited benefit of herd effects in this group. However, the small number of MSM in this study makes it difficult to draw any conclusions about possible herd effects among MSM.

The Wolfe study enhances the evidence base for strong herd effects of HPV vaccination. This study, along with other recent studies in this journal,^{13,26} contributes to the monitoring of HPV vaccine impact and can inform future HPV vaccination recommendations and cervical cancer screening strategies. The documentation of herd protection and evidence regarding herd immunity, as predicted by mathematical modeling studies, demonstrates the robustness of mathematical modeling studies that have been used to inform HPV vaccination strategies in Canada and around the world. The Wolfe study contributes to an extensive body of research which has demonstrated direct and indirect effects of HPV vaccination globally across multiple settings, which differ in program structure (e.g., female-only or sex-neutral vaccination), the vaccine offered (bivalent, quadrivalent, nonavalent), and HPV vaccination coverage.

Prior to introduction of HPV vaccination, expert opinion and mathematical models indicated that there would be declines in prevalence of HPV vaccine types, genital warts, and cervical precancers in younger age groups within the first years of HPV vaccination, followed by declines in HPV-associated cancers several decades later.²⁷ Thus far, studies of HPV vaccine impact from around the world have corroborated these predictions, with evidence of declines in HPV prevalence, anogenital warts, and cervical precancers.² Further, in settings with moderate to high vaccination coverage, benefits have been observed among unvaccinated groups, thereby corroborating model-based projections of herd protection.² We are now in the initial years of the predicted declines in HPV-associated cancers,^{28,29} and it is anticipated that there will be dramatic decreases in cervical, anal, vaginal, vulvar, and penile cancers in the upcoming decades.

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References

1. Garland SM, Kjaer SK, Muñoz N, et al. Impact and effectiveness of the quadrivalent human papillomavirus vaccine: a systematic review of 10 years of real-world experience. *Clin Infect Dis* 2016;63(4):519–27. [PubMed: 27230391]
2. Drolet M, Bénard É, Pérez N, Brisson M. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. *Lancet* 2019;394(10197):497–509. [PubMed: 31255301]
3. Spinner C, Ding L, Bernstein DI, et al. Human papillomavirus vaccine effectiveness and herd protection in young women. *Pediatrics* 2019;143(2):e20181902. [PubMed: 30670582]
4. Malagón T, Laurie C, Franco EL. Human papillomavirus vaccination and the role of herd effects in future cancer control planning: a review. *Expert Rev Vaccines* 2018;17(5):395–409. [PubMed: 29715059]
5. Ali H, Donovan B, Wand H, et al. Genital warts in young Australians five years into national human papillomavirus vaccination programme: national surveillance data. *BMJ* 2013;346:f2032. [PubMed: 23599298]
6. Fine P, Eames K, Heymann DL. “Herd immunity”: a rough guide. *Clin Infect Dis* 2011;52(7):911–6. [PubMed: 21427399]
7. Pollard AJ, Bijker EM. A guide to vaccinology: from basic principles to new developments. *Nat Rev Immunol* 2021;21(2):83–100. [PubMed: 33353987]
8. Scarbrough Lefebvre CD, Terlinden A, Standaert B. Dissecting the indirect effects caused by vaccines into the basic elements. *Hum Vaccin Immunother* 2015;11(9):2142–57. [PubMed: 26186100]
9. Brisson M, Bénard É, Drolet M, et al. Population-level impact, herd immunity, and elimination after human papillomavirus vaccination: a systematic review and meta-analysis of predictions from transmission-dynamic models. *Lancet Public Health* 2016;1(1):e8–e17. [PubMed: 29253379]
10. Brisson M, van de Velde N, Franco EL, Drolet M, Boily MC. Incremental impact of adding boys to current human papillomavirus vaccination programs: role of herd immunity. *J Infect Dis* 2011;204(3):372–6. [PubMed: 21742835]
11. Brisson M, Van de Velde N, Boily MC. Different population-level vaccination effectiveness for HPV types 16, 18, 6 and 11. *Sex Transm Infect* 2011;87(1):41–3. [PubMed: 20924049]
12. Baussano I, Lazzarato F, Ronco G, Lehtinen M, Dillner J, Franceschi S. Different Challenges in Eliminating HPV16 Compared to Other Types: A Modeling Study. *J Infect Dis* 2017;216(3):336–344. [PubMed: 28859431]

13. Munk C, Reinholdt K, Kjaer AK, et al. Prevalence of human papillomavirus (HPV) and HPV type distribution in penile samples in young men in Denmark: results 10 years after implementation of a girls-only HPV vaccination program. *J Infect Dis*. 2024;230(4):949–956 [PubMed: 38470214]
14. Tabrizi SN, Brotherton JM, Kaldor JM, et al. Assessment of herd immunity and cross-protection after a human papillomavirus vaccination programme in Australia: a repeat cross-sectional study. *Lancet Infect Dis* 2014;14(10):958–66. [PubMed: 25107680]
15. Rosenblum HG, Lewis RM, Gargano JW, Querec TD, Unger ER, Markowitz LE. Declines in prevalence of human papillomavirus vaccine-type infection among females after introduction of vaccine - United States, 2003–2018. *MMWR Morb Mortal Wkly Rep* 2021;70(12):415–420. [PubMed: 33764964]
16. Oliver SE, Unger ER, Lewis R, et al. Prevalence of human papillomavirus among females after vaccine introduction-National Health and Nutrition Examination Survey, United States, 2003–2014. *J Infect Dis* 2017;216(5):594–603. [PubMed: 28931217]
17. Markowitz LE, Hariri S, Lin C, et al. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003–2010. *J Infect Dis* 2013;208(3):385–93. [PubMed: 23785124]
18. McClung NM, Gargano JW, Bennett NM, et al. Trends in human papillomavirus vaccine types 16 and 18 in cervical precancers, 2008–2014. *Cancer Epidemiol Biomarkers Prev* 2019;28(3):602–609. [PubMed: 30792242]
19. Laprise JF, Chesson HW, Markowitz LE, Drolet M, Brisson M. Cost-effectiveness of extending human papillomavirus vaccination to population subgroups older than 26 years who are at higher risk for human papillomavirus infection in the United States. *Ann Intern Med* 2025;178(1):50–8. [PubMed: 39586101]
20. Vynnycky E, White RG. *An Introduction to Infectious Disease Modelling*. Oxford University Press; 2010:370.
21. Drolet M, Laprise JF, Chamberland É, et al. Switching from a 2-dose to a 1-dose program of gender-neutral routine vaccination against human papillomavirus in Canada: a mathematical modelling analysis. *CMAJ* 2024;196(33):E1136–e1143. [PubMed: 39374971]
22. Drolet M, Laprise JF, Brotherton JML, et al. The impact of human papillomavirus catch-up vaccination in Australia: implications for introduction of multiple age cohort vaccination and postvaccination data interpretation. *J Infect Dis* 2017;216(10):1205–1209. [PubMed: 28968800]
23. Bruni L, Albero G, Rowley J, et al. Global and regional estimates of genital human papillomavirus prevalence among men: a systematic review and meta-analysis. *Lancet Glob Health* 2023;11(9):e1345–e1362. [PubMed: 37591583]
24. Donovan B, Franklin N, Guy R, et al. Quadrivalent human papillomavirus vaccination and trends in genital warts in Australia: analysis of national sentinel surveillance data. *Lancet Infect Dis* 2011;11(1):39–44. [PubMed: 21067976]
25. Chow EPF, Machalek DA, Tabrizi SN, et al. Quadrivalent vaccine-targeted human papillomavirus genotypes in heterosexual men after the Australian female human papillomavirus vaccination programme: a retrospective observational study. *Lancet Infect Dis* 2017;17(1):68–77. [PubMed: 27282422]
26. Gray P, Wang J, Kleppe SN, Elfström KM, Dillner J. Population-based age-period-cohort analysis of declining human papillomavirus prevalence. *J Infect Dis* 2025, published online ahead of print.
27. Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER. Quadrivalent human papillomavirus vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2007;56(RR-2):1–24.
28. Kjaer SK, Dehlendorff C, Belmonte F, Baandrup L. Real-world effectiveness of human papillomavirus vaccination against cervical cancer. *J Natl Cancer Inst* 2021;113(10):1329–1335. [PubMed: 33876216]
29. Palmer TJ, Kavanagh K, Cuschieri K, et al. Invasive cervical cancer incidence following bivalent human papillomavirus vaccination: a population-based observational study of age at immunization, dose, and deprivation. *J Natl Cancer Inst* 2024;116(6):857–865. [PubMed: 38247547]