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EDITORIALS

The remarkable impact of bivalent HPV vaccine in Scotland

New analyses show substantial cross protection and herd immunity

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It was initially believed that prophylactic human papillomavirus (HPV) vaccines were probably type specific and provided protection only against infection with, and disease due to, the types of HPV the vaccines were targeted against. Given the predominance of the two most oncogenic HPV types (16 and 18) across all HPV related cancers, the two first generation vaccines (a bivalent vaccine targeting types 16 and 18 and a quadrivalent vaccine targeting types 6, 11, 16, and 18) offered important potential for meaningful cancer prevention even with no cross protection.[1]

Initial findings from the bivalent HPV vaccine trial, suggesting substantial cross protection against HPV types related to 16 and 18, were therefore met with some scepticism.[2,3] In a linked paper, Palmer and colleagues (doi:10.1136/bmj.l1161) report findings from Scotland, where the combination of high coverage with bivalent HPV vaccine, young age of screening initiation, and high quality individual level data across the population, unequivocally show high vaccine effectiveness in young women against high grade cervical disease regardless of causal HPV type.[4]

The authors used the vaccination and screening records of nine sequential birth cohorts of 20 year old women in Scotland: 20 was the age of invitation to first cervical screening until mid-2016, when the starting age was raised to 25 years. The study includes all screens taken at age 20 between 2008 and 2016, during which time women screened included unvaccinated women (2008-10), women eligible for catch-up vaccination at ages 14-17 (2011-14), and women routinely vaccinated at ages 12-13 (2015-16).

Although Scotland changed to the quadrivalent vaccine in September 2012, the vaccinated women in the study all received the bivalent vaccine. The authors identified cervical disease using both cytology and histopathology outcomes and conducted two analyses: one comparing disease rates in vaccinated cohorts with pre-vaccine cohorts, and a second comparing vaccinated and unvaccinated women within each birth cohort. Estimates of vaccine effectiveness were adjusted for deprivation and rurality—both important predictors of cervical disease in Scotland.

The findings are dramatic and document a considerable reduction in high grade cervical disease over time. The authors estimate a vaccine effectiveness of 86% (95% confidence interval 75% to 92%) for the most severe outcome of cervical intraepithelial neoplasia (CIN) grade 3 or worse in women fully vaccinated at ages 12-13 compared with the unvaccinated cohort. Notably, they report a large reduction in CIN grade 3 or worse in the most recent cohort of women compared with the pre-vaccination cohort, whether they were vaccinated or not (from a rate of 0.59% to 0.06%, an 89% decline), suggesting that interruption of HPV transmission in Scotland has created substantial herd protection.

Although HPV types 16 and 18 are known to predominate in cervical lesions among young women,[5] a reduction of over 85% against CIN grade 3 or worse caused by all HPV types clearly indicates that the cross protection documented previously in Scotland against related HPV types 31, 33, and 45[6] is translating directly into disease prevention.

This study also highlights the value of integrated registries that can systematically collect and use high quality data from screening and vaccination programmes. In its prepublication review of the paper, Jo's Trust, a cervical cancer charity, also emphasised the importance of information technology infrastructure to optimise programmes. All countries must now consider how they can best implement and evaluate vaccination, screening, and treatment programmes that support the World Health Organization's call for elimination of cervical cancer as a public health problem.[7] Scotland has shown that integrated registry systems are highly effective tools in achieving and evaluating high vaccine uptake,[8] and in assessing subsequent outcomes,[4] including screening performance.[9]

As we manage the current supply problems (including shortages) with HPV vaccines,[10] and consider whether the nonavalent HPV vaccine (which protects against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58) [11] will ever be affordable for low income countries, these new data highlight that the bivalent HPV vaccine is still a good choice for cancer prevention and that, in countries such as Scotland, might even provide protection equivalent to the nonavalent vaccine.

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We must not forget, however, the girls who were not vaccinated and the women who do not currently screen. We must work towards a world in which all girls and their families are offered, and the majority accept, HPV vaccination, wherever they live. We must also actively develop, resource, and scale-up more effective, feasible, and culturally acceptable strategies for cervical screening, such as self collection of specimens,[12] if we are ever to effectively reduce the global burden of cervical cancer.

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