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GYNAECOLOGICAL CANCER

HPV vaccine: is age just a number?

Two recent studies have reported on the safety, efficacy and performance of vaccination against human papillomavirus (HPV) in protecting women against cervical cancer.

The first study, conducted in Scotland, comprised a national immunization programme against HPV types 16 and 18 running between 2008 and 2011 and reaching girls up to the age of 18 years. Pollock *et al*. examined the effect this programme had on the incidence of low-grade and high-grade cervical abnormalities, comparing colposcopy data from a cohort of vaccinated and unvaccinated women who entered the Scottish Cervical Screening Programme.

The data showed that three doses of the bivalent vaccine decreased the incidence of virally-induced cervical intraepithelial neoplasia (CIN). Detection of CIN grades 1, 2 and 3 was significantly ($P \leq 0.0001$) reduced (29%, 50% and 55%, respectively) in individuals who received three doses of vaccine, compared with those who were unvaccinated—though only receiving two doses of the vaccine did not significantly reduce incidence of any CIN grade on statistical analysis.

"Our main finding is the 55% reduction in CIN 3 (high-grade abnormalities) associated with high uptake of the vaccine," states Kevin Pollock, lead author of the study. "However, the 29% reduction in low-grade CIN is surprising at this stage. We will follow up each annual cohort of women and in April 2016 the first cohort of young girls will be screened in Scotland, which should show the true impact of vaccination."

In a separate study published in *The Lancet*, Skinner and colleagues report on the efficacy, safety and immunogenicity of the HPV 16/18 AS04-adjuvanted vaccine in women aged >25 years, in an interim update on the VIVIANE phase III trial. Enrolment was stratified by age: 26–35 years and 36–45 years (together comprising ~90% of the cohort) and ≥46 years. Up to 15% of women in each stratum had a history of HPV infection.

Vaccination showed significant efficacy across all age groups at the combined primary end point of vaccine efficacy against 6-month persistent infection with HPV types 16 or 18, or CIN grade ≥1 associated with HPV types 16 or 18. Significant efficacy was also observed against atypical squamous cells of undetermined significance associated with HPV types 16 or 18 in all cohorts. Vaccination also conferred significant protection against HPV types 31 and 45.

The results presented in this study provide support for the argument that vaccinating women beyond the age of 25 years could provide benefit in a clinical setting. "Women over 25 years continue to be exposed to infection with HPV 16, 18 and other cancer-causing types, albeit at a lower rate than in younger women. A small percentage of these infections may persist over time, increasing the risk of high-grade cervical precancer, and eventually cancer," says study lead, Rachel Skinner. Accordingly, older women, who are not typically included in vaccination schemes, might benefit from vaccination.

Skinner continues, "we were also surprised to see evidence of protection against persistent HPV 16 and 18 infection in our entire study sample, which included women who had evidence of prior exposure to these HPV types. The proportion of women in our sample with previous HPV exposure was comparatively high, as we included a subset of women who had has a history of HPV infection or disease." That is, the vaccine could benefit women outside of a clinical trial.

These studies indicate that vaccination against HPV types 16 and 18 can greatly reduce a woman's risk of HPV infection and, ultimately, cervical cancer. That older women and not just adolescents can benefit raises the question of whether national immunization schemes require modification.

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Original articles Pollock, K. G. *et al*. Reduction of low- and high-grade cervical abnormalities associated with high uptake of the HPV bivalent vaccine in Scotland. *Br. J. Cancer* doi:10.1038/bjc.2014.479 | Skinner, S. R. *et al*. Efficacy, safety, and immunogenicity of the human papillomavirus 16/18 AS04-adjuvanted vaccine in women older than 25 years: 4-year interim follow-up of the phase 3, double-blind, randomised controlled VIVIANE study. *Lancet* doi:10.1016/S0140-6736(14)60920-X