

Editorial



A significant measure of HPV vaccine effectiveness in a high-risk population in Korea prior to a National Immunization Program

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Conflict of Interest

No potential conflict of interest relevant to this
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We learn from the paper by Seong et al. [1] that cervical cancer in young women 15 to 34 years of age in the Republic of Korea in 2015 was the third most common cancer of women [2]. Korea has adopted a national human papillomavirus (HPV) immunization program to vaccinate young girls 12 years of age (choice of bivalent or quadrivalent), at no cost to the individuals, through designated clinics and health centers and this commenced in 2016. Prior to then, both HPV vaccines were available, but very much opportunistically and at a woman's personal cost, not being reimbursable.

In adopting a new vaccination program, it is important for a multitude of reasons but particularly the investment a government has made, to measure the outcomes of such a program. To do so requires comprehensive surveillance which gives an evaluation of the real-world effects of vaccination [3]. It includes measuring vaccine coverage, vaccine acceptance, potential adverse outcomes, vaccine impact (studies which compare infection or disease in pre- and post-vaccination periods) and vaccine effectiveness (estimated by comparing prevalence or incidence of outcome measures in vaccinated versus unvaccinated individuals within similar populations and time periods). Outcomes to assess include vaccine-targeted HPV genoprevalence of HPV infection (as measured by DNA/RNA detection), vaccine-targeted HPV related diseases (including genital warts, cervical intraepithelial neoplasia (CIN) 2+ or preferably CIN3+, cervical cancers), require HPV vaccine registers (including type of vaccine, doses, intervals, age given, etc.) and cervical cancer and other HPV-related cancer registers. Various countries adopt different strategies depending on registries in existence and their sophistication and ability to interact at an information technology level.

As there is no register for HPV vaccination in Korea, this research group utilized a surrogate for this in studying a previously recruited cohort of women from a multi-center study from in five general hospitals' obstetric departments of women who were at high risk for HPV: they were all HPV DNA positive and had ASCUS or low-grade squamous intraepithelial lesion (LSIL) on a Pap test and being followed 6 monthly for five years by cytology, questionnaire and HPV DNA to measure the determinants of high-grade squamous intraepithelial lesion (CIN2+) [4].

From 1,300 women 20–60 years of age with an HPV vaccine history, (self-reported or noted from chart review) and who were infected with HPV (as defined by HPV DNA detection and genotyping using DNA micro array technology) 4, 25.8% were vaccinated (women had a choice of the quadrivalent vaccine or the bivalent vaccine: the breakdown of the uptake being 68% and 32% respectively). The researchers utilized the epidemiological characteristics and prevalence of HPV 16/18 between the vaccinated and unvaccinated. It is noteworthy that of those vaccinated, they were more likely to be younger and in their 20s and 30s (vaccinated in their 20s 54%, 30s 36% respectively), more likely to be single, with a higher education, and whilst most had completed the recommended 3 dose course (63%, 16% two doses and 20% one dose), were more likely to be sexually active at vaccination. Whilst 28.5% of those not sexually active had been vaccinated, this steadily climbed with increasing partner numbers, to 75% for those with 4 or more partners. Although mid-adult women vaccine trials show that vaccination for those sexually active are efficacious, for those vaccine-targeted genotypes with which they are already infected, the vaccines are not. Clearly being vaccinated after sexual debut has less impact than vaccination beforehand. The primary target for these prophylactic vaccines is to vaccinate early and the move to the National Immunization Program by Korea from 2016 targeting 12-year-old is to be commended [5]. It is pleasing to see the coverage thus far is excellent at 68% vaccination rate in 2016 (personal communication: Prof Miseon Kim, Seoul).

The most exciting finding in this paper is that the researchers took account of the buffer period in their evaluation of potential impact of vaccination. That is, they reviewed the prevalence of HPV 16, 18 in those vaccinated at less than, as well as greater than 12 months prior to the cytological abnormality of ASCUS/LSIL. Having a buffer period between the vaccination and the measure of HPV genoprevalence allows for “a washout period” from any potential bias from prevalent infection.

Their findings of 11% for HPV 16/18 prevalence in the vaccinated (greater than 12 months beforehand) as compared to 17% in the unvaccinated was statistically significant, thus showing a positive impact of vaccination in these women.

It would have been great to see more detail in the ages at which women were vaccinated relative to their abnormal cytology, but this was not available in the paper. Perhaps given the longitudinal nature of the follow-up of these women, more sensitivity analyses can be performed in the period between vaccination and development of abnormal cytology.

In essence, this study provides some surveillance on the effectiveness of the HPV vaccination program in Korea, in a high-risk population. With the call to action by the Director General of World Health Organization, for elimination of cervical cancer as a public health matter, we look forward to seeing an evaluation of the national HPV vaccination program that has commenced in Korea, 2016 [6]. Cervical screening in Korea is Pap cytology based, every 2 to 3 years starting from 20 to 74 years of age: the national program started in 2016 and with a participation rate of just over 50%. Ultimately should Korea move to HPV DNA screening, this would give them a built-in surveillance system for their vaccine program, as has been reported from Australia [7,8].

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