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## HPV Vaccine: A Systematic Review of 10 Years of Real-World Experience

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It has been 10 years since the quadrivalent HPV vaccine was first approved. Today, the vaccine is licensed in 129 countries. The global impact of the vaccine on the reduction of anogenital warts, cervical cancer and high grade dysplasias, as well as vulvar, vaginal, anal, penile, and oropharyngeal cancers can now be observed.

This article reports on a review of peer-reviewed manuscripts in the databases of Pubmed and Embase about the real world impact of the HPV 6/11/16/18 quadrivalent vaccine. The observational studies chosen were from January 2007 through February 2016 using pre-specified search terms and assessed for inclusion by two reviewers. The studies reviewed included manuscripts in any language excluding studies in which only the bi-valent 16/18 HPV vaccine was studied.

It is not surprising that the impact of the vaccine globally depended on the vaccine coverage, age of the cohorts at the time of vaccination, implementation of a catch up program as well as the timing of the follow up relative to vaccination. Despite the variables in the studies reviewed the results observed were consistent across studies.

Within 6 years of receiving three doses of the quadrivalent vaccine, infections in females 18-24 in Australia, and females 14-24 in the US, were reduced by 86% and 89%, respectively. A 76% reduction in infections was observed in Australian females after  $\geq 1$  dose of the vaccine for 6/11/16/18. In addition, the two countries reported an overall reduction of infections in unvaccinated females, suggesting herd protection. In Australia, where there is high vaccine uptake among females a reduction of genital warts was also observed for young men.

The studies reviewed also indicated reductions in low-grade lesions approximately as high as 45% and approximately 85% in high grade histologically confirmed cervical lesions. In each study reviewed, the greatest declines were for those females given 2-3 doses at a young age.

The study underscores that the benefits of the vaccine are greatest where it is routinely administered, and reinforces the need for HPV vaccination programs with high population coverage. Moreover, universal adoption of the HPV vaccine before sexual debut maximizes the vaccine's benefits.

Annually, >600,000 new cancer cases are attributable to HPV worldwide. Yet, in 2014 only 6.2% of females 15 years of age or younger were vaccinated globally despite wide global approval of the vaccine, including its availability in national immunization programs.

Unlike Australia where the HPV vaccine has been provided routinely to young females, the policy in the US has been an opt-in vaccine when and if it is given as an option to the caregivers of young females (and now boys). Addressing perceived safety concerns for health professionals and caregivers should be continued. However, presenting the HPV vaccine as routine and expected just as early childhood vaccinations are, is key to realizing its potential. The promise of the HPV vaccine for reducing morbidity and ultimately mortality is evidenced in the real world. Practical steps to increase vaccination uptake should be stepped up in the US and globally to make HPV related infections and cancers a rarity in the future.

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