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Commentary

Population Impact of HPV Vaccines: Summary of Early Evidence

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A B S T R A C T

Human papillomavirus (HPV) vaccines are available in the United States and around the world to prevent HPV-associated diseases including cervical cancer and genital warts. HPV vaccination is currently recommended for adolescents: target ages for routine and catch-up vaccinations vary by country. Because the time from vaccination to cancer development can be several decades, many studies are evaluating more immediate outcomes. In the 4 years since the vaccine was introduced, reductions in HPV vaccine type prevalence and genital warts have been reported in young females in the United States and other countries. Many questions remain about the long-term impact, but the initial studies show promising results for the relatively new HPV vaccine.

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Two prophylactic human papillomavirus (HPV) vaccines are available and have been introduced in many countries [1]. Both the bivalent and quadrivalent vaccines protect against HPV16 and 18 that cause 70% of cervical cancers; the quadrivalent vaccine is also directed against HPV6 and 11 that cause 90% of genital warts. Most vaccination programs recommend routine use in adolescent girls, and some offer vaccination in older females who were not previously vaccinated. More recently, some countries have added routine adolescent male vaccination with the quadrivalent vaccine to their immunization programs. Although both vaccines had high efficacy in the clinical trials [2,3], monitoring real-world effectiveness is important for program and policy [4]. Because of the long interval between infection and cancer development, efforts are under way to evaluate impact on more proximate outcomes.

Early and mid-endpoints include HPV type prevalence, genital warts (for quadrivalent vaccine), and HPV-associated cervical lesions, all of which pose unique monitoring challenges [5]. Monitoring HPV infection requires sampling from the site of infection, DNA extraction, and genotyping to evaluate trends in prevalence of HPV types. Genital warts are not notifiable in most countries. High-grade cervical lesions were used as the primary endpoint in vaccine clinical trials, but can only be detected through routine cervical cancer screening. Therefore, changes in screening could affect detection of these lesions and complicate interpretation of vaccine impact. For example, new guidelines that recommend initiation of screening at older ages and less frequent screening will be partially responsible for declines in diagnosed cervical lesions in the United States [6]. Despite these limitations, data demonstrating vaccine impact on early outcomes have become available just a few years after vaccine introduction. Results from published studies are summarized in Table 1 and described in the following sections. During the period of these evaluations, no country had recommended routine vaccination for males.

HPV Infection

Reductions in vaccine type infections among young women have been reported from several post licensure studies using consensus polymerase chain reaction assays with type-specific HPV detection. In the United States, a recent analysis of data from the National Health and Nutrition Examination Survey, a nationally representative survey of the non-institutionalized

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Table 1
Summary of published studies of HPV vaccine impact on biologic endpoints

Country (year vaccine introduced)	Data source and/or location	First author, publication year, [reference no.]	Population	Study design	Results[b]
HPV infection[a]					
Australia (2007)	Family planning clinics in Victoria	Tabrizi, 2012 [10]	Females 18–24 years	Ecologic, compared pre- to postvaccine periods	VT prevalence decreased from 28.7% (2005–2007) to 5.0% (vaccinated, 2010–2011) and 15.8% (unvaccinated, 2010–2011)
USA (2006)	Adolescent/ community health clinics in Ohio	Kahn, 2012 [9]	Females 13–26 years	Compared pre- to postvaccine periods by vaccination status	VT prevalence decreased from 31.8% (2006–2007) to 9.9% (vaccinated, 2009–2010) and 15.4% (unvaccinated, 2009–2010)
	Urban STD/ community health clinics in Indiana	Cummings, 2012 [8]	Females 14–17 years	Ecologic, compared pre- to postvaccine periods	VT prevalence decreased from 24% (1999–2005) to 5.3% (2010)
	Nationally representative survey	Markowitz, 2013 [7]	Females 14–59 years	Ecologic, compared pre- to postvaccine periods	VT prevalence decreased in 14–19 year olds from 11.5% (2003–2006) to 5.1% (2007–2010). No decrease in older age groups
Genital warts					
Australia (2007)	Sexual health clinic in Melbourne	Fairley, 2009 [11]	Females and males, all ages	Ecologic, trend analysis	New GW diagnoses decreased from 12.7% (2004–2007) to 6.6% (2008) in females <28 years and from 14.3% (2004/7) to 11.8% (2008) in heterosexual males. No decrease in females ≥28 years or homosexual males
		Read, 2011 [15]	Females and males, all ages	Ecologic, trend analysis	New GW diagnoses decreased from 18.6% (2007–2008) to 1.9% (2010–2011) in females <21 years and from 22.9% (2007–2008) to 2.9% (2010–2011) in heterosexual males <21 years. No decrease in females, heterosexual males ≥30 years or homosexual males
	Sexual health clinics throughout country	Donovan, 2011 [12]	Females and males, all ages	Ecologic, trend analysis	New GW diagnoses decreased from 11–12% (2004–2007) to 4.8% (2010–2011) in female residents aged 12–26 years and from 13–14% (2004–2007) to 8.9% (2010–2011) in heterosexual males. No decrease in females >26 years or homosexual males
		Ali, 2013 [13]	Females and males, 3 age groups (<21, 21–30, >30 years)	Ecologic, compared pre- to postvaccine periods	New GW diagnoses decreased from 11.5% (2007) to .85% (2011, unvaccinated) and 0 (2011, vaccinated) in females <21 years, from 11.3% (2007) to 3.1% (2011) in females 21–30 years, and from 18.2% (2007) to 8.9% (2011) in heterosexual males
	Medicare registry	Ali, 2013 [14]	Females and males, 15–44 years, 10-year age groups	Ecologic, trend analysis	In-patient vulvar/vaginal and penile GW treatments decreased 85% (from 285 [2007] to 42 [2011]), in females 15–24 years, 24% (from 202 [2007] to 153 [2011]), in females 25–34, 71% (from 51 [2007] to 15 [2011]) in males 15–24 years, and 59% (from 39 [2007] to 16 [2011]) in males 25–34 years. No decrease in males or females 35–44 years
New Zealand (2008)	Sexual health clinic in Auckland	Oliphant, 2011 [20]	Females and males, two age groups (<20, ≥20 years)	Ecologic, trend analysis	GW diagnoses decreased from 13.7% (2007) to 5.9% (2010) in females <20 years and from 11.5% (2007) to 6.9% (2010) in males <20 years. No decrease in older males or females
Denmark (2009)	National patient registry	Baandrup, 2013 [21]	Females and males, all ages	Ecologic, trend analysis	GW incidence per 100,000 person-years decreased from 381.5 (2008) to 39.8 (2011) in females 16–17 years. Smaller decrease in females 18–19, 20–21, 22–25, and 26–29. Nonsignificant decrease in males 22–25 and 26–29 years
		Blomberg, 2013 [16]	Females, birth cohorts eligible for vaccination (1989–99)	Retrospective cohort	Decrease in risk of GW among vaccinated (≥1 dose) girls compared with unvaccinated girls. Significant trend in relative risk from oldest to youngest cohort: .62, .25, .22, .12. No GW in vaccinated girls in youngest age cohort
Germany (2007)	Research database	Milolajczyk, 2013 [19]	Females and males, 10–79 years	Ecologic, trend analysis	New GW diagnoses per 100,000 person-years decreased from 316 (2005) to 242 (2008) in females 15–19 years
Sweden (2007)	National patient registry	Leval, 2012 [17]	Females, 10–44 years	Ecologic, trend analysis	GW incidence per 100,000 person-years decreased from 617 (2006) to 523 (2010) in females 15–19 years, from 1,038 (2006) to 885 (2010) in females 20–24 years, from 584 (2006) to 500 (2010) in females 25–29 years, and from 1,070 (2006) to 1,028 (2010) in males 20–24 years. Nonsignificant increase in older males and females