

OREGON PUBLIC HEALTH DIVISION • OREGON HEALTH AUTHORITY

HPV — ACIP AND MOTHERS AGREE: BOYS SHOULD BE VACCINATED, TOO

Human papillomaviruses (HPV) cause cervical, vaginal, vulvar, penile and oropharyngeal cancers. Among these, cervical cancer causes the most morbidity and mortality. Worldwide, cervical cancer is the 3rd most common cancer among women. In the U.S., cervical cancer was the 14th most commonly reported invasive cancer among women during 2008;* 152 new cases were diagnosed in Oregon that year, ranking us 28th among U.S. states. Recently, cervical cancer incidence and mortality appear to have increased slightly in Oregon (Figure 1).

Figure 1. Cervical cancer incidence and mortality, Oregon, 2004–2008



Among men of course, zero cases of cervical cancer were reported in Oregon during 2011. In essence, this central fact — that women bear the brunt of HPV morbidity — is the reason that vaccination of boys had not been recommended until recently.† In this *CD Summary* we explained the recent Advisory Committee on Immunization Practices (ACIP) recommendation that HPV 4-valent vaccine against HPV types 6, 11, 16 and 18 be administered to boys and young men.‡

HPV

Over 100 strains of HPV infect humans; most of these strains cause plain warts or nothing at all. Approximately 40 strains infect the genital mucosa

* <http://apps.nccd.cdc.gov/uscs/index.aspx>

† Even without detailed understanding of “dynamic transmission models,” “Markov models,” “R-naught,” sexual assortment patterns and the like, intuition is an accurate guide to the reasoning, viz. to prevent cervical cancer, vaccinate people with cervixes.

Table 1. Oncogenic risk classification of HPV strains²

Risk	HPV Types
Low	6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, CP6108
Probably High	26, 53, 66
High	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82

and skin, and 15 of these are considered to be oncogenic (Table 1).²

VACCINES

Two vaccines against HPV are currently available for use in the U.S. Gardasil®, licensed by FDA in 2006, is a quadrivalent vaccine that protects against HPV types 6, 11, 16 and 18. Together, HPV types 16 and 18 cause about 70% of cervical cancer, while non-oncogenic HPV types 6 and 11 cause about 90% of genital warts.

Cervarix®, licensed in 2009, protects against types 16 and 18, but not against 6 or 11. Gardasil® is licensed and recommended for use in both males and females; Cervarix® is used only in females (Table 2).

Table 2. HPV vaccine recommendations, by age and sex, ACIP, 2011

Age (yrs.)	Female	Male
11–21	either Cervarix® or Gardasil®	Gardasil® only
22–26		Gardasil® only (not recommended, but optional)

BENEFITS IN BOYS

Since Gardasil® was licensed, data have emerged regarding its effectiveness in boys for prevention of genital warts and anal intraepithelial neoplasia. Overall, almost 6% of adults have had genital warts.³

Though less frequent than cervical cancer, approximately 7,000 HPV-related non-cervical cancers occur annually in the U.S., 5,000 of these among men (Table 3). These include cancers of the oropharynx, anus, and penis. Approximately 87% of anal

cancers and 60% of oropharyngeal cancers are believed to be HPV-related.⁴ Gardasil’s® efficacy against HPV 6-, 11-, 16- and 18-related high-grade anal intraepithelial neoplasia, a precursor to anal carcinoma, is 75%.⁵ However, though it is presumed to have some efficacy against other HPV-related cancers, Gardasil’s® efficacy has been proven only against cervical and anal intraepithelial neoplasia and genital warts. Generally, the models that lead to the lower cost-effectiveness estimates for vaccination of boys assume some contribution to prevention of vulvar, vaginal, and oropharyngeal cancer in addition to recurrent respiratory papillomatosis.

Table 3. HPV-attributable cancers worldwide, 2002⁴

Site	Annual cases	Attributable to HPV (%)
Cervix	10,846	10,412 (96)
Oropharynx	7,360	4,637 (63)
Anus	2,547	2,371 (93)
Vulva	2,266	1,153 (51)
Vagina	601	385 (64)
Penis	828	298 (36)
All sites	22,448	17,191 (77)

COST: BENEFIT CONSIDERATIONS

Since the day Gardasil® was licensed, parents have been asking whether their boys should be vaccinated.⁵ The cost of an ounce of HPV prevention, at ~\$120/dose, is \$360 plus administration and perhaps the expense of getting to the doctor’s office three times. Is it worth it?

One early analysis estimated that adding routine vaccination of boys to routine vaccination of 12-year-old girls would cost \$442,000 for each quality-adjusted life year (QALY) saved.^{6§} However, the initial models assumed that 70% of adolescent females would be vaccinated and did not credit the

‡ www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM247722.pdf

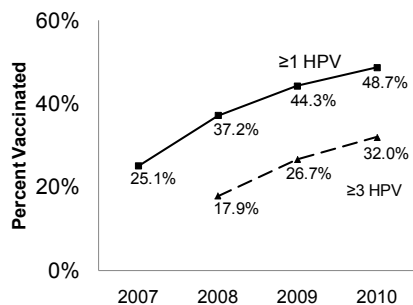
§ A commonly accepted upper limit for cost efficient public health interventions is \$50,000 per QALY.



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Figure 2. HPV vaccination among females 13–17 years of age, U.S., 2007–2010⁷



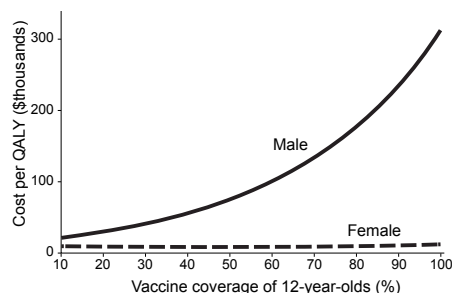
vaccine with preventing cancer in males. During 2010, an estimated 38% of Oregon females aged 13–17 years had received 3 doses of HPV vaccine, far short of the 70% figure on which cost-benefit analyses had been based.[¶] Recently, the rate of increase in coverage has decelerated (Figure 2).⁷ High rates of vaccination of girls with the highly efficacious HPV vaccine would leave little disease to be prevented by vaccinating boys. Lower rates of vaccine uptake among girls would make vaccination of boys a more cost-effective proposition: it could prevent disease not only in the vaccinated men but also cervical cancer in their non-immune female sex partners.

More recent modeling assumed vaccination rates of 20%–50% among girls and considered benefits of HPV vaccination in addition to cervical cancer prevention.^{**} Under these as-

¶ http://www2a.cdc.gov/nip/coverage/nisteen/nis_iap.asp?fmt=v&rpt=tab01_iap&qtr=Q1/2010-Q4/2010

** These include prevention of genital warts; reductions in anal, vulvar, vaginalcervical dysplasia that does not lead to cancer but requires evaluation and treatment; and prevention of anal, vulvar, vaginal, and oropharyngeal cancers and recurrent respiratory papillomatosis in infants.

Figure 3. Incremental cost per quality-adjusted life year saved for male and female vaccination programs by proportion of females covered⁸



sumptions, male vaccination projected more favorably.⁸ At 20% coverage of 12-year-old females with catch-up to 35% by age 26, Chesson and colleagues estimated that adding routine male HPV vaccination to that for females would cost \$23,600 per QALY saved. Figure 3 illustrates that incremental cost of saving a QALY by vaccinating boys is much lower therefore (desirable) when vaccination rates are low among women: for example, it would rise to \$184,300 if coverage of 12-year-old females were 75%, with catch-up to 90% by age 26. At any level of vaccine uptake, however, increasing vaccination rates among girls (if feasible) would be more cost effective than routine vaccination of boys. ACIP also considered in its recommendation the equity of vaccinating only one sex and the practical infeasibility of identifying, before onset of sexual activity, those young men who will later have sex with other men and be exposed thereby to much higher risks of anal carcinoma.^{††}

†† www.cdc.gov/vaccines/recs/acip/downloads/min-archive/min-feb11.pdf

SUMMARY

ACIP recommends vaccinating adolescent boys and girls against HPV. This represents a change in earlier recommendations for vaccinating girls only. The recommendation was changed because HPV vaccination rates among girls have been disappointing, and new data have emerged supporting efficacy of HPV vaccination against HPV-related cancers in boys and men.

FOR INFORMATION

- Oregon Immunization Program, <http://health.oregon.org/imm/>; 971-673-0300

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