

The Estimated Impact and Cost-effectiveness of Nonavalent HPV Vaccination in the United States

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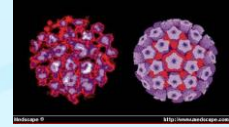
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Division of STD Prevention



Human papillomaviruses

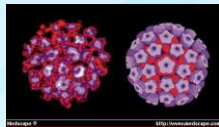
- Family of non-enveloped DNA viruses
- >150 types found in humans
- Tropism for mucosa or keratinized skin
- ~ 40 mucosal types
 - “Low risk” - non-oncogenic types
 - “High risk” - oncogenic types



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HPV epidemiology and natural history

- HPV mucosal types are acquired through sexual contact
- Most common sexually transmitted infection
 - Almost all sexually active persons will acquire
- Most infections clear on their own
 - ~90% of new infections clear within two years
- Persistent infection with a high risk HPV type can progress to cancer

Diseases associated with human papillomavirus (HPV)

- **Oncogenic types (16, 18, 31, 33, 45, 52, 58, others)**
 - Cervical cancers
 - Other cancers
 - Oropharyngeal cancers
 - Anal cancers
 - Vaginal cancers
 - Vulvar cancers
 - Penile cancers
 - High grade intraepithelial neoplasias
- **Non-oncogenic types (6, 11, others)**
 - Anogenital warts
 - Recurrent respiratory papillomatosis (RRP)
 - Low grade intraepithelial neoplasias

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Available HPV vaccines

	Bivalent (Cervarix)	Quadrivalent (Gardasil)	9-valent (Gardasil 9)
L1 VLP types	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Manufacturer	GlaxoSmithKline	Merck & Co.	Merck & Co.
First licensure in US	2009	2006	2014

~99% of HPV vaccine administered in US through 2014 has been quadrivalent vaccine

L1, Major capsid protein; VLP, virus like particle
Markowitz June 2015 ACP

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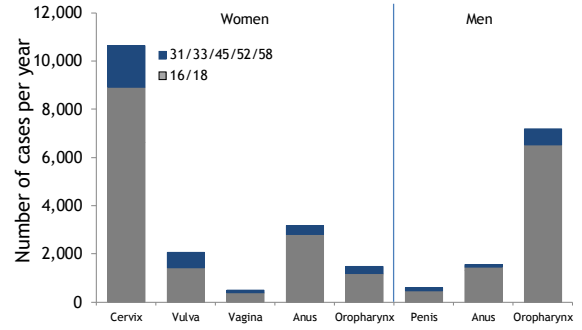
Disease burden associated with HPV types in the US

- **HPV 16/18 (targeted by bivalent, quadrivalent, 9-valent)**
 - Account for 64% of invasive HPV-associated cancers
 - 65% female, 63% male, ~21,300 cases annually
 - 66% of cervical cancers, 50% of ≥CIN2
- **HPV 6/11 (targeted by quadrivalent and 9-valent)**
 - Account for 90% of anogenital warts and most RRP
- **HPV 31,33,45,52,58 (targeted by 9-valent)**
 - Account for 10% of invasive HPV-associated cancers
 - 14% female, 4% males, ~3,400 cases annually
 - 15% of cervical cancers, 25% of ≥CIN2

≥CIN2: cervical intraepithelial neoplasia grade 2 or 3 and adenocarcinoma in situ.
MMWR 64(11), March 27, 2015

9-valent HPV vaccine

Potential for additional cancer prevention in the U.S.



Ref: 1) Jemal JNCI 2013; 2) Saraiya, JNCI (under review). Brisson October 2014 ACIP

Mathematical models critical to predict impact and cost-effectiveness of HPV vaccine strategies

- Long term benefits of HPV vaccination will not be realized for decades
 - Many adverse health outcomes
- Indirect effects (“herd effects”) of HPV vaccination

Illustration of model of cumulative, lifetime probability of acquiring HPV 16



Overview of study

Study feature	Description
Model structure	Simplified deterministic, dynamic, population-based model
Perspective	Societal The costs and benefits we included were limited to the direct costs of vaccination, the direct medical costs averted by vaccination, and the QALYs gained by HPV vaccination
Time frame	100 years
Analytic horizon	100 years+ Lifetime costs averted and lifetime QALYs gained of HPV-associated outcomes averted over 100-year period
Cervical cancer screening	Assumed to occur but not explicitly modeled
Study question	What is the cost-effectiveness of a 9-valent HPV vaccination program for both sexes in the US, compared to a quadrivalent HPV vaccination program for both sexes?

Selected model assumptions

Assumption	Description
Ages vaccinated	12-26 years (female) 12-21 years (male)
Vaccine efficacy (quadrivalent & 9-valent)	95%
Quadrivalent cross-protection efficacy against additional high-risk HPV types*	In some scenarios: HPV 31: 46.2% HPV 33: 28.7% HPV 45: 7.8% HPV 52: 18.4% HPV 58: 5.5%
Duration of vaccine protection	Lifetime
Vaccine cost per dose including \$15 per dose administration	\$145 quadrivalent \$158 9-valent

*Malagon et al. Lancet Infect Dis 2012.

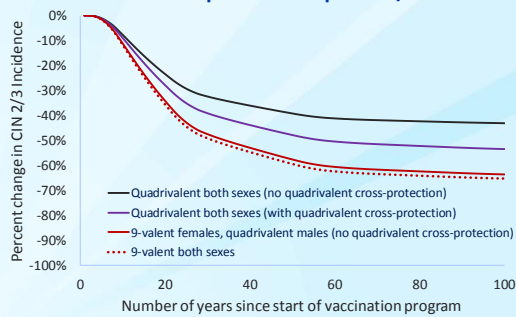
Cumulative vaccination coverage

Age (years)	Lower coverage scenario		Base case coverage scenario		Higher coverage scenario	
	Female	Male	Female	Male	Female	Male
13 to 17	37.9%	14.0%	45.5%	28.6%	80.0%	80.0%
17	48.0%	19.5%	56.4%	38.6%	80.0%	80.0%
26	55.2%	22.8%	63.9%	44.1%	80.0%	80.0%

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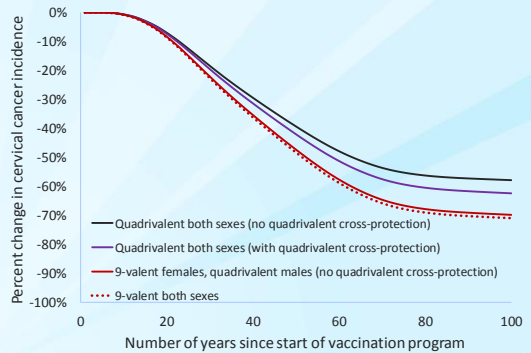
BASE CASE RESULTS

Reduction in incidence of cervical intraepithelial neoplasia 2/3



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Reduction in cervical cancer incidence



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Cost-effectiveness of 9-valent (both sexes) vs quadrivalent (both sexes) Base case results

Incremental cost per quality-adjusted life year (QALY) gained	
No quadrivalent cross-protection	With quadrivalent cross-protection
< \$0 (cost-saving)	\$8,100

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SENSITIVITY ANALYSES

Cost-effectiveness of 9-valent (both sexes) vs quadrivalent (both sexes) Sensitivity analysis: No cross protection for quadrivalent

- In one-way sensitivity analyses, 9-valent vs. quadrivalent for both sexes was cost-saving, except
 - Higher cost per 9-valent vaccine series (\$513): \$16,700 per QALY
 - Higher vaccine coverage scenario: \$3,900 per QALY
 - Lower medical costs per HPV outcome: \$6,700 per QALY
 - Lower incidence rates of HPV outcomes: \$3,900 per QALY
 - Lower % of disease caused by HPV vaccine types: \$10,900 per QALY
- In multi-way sensitivity analyses, cost-per QALY ranged from <\$0 (cost-saving) to \$12,800 in 90% of simulations

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Summary

- We found favorable cost-effectiveness ratios for 9-valent HPV vaccine across a wide range of assumptions
 - Vaccine characteristics: coverage, efficacy, cost
 - Burden of HPV-associated health outcomes
 - Medical costs, quality of life impacts, and incidence
 - Percent of health outcomes attributable to vaccine types
- Results consistent with other, more complex models
- Providing 9-valent vaccine to females accounted for most of the medical costs averted and QALYs gained by 9-valent vaccination of both sexes (vs. quadrivalent for both sexes)

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Limitations

- Our model incorporates several simplifying features
 - Does not explicitly account for cervical cancer screening
 - Does not explicitly model natural history of HPV
 - Reduction in disease burden of a given HPV type assumed proportional to reduction in cumulative exposure to the HPV type
 - Simple model of transmission dynamics
 - Does not classify the population according to sexual activity level
 - Does not explicitly model mixing of sex partners
- Uncertainty in model parameters
 - Quality of life impacts of cervical cancer precursors
 - Vaccine duration of protection
 - Model unable to account for less than lifetime duration

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Conclusions

- At current vaccine costs, 9-valent vaccination is likely cost-saving compared to quadrivalent vaccination
 - Medical costs averted by preventing outcomes related to HPV 31, 33, 45, 52, 58 exceed additional cost of 9-valent vaccine in most scenarios
- Results consistent over wide range of sensitivity analyses
 - Cost per QALY < \$0 in most scenarios, < \$20,000 in all scenarios
- Results consistent with other models
 - Consistency across 3 distinct models will likely be reassuring to decision makers

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Thank you
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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