Published in final edited form as:

Lancet Infect Dis. 2010 December ; 10(12): 845–852. doi:10.1016/S1473-3099(10)70219-X.

A cost-effectiveness analysis of targeted HPV vaccination of men who have sex with men in the United States

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Summary

Background—A vaccine targeting human papillomavirus (HPV) types 16 and 18, associated with 80% of anal cancers, has demonstrated high efficacy in males. High-risk populations such as men who have sex with men (MSM) may especially benefit from HPV vaccination. To inform immunization guidelines in the U.S., we evaluated the cost-effectiveness of HPV vaccination of MSM.

Methods—We used decision-analytic models to estimate the direct health and economic outcomes of HPV vaccination in averting HPV-related anal cancer and genital warts, varying age at vaccination, prior exposure to vaccine-targeted HPV types, prevalence of HIV, and other uncertainties.

Findings—HPV vaccination of MSM at an early age had a cost of \$15,290 per quality-adjusted life year (QALY) gained, compared to no vaccination. If MSM are vaccinated at later ages, when exposure to HPV infections is higher, the cost-effectiveness ratios become less attractive but consistently fall below \$50,000 per QALY in the majority of evaluated scenarios. Results were most sensitive to rates of anal cancer incidence, duration of vaccine protection, and HIV prevalence among MSM.

Interpretation—Our analysis suggests that, based on the current evidence, HPV vaccination of MSM is a robustly attractive strategy across a wide range of uncertainties.

Funding—J Kim is funded in part by grants from the National Cancer Institute (R01 CA93435) and the Bill and Melinda Gates Foundation (30505).

Introduction

There were 2,100 new cases of and 260 deaths from anal cancer among U.S. males in 2009. (1) Nearly 80% of these cases were associated with two oncogenic types of human papillomavirus (HPV), types 16 and 18, also responsible for 70% of cervical cancer cases. (2) While the incidence of anal cancer is far less than that of cervical cancer in the general U.S. population, men who have sex with men (MSM), particularly those who are HIV-

Author contributions

J Kim contributed to the idea and design of the study, the analysis of data, the interpretation of results, the writing of the paper, and approval of the final version.

Conflict of interest statement

J Kim has no conflicts of interest.

Ethics Committee Approval

Ethics committee approval was not required for this study.

positive, face the highest risk of anal cancer in the U.S., comparable to, if not greater than, the risk of cervical cancer among women before the era of routine cytology-based screening. (3)

Two licensed prophylactic vaccines that target HPV-16 and -18 have demonstrated high, sustained efficacy against persistent type-specific infections and cervical lesions among women unexposed to these types; the quadrivalent vaccine also targets two low-risk types, HPV-6 and -11, associated with the majority of genital warts, and has shown high efficacy against incident genital warts, as well as vaccine-type vaginal and vulvar lesions.(4–8) Based on these data, HPV vaccination guidelines since 2007 have recommended routine vaccination for females ages 11–12 (as early as 9) years and catch-up vaccination for older females up to age 26 years.(9, 10) Data on the efficacy of the quadrivalent vaccine in males suggest that prevention of vaccine-type HPV infections and diseases, particularly genital warts, may be as high as 90%.(11, 12) In October 2009, despite the recommendation for routine vaccination of females, the Centers for Disease Control and Prevention (CDC) took a permissive stance on the use of the quadrivalent HPV vaccine in males ages 9–26 in the U.S. for prevention of genital warts, falling short of recommending routine use in males.(13)

Based on more concrete data that the quadrivalent vaccine has high efficacy in preventing anal lesions in males, and specifically MSM,(14) the Advisory Committee on Immunization Practices (ACIP), which advises to the CDC, intends to revisit the evidence on vaccine efficacy in males in October 2010, creating an opportunity for a stronger recommendation of routine HPV vaccination of males. Although previous analyses have found that HPV vaccination should be targeted to pre-adolescent girls and that routine vaccination of boys may not be a good investment of health dollars unless coverage of girls remains low,(15, 16) MSM stand to benefit differentially from HPV vaccination than the general male population and therefore may represent an important target population for vaccination. There are many complex factors to be considered in evaluating strategies that target MSM for HPV vaccination, including uncertainties related to the epidemiology of HPV-related diseases and vaccine properties in MSM, as well as programmatic barriers that may impede the successful implementation of such an approach. For example, identification of MSM may not occur until older ages, after sexual initiation and exposure to HPV infections, resulting in lower vaccine effectiveness; indeed, a recent survey in Australia found that a majority of MSM would access the HPV vaccine but not until the age of 20, two years after sexual debut and after a median of 15 sexual partners.(17)

Despite these uncertainties, the potential value of vaccinating MSM is explicitly being discussed as part of the deliberations regarding HPV vaccination of males in the U.S. In particular, the recommendation to routinely vaccinate males may be swayed by evidence of the benefits and cost-effectiveness of HPV vaccination of MSM, especially if these outcomes hinge on achieving high coverage at an early age when targeting MSM may be infeasible. No single empirical study can consider all of the complex factors necessary for informed decision-making; however, the use of mathematical disease models can facilitate the synthesis of available data and the evaluation of the cost-effectiveness of alternative strategies under different scenarios of uncertainty. To inform the upcoming deliberations of the ACIP and CDC on male HPV vaccination, we used mathematical models to project the cost-effectiveness of targeted HPV vaccination of MSM in the U.S.

Methods

Analytic Overview

Markov cohort simulation models were used to synthesize epidemiological, quality of life, and cost data on HPV-related anal cancer and genital warts among MSM and to estimate the

direct health and economic consequences of targeted HPV vaccination of MSM. The models comprise mutually-exclusive health states that reflect true underlying health status of the population (e.g., no cancer, cancer, dead). The time horizon of the analysis incorporates a cohort's entire lifetime and is divided into equal time increments, during which individuals "transition" from one health state to another according to a set of transition probabilities. Life expectancy, which may be quality-adjusted for time spent in a disease state, and other outcomes can be calculated from survival curves generated by the models. In this analysis, models followed a healthy cohort of MSM starting at age 12 that faced risks of anal cancer and genital warts over the lifetime. When an incident case occurred, the model then determined whether or not that case was attributable to a vaccine-type HPV infection (HPV-16,-18 or HPV-6,-11). Individuals were subject to death from background mortality (age- and gender-specific) at anytime, or from excess mortality associated with anal cancer only.

Data and Assumptions

The data required for the analysis included age-specific incidence of disease, excess mortality rates (for anal cancer), proportion of cases attributable to vaccine-targeted HPV types, disease-specific quality of life, and average cost per case (Table 1).^(2, 18–28) Costs included direct medical costs associated with diagnosis and treatment of anal cancer and genital warts (e.g., tests, procedures, hospitalizations), and with vaccination. We assumed a composite cost per vaccinated individual of \$500, inclusive of three doses at \$120 per dose, wastage, supplies and administration, but varied this cost in sensitivity analysis. All costs were expressed in 2006 U.S. dollars.

Anal cancer incidence rates for HIV-negative and HIV-positive MSM were estimated using data from the Multicenter AIDS Cohort Study (MACS).^(18, 19) Information on the number of anal cancer cases per age group, person-time by age, and total person-time by HIV status were used to stratify overall rates of anal cancer incidence into age-specific rates by HIV status. As person-time stratified by both age and HIV status was not available, we assumed that 58% of person-time in each age group was contributed by HIV-negative individuals (as this group contributed 58% of the overall person-time), and the remaining 42% was contributed by HIV-positive individuals. To internally validate our person-time estimates, we confirmed that our overall anal cancer incidence rates in the HIV-negative group, HIV-positive group, and total group were similar to those reported by D'Souza et al.⁽¹⁹⁾ Because the HPV burden associated with rectal cancers is less well-known, we used the data on confirmed anal squamous cell cancers only in the base case analysis; however, in sensitivity analysis, we included the data on all anal and rectal cancers to provide upper bound estimates – and data from a previous cost-effectiveness analysis of anal cancer screening to provide lower bound estimates ⁽²⁹⁾ – of anal cancer incidence in HIV-negative and HIV-positive MSM.

In the base case, we assumed that the proportion of MSM who are HIV-positive in the population is 25%, based on a study of urban MSM in the U.S. conducted by the CDC,⁽³⁰⁾ but varied this proportion widely (i.e., 8% to 40%) in sensitivity analysis to reflect estimates from the National Health and Examination Surveys (NHANES) ⁽³¹⁾ and also reflect heterogeneity across populations. Excess mortality associated with anal cancer for HIV-negative MSM was based on overall 5-year survival data for anal cancers among all males, reported by the U.S. SEER Cancer registry (1975–2001);⁽²⁰⁾ for HIV-positive MSM, 5-year survival from anal cancer was based on a prospective cohort study of 8,640 HIV-positive individuals in the U.K.⁽²¹⁾ Proportion of anal cancer cases attributable to HPV-16,-18 was reported in a recent review of HPV and anal carcinoma and was not stratified by HIV status. (2) Quality of life adjustment associated with having disease assumes a health state utility ranging from 0 (death) to 1 (perfect health); for anal cancer, the health state utility was

assumed to be, on average, 0.68 over the remaining lifetime, to reflect a weighted average of stage-specific utilities by stage distribution of disease.(22) Cost per anal cancer case included diagnosis (e.g., biopsy), initial treatment (e.g., surgery or radiation), surveillance, management of metastatic disease, and terminal care.(23)

Because of the limited data on age-specific incidence of genital warts among MSM, we utilized recent data by Giuliano(24) on the overall rate of genital warts among all men (1.83 per 100 person-years), as well as rates stratified for heterosexual men (1.50 per 100 person-years) and MSM (4.70 per 100 person-years), to estimate the prevalence of MSM in the study (10.3%) and relative risk of genital warts among MSM, compared to heterosexual men (RR=3.13). These estimates were then used to stratify age-specific incidence rates of genital warts in a general population of males, reported from a study of over 3 million members of a private health insurance plan, into age-specific incidence rates of genital warts among MSM only.(25) Based on the same study, duration of genital warts was assumed to be, on average, three months,(25) and health state utility was 0.91 during the episode of warts.(27) In sensitivity analysis, we used more recent baseline age-specific incidence rates of genital warts among males from a similar population of private insurance members, reported by Hoy et al.(32) Proportion of genital warts cases attributable to HPV-6 or -11 was assumed to be 90%.(26) In the absence of information, data on genital warts among MSM were not further stratified by HIV status. Cost of treating an episode of warts included direct medical costs associated with physician office visits for diagnosis and treatment, as well as pharmacy costs for medications and analgesics.(23)

Strategies

We evaluated a strategy of targeted HPV vaccination of MSM, compared to no vaccination, under different scenarios of vaccination age (12, 20 or 26 years). A strategy of targeting MSM at age 12, while unlikely to be feasible in practice, was included to represent a “best-case” scenario, providing a lower-bound estimate of cost-effectiveness. In the base case, we assumed vaccination coverage of 50% of the MSM cohort and vaccine efficacy of 90% against HPV-16,-18 associated anal cancers and HPV-6,-11 associated genital warts over the lifetime. Vaccination was assumed to reduce only the cases attributable to vaccine-targeted HPV types and only among those who get vaccinated (i.e., vaccine cross-protective effects and herd immunity benefits were not included). We conservatively assumed that individuals with prior exposure to HPV-16,-18 and/or HPV-6,-11 received no vaccine benefit associated with those disease outcomes. At vaccination ages of 20 and 26, we varied the probability of prior exposure to vaccine-type HPV infections (from 10% to 50%), which effectively down-weighted the vaccine efficacy in reducing vaccine-type cancer or warts cases. For example, with 0% prior exposure to HPV-16,-18, the risk of developing anal cancer that is attributable to HPV-16,-18 is reduced by 90% in vaccinated individuals; however, with 10% prior exposure, the risk of developing anal cancer attributable to HPV-16,-18 is reduced by 81% ($0.90 - [0.90 \times 0.10]$). Although in the base case analysis, we assumed lifelong vaccine efficacy, we also explored the impact of shorter duration of vaccine protection (i.e., 30 years). Additional sensitivity analysis included cost-per-case and health utilities associated with anal cancer and genital warts. Given the lack of clinical guidelines for routine anal Pap screening in the U.S., we did not include anal cancer screening in the MSM population.

Analysis

The Markov models were run both without and with the vaccination strategies to generate estimates of quality-adjusted life years (QALY) gained and costs averted with respect to prevention of HPV-16,-18 associated anal cancer and HPV-6,-11 associated genital warts among MSM. Incremental cost-effectiveness ratios were calculated as the additional cost divided by the additional health benefit of HPV vaccination of MSM versus no vaccination

and were expressed as cost per QALY gained. Future costs and QALY were discounted at a rate of 3% per year, consistent with guidelines for cost-effectiveness analysis in the U.S.(33) Although there is no consensus on a threshold cost-effectiveness ratio below which an intervention would be considered “good value for money” in the U.S., we used a range of \$50,000 to \$100,000 per QALY gained as a reasonable benchmark for cost-effectiveness in this analysis.(34–37)

Role of the funding source

The funding sources had no involvement in the study design; in the collection, analysis, or interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Results

Under base case assumptions of 50% vaccination coverage and 90% vaccine efficacy, HPV vaccination of MSM at age 12 (before HPV exposure) was associated with a cost-effectiveness ratio of \$19,070 per QALY gained, compared to no vaccination, when considering anal cancer prevention only; when including genital warts benefits, the cost-effectiveness ratio decreased to \$15,290 per QALY (Figure 1). When we assumed that MSM were vaccinated at later ages (e.g., 20 or 26), with higher exposure to vaccine-type HPV infections, the cost-effectiveness ratios become less attractive, but remained below \$50,000 per QALY. For example, HPV vaccination of MSM at age 26 was \$42,200 per QALY (anal cancer only) and \$37,830 per QALY (anal cancer and genital warts), when assuming that prior exposure to all vaccine-types was 50%.

The impact of HIV prevalence among MSM was large (Figure 1, error bars), and in certain scenarios, the cost-effectiveness ratios past the threshold of \$50,000 per QALY but remained well below \$100,000 per QALY. For example, when including only anal cancer benefits, vaccinating MSM at ages 20 or 26, with at least 20% reduced efficacy due to prior HPV-16,-18 exposure, exceeded \$50,000 per QALY when HIV prevalence was decreased to 8%; when including genital warts benefits, however, the ratios were consistently below \$50,000 per QALY unless vaccination occurred at age 26 with 50% reduced vaccine efficacy. Under an assumption of 40% HIV prevalence among MSM, vaccinating MSM fell below \$30,000 per QALY, in all scenarios both with and without inclusion of genital warts benefits.

We evaluated scenarios in which prior exposure to HPV-6,-11 varied independently from that of HPV-16,-18 and found that cost-effectiveness ratios consistently fell below \$40,000 per QALY, even at older vaccine ages with high levels of prior exposure (Table 2). We also found that the variation in exposure to HPV-16,-18 had a greater impact on cost-effectiveness ratios than the variation in exposure to HPV-6,-11. For example, holding exposure to HPV-6,-11 constant at 20%, HPV vaccination of MSM at age 20 ranged from \$18,250 per QALY to \$32,780 per QALY when varying exposure to HPV-16,-18 from 10% to 50%, respectively. In contrast, holding exposure to HPV-16,-18 constant at 20%, the same strategy ranged from \$20,180 per QALY to \$22,100 per QALY when varying exposure to HPV-6,-11 from 10% to 50%, respectively. Although there are limited data on HPV exposure in males over time, a study of HIV-negative MSM in the U.S. reported prevalence of over 50% with any HPV type, 15% with high-risk types, and 30% with low-risk types by age 25; in particular, combined prevalence of HPV-16 and -18 was over 10% and of HPV-6 and -11 was nearly 20%.(38) If we used these estimates as a proxy for prior exposure to vaccine-targeted HPV types in our analysis, the cost-effectiveness ratio for vaccinating MSM at age 26 would be less than \$20,000 per QALY.

Using these data to reflect plausible estimates of prior exposure to vaccine-type HPV infections by age 26, and including the extreme scenarios in which vaccination of MSM is expected to have maximum benefit (i.e., at age 12 with 0% exposure) and minimum benefits (i.e., at age 26 with 50% exposure), we conducted a series of sensitivity analyses to evaluate the impact of important uncertainties (Table 3).^(18, 19, 23, 29, 32, 39, 40) We found that our results were most sensitive to assumptions of duration of vaccine protection and anal cancer incidence among HIV-negative and HIV-positive MSM. For example, when vaccine protection was assumed to wane completely at 30 years, vaccinating MSM at age 12 exceeded \$50,000 per QALY, and vaccinating MSM at age 26 with exposure of 10% to HPV-16,-18 and 20% to HPV-6,-11 cost \$70,610 per QALY. Vaccinating MSM at the upper age limit, assuming the highest level of exposure to all vaccine-types cost \$127,810 per QALY.

When we assumed that the estimates of anal cancer incidence included all anal and rectal cancers in the MACS population, and was therefore higher than in the base case analysis which included only confirmed anal squamous cell cancers, we found that the cost-effectiveness ratios became more attractive, with vaccination at age 12 falling below \$10,000 per QALY and vaccinating at age 26 falling below \$25,000 per QALY. In contrast, assuming much lower anal cancer incidence (roughly 10-fold less), the cost-effectiveness ratios increased considerably, ranging from \$54,880 per QALY (vaccinating at age 12) to \$142,660 per QALY (vaccinating at age 26 with 50% prior exposure).

Results were moderately sensitive to cost per vaccinated individual, although across the range of evaluated values, the ratio for MSM vaccination remained below \$50,000 per QALY. Results were insensitive to variations in costs of anal cancer or genital warts cases, health state utilities associated with anal cancer and genital warts, and revised estimates of genital warts incidence (data not shown).

Conclusions

Our analysis suggests that, based on the available data, HPV vaccination of MSM is unambiguously an attractive strategy across a wide range of uncertainties. For the most part, results were robust irrespective of both age at vaccination and proportion of MSM who have been exposed to vaccine-type HPV infections by the time vaccination occurs. The effectiveness of vaccination in reducing anal cancer cases was the overwhelming driver of cost-effectiveness results; inclusion of genital warts benefits improved (i.e., decreased) the cost-effectiveness ratios but rarely affected the overall policy conclusions for any particular strategy. To the extent that HPV vaccines are efficacious against other HPV-related health conditions, such as penile and oral cancers, vaccination of MSM will look even more attractive, although the relative contribution of vaccine-type HPV infections to these conditions are far lower than to anal cancer and genital warts. Nonetheless, as better data become available, analyses will need to be updated to include such outcomes in estimates of cost-effectiveness.

The results were most sensitive to the duration of vaccine protection (assuming complete waning at 30 years) but suggest that even vaccinating MSM at age 26 under this scenario would remain well below the upper cost-effectiveness threshold of \$100,000 per QALY, provided exposure to HPV-16 and -18 is not excessive. Similarly, cost-effectiveness results were very sensitive to the underlying rates of anal cancer. In the base case, we used what some may consider a conservative estimate of anal cancer incidence based only on squamous cell cancers; assuming higher estimates of cancer incidence that included rectal and all anal cancers in sensitivity analysis only strengthened our overall conclusions. On the other hand, we found that if anal cancer incidence among MSM decreased considerably, the

cost-effectiveness results of MSM HPV vaccination were less definitive, leaving the opportunity for other factors to become influential, such as age at vaccination and prior exposure to HPV types. Such a finding is important when one considers the increasing adoption of anal cancer screening among high-risk males that may lead to reducing cancer cases; however, it would be necessary to include the full costs and benefits of screening, diagnosis, and treatment of anal precancer before drawing firm conclusions regarding the impact of anal cancer screening on the value of HPV vaccination of MSM.

Prevalence of HIV among MSM, which governs the proportion of the MSM population who face the higher rates of anal cancer incidence, was also moderately influential on the cost-effectiveness ratios, but only under a few scenarios did the ratio exceed \$50,000 per QALY, namely when HIV prevalence was very low (8%) and prior exposure by age of vaccination was very high (50% at age 26).

Despite the uncertainty with respect to the prior exposure of HPV in the MSM population, there is consensus that health benefits are expected to be greatest when vaccinating early, ideally prior to sexual debut, after which HPV infection can be acquired quickly. Ability to achieve early uptake among this high-risk subgroup of males is challenged by a number of factors, including the age at which males self-identify as MSM; willingness to disclose sexual identity to others; acceptability of the vaccine; and social stigma of receiving a vaccine against a sexually-transmitted infection, especially if the vaccine is targeted to a subgroup with a specific sexual orientation. Largely influenced by social norms, these factors may obstruct access to a vaccine that could benefit a high-risk population who otherwise are offered no other routine services for prevention of anal cancer. Whether or not HPV vaccination of all males can or should be used as a means to achieve maximum benefits among this high-risk subgroup is unclear and is the subject of debate; however, this analysis provides compelling evidence that HPV vaccination of MSM need not occur at the earliest ages to be considered good value for money. Indeed, targeting HPV vaccination to MSM up to age 26, while not as beneficial as vaccinating MSM early, was found to have a cost-effectiveness ratio that is less than the lower-bound threshold of cost-effectiveness in the U.S. (i.e., \$50,000 per QALY), even at high levels of prior exposure to vaccine-targeted HPV types.

Despite the robust results, this analysis has important limitations to consider. First and foremost, the data on the age-related burden of anal cancer and genital warts among MSM, and especially by HIV status, are limited. As such, age-specific incidence rates of anal cancer among MSM by HIV status were estimated from the MACS population using number of anal cancer cases by age from one analysis (19) and person-years by age and HIV status from a subsequent analysis (18), and incidence rates of genital warts were not stratified by HIV status. We used disease-related cost estimates that were derived from the general U.S. population, and therefore, implicitly assumed that the cost of HPV-related diseases was also independent of that of HIV. Also because of limited data, we conservatively assumed that vaccination would be ineffective for those with prior exposure to vaccine-targeted HPV types; although preliminary data suggest that individuals with prior exposure may receive some protection against reinfection with, or reactivation of, the exposed vaccine types, the efficacy data were among women only and were subject to great uncertainty.⁽⁴¹⁾ Assuming vaccine protection among those with prior infections would improve the cost-effectiveness results, further reinforcing our conclusion that targeted HPV vaccination of MSM is an attractive intervention.

We also made several simplifying modeling assumptions. By using “static” Markov models, we captured only the direct benefits of vaccination for a single cohort of MSM. Assuming that vaccination of MSM would also yield herd immunity benefits in the population (via

reduced transmission of HPV to unvaccinated partners), we would expect that the cost-effectiveness of targeted MSM vaccination would become more attractive. The improvement in cost-effectiveness results would be even greater if reduced transmission also occurred among potential female partners and contributed to the reduction of cervical disease. The extent to which the cost-effectiveness ratios improve is uncertain, however, and would depend on many important factors for which there are limited data, including (but not limited to) achievable vaccination coverage and sexual behaviours among MSM. Finally, for simplicity, we assumed that HIV prevalence among MSM was static throughout the analysis and therefore relied on estimates that resemble cumulative exposure to HIV by the time anal cancer incidence begins to rise (i.e., 25% HIV prevalence by age 30–40 years). Although this estimate was varied across a wide range to reflect uncertainty in the data, as well as population heterogeneity, age-based HIV trends may also alter the cost-effectiveness ratio of MSM HPV vaccination. As refined data become available on the age-related exposure to HPV infections, vaccine protection against HPV transmission and disease outcomes, the complex interplay between HPV and HIV infections, and vaccine acceptability among MSM, these models will need to be revised to provide updated information on the cost-effectiveness of targeted MSM HPV vaccination.

Despite these limitations, to date, our analysis is the first to explore the potential cost-effectiveness of HPV vaccination of MSM. We found that such a strategy is highly likely to be a valuable health investment for a high-risk population that otherwise relies on no other organised prevention strategy against a highly burdensome illness (i.e., anal cancer). These findings, which were robust across different assumptions of age at vaccination, prior exposure to vaccine-targeted HPV types, and other important uncertainties, suggest that routine vaccination of all males, already shown to have diminishing value as uptake in girls increases in the U.S., may also not be the optimal means to prevent anal cancer and genital warts in MSM and that programmes targeting HPV vaccination of MSM at older ages, when more males have established and are willing to disclose their sexuality, may be an attractive approach to reaching this high-risk group.

Acknowledgments

J Kim is supported in part by grants from the National Cancer Institute (R01 CA93435) and the Bill and Melinda Gates Foundation (30505).

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Figure 1. Impact of age at vaccination, prior exposure to vaccine-targeted HPV infections, and HIV prevalence among MSM

The graph depicts the incremental cost-effectiveness ratio (y-axis) associated with a strategy of targeted HPV vaccination of MSM, varying vaccination age and % prior exposure to vaccine-type HPV infections (x-axis). The height of each bar indicates the cost-effectiveness ratios under base case assumptions (50% coverage, 90% efficacy against vaccine-type disease outcomes, and 25% HIV positivity among MSM); the red bar represents results that include anal cancer benefits only; the green bar, anal cancer and genital warts benefits. The error bars represent results associated with varying HIV positivity among MSM (upper bar, 8% positivity; lower bar, 40% positivity). Grey dotted line denotes a cost-effectiveness threshold of \$50,000 per QALY, considered a benchmark for good value for money in the U.S.

Table 1

Parameter Values for Anal Cancer and Genital Warts among MSM*

HEALTH CONDITION	MSM HIV-NEGATIVE	MSM HIV-POSITIVE
Anal cancer		
Incidence rate (per 100,000), age 16+ (18, 19)	0.01–16.44	0.09–97.92
5-year survival (%) (20, 21)	64.1	47.0
Cases attributable to HPV-16,-18 (%) (2)	78.6	
Quality of life adjustment (22) [†]	0.68	
Cost per case (\$) (23) [‡]	31,300	
Genital warts[§]		
Incidence rate (per 1,000) (24, 25)	0.09–12.87	
Cases attributable to HPV-6,-11 (%) (26)	90.0	
Quality of life adjustment (25, 27) [†]	0.91	
Cost per case (\$) (23) [‡]	430	

* Range represents age-specific values.

[†] Quality of life adjustment assumes health state utility of 0 (death) to 1 (perfect health). For anal cancer, we assumed an average health utility of 0.68 over the lifetime with disease, to reflect a weighted average of stage-specific utilities and stage distribution of disease.(20, 22) For genital warts, we assumed a health state utility of 0.91 over 3 months.(25, 27) All disease-specific utilities are multiplied to baseline age-specific utilities to estimate overall utility.(28)

[‡] Cost per case is expressed in 2006 U.S. dollars and represents the average discounted lifetime costs of a new case of disease, including direct medical costs, such as cost of procedures, hospitalizations, office visits.

[§] Data on genital warts were not stratified by HIV status.

Table 2

Cost-Effectiveness of HPV Vaccination of MSM When Varying Prior Exposure to HPV-6,-11 and HPV-16,-18 Independently*

Prior Exposure to HPV-6,-11 (%) [†]	Prior Exposure to HPV-16,-18 (%) [†]	Vaccination Age		
		Age 12	Age 20	Age 26
0	0	15,290		
10	10		17,850	19,160
	20		20,180	21,700
	50		31,850	34,680
20	10		18,250	19,470
	20		20,650	22,080
	50		32,780	35,440
50	10		19,470	20,430
	20		22,100	23,220
	50		35,740	37,830

* Values represent incremental cost-effectiveness ratios (additional cost divided by additional health benefit) of HPV vaccination of MSM, compared to no vaccination, under base case assumptions; ratios are expressed as cost per quality-adjusted life year (\$ per QALY) gained. Results include vaccine benefits in preventing vaccine-type anal cancer and genital warts among MSM. All costs are expressed in 2006 U.S. dollars.

[†] Prior exposure to vaccine-type HPV infections effectively down-weights the vaccine efficacy in reducing vaccine-type cancer or warts cases. See Methods section for details.

Table 3

Impact of Key Variables on Cost-Effectiveness Results*

Parameter	Values	Age at Vaccination (Prior HPV-16,-18 / HPV-6,-11 Exposure) [†]		
		Age 12 (0%)	Age 26 (10% / 20%)	Age 26 (50% / 50%)
Base case analysis		15,290	19,470	37,830
Duration of vaccine protection				
Finite duration	30 years	50,160	70,610	127,810
Anal cancer incidence (per 100,000) (18, 19, 29)				
High incidence	0.01–46.04 (HIV–) 0.09–143.75 (HIV+)	8,970	11,230	23,140
Low incidence	0.01–5.67 (HIV–) 0.09–14.52 (HIV+)	54,880	78,890	142,660
Cost per vaccinated individual				
Low cost	\$360	9,760	12,910	26,100
High cost	\$600	19,240	24,150	46,210
Anal cancer cost per case (23)				
High cost	\$60,800	12,790	16,840	35,220
Low cost	\$15,200	16,650	20,910	39,260
Genital warts cost per case (23, 32)				
High cost	\$810	13,690	18,440	36,700
Low cost	\$360	15,580	19,660	38,040
Anal cancer health utility (29, 39)				
Low utility	0.50	14,170	17,980	34,960
High utility	0.88	16,750	21,440	41,630
Genital warts health utility (39, 40)				
Low utility	0.87	14,830	19,090	37,020
High utility	0.96	16,300	20,270	39,570

* Values represent incremental cost-effectiveness ratios (additional cost divided by additional health benefit) of HPV vaccination of MSM, compared to no vaccination, under base case assumptions; ratios are expressed as cost per quality-adjusted life year (\$ per QALY) gained. Results include vaccine benefits in preventing vaccine-type anal cancer and genital warts among MSM. All costs are expressed in 2006 U.S. dollars.

[†] Prior exposure to vaccine-type HPV infections effectively down-weights the vaccine efficacy in reducing vaccine-type cancer or warts cases. See Methods section for details.