Adjuvant HPV Vaccination for Anal Cancer Prevention in HIV-Positive Men Who Have Sex With Men: The Time is Now

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Abstract

Importance—Outcomes of treating high-grade squamous intraepithelial lesions (HSIL), a precursor to anal cancer, remain uncertain. Emerging evidence shows that post HSIL treatment adjuvant quadrivalent human papillomavirus (qHPV) vaccination improves the effectiveness of treatment. However, no recommendations exist regarding the use of qHPV vaccine as an adjuvant

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form of therapy. Our objective was to determine whether post-treatment adjuvant vaccination should be adopted in HIV-infected MSM (individuals at highest risk for anal cancer) on the basis of cost-effectiveness determined using existing evidence or whether future research is needed.

Methods—We developed a Markov (state-transition) cohort model to assess the cost-effectiveness of post-treatment adjuvant HPV vaccination of 27 years or older HIV-infected MSM. We first estimated cost-effectiveness and then performed value-of-information (VOI) analysis to determine whether future research is required by estimating the expected value of perfect information (EVPI). We also estimated expected value of partial perfect information (EVPPI) to determine what new evidences should have highest priority.

Results—With the incremental cost-effectiveness ratio (ICER) of $71,937/QALY, "treatment plus vaccination" was the most cost-effective HSIL management strategy using the willingness-to-pay threshold of 100,000/QALY. We found that population-level EVPI for conducting future clinical research evaluating HSIL management approaches was US$12 million (range $6–$20 million). The EVPPI associated with adjuvant qHPV vaccination efficacy estimated in terms of hazards of decreasing HSIL recurrence was $0 implying that additional data from a future study evaluating efficacy of adjuvant qHPV vaccination will not change our policy conclusion that "treatment plus vaccination" was cost-effective. Both the ICER and EVPI were sensitive to HSIL treatment compliance.

Conclusion—Post-treatment adjuvant qHPV vaccination in HIV-infected MSM aged 27 or above is likely to be cost-effective. Use of adjuvant qHPV vaccination could be considered as a potential strategy to reduce rising anal cancer burden among these high-risk individuals.

INTRODUCTION

The incidence of anal cancer is 80 times higher in HIV-infected men who have sex with men (MSM) than the general population in the United States [1, 2]. Infection with human papillomavirus (HPV), particularly types 16 or 18, is considered the most significant risk factor for anal cancer [3]. Persistent HPV infection may lead to anal high-grade squamous intraepithelial lesions (HSIL), which might ultimately progress to invasive anal cancer [4].

Effective management of HSIL might prevent or slow down progression to invasive anal cancer; however, how best to manage HSIL is controversial as the benefits of treatment are not demonstrated by clinical trials. For this reason, there is no established standard of care. Treatment using ablation is the most commonly accepted strategy. However, HSIL recurs in about 60–70% of patients within 1 year following ablation and despite treatment for recurrent lesions [5], patients are at risk of progressing to invasive anal cancer [5–8]. Tong et al and data from the Study of Prevention of Anal Cancer (SPANC) demonstrated that HSIL might naturally regress [9]. Furthermore, given that treatment is associated with morbidity [5, 10], some suggest delaying HSIL treatment and actively monitoring patients until

occurrence of early invasive cancer when treatment is known to be efficacious where five-year cancer-specific survival of 95% is achievable [11–13].

Recent data show that the effectiveness of anal HSIL treatment could be improved by the addition of post-treatment adjuvant quadrivalent human papillomavirus (qHPV) vaccination because vaccination decreases the risk of recurrence and has the potential to decrease subsequent progression to invasive anal cancer [14, 15]. Similarly, studies have shown benefits of adjuvant qHPV vaccination for prevention of recurrent cervical intraepithelial neoplasia (CIN), oral papillomas, anal condyloma, and respiratory and laryngeal papillomatosis (other HPV-associated diseases) [16]. Data from the SPERANZA randomized clinical trial (RCT) showed that the qHPV vaccine is efficacious after loop electrosurgical excision procedure (LEEP) treatment for CIN—over the median follow-up of 27 months, 11 out of 162 patients in control group developed a cervical recurrence (6%) while 2 out of 162 vaccinated women recurred (1%) (p=0.0199) [17]. Although clinical trials found no evidence on efficacy of HPV vaccination for prevention of anal persistent HPV infection [18], no empirical trial data exist regarding the effectiveness of adjuvant vaccination for prevention of recurrent anal HSIL or anal cancer in HIV-infected individuals. Considering this uncertainty, a modeling based analysis showed that "treatment plus vaccination" could be a cost-effective HSIL management strategy even under the assumption of worst-case efficacy of reducing HSIL recurrence for only up to 2 years [19]. Therefore, the questions then arise: Should the guidelines consider implementing post-treatment adjuvant qHPV vaccination despite the lack of direct evidence from empirical studies? Or should further data be collected from additional studies before making a decision?

In this study, we investigated above tradeoffs by conducting a value of information (VOI) analysis, which provides a unique perspective on the need for conducting further research, including randomized clinical trials, before making a policy decision, and an indication of the amount that society should be willing to spend to gain additional information and reduce uncertainty through further research about unknown factors (e.g., adjuvant qHPV vaccine efficacy, disease natural history, etc.). VOI analysis has been successfully used in risk analysis [20] and has recently been recommended to evaluate healthcare technologies by the Second Panel on Cost-Effectiveness in Health and Medicine, as well as by multiple agencies including the Agency for Healthcare Research and Quality (AHRQ) and the Patient-Centered Outcomes Research Institute (PCORI) in the United States [21–27]. Therefore, our objective was to determine if additional clinical studies were necessary or if the currently available data, even with uncertainty, were sufficient to inform post-treatment adjuvant HPV vaccination recommendations.

METHODS

Model overview and comparators

To conduct VOI analysis, we used a previously developed and validated state-transition model that simulated the natural history of anal carcinoma in HIV-infected MSM and followed patients after treatment for initial HSIL for any risk of subsequent recurrence or potential cancer [19, 28] (Appendix S1.1). The model compared four strategies: do nothing, active monitoring (using annual digital anorectal examination (DARE) and high resolution

anoscopy (HRA)), treatment for HSIL (using ablation), and treatment plus adjuvant qHPV vaccination [16] (Appendix S1.2). The schematic model structure of the natural history of anal carcinoma and potential disease progression after HSIL treatment is presented in Appendix Figure F1.1.

Baseline cohort and disease transition

The hypothetical baseline cohort was comprised of 27 year or older HIV-infected MSM who have been diagnosed with HSIL in the U.S. We defined the Markov health states capturing anal carcinogenesis as: normal, low-grade squamous intraepithelial lesions (LSIL), HSIL, invasive anal cancer, HSIL recurrence, and death. In addition to these, the model included health states for HIV progression based on the patient's CD4 count (i.e., CD4 >500 cells/mm^3, CD4 between 200–500 cells/mm^3, and CD4 <200 cells/mm^3). Patient CD4 count, rates of HSIL progression or regression, and natural history post initial regression were obtained from the literature or calibrated using a separate natural history model for anal carcinogenesis (Appendix S1.3; Appendix Table T1.1 and T1.2) [2, 9, 19, 29–31]. Our model also considered the possibility of receiving antiretroviral therapy (ART) and the impact of change in CD4 count on anal carcinogenesis.

Effectiveness parameters

We defined treatment effectiveness as probability of HSIL recurrence post-treatment for initial HSIL. (Appendix Table T1.2) We defined vaccine effectiveness as the hazards (probability that an individual at a given time has an event) of developing recurrent HSIL that ultimately transitions to anal cancer (Appendix Table T1.3) [14, 28, 32]. Patients not receiving any care (do nothing) followed natural history of the disease where stage-specific anal cancer was diagnosed symptomatically while active monitoring led to early detection of early invasive anal cancer (Appendix Table T1.2).

Cost and utilities

Cost data were estimated using the Surveillance, Epidemiology, and End Results (SEER) database and Medicare claims (Appendix Table T1.4) as well as obtained from published studies [28, 29, 33]. Health-state utilities (preference-based valuation of quality of life) were identified from the literature (Appendix Table T1.4) [29].

Value of information analysis

The first step to conduct a value of information analysis was to conduct a probabilistic sensitivity analysis (PSA). We used 10,000 Monte Carlo runs to sample the probability distributions for all model parameters. We then estimated the cost-effectiveness of each HSIL management strategy using the average of the PSA runs. The decision uncertainty was presented using the cost-effectiveness acceptability frontier that provides a graphical illustration of the probability that the alternative with the highest net benefit will be cost-effective [34].

Next, we estimated the expected value of perfect information (EVPI) [35], which provided the maximum amount the healthcare system would be willing to pay to achieve perfect information about the clinical and economic value of the HSIL management approach. We

first estimated patient-level EVPI, which is the difference between the payoff (expected net benefit) with perfect information and current information [36, 37]. Given that observational studies have shown that individuals who have had HSIL treatment were less likely to progress to anal cancer for at least 10 years [7, 8], We further assumed that the optimal strategy remains a viable alternative for prevention of anal cancer in MSM between 10 to 30 years (where the base case time horizon was assumed to be 20 years).

We then estimated the population-level EVPI by multiplying the individual EVPI by the number of MSM who would be potentially benefited over the next 20 years, discounted at an annual rate of 3%. To determine the population of men who will potentially benefit, we used population projection data from the US Census Bureau [38], proportion of MSM in the US from Urban Health data [39], prevalence of HIV in the US among MSM [40], and current and projected incidence of anal cancer in MSM [41, 42] (Appendix 2). Finally, we estimated EVPI by assuming the time-frame to be either 10 years or 30 years.

Similarly, we estimated the patient-level and then population-level expected value of partial perfect information (EVPPI) to find how much the healthcare system would be willing to pay to resolve uncertainty around specific parameters. This indicates what new evidence (studies) should have the highest priority when undertaking additional studies (i.e., parameters with highest informational value). This was estimated using a two-level simulation process [26], where outer simulation loop values were drawn for parameter of interest and inner loop values were drawn for all other parameters [26]. The EVPPI was estimated as the difference between the expected value with perfect and current information about the parameter(s). Particularly, we estimated the EVPPI for the group of parameters that characterize HSIL progression or regression and LSIL progression or regression in patients not treated for HSIL, and adjuvant HPV vaccination efficacy and HSIL treatment efficacy in patients receiving treatment for HSIL.

Sensitivity analysis

HSIL recurrence rate remains high and patients are likely to be lost to follow-up; therefore, we first determined cost-effectiveness and value of future research by varying treatment compliance. Since efficacy of adjuvant qHPV vaccination was a major assumption for this study, we performed sensitivity analysis to evaluated EVPI and EVPPI under the worst case scenario (i.e., lowest possible efficacy) of adjuvant qHPV vaccination efficacy. For this analysis, we assumed that that the efficacy of adjuvant qHPV vaccination was only 2% (range 0%–78%) for the time duration of first two years post treatment for initial HSIL. Then after, we assumed that there was no difference in recurrence among individuals who received adjuvant vaccine versus individuals who did not receive the vaccine post treatment.

RESULTS

Model validation

We validated our model by comparing natural history model-predicted 1-year, 2-year, and 3-year cumulative risks of HSIL to the cumulative risks reported by Burgos et al [43]. Model accuracy was established as the cumulative risks predicted by the model were within the

95% confidence interval of the cumulative risks reported in the literature. Detailed model validation is presented in Supplementary Appendix 3 and elsewhere [19, 28].

Cost-effectiveness

Based on the current evidence, we found that "do nothing" was likely to be a cost-effective strategy if the willingness-to-pay (WTP) threshold is below $71,937 per QALY. If the WTP threshold is greater than or equal to $71,937 per QALY, then "HSIL treatment plus vaccination" was optimal. At the WTP threshold of $100,000/QALY, "HSIL treatment plus vaccination" was likely to be most optimal with 73% probability. Detailed clinical and economic outcomes by strategies are listed in Table 1. The uncertainty associated with these strategies is represented using the cost-effectiveness acceptability frontier (Figure 1a). We also present cost-effectiveness acceptability curves (Appendix Figures F4.3 and F4.4).

Value of perfect information

Figure 1a presents the EVPI for HIV-infected MSM over WTP thresholds ranging from $0 per QALY to $200,000 per QALY. Assuming that the HSIL management approaches would remain viable for prevention of anal cancer over 20 years, the EVPI at the WTP of $100,000/QALY was $12 million (peak EVPI was $21 million). This implies that future clinical research evaluating HSIL management approaches could be potentially worthwhile as long as the cost of research is below $12 million.

When the time-frame for the analysis was decreased to 10 years, the potential value of further information dropped to $6 million, when the time–frame for the analysis was increased to 30 years, the potential value of further information increased to $20 million (Appendix Figure F4.1.).

Value of partial perfect information

The EVPPI of adjuvant qHPV vaccination efficacy was $0 at the WTP threshold of $100,000/QALY (Figure 1b). This implies that additional evidence on efficacy of adjuvant qHPV vaccination is not needed prior to implementation of post-treatment adjuvant HPV vaccination policy. In other words, despite uncertainty regarding the efficacy of adjuvant qHPV vaccination, treatment plus vaccination will remain the most cost-effective strategy.

Similarly, the EVPPI for HPV 16/18 reinfection, HSIL treatment effectiveness, and adjuvant qHPV vaccination efficacy were $0 at the WTP threshold of $100,000/QALY implying that additional future research in these individual variables will not change the cost-effectiveness results.

We found that the EVPPI was highest for LSIL progression or regression (peak EVPPI at $8.1 million), followed by HSIL progression or regression (peak EVPPI at $7.1 million). At the WTP threshold of $100,000/QALY, these values were $1.5 million and $0.5 million, respectively. High EVPPI associated with these parameters indicate that a more precise estimate of the LSIL and HSIL natural history may be required; this in turn would require an experimental design.

Sensitivity analysis

Both the ICER and EVPI were sensitivity to HSIL treatment compliance. When loss to follow-up was varied in the range of 20% to 80%, the ICER varied from $66,653/QALY to $145,517/QALY and peak EVPI varied from $20.8 million to $26.9 million (Figures 2a–2d). When borderline adjuvant vaccine efficacy was assumed, the ICER of treatment plus adjuvant qHPV vaccination compared with do nothing was increased to $87,982/QALY. (Figure 3a; Appendix Table T4.1). The EVPI under this scenario of borderline vaccine efficacy at the WTP threshold of $100,000/QALY increased to $21 million (range $10 million to $34 million) (Figure 3a and Appendix Figure 4.2). The peak EVPI was $24 million (range $12 million to $38 million). The EVPPI at $100,000/QALY when borderline efficacy was assumed was $6 million (peak EVPPI at $11 million) for LSIL progression or regression followed by $5 million (peak at $9 million) for HSIL progression or regression (Figure 3b).

DISCUSSION

With increasing health care expenditures, value-based care has received significant attention in recent years [44–46]. There is an increasing demand for value-based cancer research with emphasis on improvement in clinical trial efficiency and cancer outcomes in order to increase the body of knowledge derived from scarce research funding without sacrificing scientific rigor [44]. Likewise, there is an urgent need to determine research priorities that will facilitate precision medicine. Our analysis provides a unique perspective on the value of future adjuvant qHPV vaccination research that by evaluating the impact of uncertainty regarding vaccine efficacy and other study variables on decision making, systematically determines future research needs with the objective to achieve the maximum return on limited healthcare resources and at the same time, maximize population health.

Previous studies evaluated the effectiveness or cost-effectiveness of adjuvant HPV vaccination compared to HSIL treatment alone (i.e., adding HPV vaccination to HSIL treatment regimen) [14, 15, 47] or determined the cost-effectiveness of HSIL management [19] or surveillance after HSIL treatment [48]. No guidelines exist for anal HSIL management and given the uncertainty associated with the efficacy of HSIL treatment and adjuvant HPV vaccination, in the present study, we first comprehensively compared the outcomes of all potential HSIL management options and then conducted value-of-information analysis to determine the value of future research needed to resolve all possible uncertainty among HIV-infected MSM. Finally, we determined future high priority research by identifying parameters with highest informational value.

We found that post-treatment adjuvant qHPV vaccination is likely to be a cost-effective strategy for management of HSIL and implementation of post-treatment adjuvant HPV vaccination policy sooner rather than later should be of high priority because the future data is unlikely to change the conclusion that treatment plus adjuvant qHPV vaccination would be most cost-effective. Our conclusion is based on a detailed cost-effectiveness and value of information analysis, which evaluated a tradeoff between making a decision with current, uncertain, information versus waiting to reduce uncertainty with additional research. The VOI analysis suggested that potential HSIL management research in HIV-infected MSM

who are 27 years or older could potentially be worthwhile if the total cost of research is below $12 million (range $6 million – $20 million). Under an alternative assumption of borderline adjuvant qHPV vaccination efficacy, where adjuvant vaccine efficacy was at its extreme lower-bound, the maximum value of potential research increased to $21 million (range $10 million to $34 million).

To our knowledge, no previous study has evaluated the value of conducting future research for prevention of anal cancer. Our findings will help prioritize future research that will ultimately help reduce uncertainty about unobserved study variables. The reduction in uncertainty in some parameters will not affect results of future cost-effectiveness analysis. For example, future studies evaluating adjuvant qHPV vaccination efficacy, HSIL treatment effectiveness, and HPV reinfection and clearance where EVPPI was $0. The significance of this finding is that despite the uncertainty about these parameters, particularly about the efficacy of adjuvant qHPV vaccination, treatment plus adjuvant vaccination remains the most cost-effective strategy. Any future research in these parameters is unlikely to change the policy conclusion that HSIL treatment plus adjuvant HPV vaccination is cost-effective in HIV-infected MSM.

We also identified areas of future research that should have a high priority. First, future studies evaluating the natural history (progression or regression) of LSIL was likely to be of highest priority, based on its highest EVPPI. Substantial uncertainty exists about the natural history of LSIL. For instance, three studies reported LSIL progression or regression [9, 43, 49]. Two of these followed a cohort of patients [43, 49] and one retrospectively performed clinical audit.[9] All reported progression in the range of 4.7% to 11.6% per year [9, 43, 49]. In addition, all reported that the progression rate increases with age and decreases with reduced CD4 count. No study reported spontaneous LSIL regression. Such a study along with additional research to resolve uncertainty related to evaluation of age-specific progression or regression could potentially be worthwhile as long as the total cost of future research remains below $1.5 million.

The second highest priority future research should focus on measuring HSIL progression or regression in patients not receiving treatment for HSIL. In a recent meta-analysis, Machalek et al (2012) [2] theoretically calculated the progression rate of HSIL to cancer to be 1 in 377 HIV-infected MSM per year, and previous modeling-based studies have shown that progression is likely to increase with age [28, 50]; however, none of these estimates were based on empirical studies. Tong et al (2013) evaluated regression of HSIL and found that regression rate decreases with age [9]. Further research to evaluate HSIL progression and regression could potentially be worthwhile if it cost less than $0.5 million. The low EVPPI implies that the precise estimates for this variable might be obtained from less costly methods, such as observational studies.

Our study's inherent limitation is that it only evaluates the uncertainties captured by the economic evaluation model. The analysis does not take into account parameters that may apply to particular individuals—for example, vaccination side effects like allergic reactions, pain, and fainting. We did not consider these side effects because they are extremely rare. In most instances, when they occur, these side effects have little to no impact on the overall

cost-effectiveness of the vaccine. Second, we estimated the outcomes assuming a time frame of 20 years over which post-treatment adjuvant HPV vaccination might remain efficacious for prevention of anal cancer. As there is uncertainty over long term duration and degree of protection of treatment and adjuvant vaccination, we performed sensitivity analysis varying this time-frame in the range of 10 to 30 years.

In conclusion, treatment plus vaccination is potentially the most cost-effective approach for HSIL management. If implemented sooner rather than later, post-treatment adjuvant qHPV vaccination has the potential to decrease the incidence of preventable invasive anal cancer and save a large sum of healthcare dollars that would otherwise be spent on treatment for recurrent HSIL and invasive cancer. Therefore, adjuvant qHPV vaccination of HIV-infected MSM aged 27 years or older and who have had treatment for HSIL should be considered.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Research highlights

- We examined value of adoption of adjuvant qHPV vaccine for anal cancer prevention.

- We performed cost-effectiveness and value of information analysis.

- HPV vaccination is cost-effective for managing HIV-positive MSM with HSIL.

- Future clinical research data will not change this policy conclusion.

- Implementing adjuvant HPV vaccination soon will provide excellent value for money.
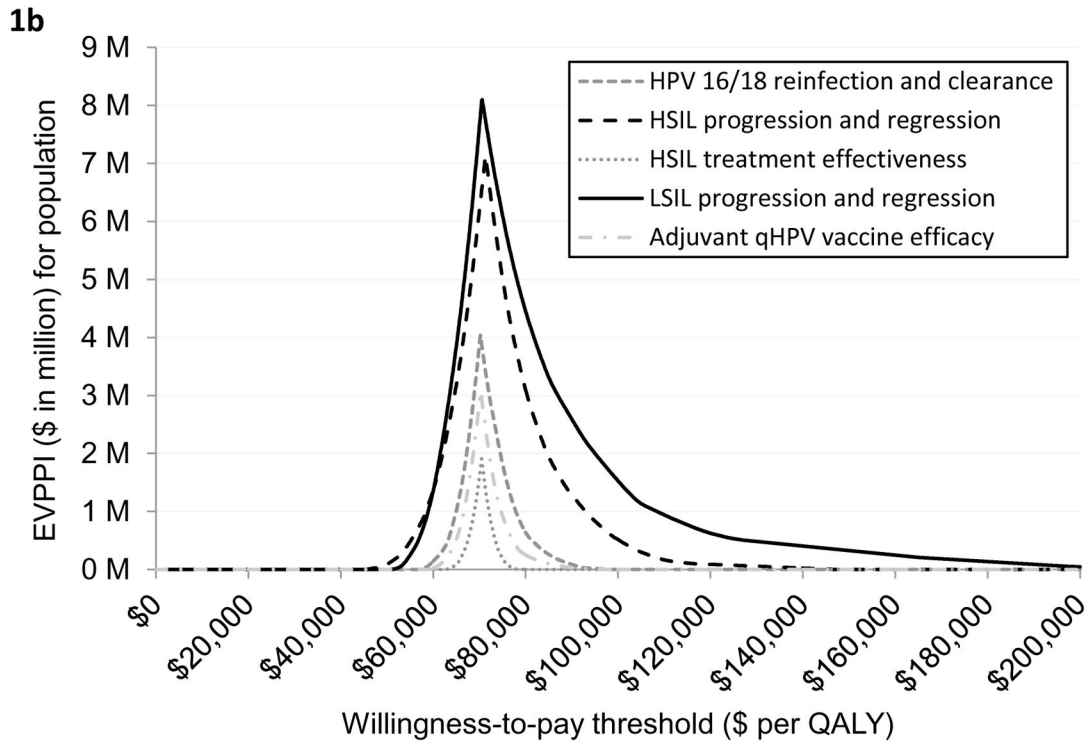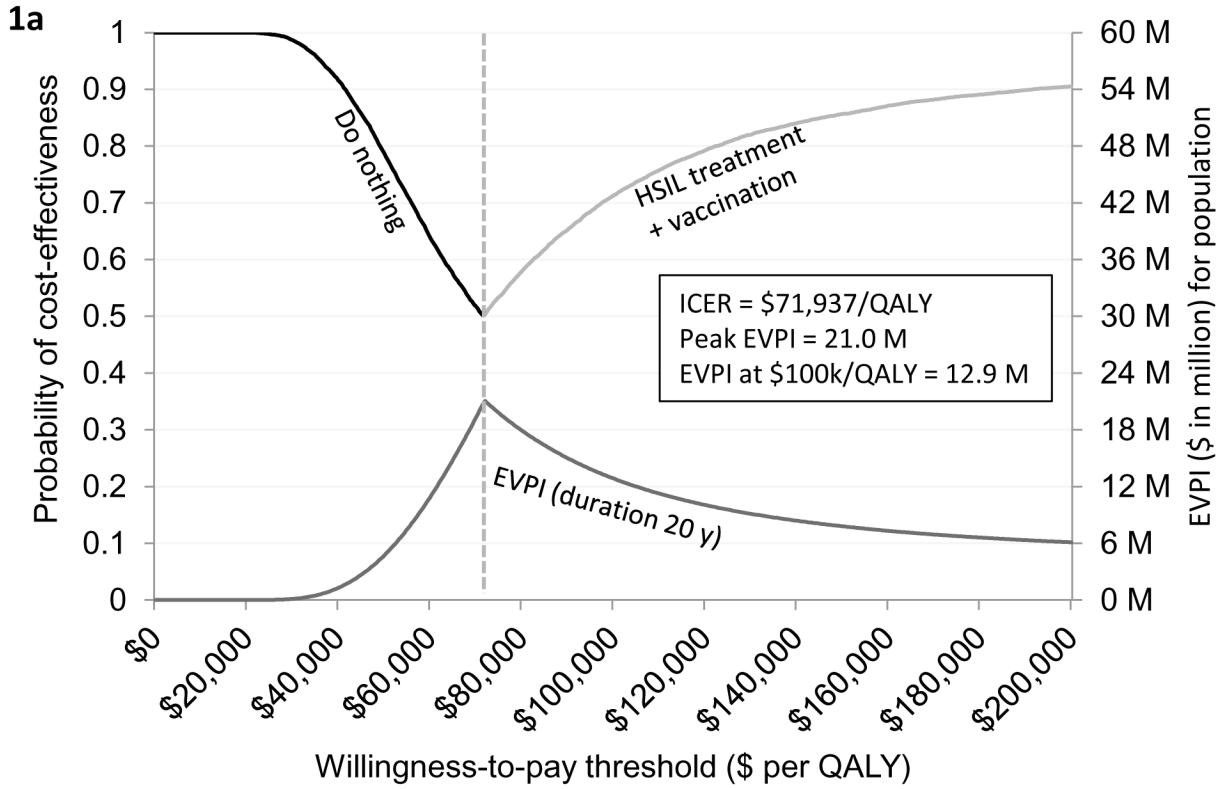
1a

1b

Figure 1. Cost-effectiveness acceptability frontier and expected value of perfect and partial perfect information
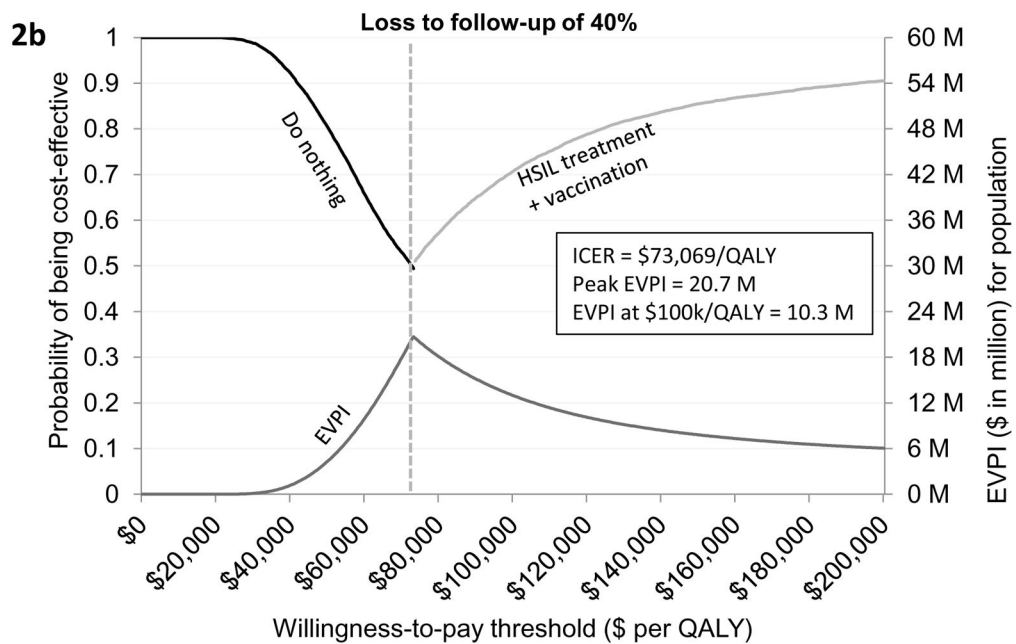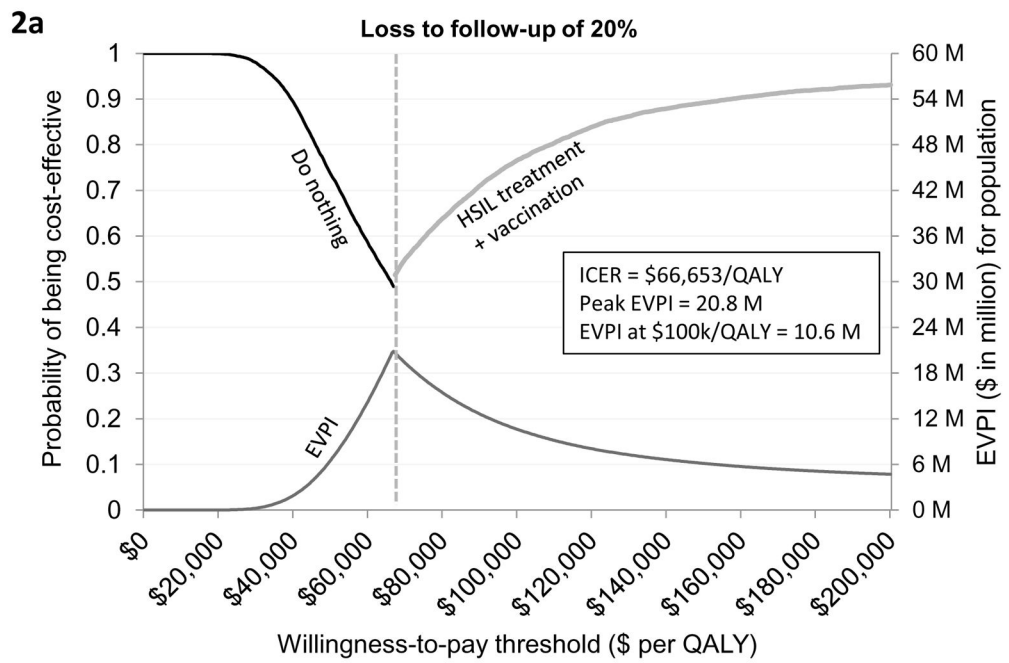
Figure 1a provides a graphical illustration of the uncertainty associated with the optimal strategy over a range of values for the willingness-to-pay thresholds. As seen in the figure, do nothing was the optimal strategy if the willingness-to-pay (WTP) threshold was below $71,937 per QALY. If the WTP threshold was greater than $71,937 per QALY then HSIL treatment plus adjuvant vaccination was the optimal strategy. The secondary vertical axis of the figure illustrates the EVPI associated with HSIL management in HIV-infected MSM. As seen in the figure, the value of further investigation was $12 million at the WTP threshold of $100,000 per QALY. Figure 1b shows EVPPI associated among HIV-infected MSM. Solid black, dashed black, dashed gray, dashed and dotted gray, and dotted gray lines represent the parameters LSIL progression and regression, HSIL progression and regression, HPV 16/18 reinfection and clearance, adjuvant qHPV vaccination efficacy, and HSIL treatment effectiveness, respectively. As seen in the figure, at the WTP threshold of $100,000 per QALY, the EVPPIs for LSIL progression and regression and HSIL progression and regression were $1.5 million and $0.5 million, respectively.

Abbreviations: EVPI, expected value of perfect information; EVPPI, expected value of partial perfect information; ICER, incremental cost-effectiveness ratio; HSIL, high-grade squamous intraepithelial lesions; QALY, quality-adjusted life-year.
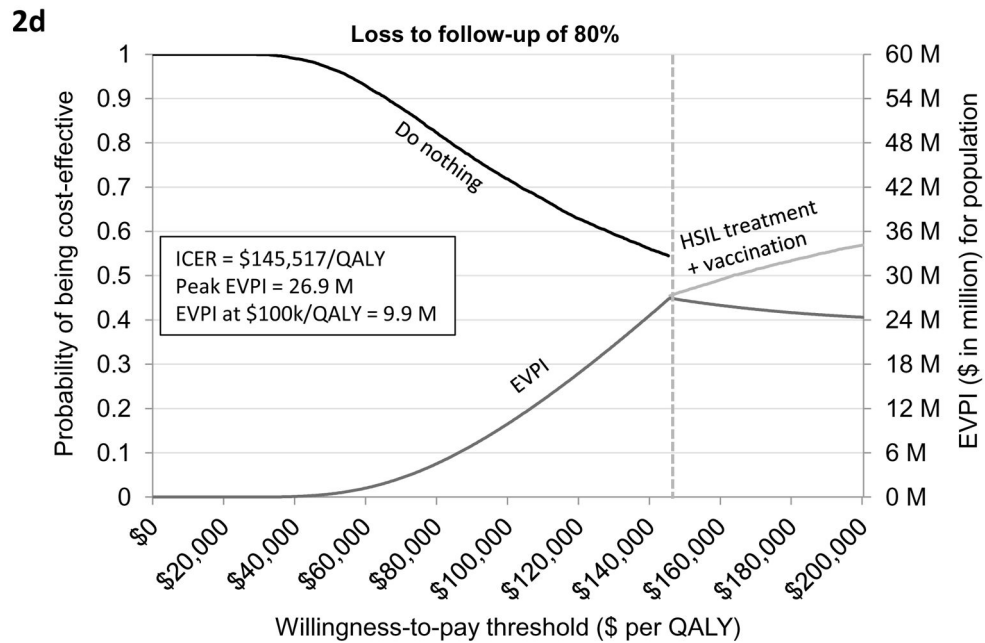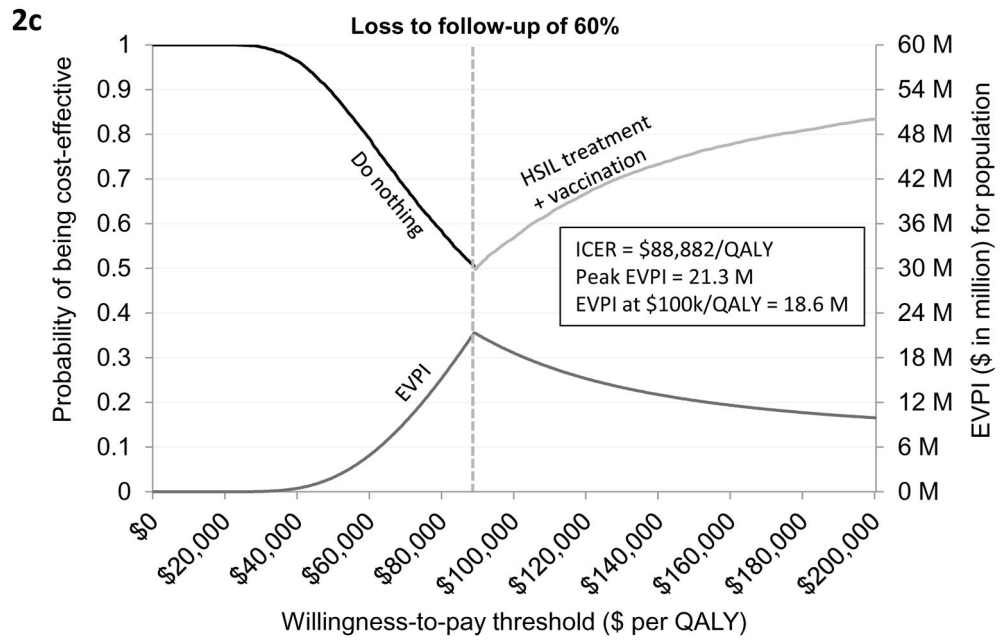
2a

Loss to follow-up of 20%

ICER = $66,653/QALY
Peak EVPI = 20.8 M
EVPI at $100k/QALY = 10.6 M

2b

Loss to follow-up of 40%

ICER = $73,069/QALY
Peak EVPI = 20.7 M
EVPI at $100k/QALY = 10.3 M

2c

Loss to follow-up of 60%

Do nothing

HSIL treatment + vaccination

ICER = $88,882/QALY
Peak EVPI = 21.3 M
EVPI at $100k/QALY = 18.6 M

EVPI

Probability of being cost-effective

EVPI ($ in million) for population

Willingness-to-pay threshold ($ per QALY)

2d

Loss to follow-up of 80%

Do nothing

HSIL treatment + vaccination

ICER = $145,517/QALY
Peak EVPI = 26.9 M
EVPI at $100k/QALY = 9.9 M

EVPI

Probability of being cost-effective

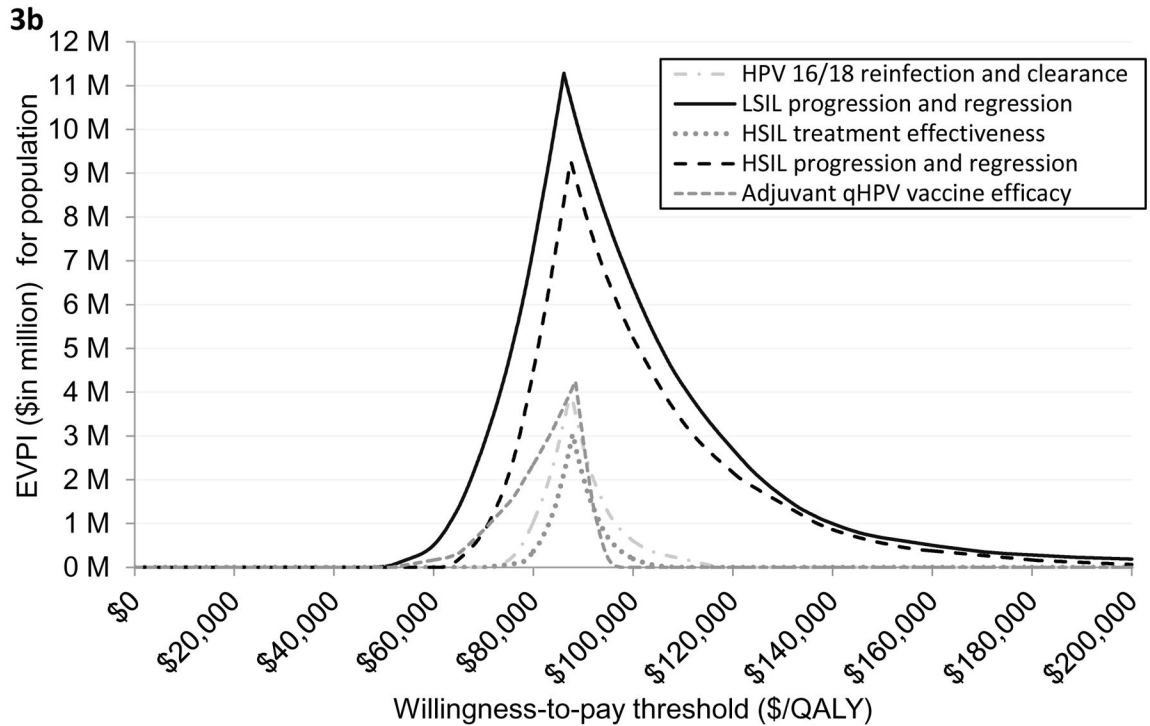EVPI ($ in million) for population

Willingness-to-pay threshold ($ per QALY)
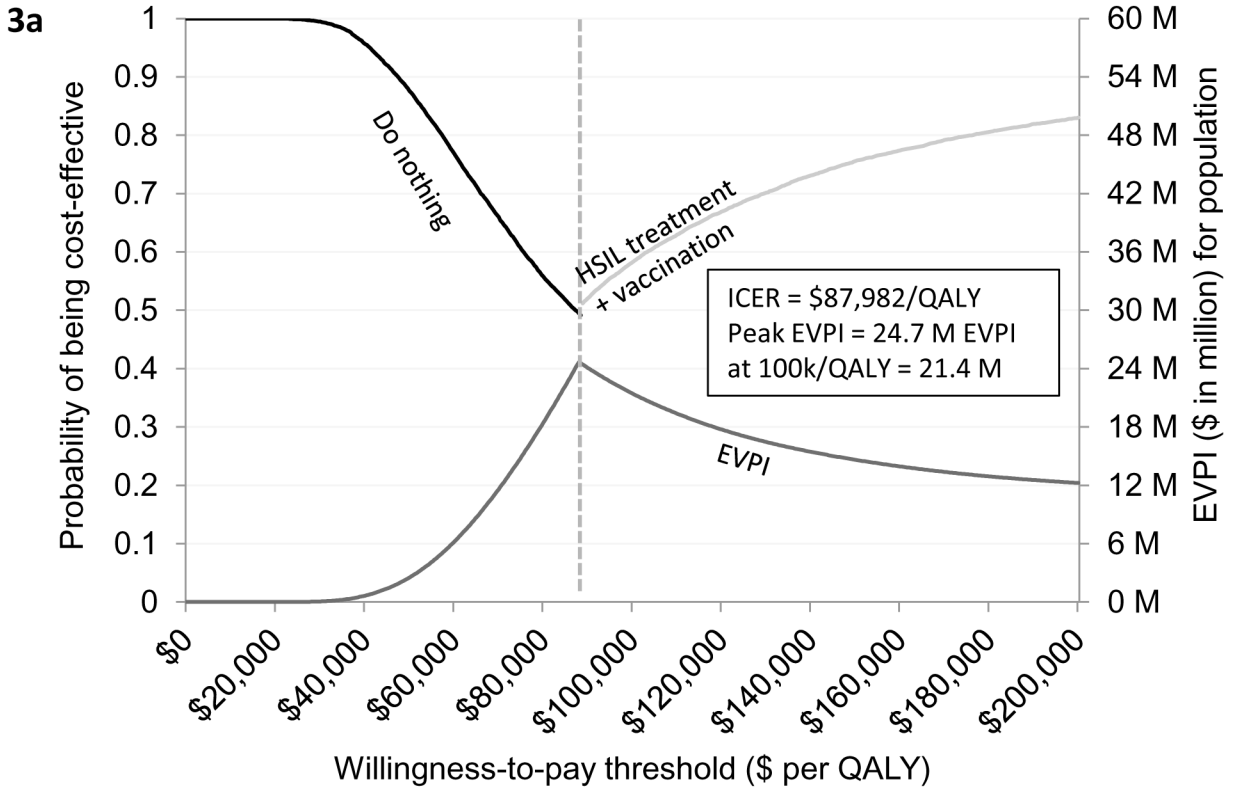
Figure 2. Cost-effectiveness acceptability frontier and expected value of perfect information by treatment compliance (loss to follow-up of 20% to 80%)

Figure 2 depicts cost-effectiveness acceptability frontier and expected value of perfect information when loss to follow-up was varied from **(A)** 20% to **(B)** 40%, **(C)** 60%, and **(D)** 80%.

3a

ICER = $87,982/QALY
Peak EVPI = 24.7 M EVPI
at 100k/QALY = 21.4 M

3b

Legend:
- HPV 16/18 reinfection and clearance
- LSIL progression and regression
- HSIL treatment effectiveness
- HSIL progression and regression
- Adjuvant qHPV vaccine efficacy

Figure 3. Cost-effectiveness acceptability frontier and expected value of perfect information assuming worst-case adjuvant qHPV vaccination efficacy

Figure 3a provides a graphical illustration of the uncertainty associated with the optimal strategy over a range of values for the willingness-to-pay thresholds under the assumption of worst-case adjuvant qHPV vaccination efficacy. As seen in the figure, do nothing was the optimal strategy if the willingness-to-pay (WTP) threshold was below $87,982 per QALY. If the WTP threshold was greater than $87,982 per QALY then HSIL treatment plus adjuvant vaccination was the optimal strategy. The secondary vertical axis of the figure illustrates the EVPI associated with HSIL management in HIV-infected MSM when worst-case adjuvant qHPV vaccination efficacy was assumed. As seen in the figure, the value of further investigation was $21 million at the WTP threshold of $100,000 per QALY. Figure 3b shows EVPPI associated among HIV-infected MSM. Solid black, dashed gray, dashed brown, dashed and dotted blue, and dotted green lines represent the parameters LSIL progression and regression, HSIL progression and regression, adjuvant qHPV vaccination efficacy, HPV 16/18 reinfection and clearance, and HSIL treatment effectiveness, respectively. As seen in the figure, at the WTP threshold of $100,000 per QALY, the EVPPIs for LSIL progression and regression and HSIL progression and regression were $6 million and $5 million, respectively.

Abbreviations: EVPI, expected value of perfect information; EVPPI, expected value of partial perfect information; ICER, incremental cost-effectiveness ratio; HSIL, high-grade squamous intraepithelial lesions; QALY, quality-adjusted life-year

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Table 1

Cost-effectiveness analysis

Strategy	Lifetime Cost, $	QALYs	ICER, $ per QALY	Cumulative anal cancer incidence, %	Cumulative anal cancer mortality, %
Do nothing	367,911	12.93	–	8%	5%
Active monitoring/watchful waiting	372,268	12.95	Weakly Dominated[†]	8%	4%
Treat HSIL	379,056	13.04	Weakly Dominated[†]	3%	2%
Treat HSIL+ adjuvant qHPV vaccination	379,458	13.09	71,937	2%	1%

Abbreviations: QALYs, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; HSIL, high-grade squamous intraepithelial lesions; qHPV, quadrivalent human papillomavirus vaccine