

Supplementary Appendix to
Evaluating Cost-effectiveness of 9-valent HPV Vaccination for Men Who Have Sex with
Men by HIV Status in Hong Kong

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lementary Table S1. Annual HPV infection rates by age group and HIV status in MSM.

Age Group	HIV+/HR-HPV	HIV+/LR-HPV	HIV-/HR-HPV	HIV-/LR-HPV
12–18	0.2027	0.1720	0.1398	0.1186
19–27	0.2027	0.1720	0.1398	0.1186
28–44	0.4054	0.3440	0.2796	0.2372
≥45	0.2027	0.1720	0.1398	0.1186

MSM = men who have sex with men; HPV = human papillomavirus; HR-HPV = high-risk human papillomavirus; LR-HPV = low-risk human papillomavirus; HIV = human immunodeficiency virus.

The overall HPV incidence is from a an observational cohort study [1]. To derive age-specific infection rates for high risk HPV types and low risk HPV types and HIV statuses among MSM, we used the following formula based on age group weighting (Supplementary Table S3) and relative incidence: $P_i = k \times r_i$ (k =Total susceptibility / $\sum w_i \times r_i$)

To estimate the incidence of high-risk (HR) and low-risk (LR) HPV in HIV-positive MSM, we used the prevalence ratio between HIV-positive (92.6%) and HIV-negative (63.9%) MSM [2], giving a ratio of approximately 1.45. Assuming susceptibility increases proportionally with prevalence, we multiplied the known susceptibility in HIV-negative MSM (HR-HPV: 0.0171; LR-HPV: 0.0142) by this ratio. The estimated susceptibilities in HIV-positive MSM are therefore 0.0248 for HR-HPV and 0.0206 for LR-HPV. This simplified approach assumes a direct relationship and may not account for other influencing factors.

The incidence rates of HPV infection were assumed to be different among these four groups. The age-stratified HPV incidences were assumed to be 1:1:2:1 among the 12-18, 19-27, 28-44 and ≥45 age groups, to reflect the higher overall incidences of genital warts and anal cancer among the intermediate male age group [3].

Supplementary Table S2. Age-specific natural background mortality rates.

Annual all-cause mortality rate by HIV status and age (%).	HIV-	HIV+
11–14 years	0.0083	0.018094
15–19 years	0.0215	0.04687
20–24 years	0.0322	0.070196
25–29 years	0.0466	0.101588
30–34 years	0.0622	0.135596
35–39 years	0.0833	0.181594
40–44 years	0.1253	0.273154
45–49 years	0.1990	0.4338
50–54 years	0.3107	0.677326
55–59 years	0.5293	1.153874
60–64 years	0.8374	1.825532
65–69 years	1.2641	2.755738
70–74 years	2.1524	4.692232
74–79 years	3.4555	7.53299
80–84 years	6.0256	13.135808
85+ years	12.2915	26.79547

HIV = human immunodeficiency virus; HIV– = HIV-negative individuals; HIV+ = HIV-positive individuals

The monthly all-cause mortality rates for HIV-negative MSM were based on age-specific mortality rates for males in Hong Kong [4]. For HIV-positive MSM, a higher mortality risk was applied by incorporating a monthly mortality risk ratio of 2.18, as reported in a previous study [5]

Supplementary Table S3. The proportion of MSM age groups

Age Group	Proportion
12–18	0.1422
19–27	0.2478
28–44	0.4654
≥45	0.1456

To adjust the proportions according to the newly defined age groups (12-18, 19-27, 28-44, ≥41), we'll need to redistribute the existing age group data (≤20, 21-30, 31-40, ≥41) into the new categories. We'll assume a uniform distribution within each group for this calculation [6].

MSM age groups	[7]
12-20	9.6%
21-30	42%
31-40	32.9%
≥41	15.6%

Supplementary Table S4. Age-specific natural background mortality rates.

Annual all-cause mortality rate by HIV status and age (%).	HIV-	HIV+
11–14 years	0.0083	0.018094
15–19 years	0.0215	0.04687
20–24 years	0.0322	0.070196
25–29 years	0.0466	0.101588
30–34 years	0.0622	0.135596
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Supplementary Table S4. HPV vaccination strategies for MSM.

Strategy	Age groups			
	12-14	15-27	28-44	≥45
One-group-targeted strategies				
All MSM	1	0	0	0
	0	1	0	0
	0	0	1	0
	0	0	0	1
HIV+ MSM	1	0	0	0
	0	1	0	0
	0	0	1	0
	0	0	0	1
Two-group-targeted strategies				
All MSM	1	1	0	0
	1	0	1	0
	1	0	0	1
	0	1	1	0
	0	1	0	1
	0	0	1	1
HIV+ MSM	1	1	0	0
	1	0	1	0
	1	0	0	1
	0	1	1	0
	0	1	0	1
	0	0	1	1
Three-group-targeted strategies				
All MSM	1	1	1	0
	1	1	0	1
	1	0	1	1
	0	1	1	1
HIV+ MSM	1	1	1	0
	1	1	0	1

	1	0	1	1
	0	1	1	1
Three-group-targeted strategies				
All MSM	1	1	1	1
HIV+ MSM	1	1	1	1

MSM = men who have sex with men; Number "0" represents no vaccine, "1" represents vaccine.

Supplementary S1. Transition probabilities assumption.

1. HR-HPV to LG-AIN

Data on the Infected → LGAIN rate for HIV-positive MSM was not found in recent studies. Thus, we used data from a 1998 study by Palefsky et al. which measured AIN progression in 143 HIV positive and 131 HIV negative individuals for 2 years and also the number of HPV strains they were infected with [39]. The rate of progression in HIV positive individuals infected with either a single or multiple HIV strains was 0.58/person-year (95 cases in 165 person-years), and the rate of progression in HIV negative individuals was 0.30/person-year (32 cases in 106 person-years). Thus, the rate of Infected → LGAIN for HIV-positive MSM is 1.9 times that of HIV-negative MSM. The rates of progression in HIV negative individuals we estimated were similar to 0.078 [8], So the HIV positive MSM HR-HPV to LGAIN is 0.1482

2. LR-HPV to GW

LR-HPV infections were found in anogenital warts among MSM, with a prevalence of 75.9% in HIV-positive individuals and 41.7% in HIV-negative individuals [9]. This indicates that HIV-positive MSM have a higher risk of multiple LR-HPV infections compared to HIV-negative MSM, with a risk ratio of approximately 1.82. According to a MSM modelling study [10], the probability of LR-HPV to genital warts in MSM is 0.29. Therefore, for HIV-positive MSM, we assumed the probability of LR-HPV leading to GW is $0.29 * 1.82 = 0.5278$.

3. HG-AIN to Anal cancer

Annual transition probabilities from HG-AIN to anal cancer [11]

Age (years)	Mean
12-35	0.0009
36-45	0.0014
>45	0.0045

4. Supplementary Table S5. Transition probabilities from HG-AIN to anal cancer among HIV- MSM.

MSM HIV-		MSM HIV+	
Age (years)	Mean	Age (years)	Mean
12-35	0.0009	12-35	0.0099
36-45	0.0014	36-45	0.0154
>45	0.0045	>45	0.0495

Annual rates estimated from Machalek et al. [2], 1 in 377 in HIV-positive MSM and 1 in 4196 in HIV-negative MSM, with a risk ratio of 11:1. We assumed the annual rate for HIV-positive individuals is 11 times that of HIV-negative individuals.

5. LG-AIN to HG-AIN

Data on the LGAIN → HGAIN rate for MSM by HIV status was not found in recent studies. Thus, we used data from a 1998 study by Palefsky et al. which measured incident HSIL (high-grade squamous intraepithelial lesion) in 277 HIV positive and 211 HIV negative individuals with 4 years of follow-up [39]. Of 135 HIV-positive MSM and 34 HIV-negative with LSIL (low-grade squamous intraepithelial lesion) or ASCUS (atypical squamous cells of undetermined significance) at baseline, 62 and 11 had HSIL by either cytology or histology within 4 years, for yearly rate of progression of 0.149 (416 person-years) and 0.096 (114 person-years), respectively. Thus, the rate of LGAIN → HGAIN for HIV-positive MSM is 1.5 times that of HIV-negative MSM. We use TreeAge Pro 2022 to transit the rate into probability by using function ratetoprob

6. Supplementary Table S7. Anal cancer mortality among MSM stratified by age and HIV status.

The cancer	MSM HIV-		MSM HIV+		anal
	Age (years)	Mean	Age (years)	Mean	
	12-29	0.0000	12-29	0.0000	
	30-39	0.0564	30-39	0.122952	
	40-49	0.2064	40-49	0.449952	
	50-59	0.1452	50-59	0.316536	
	>59	0.2208	>59	0.481344	

mortality data for MSM who are HIV-negative comes from the Hong Kong Hospital Authority's local data. The death rate for HIV-positive individuals was found to be 2.18 times greater [5]. We assume that the death rate for every age group is consistently 2.18 times higher among MSM who are HIV-positive. Therefore, to estimate the mortality rates for HIV-positive individuals, we multiply the HIV-negative data by 2.18.

7. Anal cancer to Cured

The monthly transition probability for HIV-negative MSM from anal cancer to cancer cured is 0.0166, based on local data from the Hospital Authority. A retrospective cohort study found that the 5-year anal cancer-specific survival rates for HIV-negative and HIV-positive males are 80.5% and 72.5%, respectively [12]. The ratio of these survival rates is approximately 1:0.9. The cured rate of anal cancer among MSM is from [13]

8. LR-HPV, HR-HPV to Susceptible

Among people living with HIV, the HPV clearance rate is approximately halved, with a pooled relative risk (RR) of 0.53 (95% CI: 0.42 to 0.67) [14]. To adjust for the reduced clearance rate among HIV-positive individuals, we multiply the transition probabilities by the RR: For LR-HPV HR-HPV to Susceptible: $0.146 * 0.53 = 0.0774$

Supplementary Table S8. Number and Proportion of Anogenital Warts and Anal Cancer Cases Prevented under 9vHPV (70% Coverage)

				Incidence of anogenital warts	Incidence of anal cancer
Base-case				1438.1 per 100,000 years	2.03 per 100,000 person-years
Strategy				Prevented anogenital warts	Prevented anal cancers
Age groups					
12-18	19-27	28-44	≥45		
Strategies preventing the most anogenital warts					
One-group-targeted strategies					
0	0	1	0	38330000 (26.7%)	105500 (52.0%)
Two-group-targeted strategies					
0	1	1	0	55750000 (38.8%)	117700 (58.0%)
Three-group-targeted strategies					
1	1	1	0	65800000 (45.8%)	125900 (62%)
Strategies preventing the most anal cancer					
One-group-targeted strategies					
0	0	1	0	38330000 (26.7%)	105500 (52.0%)
Two-group-targeted strategies					
0	1	1	0	55750000 (38.8%)	117700 (58.0%)
Three-group-targeted strategies					
0	1	1	1	65600000 (45.6%)	138500 (68.2%)
Four-group-targeted strategies					
1	1	1	1	75640000 (52.5%)	143000 (70.4%)

Supplementary Table S9. The ICER values of different HPV vaccination strategies in sensitivity analyses.

	Strategy							
	All 12-18	All 12-18 & 28-44	All 12-44	All ≥ 12	HIV + 12-18	HIV+ 12-18 & 28-44	HIV+ 12-18 & ≥ 28	HIV+ ≥ 12
Vaccine price for both adolescent and adult								
25%	580.4	6128.4	7522.6	8094.1	Cost saving	Cost saving	Cost saving	57.6
-25%	Cost saving	2255.9	3099.0	3966.0	Cost saving	Cost saving	Cost saving	Cost saving
50%	1400.5	8064.6	9734.4	10418.8	Cost saving	Cost saving	322.5	1038.8
Vaccine Efficacy Duration and time horizon								
Protection of 10 years/ 20 year horizon				undominated				
Protection of 10 years/ 5 year horizon	10465.6	24565.3	29466.9	31526.2	Cost saving	6631.0	7882.8	9717.4
Protection of 20 years/ life time horizon				undominated				

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