Appendix 1. Additional information on the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model

The PRIME model is a model developed by the World Health Organization (WHO) to estimate country-specific cost-effectiveness of HPV vaccination among females. It models the effect of the vaccine by incorporating the reduction in age-dependent incidence of cervical cancer as a result of vaccination. The model assumes that the individuals finish all doses of the vaccine and the vaccine provides lifelong protection. Also, it does not consider herd immunity.

The model is pre-populated with country-specific input data. However, it also allows customization of the input data. We changed the inputs of target age group, price of vaccine, delivery costs (adjusted based on the default input), and cancer treatment costs. We also changed the Chinese-specific data of the proportion of cervical cancer attributable to HPV types 16/18 to that of HPV types 16/18/31/33/45/52/58 for the analysis of the 9-valent vaccine.

To cross-validate the model, the developers of the model extracted input data from previous HPV modeling studies and calculated the results using the PRIME model. The results were then compared with the previous studies, the difference from published results was tested using Cohen's Kappa (0.845; indicates near perfect agreement). The developers showed that there was good agreement.

The model was adopted to evaluate the cost-effectiveness of HPV vaccination in Vietnam as a country-specific application in addition to multi-country application.(1) More details of the model have been described elsewhere.(2)

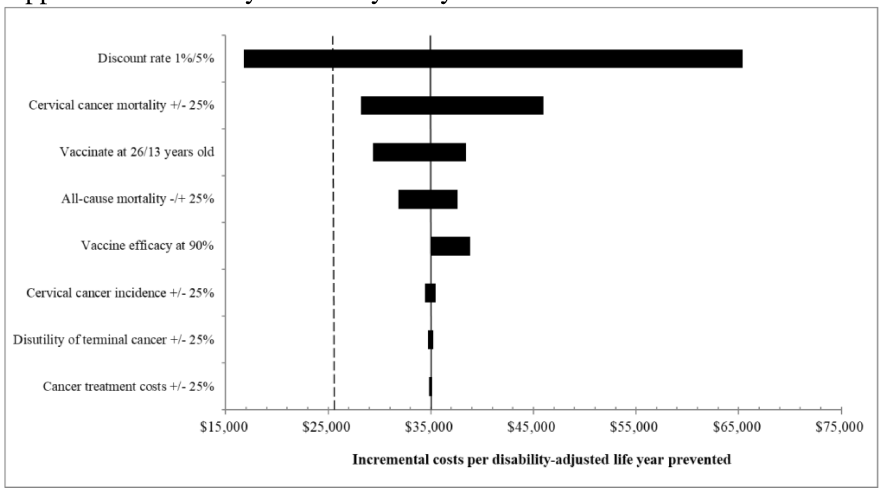
Appendix 2. Very small chances of prior HPV infection among the 16 years old Chinese females

In the base-case analysis, the target age group was 16 years old females because this was the youngest age group among the approved population for the use of the 9-valent vaccine in China. In China, the vast majority of the female individuals in this age are not infected with HPV. According to a study by Zhao et el., 6.9% of females in the age group 15-19 years old were sexually active in 2012.(3) This number should be lower for those who aged 16 years since this age is closer to the younger bound of the age group. Another study in the same year by Guo et al. confirmed that sexual debut before age 18 was rare in China.(4) Granted, the estimates were not necessarily accurate since there might be social desirability bias and the situation could have evolved, but it is impossible to speculate on how substantial the bias and the change were. However, it is reasonable to think the proportion of sexually active individuals in the 16 years old females is still very low in China. Therefore, most 16 years old still did not have sexual debut and did not expose to HPV although a very small proportion of them would have had sexual debut. Additionally, taking into consideration that most of those who had sexual debut would not have been infected, the proportion of uninfected individuals in the age group of 16 years old would be even higher than the proportion without sexual debut.

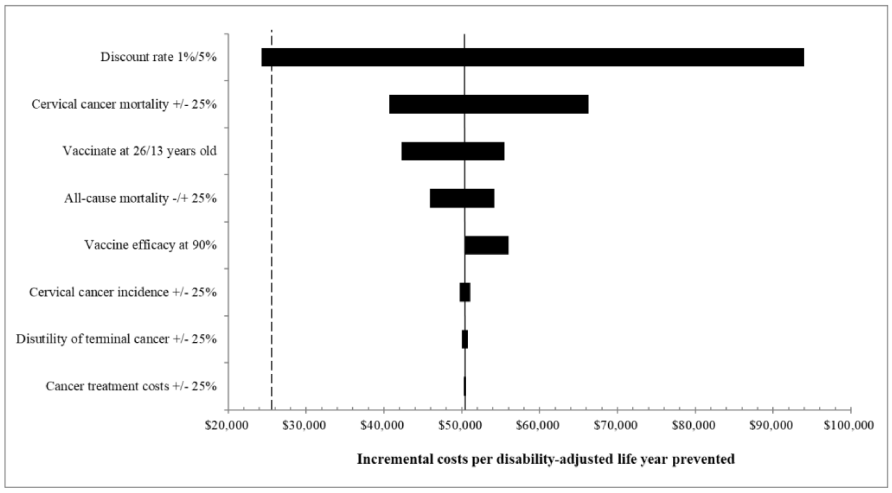
Appendix 3. Additional information on the base-case results.

	Not receiving vaccination	9-valent vaccine	quadrivalent vaccine	bivalent vaccine
Discounted expected lifetime treatment costs of cervical cancer per individual (HPV types 16/18/31/33/45/52/58)	$17	$0	NA	NA
Discounted expected lifetime treatment costs of cervical cancer per individual (HPV types 16/18)	$13	NA	$0	$0
Total costs with vaccination	NA	$628	$393	$291
Discounted expected life years lost due to cervical cancer (HPV types 16/18/31/33/45/52/58)	0.0250	0	NA	NA
Discounted expected life years lost due to cervical cancer (HPV types 16/18)	0.0188	NA	0	0
Discounted non-fatal DALYs due to cervical cancer (HPV types 16/18/31/33/45/52/58)	0.0015	0	NA	NA
Discounted non-fatal DALYs due to cervical cancer (HPV types 16/18/31/33/45/52/58)	0.0011	NA	0	0
Discounted net costs	NA	$611	$380	$278
Discounted DALYs prevented	NA	0.0265	0.0199	0.0199
ICER vs. not being vaccinated	NA	$23,012	$19,061	$13,944

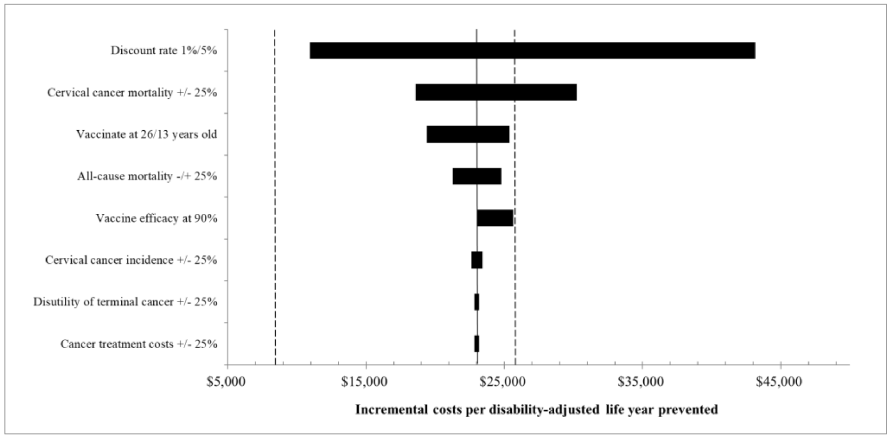
Appendix 4. One-way sensitivity analyses of the 9-valent HPV vaccine



a. Sensitivity analysis results of comparing the 9-valent vaccine with the quadrivalent vaccine. The dash line on the left represents the cost-effective threshold.



b. Sensitivity analysis results of comparing the 9-valent vaccine with the bivalent vaccine. The dash line on the left represents the cost-effective threshold.



c. Sensitivity analysis results of comparing the 9-valent vaccine with no vaccination. The left and right dash lines represent the highly cost-effective and cost-effective thresholds, respectively.

Appendix 5. An example of discounted results vs. undiscounted results. The sensitivity analysis result that vaccinating at older ages was more cost-effective is counter-intuitive. It was because the loss of DALYs prevented caused by discounting exceeds the gain of DALYs prevented by vaccinating earlier. To further illustrate this, we present below an example using the default PRIME model without customizing any parameters except age.

Hence, the results in the example only demonstrate how discounting affects model outputs and are not comparable to the results in the current study.

	Vaccinate at 16 years old		Vaccinate at 26 years old	
	Undiscounted	Discounted	Undiscounted	Discounted
Net costs	$42	$43	$42	$44
DALYs prevented	0.0482	0.0158	0.0445	0.0188
Incremental costs per DALY prevented	$867	$2,751	$945	$2,316

Abbreviations: DALY, disability-adjusted life year; PRIME, the Papillomavirus Rapid Interface for Modelling and Economics (PRIME).

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