Supplementary Materials

Supplementary Material 1: References and assumptions for vaccine effectiveness used in the model against CC, CIN1/2/3 and GW for 2D-AS04-HPV-16/18v, 2D-4vHPVv and 2D/3D-9vHPVv

To approximate vaccine effectiveness, the model used vaccine efficacy (VE) as a proxy. Based on local expert opinion, the study used VE estimates irrespective of human papillomavirus (HPV) type, which were taken from clinical trials for girls and women who were naïve to HPV infection at study entry; they were considered most representatives of 12-year-old girls (i.e. 7th grade), the cohort of interest in this analysis. It should be noted that VE against 'any grade' or cervical intraepithelial neoplasia (CIN) grade 1 (CIN1) or higher (CIN1+) was used as proxy effectiveness against CIN1; VE against CIN grade 2 (CIN2) or higher (CIN2+) as proxy effectiveness against CIN2/3 and VE against CIN grade 3 (CIN3) or higher (CIN3+) as proxy effectiveness against cervical cancer (CC).

VE against CIN1/CIN1+, CIN2/CIN2+ and CIN3/CIN3+, irrespective of the causative HPV types, has been reported for the AS04-adjuvanted HPV-16/18 vaccine (AS04-HPV-16/18v) and the human papillomavirus 6/11/16/18 vaccine (4vHPVv), respectively (Lehtinen et al., 2012; Munoz et al., 2010). However, VE for the human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine (9vHPVv), irrespective of the causative HPV type, has been reported against 'any grade' and CIN2+ but not for CIN3/CIN3+ (Merck Sharp & Dohme Corp., 2015). Therefore, VE against CIN3/CIN3+ for 9vHPVv was projected based on available data from a study by Joura et al. (2014) and the clinical trial synopsis of 9vHPVv (Merck Sharp & Dohme Corp., 2015).

Joura et al. (2014) reported the contribution of seven oncogenic HPV types (HPV16/18/31/33/45/52/58) to cases of CIN1, CIN2 and CIN3 in the placebo arms of the

4vHPVv phase III clinical trials. As these oncogenic types are targeted by 9vHPVv, the authors estimated 9vHPVv would prevent the development of CIN1, CIN2 and CIN3 to the extent to which these HPV types were causing the CIN stages within the population. As explained in section "Vaccine effectiveness", the adjusted VE of 9vHPVv against CIN3/CIN3+ was estimated at 79.6% (Table S 1).

Table S 1: Estimated VE of 9vHPVv against cervical intraepithelial neoplasia grade 3 (or higher), irrespective of the causative HPV type

Endpoint in the model	**Expected VE (%)**			**Observed VE[§] (%) (Merck Sharp & Dohme Corp., 2015)**	**Ratio (expected VE / observed VE; %)**	**Adjusted VE (%)**
	Min (Joura et al., 2014)	**Max (Joura et al., 2014)**	**Average**			
CIN1 (proxy for CIN1/CIN1+ or "any grade")	43.0	55.0	49.0	47.1	96.1	-
CIN2/3 (proxy for CIN2/CIN2+)	70.0	78.0	74.0	62.8	84.9	-
CC (proxy for CIN3/CIN3+)	85.0	91.0	88.0	-	Average: 90.5	88.0 * 90.5 = 79.6

[§]In HPV naïve population. It is however unclear whether the selected cohort received all 3 doses or at least one dose of the vaccine and had protocol violations.

9vHPVv, human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine; CC, cervical cancer; CIN1/2/3 (+), cervical intraepithelial neoplasia grade 1/2/3 (or higher); HPV, human papillomavirus; VE, vaccine efficacy

Supplementary Material 2: Transition probabilities used in the base-case analysis

The transition probabilities used in the model were mainly taken from previous Taiwan human papillomavirus (HPV) cost-effectiveness analyses (Demarteau et al., 2012; Suárez et al., 2008), updated with local or more recent available data (Health Promotion Administration - Ministry of Health and Welfare - Taiwan; Ministry of Health and Welfare - Taiwan, 2013; Sanders and Taira, 2003; Shen et al., 2016; Van de Velde et al., 2007; Woodhall et al., 2011). The updated data are italicised in the table.

Table S 2: Transition probabilities used in the base-case analysis

Parameter	**Estimate**	**References**
Progression probabilities		
Oncogenic HPV progression to CIN1	7.9%*	Demarteau et al. (2012); Suárez et al. (2008)
Non-oncogenic HPV progression to CIN1	*3.6%*	*Van de Velde et al. (2007); Sanders and Taira (2003)*
Non-oncogenic HPV progression to GW	*0.0% - 2.9%*	*Calibrated against the reported age-specific GW incidence in Taiwan (Ministry of Health and Welfare - Taiwan, 2013) (Table 2)*
Oncogenic CIN1 progression to CIN2/3	9.1%	Demarteau et al. (2012); Suárez et al. (2008)
CIN2/3 progression to persistent CIN2/3	11.4%	Demarteau et al. (2012); Suárez et al. (2008)
Persistent CIN2/3 progression to CC	*0.0% - 3.6%*	*Calibrated against the reported age-specific CC incidence in Taiwan (Health Promotion Administration - Ministry of Health and Welfare - Taiwan) (Table 2)*
CC to death	*6.7%*	*Estimated based on a 5-year survival rate of 70.8% (Shen et al., 2016). It was assumed that CC patients alive after 5 years were cured.* *Calibrated against the reported age-specific CC mortality in Taiwan (Health Promotion Administration - Ministry of Health and Welfare - Taiwan) (Table 2).*
Regression probabilities		
Oncogenic/non-oncogenic HPV regression	51.6%	Demarteau et al. (2012); Suárez et al. (2008)

Parameter	Estimate	References
Oncogenic/non-oncogenic CIN1 regression to no HPV	44.9%	Demarteau et al. (2012); Suárez et al. (2008)
CIN2/3 regression to no HPV	22.7%	Demarteau et al. (2012); Suárez et al. (2008)
CC regression to no HPV (CC cured)	*21.8%*	*Estimated based on a 5-year survival rate of 70.8% (Shen et al., 2016). It was assumed that CC patients alive after 5 years were cured.*
GW resistance probability		
GW resistant	*29.0%*	*Estimated based on the proportion of females in the UK population with a recurrent episode of GW (Woodhall et al., 2011).*

*4.9% (referenced data) + 3.0% to allow calibration of the model

CC, cervical cancer; CIN1/2/3, cervical intraepithelial neoplasia grade 1/2/3; GW, genital warts; HPV, human papillomavirus

Supplementary Material 3: Epidemiological data incorporated as data input into the model

In addition to cervical cancer (CC) incidence/mortality and genital warts (GW) incidence data described in Table 2, other epidemiological data were incorporated into the model as input data: human papillomavirus (HPV) incidence (non-oncogenic and oncogenic), all-cause mortality in the general female population, and distribution of CC incidence by stage, retrieved from published source as described here below.

Genital warts incidence

The GW incidence data were derived from an analysis of the National Health Insurance Research Database (NHID) for the year 2012 (Ministry of Health and Welfare - Taiwan, 2013) (Table 2). GW incident cases in 2012 were defined as cases that were identified as prevalent cases in 2012 but not in 2011. GW patients were identified as having at least three outpatient claims with major/minor ICD-9-CM code 078.11 (*condyloma acuminatum*) within three months in a given year, or as having received GW treatment procedures in any outpatient claims with major/minor ICD-9-CM code 078.11. The model assumed that a patient did not develop more than one case of GW within a year.

HPV incidence (non-oncogenic and oncogenic)

The annual incidence of oncogenic HPV was derived from the prevalence. Due to variance between age-groups in the prevalence, a polynomial trendline was fitted to generate a continuous function for the prevalence. The following formulae of a 5-power calculation was used to calculate the continuous function for the prevalence of each age group:

C5*age^5+C4*age^4+C3*age^3+C2*age^2+C1*age^1+b = prevalence for the given age, where *C1–C5* represent the coefficients on each term and *b* the constant[1].

As only the overall HPV prevalence has been reported in previous population-based cohort studies in Taiwan, the reported ratio between the oncogenic HPV and the overall HPV prevalence (21.8% / 29.0%) was used to determine oncogenic HPV prevalence for women ≥30 years old (Chao et al., 2008; Chen et al., 2011; Richardson et al., 2003). For women <30 years old, the prevalence of oncogenic HPV was derived from a nationwide cross-sectional study of outpatients from 51 obstetrics-gynaecology clinics in Taiwan (personal communication). The polynomial trend of oncogenic HPV prevalence was then determined based on the estimated oncogenic HPV prevalence (Table S 3). Both the regression probability from oncogenic HPV to no HPV and the progression probability from oncogenic HPV to cervical intraepithelial neoplasia grade 1 (CIN1) were also assumed to remain consistent across age-groups.

Once the annual incidence of oncogenic HPV was estimated, the annual incidence of non-oncogenic HPV was determined based on the reported ratio between the non-oncogenic HPV and oncogenic HPV incidence (1.24% / 1.4%) (Richardson et al., 2003). These oncogenic and non-oncogenic HPV incidence data were used to estimate the probability of HPV infection in the model (Table S 3).

[1]Oncogenic HPV prevalence for a given age = [(1.02160*10^-8)*age^5]+[(-2.50177*10^-6)*age^4]+(0.00023*age^3)+(-0.00999*age^2)+(0.19672*age^1)+(-1.25897).

Table S 3: Age-specific oncogenic and non-oncogenic HPV incidence used in the model

Age-groups (years of age)	Oncogenic HPV prevalence (estimated; %) (Chao et al., 2008; Chen et al., 2011; Richardson et al., 2003) (personal communication)	Oncogenic HPV prevalence (trendline; %)	Oncogenic HPV incidence (trendline; %)	Non-oncogenic HPV incidence (trendline; %) (Richardson et al., 2003)
15-20	11.7%	14.3%	11.9%	10.6%
21-29	15.8%	15.5%	10.6%	9.4%
30-39	9.5%	10.6%	6.9%	6.1%
40-49	9.4%	9.4%	6.2%	5.5%
50-59	11.4%	11.4%	7.5%	6.7%
60-65	12.6%	11.3%	7.8%	6.9%
>65	8.0%	8.3%	7.7%	6.7%

HPV, human papillomavirus

All-cause mortality in the general female population

The age-specific all-cause mortality probabilities in the general female population in Taiwan in 2016 were derived from the life tables produced by the Taiwan Ministry of the Interior - Department of Statistics (Table S 4). These estimates reflect death by all causes and were incorporated into the model in addition to the CC-specific mortality.

Table S 4: Age-specific all-cause mortality probability in the general female population in Taiwan (Ministry of the Interior - Department of Statistics)

Age-groups (years of age)	Mortality probability (%)
<15	0.0373
15-19	0.0196
20-24	0.0255
25-29	0.0331
30-34	0.0513
35-39	0.0768
40-44	0.1083
45-49	0.1647
50-54	0.2538
55-59	0.3649
60-64	0.5369
65-69	0.9011
70-74	1.5861
75-79	2.7807
80-84	4.8096
≥85	13.5135*

*Life expectancy at age 85 among the female Taiwanese is reported at 7.40 in 2016. Thus, the formulae of 1/7.40 is applied as the annual mortality probability from age 85 until the end of the cycle.

Distribution of CC incidence by stage

Distribution of CC incidence by stage in 2014 was derived from the Taiwan Cancer Registry Annual Report (Taiwan Cancer Registry Center, 2014). Since the model did not account for patients with 'unknown stage', these patients were disregarded and the proportion of CC incident cases was re-calculated. These re-weighted estimates were included in the model to weigh disutility weights in estimating quality-adjusted life year (QALY) loss (Table S 5).

Table S 5: Distribution of CC incidence by stage

Stage	Reported CC incidence (%)	Re-weighted CC incidence (%)
I	43.6	46.4
II	26.3	28.0
III	12.0	12.8
IV	12.1	12.8
Unknown	6.0	-
Total	100.0	100.0

CC: cervical cancer

Supplementary Material 4: Parameters of vaccination, treatment and screening practices in Taiwan used in the model

Parameter	Estimate	References
Vaccination		
Vaccination population size of cohort	120,000	Department of Household Registration - M.O.I. (2016)
Vaccination coverage	89.0%	Lee et al. (2012)
Duration of immunity	Lifelong	The same assumption has been made in the base-case analysis of other HPV CE analyses (Dasbach et al., 2008; Elbasha et al., 2007; French et al., 2007; Goldie et al., 2007; Liu et al., 2010; Rogoza et al., 2008)
Treatment		
CIN2/3 treatment (% treated)	100.0%	Local expert opinion based on clinical practice in Taiwan
CIN2/3 treated (% efficacy)	90.0%	Sanders and Taira (2003)
CIN1 treatment (% treated)	0.0%	Local expert opinion based on clinical practice in Taiwan
CIN1 treated (% efficacy)	90.0%	Sanders and Taira (2003)
Frequency of screening	Every year	Koong et al. (2006); Cervical Cancer Screening Registry System Annual Report, Republic of China, Taiwan 2014 (Health Promotion Administration - Ministry of Health and Welfare - Taiwan, 2014)
Pap screening		
Screening ages (years)	Starting at 30*	Koong et al. (2006); Chow et al. (2010); and expert opinion
Screening coverage (%)	27.6%	Cervical Cancer Screening Registry System Annual Report, Republic of China, Taiwan, 2014 (Health Promotion Administration - Ministry of Health and Welfare - Taiwan, 2014)
Proportion of positive Pap smear (%)	1.3%	Cervical Cancer Screening Registry System Annual Report, Republic of China, Taiwan, 2014 (Health Promotion Administration - Ministry of Health and Welfare - Taiwan, 2014)
Sensitivity of conventional cytology for CIN1 or LSIL (%)	63.0%	Fahey et al. (1995)

Parameter	Estimate	References
Sensitivity of conventional cytology for CIN2/3+ or HSIL+ (%)	81.9%	Chao et al. (2008)

*No ending age

CE, cost-effectiveness; CIN1/2/3(+), cervical intraepithelial neoplasia grade 1/2/3 (or higher); HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; Pap, Papanicolaou

Supplementary Material 5: Screening, vaccination and treatment costs incorporated in the model

The costs of screening, vaccination and treatment of genital warts (GW), cervical intraepithelial neoplasia (CIN) lesions and cervical cancer (CC) were Taiwan-specific, derived from patient registries/databases and validated by local experts (Table S 6). Vaccine costs of the AS04-adjuvanted HPV-16/18 vaccine (AS04-HPV-16/18v), the human papillomavirus 6/11/16/18 vaccine (4vHPVv) and the human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine (9vHPVv) were determined based on their price levels in the Taiwanese private market and price parity was assumed between AS04-HPV-16/18v and 4vHPVv. All cost estimates were inflated to year 2016 by using the medical care services Consumer Price Index (CPI) in Taiwan (National Statistics - Republic of China (Taiwan), 2018).

Table S 6: The cost-per-case estimates used in the base-case analysis

Parameter	Description	Cost per case (NT$)	Notes and references
Treatment cost of CC	Treatment costs (including all costs associated with inpatient and outpatient claims) related to CC, incurred within the first, second, third, fourth and fifth years after CC diagnosis	1st year: 388,274 2nd year: 83,308 3rd year: 54,271 4th year: 39,653 5th year: 28,624 5-year average: 594,130	NHI-related costs were estimated for each year from the first year up to the fifth year after the diagnosis of ICD-O-3 code C53 (malignant neoplasm of cervix uteri). Average annual treatment cost (NT$ 160,009) was estimated based on the 5-year average treatment cost of CC, which was then divided by the average duration (years) of CC estimated in the model. References: Taiwan Cancer Registry (Department of Statistics - Ministry of Health and Welfare - Taiwan), NHID (Ministry of Health and Welfare - Taiwan, 2013); Data examined: 1-Jan-2008 – 31-Dec-2015
Treatment cost of CIN2/3	Treatment costs (including all costs	11,245	All outpatient and inpatient claims with major/minor ICD-9-CM codes 622.x (non-inflammatory disorders of cervix), 233.1

Parameter	Description	Cost per case (NT$)	Notes and references
	associated with inpatient and outpatient claims) related to CIN2/3, incurred within a year after diagnosis		(carcinoma in situ of cervix uteri), V723 (gynaecological examination), or V762 (screening for malignant neoplasms of cervix), which occurred within 365 days after the index date (date when patients met the criteria of having biopsy results of CIN2/3 in a given year without CC in a given year or in the previous years), and who did not meet any of the following criteria were included in the estimation of CIN2/3 treatment costs: • Had biopsy results of CC within 365 days after the index date; or • Had major/minor ICD-9-CM code 180 (malignant neoplasm of cervix uteri) within 365 days after the index date; or • Died within 365 days after the index date References: Biopsy datasets (Pap Smear Task Force), NHID (Ministry of Health and Welfare - Taiwan, 2013) Data examined: 1-Jan-2011 – 31-Dec-2013
Follow-up treatment cost for CIN2/3	Cost of follow-up (including consultation and screening costs), incurred in the year following CIN2/3 detection and treatment	2,266	Based on local expert opinion, it was assumed that on average, a patient in Taiwan would be followed up three times in the year subsequent to detection and treatment of CIN2/3. One session of curative screening was estimated at NT$ 430 and consultation per visit was estimated at NT$ 325. The cost of consultation per visit was estimated as the average of medical centre/regional hospital consultation fee (NT$ 304), district hospital consultation fee (NT$ 325), and clinic consultation fee (NT$ 347) since consultation fees differ for each medical service provider. Reference: National Health Insurance Administration - Ministry of Health and Welfare - Taiwan (2016)
Treatment cost of CIN1	Treatment costs (including all costs associated with inpatient and outpatient claims) related to CIN1, incurred within a year after	2,962	All outpatient and inpatient claims with major/minor ICD-9-CM codes 622.x (non-inflammatory disorders of cervix), V723 (gynaecological examination) or V762 (screening for malignant neoplasms of cervix) which occurred within 365 days after the index date (earlier date when patients met the criteria of having either biopsy results of CIN1 in a given year without CIN2/3 or

Parameter	Description	Cost per case (NT$)	Notes and references
	diagnosis		CC in a given year or in the previous years, OR cytological results of LSIL in a given year without biopsy results of CIN2/3 or CC in a given year or in the previous years) and who did not meet any of the following criteria were included in the estimation of CIN1 treatment costs: • Had biopsy results of CIN2/3 or CC within 365 days after the index date; or • Had major/minor ICD-9-CM codes 180 (malignant neoplasm of cervix uteri)/233.1 (carcinoma in situ of cervix uteri) within 365 days after the index date; or • Died within 365 days after the index date References: Biopsy datasets (Pap Smear Task Force), Pap smear test datasets (Pap Smear Task Force), NHID (Ministry of Health and Welfare - Taiwan, 2013) Data examined: 1-Jan-2011 – 31-Dec-2013
Follow-up treatment cost for CIN1	Cost of follow-up (including consultation and screening costs) incurred in the year following CIN1 detection and treatment	1,511	Based on local expert opinion, it was assumed that on average, a patient in Taiwan would be followed up twice in the year subsequent to detection and treatment of CIN1. One session of curative screening was estimated at NT$ 430 and consultation per visit was estimated at NT$ 325 on average. Reference: National Health Insurance Administration - Ministry of Health and Welfare - Taiwan (2016)
Treatment cost of GW	Treatment costs (including all costs associated with inpatient and outpatient claims) related to GW, incurred within a year after GW diagnosis	6,170	All outpatient and inpatient claims with major/minor ICD-9-CM code 078.11 (*condyloma acuminatum*) which occurred 365 days after the index date (earlier date when patients met the criteria of either having at least three outpatient claims with major/minor ICD-9-CM code 078.11 within 3 months in a given year OR receiving any GW treatment procedures in any outpatient claims with major/minor ICD-9-CM code 078.11) were included in the estimation of GW treatment costs. Reference: NHID (Ministry of Health and Welfare - Taiwan,

Parameter	Description	Cost per case (NT$)	Notes and references
			2013) Data examined: 1-Jan-2011 – 31-Dec-2013
Cost of regular screening for a woman with negative Pap smear	Screening costs (including costs of Pap smear sampling/pelvic cavity examination and cervical cytopathological examination) for a woman with negative Pap smear	430	For a patient who had a negative Pap smear result, it was assumed that only preventive screening would be recommended (i.e., no need for curative screening, confirmatory test or further consultations). Total cost included one session of Pap smear sampling/pelvic cavity examination (NT$ 230) and one session of cervical cytopathological examination (NT$ 200). Reference: National Health Insurance Administration - Ministry of Health and Welfare - Taiwan (2016)
Cost of regular screening for a woman with positive Pap smear	Screening costs (including costs of preventive and curative screening, confirmatory test and consultation) for a woman with positive Pap smear	2,966	For a patient who had a positive Pap smear result, it was assumed that preventive screening, curative screening, confirmatory test and further consultations would be recommended. The cost of a confirmatory test was estimated as the average of the fee for cervical biopsy, colposcopy, endocervical curettage, cervical conisation, and cryosurgery or electrosurgery of cervix. Total cost included one session of preventive screening (NT$ 430), two sessions of curative screening (NT$ 860), average cost of a confirmatory test (NT$ 1,026) and two consultation visits (NT$ 651). Reference: National Health Insurance Administration - Ministry of Health and Welfare - Taiwan (2016)
Cost of AS04-HPV-16/18v	Cost of vaccination per dose (including the vaccine cost and the administration costs)	3,600	Vaccination administration cost was NT$ 100 per dose. Reference: Centers for Disease Control - Taiwan (2016)
Cost of 4vHPVv		3,600	Vaccination administration cost was NT$ 100 per dose. Reference: Centers for Disease Control - Taiwan (2016)
Cost of 9vHPVv		5,100	Vaccination administration cost was NT$ 100 per dose. Reference: Centers for Disease Control - Taiwan (2016)

4vHPVv, human papillomavirus 6/11/16/18 vaccine; 9vHPVv, human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CC: cervical cancer; CIN1, cervical intraepithelial neoplasia grade 1; CIN2/3, cervical intraepithelial neoplasia grade 2 or 3; GW: genital warts; ICD-O-3: International Classification of Diseases for Oncology, 3rd Edition; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; LSIL, low-grade squamous intraepithelial lesion; NHI: National Health Insurance; NHID: National Health Insurance Research Database; NT$: New Taiwan dollar; Pap: Papanicolaou

Supplementary Material 6: Parameters and their variability in univariate and probabilistic sensitivity analyses

Two types of sensitivity analyses were performed: a univariate sensitivity analysis and a probabilistic sensitivity analysis (PSA), to assess the robustness of the model results. The analyses used relevant ranges for each variable such as the minimum and maximum values of the confidence interval (CI) or a variation of 20% higher or lower than the base-case.

Table S 7: Parameters and their variability in univariate and probabilistic sensitivity analyses

Parameter		Base-case	Univariate sensitivity analysis range	PSA distribution and range
Discounting (%)				
Costs		3.0[a]	0.0 - 5.0	N/A
Health outcomes		3.0[a]	0.0 - 3.0	
Epidemiology				
Oncogenic HPV infection incidence (%)		5.9 - 12.4	± 20.0%	Multiplied by a uniform distribution from 0.8 to 1.2
Vaccine effectiveness irrespective of the causative HPV type (%)				
AS04-HPV-16/18v	CC	93.2	78.9 - 98.7[b]	Beta distribution based on relevant univariate sensitivity analysis range as 95% CI
	CIN2/3	64.9	52.7 - 74.2[b]	
	CIN1	50.3	40.2 - 58.8[b]	
	GW	0.0	0.0 - 50.9[b,c]	
4vHPVv	CC	43.0	13.0 - 63.2[b]	
	CIN2/3	42.7	23.7 - 57.3[b]	
	CIN1	29.7	17.7 - 40.0[b]	
	GW	82.8	74.3 - 88.8[b]	
9vHPVv	CC	79.6	63.7 - 95.6[b,d]	
	CIN2/3	62.8	34.8 - 78.8[b]	
	CIN1	47.1	30.6 - 59.7[b]	

	GW	94.6	75.7 - 100.0[b,e]	
Costs (NT$)[f]				
AS04-HPV-16/18v (per dose)		3,600[g]	2,880 - 4,320 (± 20.0%)	N/A
4vHPVv (per dose)		3,600[g]	2,880 - 4,320 (± 20.0%)	
9vHPVv (per dose)		5,100	4,320 - 7,200 (120.0% - 200.0% of 4vHPVv)[h]	
Screening cost (annual cost per woman)	Negative Pap smear	430	344 - 516 (± 20.0%)	Multiplied by a uniform distribution from 0.8 to 1.2
	Positive Pap smear	2,966	2,373 - 3,560 (± 20.0%)	
Treatment cost of CIN1 (annual cost per case)		2,962	2,369 - 3,554 (± 20.0%)	Log-normal distribution based on base-case estimate as mean and SD=39[i] (Ministry of Health and Welfare - Taiwan, 2013); Pap smear test datasets (Pap Smear Task Force); Biopsy datasets (Pap Smear Task Force)
Treatment cost of CIN2/3 (annual cost per case)		11,245	8,996 - 13,493 (± 20.0%)	Log-normal distribution based on base-case estimate as mean and SD=226[i] (Ministry of Health and Welfare - Taiwan, 2013); Biopsy datasets (Pap Smear Task Force)
Treatment cost of GW (annual cost per case)		6,170	4,936 - 7,405 (± 20.0%)	Log-normal distribution based on base-case estimate as mean and SD=139[i] (Ministry of Health and Welfare - Taiwan, 2013)
Treatment cost of CC (annual cost per case)		160,009	128,007 - 192,010 (± 20.0%)	Log-normal distribution based on five-year mean treatment cost of NT$594,130 and SD estimate of 5,686 divided by the average CC duration estimated in the model[i] (Department of Statistics - Ministry of Health and Welfare - Taiwan; Ministry of Health and Welfare - Taiwan,

				2013)
QALY loss				
GW		0.0396	0.0317 - 0.0476 (± 20.0%)	Multiplied by a uniform distribution from 0.8 to 1.2
CIN1 screening-detected		0.0766	0.0613 - 0.0919 (± 20.0%)	
CIN2/3 screening-detected		0.0230	0.0184 - 0.0277 (± 20.0%)	
CC treated		0.3830	0.3064 - 0.4596 (± 20.0%)	
CC cured		0.1035	0.0828 - 0.1242 (± 20.0%)	
Screening, vaccination and treatment practice				
Starting age of regular screening (years)[j]		30	25 - 35	N/A
Ending age of regular screening (years)		107[j]	70 - 107	
Frequency of regular re-screening (years)		1	1 - 5	
Sensitivity of conventional cytology (%)	CIN1	63.0%	50.4% - 75.6% (± 20.0%)	Beta distribution based on reported 95% CI : 55.0% - 71.0% (Fahey et al., 1995)
	CIN2/3+	81.9%	65.5% - 98.3% (± 20.0%)	Beta distribution based on estimated 95% CI : 71.0% - 90.0% (Chao et al., 2008)
Proportion of patients being treated for CIN1		0.0%	0.0 - 20.0%	Multiplied by a uniform distribution from 0.0 to 0.2
Proportion of treatment for CIN1 being successful		90.0%	70.0 - 100.0%	Multiplied by a uniform distribution from 0.8 to 1.2 (with maximum of 100%)
Proportion of patients being treated for CIN2/3		100.0%	80.0 - 100.0%	Multiplied by a uniform distribution from 0.8 to 1.2 (with maximum of 100%)
Proportion of treatment for CIN2/3 being successful		90.0%	70.0 - 100.0%	Multiplied by a uniform distribution from 0.8 to 1.2 (with maximum of 100%)
Transition probabilities (%)				
Oncogenic HPV progression to CIN1		7.9%[k]	N/A	Beta distribution with base-case estimate as mean and SD=0.009 (Demarteau et al., 2012; Li et al., 2015)
Non-oncogenic HPV progression to CIN1		3.6%		Beta distribution with base-case estimate as mean and SD being equal to 25% of

			the difference between 3.0% and 5.0% (Sanders and Taira, 2003)
Oncogenic CIN1 progression to CIN2/3	9.1%		Beta distribution with base-case estimate as mean and SD=0.021 (Demarteau et al., 2012; Li et al., 2015)
CIN2/3 progression to persistent CIN2/3	11.4%		Beta distribution with base-case estimate as mean and SD=0.01175 (Demarteau et al., 2012)
CC to death	6.7%		Multiplied by a uniform distribution from 0.8 to 1.2 (Demarteau et al., 2012; Li et al., 2015)
Oncogenic/non-oncogenic HPV regression	51.6%		Beta distribution with base-case estimate as mean and SD=0.14 (Demarteau et al., 2012)
Oncogenic/non-oncogenic CIN1 regression to no HPV	44.9%		Beta distribution with base-case estimate as mean and SD=0.142 (Demarteau et al., 2012)
CIN2/3 regression to no HPV	22.7%		Beta distribution with base-case estimate as mean and SD=0.058 (Li et al., 2015)
CC regression to no HPV (CC cured)	21.8%		Multiplied by a uniform distribution from 0.8 to 1.2 (Demarteau et al., 2012; Li et al., 2015)
GW resistance	29.0%		Multiplied by a uniform distribution from 0.8 to 1.2 (Demarteau et al., 2012)

[a]Discount rate of 3.0% was applied for both costs and health outcomes in accordance with the Taiwanese pharmacoeconomic recommendations (Center for Drug Evaluation, 2014; International Society for Pharmacoeconomics and Outcome Research, 2006).

[b]Sensitivity analysis assessed vaccine effectiveness based on the best (i.e. the upper limit of AS04-HPV-16/18v effectiveness combined with the lower limit of 4vHPVv/9vHPVv effectiveness) and the worst scenario (i.e. the lower limit of AS04-HPV-16/18v effectiveness combined with the upper limit of 4vHPVv/9vHPVv effectiveness) for AS04-HPV-16/18v.

[c]Based on the observation of continued decline in GW incidence among females who were vaccinated with AS04-HPV-16/18v in England, supported by clinical evidence (Canvin et al., 2016; Public Health England, 2012; Szarewski et al., 2013).

[d]Due to limited data available, mean vaccine effectiveness was projected based on available data from Joura *et al*. 2014 and the clinical trial synopsis (Joura et al., 2014; Merck Sharp & Dohme Corp., 2015). The sensitivity analysis range is ± 20% of the mean.

[e]Reported 95% CI is 66.0% - 94.3% but it is considered inaccurate as the higher bound (94.3%) is lower than the mean (Giuliano et al., 2014). The range suggested is based on ±20% with a maximum of 100%.

[f]Cost estimates were inflated to year 2016 by using the medical care services Consumer Price Index (CPI) in Taiwan (National Statistics - Republic of China (Taiwan), 2018). In 2016, the medical care CPI was 103.6 (the base year is 2010) in Taiwan.

[g]Price parity between AS04-HPV-16/18v and 4vHPVv was assumed.

[h]Given the recent entry of the 9vHPVv in the Taiwanese market, a broad range (120%-200%) of 4vHPVv was explored.

[i]Standard deviations have been retrieved or estimated based on data from Taiwan Cancer Registry (Department of Statistics - Ministry of Health and Welfare - Taiwan), NHID (Ministry of Health and Welfare - Taiwan, 2013), Pap smear test datasets (Pap Smear Task Force) and Biopsy datasets (Pap Smear Task Force).

[j]End of model cycle.

[k]4.9% (referenced data) + 3% to allow calibration of the model.

4vHPVv, human papillomavirus 6/11/16/18 vaccine; 9vHPVv, human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CC, cervical cancer; CI, confidence interval; CIN1/2/3, cervical intraepithelial neoplasia grade 1/2/3; GW, genital warts; HPV, human papillomavirus; N/A, not applicable; NT$, New Taiwan dollar; Pap, Papanicolaou; PSA, probabilistic sensitivity analysis; QALY, quality-adjusted life year; SD, standard deviation

Supplementary Material 7: Estimated number of cases, total costs, LYs and QALYs gained for each of the interventions, and incremental outcomes (per person)

Results	Screening only	2D-AS04-HPV-16/18v+scr	2D-4vHPVv+scr	2D-9vHPVv+scr	3D-9vHPVv+scr	2D-AS04-HPV-16/18v+scr compared with			
						Screening only	2D-4vHPVv+scr	2D-9vHPVv+scr	3D-9vHPVv+scr
Undiscounted number of cases									
CC cases	0.0044	0.0009	0.0029	0.0014	0.0014	-0.0035	-0.0020	-0.0006	-0.0006
CC deaths	0.0013	0.0002	0.0008	0.0004	0.0004	-0.0010	-0.0006	-0.0002	-0.0002
Screening-detected CIN2/3 cases	0.0059	0.0014	0.0039	0.0021	0.0021	-0.0046	-0.0026	-0.0008	-0.0008
Screening-detected CIN1 cases	0.0741	0.0370	0.0467	0.0268	0.0268	-0.0371	-0.0098	0.0101	0.0101
GW cases	0.0176	0.0176	0.0052	0.0032	0.0032	0.0000	0.0124	0.0144	0.0144
LY gained	45.9072	46.0273	45.9579	46.0074	46.0074	0.1200	0.0693	0.0199	0.0199
QALY gained	45.8824	46.0199	45.9428	45.9998	45.9998	0.1375	0.0771	0.0202	0.0202
Undiscounted costs (NT$)									
Vaccination	0	6,408	6,408	9,078	13,617	6,408	0	-2,670	-7,209
CC treatment	2,163	426	1,423	712	712	-1,737	-997	-286	-286
CIN2/3 treatment	89	20	58	32	32	-69	-38	-12	-12
CIN1 treatment	220	110	139	80	80	-110	-29	30	30
GW treatment	152	152	45	27	27	0	108	125	125
Screening	3,378	3,418	3,412	3,431	3,431	40	6	-13	-13
Total cost	6,002	10,534	11,486	13,359	17,898	4,533	-951	-2,825	-7,364
Discounted cost (NT$) and health outcomes									
Total cost	2,223	7,993	8,286	10,680	15,219	5,770	-293	-2,687	-7,226
LY gained	24.7269	24.7556	24.7389	24.7508	24.7508	0.0287	0.0167	0.0048	0.0048

Results	Screening only	2D-AS04-HPV-16/18v+scr	2D-4vHPVv+scr	2D-9vHPVv+scr	3D-9vHPVv+scr	2D-AS04-HPV-16/18v+scr compared with			
						Screening only	2D-4vHPVv+scr	2D-9vHPVv+scr	3D-9vHPVv+scr
QALY gained	24.7158	24.7523	24.7321	24.7474	24.7474	0.0365	0.0201	0.0049	0.0049
ICER per QALY gained (NT$)						158,157	AS04-HPV-16/18v+scr dominates 2D-4vHPVv+scr	AS04-HPV-16/18v+scr dominates 2D-9vHPVv+scr	AS04-HPV-16/18v+scr dominates 3D-9vHPVv+scr

2D, two-dose; 3D, three-dose; 4vHPVv, human papillomavirus 6/11/16/18 vaccine; 9vHPVv, human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CC, cervical cancer; CIN1, cervical intraepithelial neoplasia grade 1; CIN2/3, cervical intraepithelial neoplasia grade 2 or 3; GW, genital warts; HPV, human papillomavirus; ICER, incremental cost-effectiveness ratio; LYs, life years; NT$, New Taiwan dollar; QALY, quality-adjusted life year; scr, screening

Supplementary Material 8: Results of the scenario analyses

Results for each scenario	2D-AS04-HPV-16/18v+screening compared with			
	Screening only	2D-4vHPV v+scr	2D-9vHPV v+scr	3D-9vHPV v+scr
Total discounted costs (NT$) per person				
Limited immunity	5,817	-270	-2,685	-7,224
Higher GW incidence	5,770	-157	-2,529	-7,068
Vaccine tender prices	2,566	-293	-1,263	-3,488
Total discounted QALY-gained per person				
Limited immunity	0.0346	0.0191	0.0047	0.0047
Higher GW incidence	0.0365	0.0192	0.0039	0.0039
Vaccine tender prices	0.0365	0.0201	0.0049	0.0049
ICER per QALY gained (NT$)				
Limited immunity	168,163	2D-AS04-HPV-16/18v+scr dominates 2D-4vHPVv+scr	2D-AS04-HPV-16/18v+scr dominates 2D-9vHPVv+scr	2D-AS04-HPV-16/18v+scr dominates 3D-9vHPVv+scr
Higher GW incidence	158,161	2D-AS04-HPV-16/18v+scr dominates 2D-4vHPVv+scr	2D-AS04-HPV-16/18v+scr dominates 2D-9vHPVv+scr	2D-AS04-HPV-16/18v+scr dominates 3D-9vHPVv+scr
Vaccine tender prices	70,335	2D-AS04-HPV-16/18v+scr dominates 2D-4vHPVv+scr	2D-AS04-HPV-16/18v+scr dominates 2D-9vHPVv+scr	2D-AS04-HPV-16/18v+scr dominates 3D-9vHPVv+scr

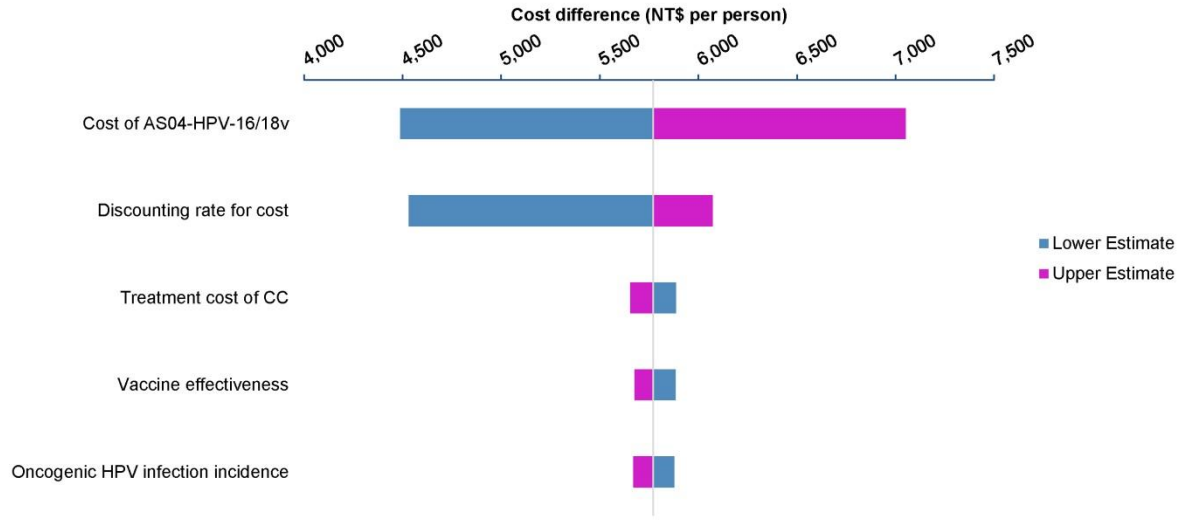
2D, two-dose; 3D, three-dose; 4vHPVv, human papillomavirus 6/11/16/18 vaccine; 9vHPVv, human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CC, cervical cancer; CIN1, cervical intraepithelial neoplasia grade 1; CIN2/3, cervical intraepithelial neoplasia grade 2 or 3; GW, genital warts; HPV,

human papillomavirus; ICER, incremental cost-effectiveness ratio; LYs, life years; NT$, New Taiwan dollar; QALY, quality-adjusted life year; scr, screening

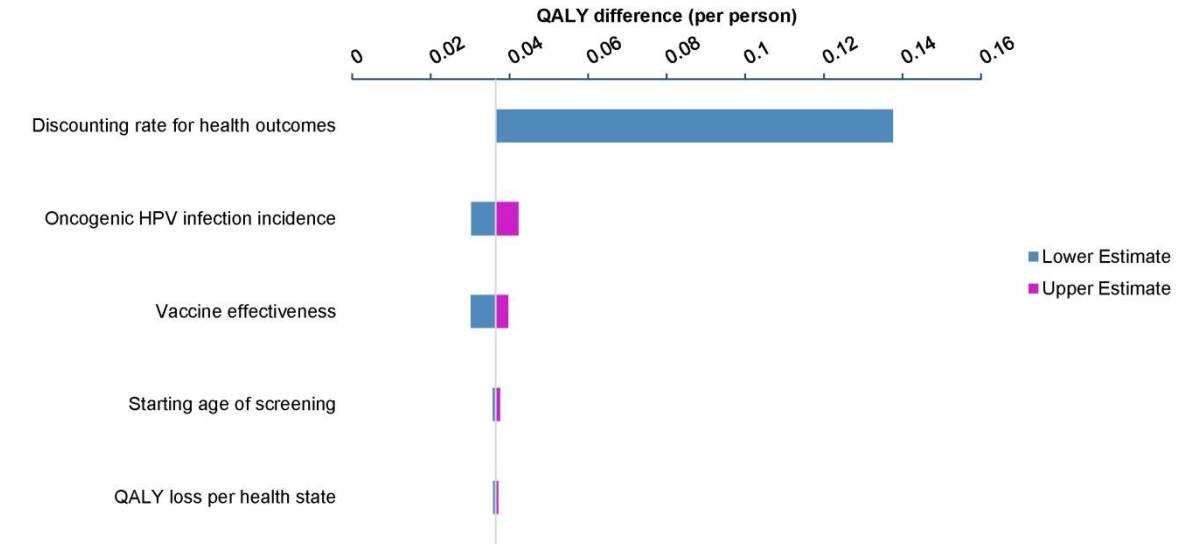
Supplementary Material 9: Results of the univariate sensitivity analysis

Figure S 1: Univariate sensitivity analysis between 2D-AS04-HPV-16/18v+screening and screening only on cost (A), QALY (B) and ICER (C) per person (5 most influential variables)

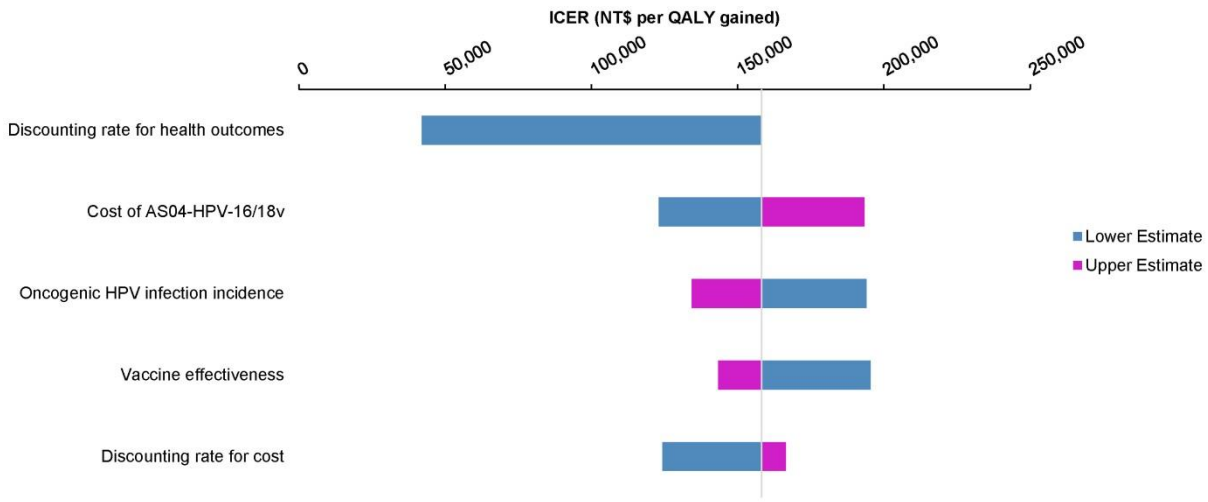
A



B



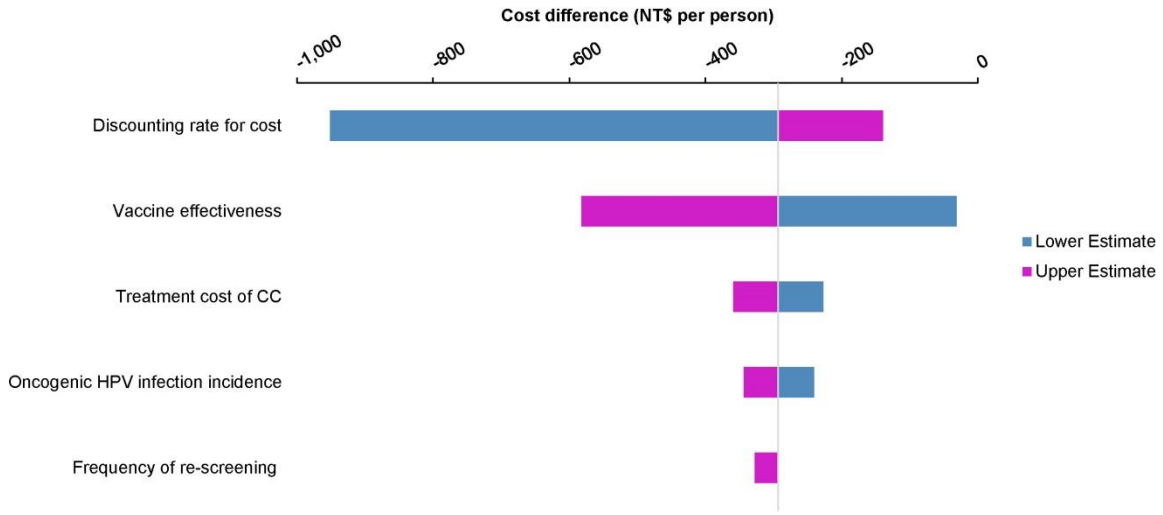
C



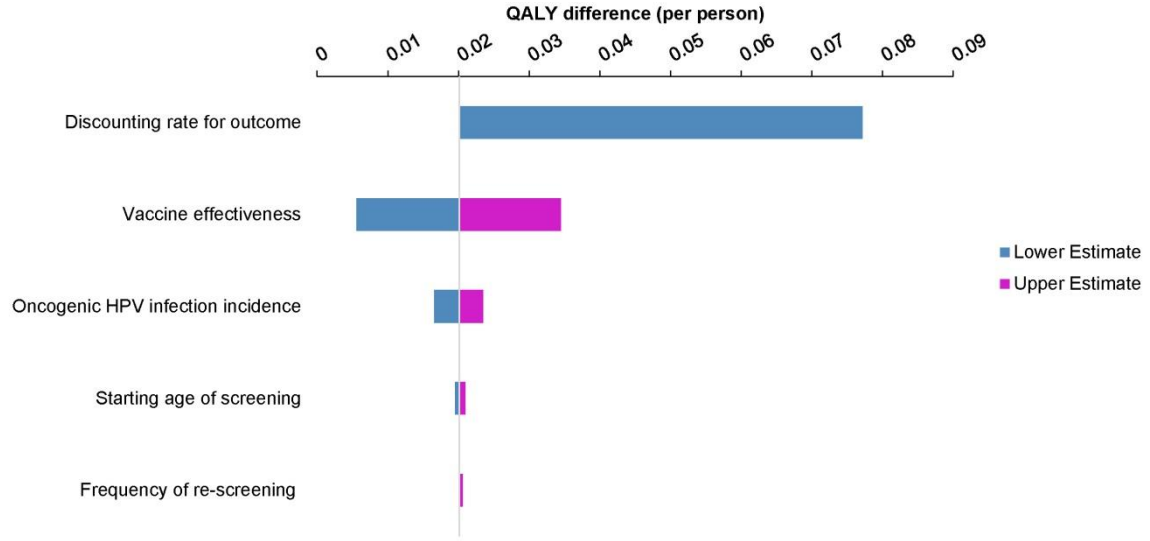
2D, two-dose; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CC, cervical cancer; HPV, human papillomavirus; ICER, incremental cost-effectiveness ratio; NT$, New Taiwan dollar; QALY, quality-adjusted life year

Figure S 2: Univariate sensitivity analysis between 2D-AS04-HPV-16/18v+screening and 2D-4vHPVv+screening on cost (A) and QALY (B) per person (5 most influential variables)

A



B

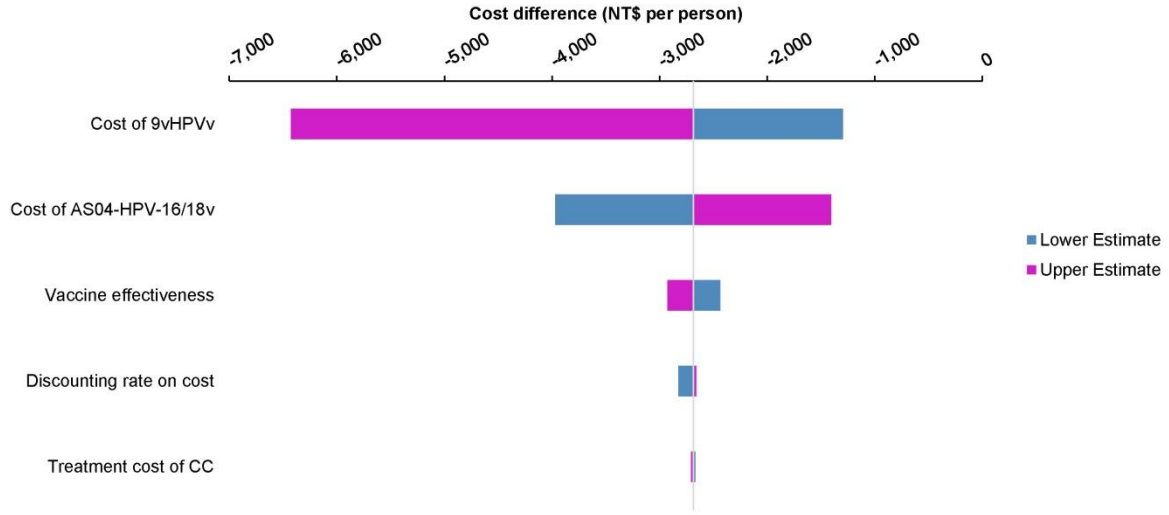


2D, two-dose; 4vHPVv, human papillomavirus 6/11/16/18 vaccine; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CC, cervical cancer; HPV, human papillomavirus;

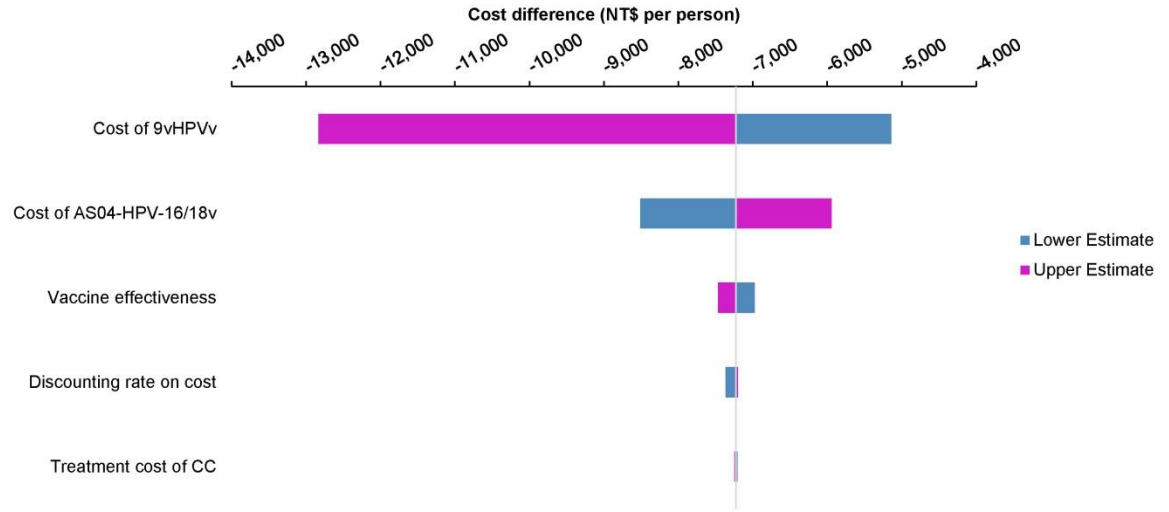
ICER, incremental cost-effectiveness ratio; NT$, New Taiwan dollar; QALY, quality-adjusted life year

Figure S 3: Univariate sensitivity analysis between 2D-AS04-HPV-16/18v+screening and 2D/3D-9vHPVv+screening on cost (A: 2D-9vHPVv and B: 3D-9vHPVv) and QALY (C) per person (5 most influential variables)

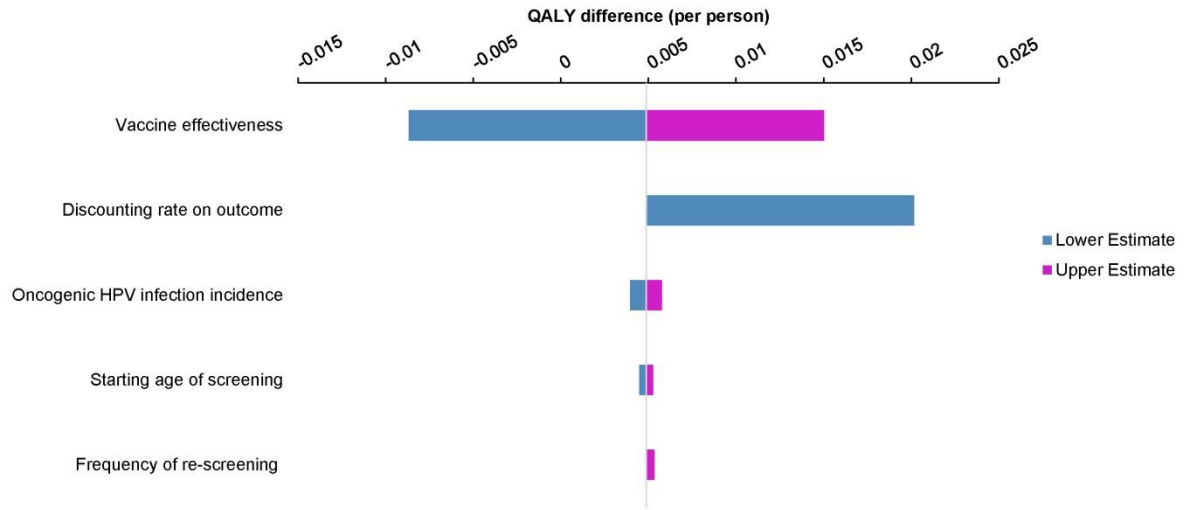
A



B



C



2D, two-dose; 3D,three-dose; 9vHPVv, human papillomavirus 6/11/16/18/31/33/45/52/58 vaccine; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CC, cervical cancer; HPV, human papillomavirus; NT$, New Taiwan dollar; QALY, quality-adjusted life year

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