

Appendix A

A.1. AS04-adjuvanted HPV-16/18 vaccine (Cervarix, GSK; AS04-HPV-16/18v)

AS04-HPV-16/18v contains a proprietary adjuvant system (AS04; adjuvant system containing 50 µg of 3-O-desacyl-4'-monophosphoryl lipid A adsorbed on aluminium salt [500 µg Al³⁺]), which has been shown to produce an enhanced immune response compared with a formulation with aluminium salt only (Giannini et al., 2006).

A.2. Supplementary methods

A single-round consultation with two Malaysian clinical experts (RS and CMY, co-authors of this paper) was held in March and April 2015 with a single expert present at each meeting.

Both experts are obstetrics & gynaecology experts undertaking current practice in Malaysia.

Each meeting was organised around presenting the key input parameters for discussion and endorsement. Specific discussion points were around cervical intraepithelial neoplasia (CIN) treatment patterns, cervical cancer (CC) mortality, CC screening coverage and frequency, and genital warts incidence and treatment. Both experts suggested that CC mortality and screening frequency were important variables that necessitated specific attention. Genital warts incidence was suggested a lesser health issue in Malaysia.

Both experts agreed with the data inputs and assumptions.

Appendix B

Table B.1. Age-specific mortality rates among the female population of Malaysia (Department of Statistics Malaysia, 2015; Jabatan Perangkaan Malaysia (Department of Statistics Malaysia))

Age group (years)	Age-specific mortality rate (per thousand residents)
0-1	0.00550
0 - 4	0.00146
5 - 9	0.00102
10-14	0.00110
15 - 19	0.00161
20 - 24	0.00187
25 - 29	0.00228
30 - 34	0.00326
35 - 39	0.00531
40 - 44	0.00801
45 - 49	0.01341
50 - 54	0.02245
55 - 59	0.03396
60 - 64	0.05336
65 - 69	0.08106
70 - 74	0.14849
75 - 79	0.24058
80+	1.00000

Table B.2. Human papillomavirus (HPV) incidence used in the model, based on prevalence data (Bruni et al., 2015)

Age group (years)	HPV incidence range in the model (among females)
<15	0
15-19	0.07292 - 0.07765
20-24	0.05403 - 0.0694
25-29	0.04223 - 0.05077
30-34	0.04013 - 0.0412
35-39	0.04046 - 0.04142
40-44	0.04003 - 0.04145
45-49	0.03543 - 0.03929
50-54	0.03063 - 0.0344
55-59	0.02474 - 0.02976
60-64	0 - 0.02234
65-69	N/A
70-74	N/A
+75	N/A

Table B.3. Female genital warts incidence in Japan (Kumamoto et al., 2004)

Age groups (years)	Incidence of 1st attack genital warts
<15	0.0 (assumption)
15-19	87.8
20-24	146.3
25-29	112.3
30-34	48.3
35-39	32.0
40-49	5.7
50-54	5.6
55-59	2.3
60-64	1.2
≥65	0.0 (assumption)

Appendix C

Table C.1. Natural history of HPV infection

Parameter	Yearly transition probabilities	References
<i>Low-risk HPV</i>		
[No HPV] to [Low-risk HPV]	0 - 0.067	Age specific (Kumamoto et al., 2004; Richardson et al., 2003)
[Low-risk HPV] to [No HPV]	0.516	(Richardson et al., 2003)
[Low-risk HPV] to [Genital warts]*	0.0001 - 0.0592	Age-specific genital warts incidence (Kumamoto et al., 2004) and calibration
[Low-risk HPV] to [Low-risk CIN1]	0.036	(Van de Velde et al., 2007)
[Low-risk CIN1] to [No HPV]	0.500	(Van de Velde et al., 2007)
<i>Oncogenic HPV</i>		
[No HPV] to [Oncogenic HPV]	0 - 0.076	Age specific derived from (Bruni et al., 2015) Transition probability specific for Malaysia
[Oncogenic HPV] to [No HPV]	0.293 - 0.553	Age specific (Goldie et al., 2004; Melnikow et al., 1998; Moscicki et al., 2001; Schlecht et al., 2003)
[Oncogenic HPV] to [Oncogenic CIN1]	0.049	(Goldie et al., 2004; Sanders and Taira, 2003; Van de Velde et al., 2007)
[Oncogenic HPV] to [CIN2/3]	0	Assumption
[Oncogenic CIN1] to [No HPV]	0.449	Natural regression (Sanders and Taira, 2003; Van de Velde et al., 2007)
[Oncogenic CIN1] to [CIN2/3]	0.125	(Melnikow et al., 1998) including calibration
[CIN2/3] to [No HPV]	0.227	(Sanders and Taira, 2003; Van de Velde et al., 2007)
[CIN2/3] to [Oncogenic CIN1]	0	Spontaneous regression from [CIN2/3] to [CIN1] assumed to be 0 as all regressions assumed to go straight to [No HPV]
[CIN2/3] to [Persistent CIN2/3]	0.114	(Melnikow et al., 1998)
[Persistent CIN2/3] to [No HPV]	0.227	(Sanders and Taira, 2003; Van de Velde et al., 2007)
[Persistent CIN2/3] to [Cancer]	0.001 - 0.648	Age specific; from calibration
[Cancer] to [Death cancer]	0.106	Based on proportion of cervical cancer patients still alive after 5 years (assumed to be cured, N=6,130) and expected 5-year cumulative number of cases ($N = 2,145 \times 5 = 10,725$) = $6,130/10,725 = 0.5716$ The annual CC mortality rate was calculated as $1 - 0.5716^{(1/5)} = 10.6\%$ Data retrieved from Globocan 2012 (Ferlay et al., 2013) Transition probability specific for Malaysia
[Cancer] to [Cancer cured]	0.156	The annual cervical survival rate was calculated as $1 - (1 - 0.5716)^{(1/5)} = 15.6\%$ (Ferlay et al., 2013) Transition probability specific for Malaysia
<i>Screening parameters</i>		
Pap sensitivity CIN1	0.580	Based on "screening" from (Fahey et al., 1995)
Proportion of CIN1 treated	0	(MoH Malaysia and Academy of Medicine, 2003)
Pap sensitivity CIN2/3	0.610	Based on "CIN2" from (Fahey et al., 1995)
Proportion of CIN2/3 treated	1.00	Expert opinion
CIN2/3 treatment success	0.90	(Van de Velde et al., 2007)

* Based on female genital warts incidence data from the National Surveillance of Sexually Transmitted Diseases of Japan (Appendix Table B.3). Yearly transition probabilities were assumed to be independent of region/country and were maintained from previous published models (Demarteau and Standaert, 2010).
CIN1/2/3, cervical intraepithelial neoplasia grade 1/2/3; HPV, human papillomavirus

C1b Cost methods

Part of these methods have been described in (Aljunid et al., 2010).

Treatment cost

In order to assess the average direct costs per patient associated with cervical cancer, a retrospective review of patient records from four hospitals from the period January 2007 to December 2008 was

performed to identify cervical cancer patients and to characterise resource use in these patients. The four hospitals chosen in this study (one teaching hospital in Kuala Lumpur and three government hospitals in Central, Northern and East Coast region of Malaysia) are geographically dispersed and were carefully selected to provide data representative of the whole country. A total of 444 hospital admissions attributable to cervical cancer were identified at the selected hospitals, classified according to the ICD-10 code C53 for malignant neoplasm of the cervix uteri. Cervical cancer cases were categorised according to cancer stage.

The clinical treatment pathways and annual resource use (number of visits, medication use and procedures) of patients with precancerous lesions were estimated by an expert panel comprising obstetricians, pathologists, oncologists, radiotherapists, public health specialists and nurses as follows:

- Management of CC starts with Pap smear screening. The participants reported that around 0.86% to 3.1% of the results are abnormal. Out of these abnormal smears, 70% are usually ASCUS (atypical squamous cells of undetermined significance) which needs a repeat smear within 6 months. 30% are pathological in nature with colposcopic procedure to determine the diagnosis.
- Usually based on colposcopic examinations 40% are LGSIL (low-grade squamous intraepithelial lesion). The cytological slide needs to be reviewed by the pathologist to determine whether they are normal or abnormal. A normal result requires a repeat smear within 4-6 months and 2 repeated normal smears will entail the patient to a 3 yearly follow up. If a repeated smear turns out to be abnormal, a repeated colposcopy needs to be done. An abnormal result will require the patient to undergo Cone, LEEP (loop electrosurgical excision procedure) or LLETZ (large loop excision of the transformation zone) procedure.
- Another 60% are HGSIL (high-grade squamous intraepithelial lesion) which requires biopsy to determine the stage of the disease. From this biopsy usually 60% will turn out to be CIN1, 35% CIN2/3 and another 5% Invasive. 80% of CIN1 cases need a repeat smear within 6 months and out of that 80% will need a repeat colposcopy while 20% of CIN1 cases need cryotherapy either by ablation or excision. 95% of CIN2/3 cases need an excision either by Cone, LEEP or LLETZ procedure. Another 5% will end up requiring Total Abdominal Hysterectomy (TAH).
- Invasive are disease stages 1, 2, 3 and 4. Usually 20% are Stage 1, 30% Stage 2, another 30% Stage 3 and 20% Stage 4. 90% of the patients in Stage 1 require surgical intervention and 10% end-up with chemotherapy. Patients in Stage 2-4a require either surgery or combined chemo-radiotherapy or both while Stage 4b usually requires palliative treatment.

Overhead cost

Top-down costing

A top-down costing approach is employed to estimate the cost of treatment for in- and out-patient care. Clinical Cost Modelling Software Version 2.1 (CCM Ver. 2.1) is used to distribute the cost from Top Level Cost Centres to Intermediate and Patient Cost Centre. The final cost endpoint calculated using this methodology was cost per day of stay per patient with CC. In imputing the cost the following conventions were used:

Capital Cost

Costs of buildings and fixtures have been included according to the life span of the building estimated at 20 years with an annual depreciation of 5%, i.e. a 12.46 annualisation factor. This value was then applied in proportion to the area utilised for activities within the scope of the study. Costs of instruments have been determined at a life span of 5 years with an annual depreciation of 20%. Costs of transportation/vehicles have been calculated with the assumption of a life span of 5 years with an annual depreciation of 20%, i.e. a 4.32 annualisation factor. Only vehicles used within the activity scope of this study were considered.

Recurrent Cost

Emolument costs including salaries, bonuses and allowances to healthcare personnel involved in each activity within the scope of the study were applied according to the time ratio allotted to the relevant activities. The total gross income of individual healthcare personnel was divided by 10,400 to calculate an emolument cost per minute (assuming there are 260 total days of work, with each day consisting of 8 hours). The costs of supplies were calculated as the total cost of all purchases of medication and non-medication items (slides, reagent, disposable gloves, disposable speculum and spatulas etc.) used for the activities related to the study. Utility costs due to water, electricity supply, telephone and waste maintenance were calculated according to area of use for activities within the scope of the study.

C.2. Randomised controlled trials used to determine AS04-HPV-16/18v and HPV-6/11/16/18 vaccine (4vHPVv) efficacy

(Brown et al., 2009; Paavonen et al., 2009; Skinner et al., 2009; The FUTURE II Study Group, 2007; Tjalma et al., 2009).

Table C.3. Estimation of vaccine effectiveness

Parameter	HPV type distribution	Vaccine efficacy AS04-HPV-16/18v (95% CI)	Vaccine efficacy 4vHPVv (95% CI)
<i>CIN1</i>			
HPV-16/18	25.10% (South-East Asia) (Bruni et al., 2015)	98% - assumed same as for CIN2+ (Paavonen et al., 2009)	98% - assumed same as for CIN2+ (The FUTURE II Study Group, 2007)
Grouped non-vaccine types (HPV 31/33/35/39/45/51/52/56/58/59)	58.10% (South-East Asia) (Bruni et al., 2015)	47.7% (28.9–61.9%) (Paavonen et al., 2009; Tjalma et al., 2009)	23.4% (7.8–36.4%) (Brown et al., 2009)
HPV-6/11	4.40% (South-East Asia) (Bruni et al., 2015)	0%	98% - assumed same as for CIN2+ HPV-16/18 (The FUTURE II Study Group, 2007)
Overall effectiveness		52.31%	42.51%
<i>Genital warts</i>			
HPV-6/11	90% (expert opinion)	0%	98% - assumed same as for CIN2+ HPV-16/18 (The FUTURE II Study Group, 2007)
Overall effectiveness		0%	88.20%
<i>CIN2/3</i>			
HPV-16/18	49.30% (Bruni et al., 2015)	98% (Paavonen et al., 2009)	98% (The FUTURE II Study Group, 2007)
Grouped non-vaccine types (HPV 31/33/35/39/45/51/52/56/58/59)	50.60% (Bruni et al., 2015)	68.4% (45.7–82.4%) (Paavonen et al., 2009; Skinner et al., 2009)	32.5% (6.0–51.9%) (Brown et al., 2009)
Overall effectiveness		82.92%	64.76%
<i>Cervical cancer</i>			
HPV-16/18	59.26%* (Bruni et al., 2015)	98% - assumed same as for CIN2+ (Paavonen et al., 2009)	98% - assumed same as for CIN2+ (The FUTURE II Study Group, 2007)
Grouped non-vaccine types (HPV 31/33/35/39/45/51/52/56/58/59)	38.86%* (Bruni et al., 2015)	68.4% (45.7–82.4%) (Paavonen et al., 2009; Skinner et al., 2009)	33% (6–52%) (Brown et al., 2009)
Overall effectiveness		84.66%	70.71%

* Values were normalised to 100% as the individual HPV type prevalences added up to 149.5% 4vHPVv, HPV-6/11/16/18 vaccine; AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine; CIN1/2/3, cervical intraepithelial neoplasia grade 1/2/3; HPV, human papillomavirus

C.4. Clinical trials used to determine efficacy against non-vaccine HPV types:

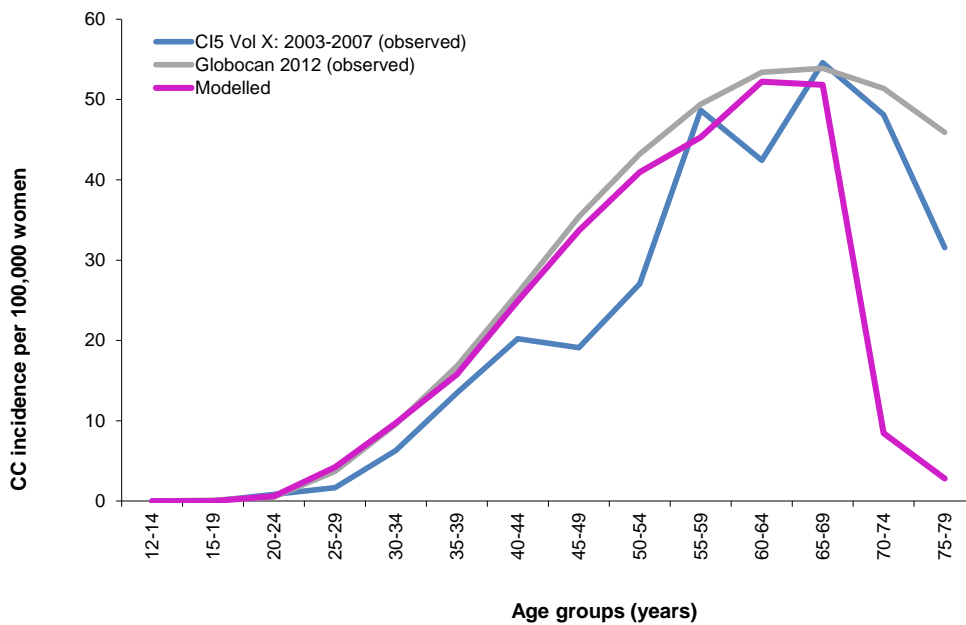
(Brown et al., 2009; Paavonen et al., 2009; Skinner et al., 2009; Tjalma et al., 2009)

Non-vaccine types included: HPV types 31/33/35/39/45/51/52/56/58/59

C.5. HPV cost-effectiveness analyses used for yearly disutilities

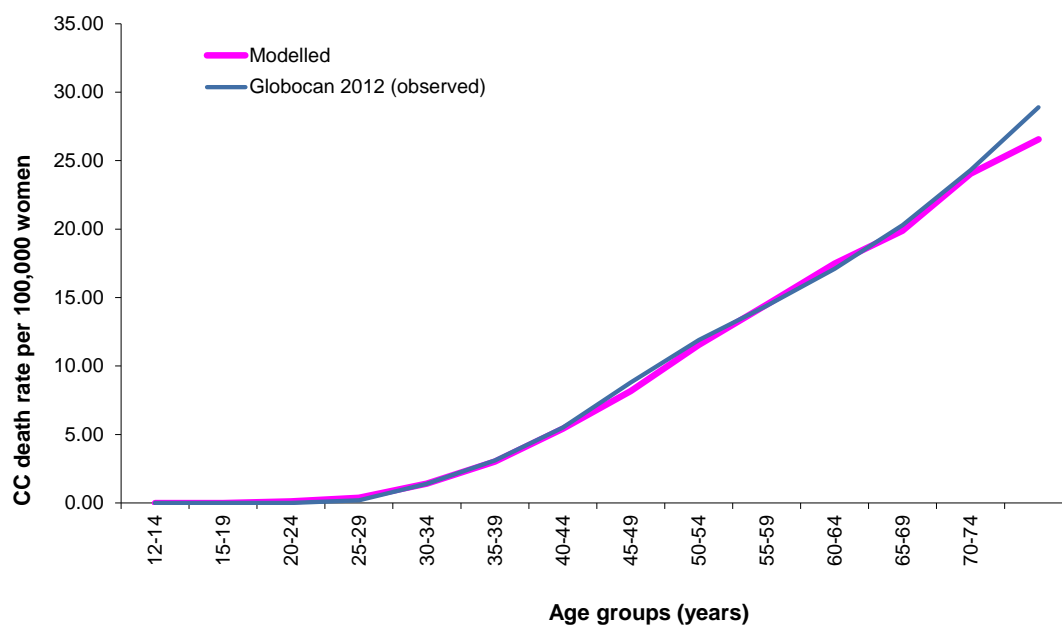
(Gold et al., 1998; Goldie et al., 2004; Insinga et al., 2005b; Institute of Medicine, 2000; Myers et al., 2004; Woodhall et al., 2011). HPV cost-effectiveness analyses were used to determine the yearly disutilities for precancerous and cancerous states (genital warts 0.018; CIN1/2/3-detected 0.0128; cancer 0.2730; cured cancer 0.062; death 1).

Fig. C.6. Observed vs. modelled cervical cancer incidence (Ferlay et al., 2013; World Health Organization (WHO), 2014)



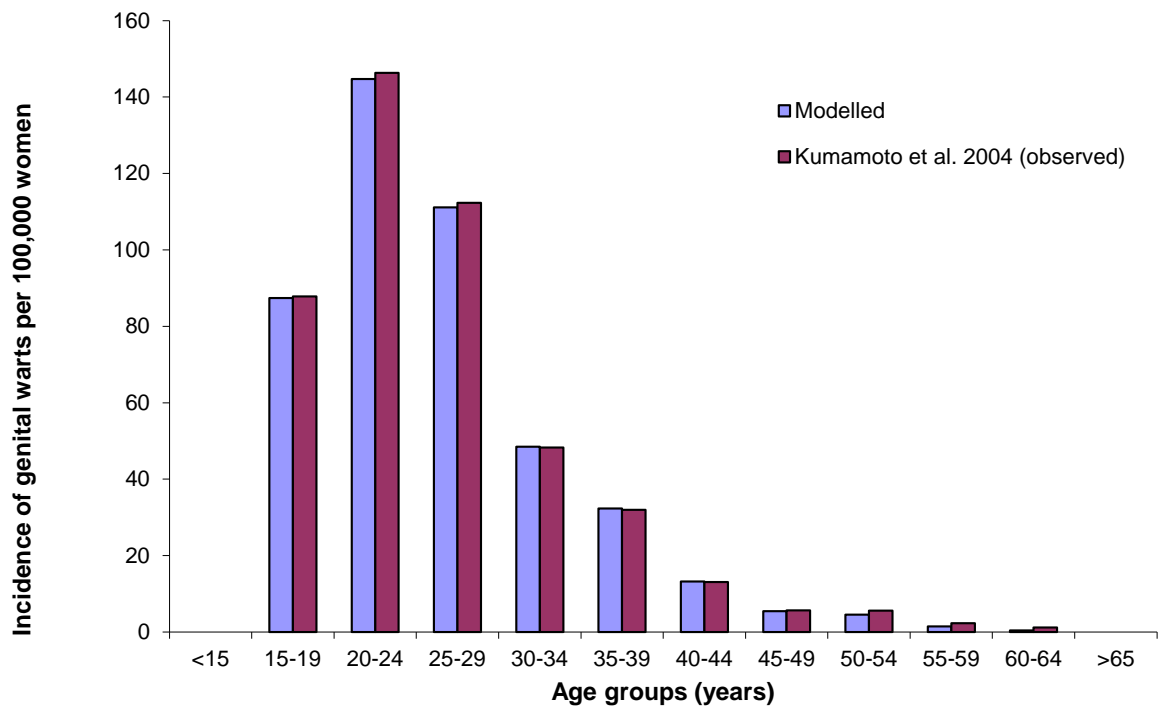
CC, cervical cancer; CI5, Cancer Incidence in Five Continents

Fig. C.7. Observed vs. modelled cervical cancer mortality (Ferlay et al., 2013)



CC, cervical cancer

Fig. C.8. Modelled vs. observed annual incidence (per 100,000 women) of genital warts (Japan data) (Kumamoto et al., 2004)



Appendix D

Table D.1. Input variables values for one-way sensitivity analysis

	Base case	Min	Max
Vaccine efficacy cross protection CIN1			
AS04-HPV-16/18v	47.7%	28.9%	61.9%
4vHPV	23.4%	7.8	36.4
Vaccine efficacy cross protection CIN2/3 and CC			
AS04-HPV-16/18v	68.4%	45.7%	82.4%
4vHPV	32.5%	6.0%	51.9%
Discount rate	3%	1.5%	5%
HPV oncogenic infection rate in population	0 - 0.076	-20%	+20%
HPV-16/18 in CIN1	25.10%	20.08%	30.12%
HPV-16/18 in CIN2/3	49.30%	39.44%	59.16%
HPV-16/18 in CC	59.26%	47.41%	71.11%
Distribution cross protection HPV types CIN1	58.10%	46.48%	69.72%
Distribution cross protection HPV types CIN2/3	50.6%	40.5%	60.7%
HPV-6/11 in genital warts	90%	72%	100%
Distribution cross protection HPV types CC	38.86%	31.09%	46.63%
Disutility			
CIN1	0.0128	0.0102	0.0154
CIN2/3	0.0128	0.0102	0.0154
CC	0.2730	0.2184	0.3276
CC cured	0.0620	0.0496	0.0744
GW	0.0180	0.0144	0.0216
Regular screening coverage	59.7%	47.8%	71.6%
Pap screen sensitivity CIN1	58.0%	46.4%	69.6%
Pap screen sensitivity CIN2/3	61.0%	48.8%	73.2%
Cost			
Negative pap	MYR 30	MYR 24	MYR 36
False positive pap	MYR 1,190	MYR 952	MYR 1,428
CIN1	MYR 1,102	MYR 882	MYR 1,322
Genital warts	MYR 1,833.63	MYR 1,466.9	MYR 2,200.36
CIN2/3	MYR 2,461	MYR 1,969	MYR 2,953
CC	MYR 62,537.43	MYR 50,030	MYR 75,045
vaccine	MYR 134	MYR 107.2	MYR 160.8

4vHPV, HPV-6/11/16/18 vaccine (*Gardasil*); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (*Cervarix*); CC, cervical cancer; CIN1/2/3, cervical intraepithelial neoplasia grade 1/2/3; GW, genital warts; HPV, human papillomavirus; MYR, Malaysian Ringgits; Pap, Papanicolaou test

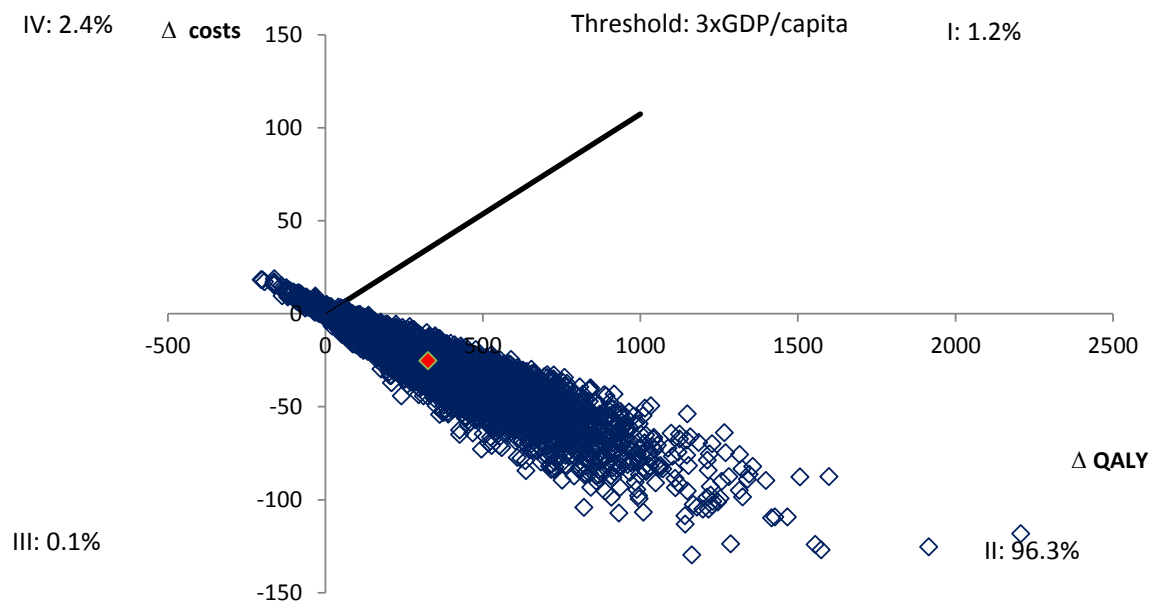
Table D.2. Input variables values for probabilistic sensitivity analysis

Health states	Distribution	Source
Age-specific mortality	Uniform distribution (–; –)	Assumption. Multiplied at each age by a uniform distribution from 0.8– 1.2
Oncogenic HPV infection		
[Oncogenic HPV] to [No HPV]	Uniform distribution (0.234-0.442; 0.352-0.664)	Assumption. Multiplied at each age by a uniform distribution from 0.8– 1.2
[Oncogenic HPV] to [CIN1]	Normal distribution 0.049 (SD 0.009)	(Moscicki et al., 2001)
[Oncogenic HPV] to [CIN2/3]	Fix (0)	Assumption
[Oncogenic CIN1] to [Cancer cured]	Normal distribution 0.449 (SD 0.142)	(Sanders and Taira, 2003; Van de Velde et al., 2007)
[CIN1] to [CIN2/3]	Normal distribution 0.125 (SD 0.021)	(Melnikow et al., 1998; Sanders and Taira, 2003; Van de Velde et al., 2007)
[CIN2/3] to [Cancer cured]	Normal distribution 0.227 (SD 0.058)	(Melnikow et al., 1998)
[CIN2/3] to [Oncogenic CIN1]	Fix (0)	Assumption
[CIN2/3] to [Persistent CIN2/3]	Uniform distribution (0.091-0.137)	(Melnikow et al., 1998)
[Persistent CIN2/3] to [Cancer]	Uniform distribution (0.001 – 0.518; 0.001 – 0.778)	Assumption. Multiplied at each age by a uniform distribution from 0.8– 1.2
% CIN2/3 detected undergoing treatment	Fix (1)	Assumption
CIN2/3 treatment success	Uniform distribution (0.72 – 1)	Assumption based on expert opinion
[Cancer] to [Death from CC]	Uniform distribution (0.085-0.127)	Assumption
[Cancer] to [Cancer cured]	Uniform distribution (0.125-0.187)	Assumption
Low-risk HPV infection		
[Low-risk HPV] to [No HPV]	Uniform distribution (0.413-0.619)	(Richardson et al., 2003)
[Low-risk HPV] to [Genital warts]	Uniform distribution (0.0001-0.0474; 0.0001-0.071)	Multiplied at each age by a uniform distribution from 0.8-1.2 (Kumamoto et al., 2004)
[Low-risk HPV] to [Low-risk CIN1]	Normal distribution 0.036 (SD 0.005)	(Van de Velde et al., 2007)
% GW resistant	Uniform distribution (0.28-0.42)	(Woodhall et al., 2011)
[Low-risk CIN1] to [No HPV]	Normal distribution 0.500 (SD 0.145)	(Van de Velde et al., 2007)
Cost of regular screening for subjects with negative pap smear	Uniform distribution (MYR 24-MYR 36)	Expert panel
Cost of regular screening for positive pap smear subject, plus colposcopy/biopsy	Uniform distribution (MYR 952 – MYR 1,428)	Expert panel
Treatment cost of CIN1	Uniform distribution (MYR 1,681.6 - MYR 2,522.4)	Expert panel
Treatment cost of CIN2/3	Uniform distribution (MYR 1,968.8 – MYR 2,953.2)	Expert panel
Average yearly treatment cost for GW and resistant GW in females	Uniform distribution MYR 1,467.2 - MYR 2,200.8	Expert panel
Composite average yearly treatment costs accounting for each stage of CC	Uniform distribution (MYR 50,029.6 - MYR 75,044.4)	Expert panel
Price vaccine per dose (both vaccine)	Fix (MYR 107.2 - MYR 160.8)	Assumption
Disutilities		
No HPV	Fix (0)	
HPV, CIN1, CIN2/3 undetected	Fix (0)	
CIN1 detected	Uniform distribution (0.010–0.015)	(Insinga et al., 2005a; Myers et al., 2004)
CIN2/3 detected	Uniform distribution (0.010–0.015)	(Insinga et al., 2005a; Myers et al., 2004)
GW	Uniform distribution (0.014–0.022)	(Gold et al., 1998; Myers et al., 2004)
Cancer	Uniform distribution (0.218–0.328)	(Insinga et al., 2005a; Myers et al., 2004)
Cancer cured	Uniform distribution (0.050–0.074)	(Insinga et al., 2005a; Myers et al., 2004)

Death	Fix (1)	
Screening effectiveness		
CIN1 detected	Normal distribution 0.58 (SD 0.045)	(Fahey et al., 1995)
CIN2/3 detected	Normal distribution 0.61 (SD 0.045)	(Fahey et al., 1995)
Vaccine effectiveness		
AS04-HPV-16/18v effectiveness against 16/18	Fix (0.980)	(Paavonen et al., 2009)
AS04-HPV-16/18v effectiveness against other 10 HPV-types in CIN1	Normal distribution 0.477 (SD 0.083)	(Paavonen et al., 2009; Tjalma et al., 2009)
AS04-HPV-16/18v effectiveness against other 10 HPV-types in CIN2/3	Normal distribution 0.684 (SD 0.083)	(Paavonen et al., 2009; Skinner et al., 2009)
AS04-HPV-16/18v effectiveness against other 10 HPV-types in CC	Normal distribution 0.684 (SD 0.083)	(Paavonen et al., 2009; Skinner et al., 2009)
4vHPVv effectiveness against 16/18	Fix (0.980)	(The FUTURE II Study Group, 2007)
4vHPVv effectiveness against other 10 HPV-types in CIN1	Normal distribution 0.231 (SD 0.072)	(Brown et al., 2009)
4vHPVv effectiveness against other 10 HPV-types in CIN2/3	Normal distribution 0.332 (SD 0.111)	(Brown et al., 2009)
4vHPVv effectiveness against other 10 HPV-types in CC	Normal distribution 0.332 (SD 0.111)	(Brown et al., 2009)
4vHPVv effectiveness against HPV-6/11	Normal distribution 0.980 (SD 0.065)	(Garland et al., 2007; The FUTURE II Study Group, 2007; Villa, 2006)
HPV type distribution		
HPV-6/11 in CIN1	Uniform distribution (0.04 - 0.05)	(Bruni et al., 2015)
HPV-16/18 in CIN1	Uniform distribution (0.2 - 0.3)	(Bruni et al., 2015)
HPV-16/18 in CIN2/3	Uniform distribution (0.39 - 0.59)	(Bruni et al., 2015)
HPV-16/18 in CC	Uniform distribution (0.47 - 0.71)	(Aubin et al., 2008; Garland et al., 2009)
HPV-6/11 in GW	Normal distribution (0.72 - 1)	(Bruni et al., 2015)

4vHPVv, HPV-6/11/16/18 vaccine (*Gardasil*); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (*Cervarix*); CC, cervical cancer; CIN1/2/3, cervical intraepithelial neoplasia grade 1/2/3; GW, genital warts; HPV, human papillomavirus; lr, low risk; MYR, Malaysian Ringgits; Pap, Papanicolaou test; SD, standard deviation.

Fig. D.3. Probabilistic sensitivity analysis result



GDP, gross domestic product; QALY, quality-adjusted life year

Appendix E

Table E.1. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPVv, cost outcomes base-case mortality

Cost outcomes (MYR)	Duration (year)	4vHPVv									
		10	15	20	25	30	35	40	45	50	100
AS04-HPV-16/18v	10	-MYR 14,286,390	-MYR 11,588,074	-MYR 8,884,296	-MYR 6,530,295	-MYR 4,490,474	-MYR 2,809,284	-MYR 1,528,112	MYR 3,020,305	MYR 3,189,125	MYR 3,192,056
	15	-MYR 18,615,966	-MYR 15,917,650	-MYR 13,213,872	-MYR 10,859,871	-MYR 8,820,050	-MYR 7,138,860	-MYR 5,857,688	-MYR 1,309,271	-MYR 1,140,451	-MYR 1,137,521
	20	-MYR 23,244,632	-MYR 20,546,316	-MYR 17,842,538	-MYR 15,488,537	-MYR 13,448,716	-MYR 11,767,526	-MYR 10,486,354	-MYR 5,937,937	-MYR 5,769,117	-MYR 5,766,187
	25	-MYR 27,265,845	-MYR 24,567,530	-MYR 21,863,752	-MYR 19,509,751	-MYR 17,469,929	-MYR 15,788,740	-MYR 14,507,568	-MYR 9,959,150	-MYR 9,790,331	-MYR 9,787,400
	30	-MYR 30,761,019	-MYR 28,062,703	-MYR 25,358,925	-MYR 23,004,924	-MYR 20,965,103	-MYR 19,283,913	-MYR 18,002,741	-MYR 13,454,324	-MYR 13,285,504	-MYR 13,282,573
	35	-MYR 33,620,630	-MYR 30,922,314	-MYR 28,218,536	-MYR 25,864,535	-MYR 23,824,714	-MYR 22,143,524	-MYR 20,862,352	-MYR 16,313,935	-MYR 16,145,115	-MYR 16,142,185
	40	-MYR 39,278,779	-MYR 36,580,463	-MYR 33,876,685	-MYR 31,522,684	-MYR 29,482,863	-MYR 27,801,673	-MYR 26,520,502	-MYR 21,972,084	-MYR 21,803,264	-MYR 21,800,334
	45	-MYR 40,592,451	-MYR 37,894,135	-MYR 35,190,357	-MYR 32,836,356	-MYR 30,796,535	-MYR 29,115,345	-MYR 27,834,173	-MYR 23,285,756	-MYR 23,116,936	-MYR 23,114,005
	50	-MYR 40,973,646	-MYR 38,275,331	-MYR 35,571,553	-MYR 33,217,552	-MYR 31,177,730	-MYR 29,496,541	-MYR 28,215,369	-MYR 23,666,951	-MYR 23,498,132	-MYR 23,495,201
100	-MYR 40,980,237	-MYR 38,281,921	-MYR 35,578,143	-MYR 33,224,142	-MYR 31,184,321	-MYR 29,503,131	-MYR 28,221,959	-MYR 23,673,542	-MYR 23,504,722	-MYR 23,501,792	

4vHPVv, HPV-6/11/16/18 vaccine (Gardasil); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (Cervarix); MYR, Malaysian Ringgits

Table E.2. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPV, QALY outcomes, base-case mortality

QALY	Duration (year)	4vHPV									
		10	15	20	25	30	35	40	45	50	100
AS04-HPV-16/18v	10	222.1	203.1	183.8	169.6	160.2	155.3	153.4	153.0	152.9	152.9
	15	265.3	246.3	227.0	212.7	203.3	198.5	196.6	196.1	196.1	196.1
	20	309.2	290.2	270.9	256.7	247.3	242.4	240.5	240.1	240.0	240.0
	25	341.7	322.7	303.4	289.2	279.8	274.9	273.0	272.6	272.6	272.6
	30	363.2	344.2	324.9	310.6	301.2	296.3	294.5	294.0	294.0	294.0
	35	374.3	355.3	336.0	321.7	312.4	307.5	305.6	305.1	305.1	305.1
	40	378.0	359.0	339.7	325.4	316.0	311.1	309.3	308.8	308.8	308.8
	45	379.6	360.6	341.3	327.0	317.6	312.8	310.9	310.4	310.4	310.4
	50	379.6	360.6	341.3	327.1	317.7	312.8	310.9	310.5	310.4	310.4
100	379.6	360.6	341.3	327.1	317.7	312.8	310.9	310.4	310.4	310.4	

4vHPVv, HPV-6/11/16/18 vaccine (Gardasil); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (Cervarix)

Table E.3. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPVv, ICER, base-case mortality

ICER	Duration (year)	4vHPVv										
		10	15	20	25	30	35	40	45	50	100	
AS04-HPV-16/18v	10	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	15	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	20	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	25	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	30	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	35	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	40	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	45	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	50	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	100	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	

4vHPVv, HPV-6/11/16/18 vaccine (*Gardasil*); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (*Cervarix*)

Table E.4. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPVv, Cost outcomes mortality (Razak et al., 2013)

Cost outcomes (MYR)	Duration (year)	4vHPVv									
		10	15	20	25	30	35	40	45	50	100
AS04-HPV-16/18v	10	-MYR 19,037,353	-MYR 16,083,774	-MYR 13,058,630	-MYR 10,393,505	-MYR 8,049,836	-MYR 6,102,700	-MYR 4,630,799	MYR 11,527	MYR 231,753	MYR 235,530
	15	-MYR 23,947,192	-MYR 20,993,612	-MYR 17,968,469	-MYR 15,303,344	-MYR 12,959,675	-MYR 11,012,538	-MYR 9,540,637	-MYR 4,898,311	-MYR 4,678,085	-MYR 4,674,309
	20	-MYR 29,307,681	-MYR 26,354,101	-MYR 23,328,958	-MYR 20,663,833	-MYR 18,320,164	-MYR 16,373,027	-MYR 14,901,126	-MYR 10,258,800	-MYR 10,038,574	-MYR 10,034,798
	25	-MYR 34,040,125	-MYR 31,086,546	-MYR 28,061,402	-MYR 25,396,277	-MYR 23,052,608	-MYR 21,105,472	-MYR 19,633,571	-MYR 14,991,245	-MYR 14,771,019	-MYR 14,767,242
	30	-MYR 38,230,277	-MYR 35,276,697	-MYR 32,251,554	-MYR 29,586,429	-MYR 27,242,760	-MYR 25,295,623	-MYR 23,823,722	-MYR 19,181,396	-MYR 18,961,170	-MYR 18,957,394
	35	-MYR 41,696,998	-MYR 38,743,419	-MYR 35,718,275	-MYR 33,053,151	-MYR 30,709,481	-MYR 28,762,345	-MYR 27,290,444	-MYR 22,648,118	-MYR 22,427,892	-MYR 22,424,115
	40	-MYR 47,585,382	-MYR 44,631,803	-MYR 41,606,659	-MYR 38,941,534	-MYR 36,597,865	-MYR 34,650,729	-MYR 33,178,828	-MYR 28,536,502	-MYR 28,316,276	-MYR 28,312,499
	45	-MYR 49,316,290	-MYR 46,362,711	-MYR 43,337,567	-MYR 40,672,442	-MYR 38,328,773	-MYR 36,381,637	-MYR 34,909,736	-MYR 30,267,410	-MYR 30,047,184	-MYR 30,043,407
	50	-MYR 49,813,564	-MYR 46,859,985	-MYR 43,834,841	-MYR 41,169,716	-MYR 38,826,047	-MYR 36,878,911	-MYR 35,407,009	-MYR 30,764,684	-MYR 30,544,457	-MYR 30,540,681
100	-MYR 49,822,058	-MYR 46,868,478	-MYR 43,843,335	-MYR 41,178,210	-MYR 38,834,541	-MYR 36,887,404	-MYR 35,415,503	-MYR 30,773,177	-MYR 30,552,951	-MYR 30,549,175	

4vHPVv, HPV-6/11/16/18 vaccine (Gardasil); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (Cervarix); MYR, Malaysian Ringgits

Table E.5. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPV, QALY outcomes, mortality (Razak et al., 2013)

QALY	Duration (year)	4vHPV									
		10	15	20	25	30	35	40	45	50	100
AS04-HPV-16/18v	10	332.7	306.2	280.3	262.0	250.9	245.9	244.6	244.6	244.9	244.9
	15	392.6	366.2	340.2	322.0	310.8	305.8	304.5	304.5	304.8	304.8
	20	451.7	425.3	399.3	381.0	369.9	364.9	363.6	363.6	363.9	363.9
	25	493.4	466.9	441.0	422.7	411.6	406.6	405.3	405.3	405.5	405.6
	30	518.7	492.3	466.4	448.1	437.0	431.9	430.7	430.6	430.9	430.9
	35	530.2	503.7	477.8	459.5	448.4	443.4	442.1	442.1	442.3	442.4
	40	533.6	507.2	481.2	462.9	451.8	446.8	445.5	445.5	445.8	445.8
	45	533.1	506.7	480.7	462.4	451.3	446.3	445.0	445.0	445.3	445.3
	50	532.4	506.0	480.0	461.8	450.6	445.6	444.3	444.3	444.6	444.6
100	532.4	506.0	480.0	461.8	450.6	445.6	444.3	444.3	444.6	444.6	

4vHPV, HPV-6/11/16/18 vaccine (Gardasil); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (Cervarix); MYR, Malaysian Ringgits

Table E.6. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPVv, ICER, mortality (Razak et al., 2013)

ICER	Duration (year)	4vHPV										
		10	15	20	25	30	35	40	45	50	100	
AS04-HPV-16/18v	10	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx very C/E	Cx very C/E	Cx very C/E
	15	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	20	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	25	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	30	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	35	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	40	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	45	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	50	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	100	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant

4vHPV, HPV-6/11/16/18 vaccine (*Gardasil*); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (*Cervarix*); MYR, Malaysian Ringgits

Table E.7. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPV, HPV-16/18 distribution unadjusted

Cost outcomes (MYR)	4vHPV										
	Duration (year)	10	15	20	25	30	35	40	45	50	100
AS04-HPV-16/18v	10	MYR 6,627,899	MYR 9,609,605	MYR 12,547,452	MYR 15,067,210	MYR 17,203,293	MYR 18,922,072	MYR 20,199,095	MYR 23,999,376	MYR 24,156,911	MYR 24,159,430
	15	MYR 2,291,509	MYR 5,273,215	MYR 8,211,063	MYR 10,730,820	MYR 12,866,903	MYR 14,585,682	MYR 15,862,706	MYR 19,662,986	MYR 19,820,521	MYR 19,823,040
	20	-MYR 2,222,697	MYR 759,009	MYR 3,696,856	MYR 6,216,614	MYR 8,352,696	MYR 10,071,475	MYR 11,348,499	MYR 15,148,779	MYR 15,306,315	MYR 15,308,834
	25	-MYR 6,083,558	-MYR 3,101,852	-MYR 164,005	MYR 2,355,753	MYR 4,491,836	MYR 6,210,615	MYR 7,487,638	MYR 11,287,919	MYR 11,445,454	MYR 11,447,973
	30	-MYR 9,370,122	-MYR 6,388,416	-MYR 3,450,569	-MYR 930,811	MYR 1,205,272	MYR 2,924,051	MYR 4,201,074	MYR 8,001,355	MYR 8,158,890	MYR 8,161,409
	35	-MYR 12,006,766	-MYR 9,025,060	-MYR 6,087,213	-MYR 3,567,455	-MYR 1,431,373	MYR 287,406	MYR 1,564,430	MYR 5,364,710	MYR 5,522,246	MYR 5,524,765
	40	-MYR 16,833,766	-MYR 13,852,060	-MYR 10,914,213	-MYR 8,394,455	-MYR 6,258,373	-MYR 4,539,594	-MYR 3,262,570	MYR 537,710	MYR 695,246	MYR 697,765
	45	-MYR 17,949,807	-MYR 14,968,101	-MYR 12,030,253	-MYR 9,510,496	-MYR 7,374,413	-MYR 5,655,634	-MYR 4,378,610	-MYR 578,330	-MYR 420,795	-MYR 418,276
	50	-MYR 18,256,616	-MYR 15,274,911	-MYR 12,337,063	-MYR 9,817,306	-MYR 7,681,223	-MYR 5,962,444	-MYR 4,685,420	-MYR 885,140	-MYR 727,605	-MYR 725,085
100	-MYR 18,261,522	-MYR 15,279,817	-MYR 12,341,969	-MYR 9,822,212	-MYR 7,686,129	-MYR 5,967,350	-MYR 4,690,326	-MYR 890,046	-MYR 732,511	-MYR 729,991	

4vHPV, HPV-6/11/16/18 vaccine (*Gardasil*); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (*Cervarix*); MYR, Malaysian Ringgits

Table E.8. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPV, HPV-16/18 distribution unadjusted

QALY	4vHPV										
	Duration (year)	10	15	20	25	30	35	40	45	50	100
AS04-HPV-16/18v	10	-42.7	-63.5	-84.4	-99.7	-109.7	-114.9	-116.8	-117.3	-117.3	-117.3
	15	-2.4	-23.1	-44.0	-59.4	-69.4	-74.5	-76.5	-76.9	-77.0	-77.0
	20	38.2	17.5	-3.4	-18.7	-28.8	-33.9	-35.8	-36.3	-36.3	-36.3
	25	68.1	47.3	26.4	11.1	1.1	-4.0	-6.0	-6.5	-6.5	-6.5
	30	87.6	66.8	46.0	30.6	20.6	15.5	13.5	13.0	13.0	13.0
	35	97.6	76.9	56.0	40.6	30.6	25.5	23.5	23.1	23.0	23.0
	40	100.9	80.1	59.2	43.9	33.9	28.7	26.8	26.3	26.3	26.3
	45	102.3	81.6	60.7	45.4	35.4	30.2	28.3	27.8	27.8	27.8
	50	102.4	81.6	60.7	45.4	35.4	30.3	28.3	27.8	27.8	27.8
100	102.4	81.6	60.7	45.4	35.4	30.3	28.3	27.8	27.8	27.8	

4vHPV, HPV-6/11/16/18 vaccine (*Gardasil*); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (*Cervarix*); MYR, Malaysian Ringgits

Table E.9. Two-way sensitivity analysis on duration of cross-protection AS04-HPV-16/18v vs. 4vHPV, HPV-16/18 distribution unadjusted

		4vHPV									
		10	15	20	25	30	35	40	45	50	100
AS04-HPV-16/18v	10	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated
	15	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated
	20	Cx dominant	Cx C/E	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated
	25	Cx dominant	Cx dominant	Cx dominant	Cx not C/E	Cx not C/E	Cx dominated	Cx dominated	Cx dominated	Cx dominated	Cx dominated
	30	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx C/E	Cx not C/E	Cx not C/E	Cx not C/E	Cx not C/E	Cx not C/E
	35	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx very C/E	Cx C/E	Cx not C/E	Cx not C/E	Cx not C/E
	40	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx very C/E	Cx very C/E	Cx very C/E
	45	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	50	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant
	100	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant	Cx dominant

4vHPV, HPV-6/11/16/18 vaccine (*Gardasil*); AS04-HPV-16/18v, AS04-adjuvanted HPV-16/18 vaccine (*Cervarix*); MYR, Malaysian Ringgits

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