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           | 0.14949                                              |
| 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 |
|-----------|-------------------------------|------------|
| **Low-risk HPV** | | |
| [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) |
| **Oncogenic HPV** | | |
| [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*5 = 10,725) = 6,130/10,725 = 0.5716 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 |

#### Screening parameters

| Parameter | Value | Reference |
|-----------|-------|-----------|
| 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 |

#### 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 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 chemoradiotherapy 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-medicinal 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) |
|-----------|-----------------------|-----------------------------------------|----------------------------------|
| **CIN1**  |                       |                                         |                                  |
| 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% |
| **Genital warts** | | | |
| 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% |
| **CIN2/3** | | | |
| 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% |
| **Cervical cancer** | | | |
| 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 4vHPV                      | 47.7%     | 28.9% | 61.9% |
| AS04-HPV-16/18v                 | 23.4%     | 7.8   | 36.4  |
| **Vaccine efficacy cross protection** |           |       |       |
| CIN2/3 and CC 4vHPV             | 68.4%     | 45.7% | 82.4% |
| AS04-HPV-16/18v                 | 32.5%     | 6.0%  | 51.9% |
| **Discount rate**               | 5%        | 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                  | 50.10%    | 46.48%| 69.72%|
| 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 34| 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|
| Disutility 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.
| 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) | (Moskicki 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 |
| [Persistent CIN2/3] to [Cancer] | Uniform distribution (0.091–0.137) | (Melnikow et al., 1998) |
| % 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 (0.216–0.328) | (Insinga et al., 2005a; Myers et al., 2004) |
| Cancer cured | Uniform distribution (0.050–0.074) | (Insinga et al., 2005a; Myers et al., 2004) |

**Table D.2. Input variables values for probabilistic sensitivity analysis**
| 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 effect against 16/18 | Fix (0.980) (Paavonen et al., 2009) |
| AS04-HPV-16/18v effect 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 effect 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 effect 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

IV: 2.4%

II: 96.3%

Threshold: 3xGDP/capita

I: 1.2%

III: 0.1%
### 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) | 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 15,786,740 | 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 25,864,353 | 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 40,582,451 | 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 36,281,921 | MYR 35,378,143 | MYR 33,224,142 | MYR 31,184,321 | MYR 29,503,131 | MYR 26,221,959 | 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 Ringgit

### 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) | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 100 |
|------|-----------------|----|----|----|----|----|----|----|----|----|-----|
| AS04-HPV-16/18v | 10              | 222.1 | 203.1 | 188.3 | 168.6 | 160.2 | 155.3 | 153.4 | 153.0 | 152.9 | 152.9 |
|       | 15              | 265.3 | 246.3 | 227.0 | 212.7 | 203.5 | 198.5 | 196.6 | 196.1 | 196.1 | 196.1 |
|       | 20              | 309.2 | 290.2 | 276.9 | 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 | 327.0 | 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) | 10   | 15   | 20   | 25   | 30   | 35   | 40   | 45   | 50   | 100  |
|-------|-----------------|------|------|------|------|------|------|------|------|------|------|
|       |                 |      |      |      |      |      |      |      |      |      |      |
|       | AS04-HPV-16/18v |      |      |      |      |      |      |      |      |      |      |
| 10    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 15    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 20    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 25    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 30    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 35    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 40    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 45    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 50    | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |
| 100   | Cx dominant     | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   | Cx   |

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) | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 100 |
|---------------------|-----------------|----|----|----|----|----|----|----|----|----|-----|
| AS04-HPV-16/18v     | 4vHPVv          | 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 4,888,311 | MYR 4,878,085 | 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 35,716,275 | 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 38,941,634 | MYR 36,597,865 | MYR 34,650,729 | MYR 33,178,828 | MYR 29,536,502 | 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) | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 100 |
|----------|-----------------|----|----|----|----|----|----|----|----|----|-----|
| AS04-HPV-16/18v | 4vHPVv          | 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 | 442.9 | 442.9 |
| 40       | 533.6           | 507.2 | 481.2 | 462.9 | 451.8 | 446.8 | 445.5 | 445.5 | 445.9 | 445.9 |
| 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) | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 100 |
|------|----------------|----|----|----|----|----|----|----|----|----|-----|
| 4vHPV |               |    |    |    |    |    |    |    |    |    |     |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |
|      | Cx dominant    | Cx dominant | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx | Cx |

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 | AS04-HPV-16/18v | AS04-HPV-16/18v adjuvanted |
|---------------------|-------|----------------|---------------------------|
|                     | 10    | 15             | 20                        | 25          | 30       | 35       | 40       | 45       | 50       | 100      |
| Duration (year)     | 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 |
|                     | 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 |
|                     | 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 |
|                     | 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 |
|                     | 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  |
|                     | 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  |
|                     | 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    |
|                     | 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    |
|                     | 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    |
|                     | MYR 18,261,322 | MYR 15,279,817 | MYR 12,341,969            | MYR 9,822,212  | MYR 7,688,129  | 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 | Duration (year) | 4vHPV | AS04-HPV-16/18v | AS04-HPV-16/18v adjuvanted |
|------|----------------|-------|----------------|---------------------------|
|      | 10             | 15    | 20             | 25                        | 30         | 35        | 40         | 45         | 50         | 100        |
|      | -42.7          | -63.5 | -84.4          | -99.7                     | -109.7     | -114.9    | -116.8     | -117.3     | -117.3     | -117.3     |
|      | -2.4           | -23.1 | -44.0          | -59.4                     | -69.4      | -74.5     | -76.9      | -77.0      | -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      | 13.0       | 13.0       | 13.0       | 13.0       |
| 35   | 97.6           | 76.9  | 56.0           | 40.6                      | 30.6       | 20.5      | 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   |
|-------|--------|--------|--------|--------|--------|--------|--------|--------|--------|-------|
| 10    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 15    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 20    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 25    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 30    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 35    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 40    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 45    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 50    | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |
| 100   | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx     | Cx    |

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

Aljunid S, Zafar A, Saperi S, Amrizal M (2010). Burden of disease associated with cervical cancer in Malaysia and the potential costs and consequences of HPV vaccination. Asian Pac J Cancer Prev, 11, 1551-9.

Aubin F, Pretet JL, Jacquard AC, et al (2008). Human papillomavirus genotype distribution in external acuminata condylomata: a Large French National Study (EDiTH IV). Clin Infect Dis, 47, 610-5.

Brown DR, Kjaer SK, Sigurdsson K, et al (2009). The impact of quadrivalent human papillomavirus (HPV; types 6, 11, 16, and 18) L1 virus-like particle vaccine on infection and disease due to oncogenic nonvaccine HPV types in generally HPV-naive women aged 16-26 years. J Infect Dis, 199, 926-35.

Bruni L, Barrionuevo-Rosas L, Albero G, et al (2015). Information Centre on HPV and Cancer (HPV Information Centre): Human Papillomavirus and Related Diseases in Malaysia - Summary Report 19 April 2017. http://www.hpvcentre.net/dataquery.php (accessed 05 October 2015).

Demarteau N, Standaert B (2010). Modelling the economic value of cross- and sustained-protection in vaccines against cervical cancer. J Med Econ, 13, 324-38.

Department of Statistics Malaysia (2015). Population by age and sex, Malaysia, 2014. http://pqi.stats.gov.my/searchBI.php?tahun=2014&kodData=2&kodJadual=1&kodCiri=3&kodNegeri=0 0 (accessed 30 September 2015).

Fahey MT, Irwig L, Macaskill P (1995). Meta-analysis of Pap test accuracy. Am J Epidemiol, 141, 680-9.

Ferlay J, Soerjomataram I, Ervik M, et al (2013). GLOBOCAN 2012 v1.0, Cancer incidence and mortality worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer (IARC); 2013. http://globocan.iarc.fr (accessed 31 January 2014).

Garland SM, Hernandez-Avila M, Wheeler CM, et al (2007). Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. N Engl J Med, 356, 1928-43.

Garland SM, Steben M, Sings HL, et al (2009). Natural history of genital warts: analysis of the placebo arm of 2 randomized phase III trials of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine. J Infect Dis, 199, 805-14.

Giannini SL, Hanon E, Moris P, et al (2006). Enhanced humoral and memory B cellular immunity using HPV16/18 L1 VLP vaccine formulated with the MPL/aluminium salt combination (AS04) compared to aluminium salt only. Vaccine, 24, 5937-49.

Gold MR, Franks P, McCoy KL, Fryback DG (1998). Toward consistency in cost-utility analyses: using national measures to create condition-specific values. Med Care, 36, 778-92.

Goldie SJ, Kohli M, Grima D, et al (2004). Projected clinical benefits and cost-effectiveness of a human papillomavirus 16/18 vaccine. J Natl Cancer Inst, 96, 604-15.

Insiinga RP, Dasbach EJ, Elbasha EH (2005a). Assessing the annual economic burden of preventing and treating anogenital human papillomavirus-related disease in the US: analytic framework and review of the literature. Pharmacoeconomics, 23, 1107-22.
Inسینگا RP, Glass A, Rush B (2005b). Health state transitions following an abnormal pap smear: implications for health utility assessment in cost-effectiveness analyses. Abstract W-02 presented at the 22nd International Papillomavirus Conference & Clinical Workshop, 30 April - 6 May 2005, Vancouver, BC, Canada.

Institute of Medicine (2000). Vaccines for the 21st Century: A Tool for Decisionmaking. In: The National Academies Press. Washington, DC, USA.

Jabatan Perangkaan Malaysia (Department of Statistics Malaysia) (2014). Jadual hayat Ringkas (Abridged life tables) Malaysia 2011-2014. http://www.statistics.gov.my (accessed 13 February 2015).

Kumamoto Y, Tsukamoto J, Sugiyama T, et al (2004). National surveillance of sexually transmitted diseases of Japan in 2002. Japanese Journal of Sexually Transmitted Diseases, 15, 17-45.

Melnikow J, Nuovo J, Willan AR, Chan BK, Howell LP (1998). Natural history of cervical squamous intraepithelial lesions: a meta-analysis. Obstet Gynecol, 92, 727-35.

MoH Malaysia, Academy of Medicine (2003). Management of cervical cancer. Clinical Practice Guidelines. http://www.acadmed.org.my/cpg/CPG-Management%20of%20CervicalCancer.pdf (accessed 01 December 2015).

Moscicki AB, Hills N, Shiboski S, et al (2001). Risks for incident human papillomavirus infection and low-grade squamous intraepithelial lesion development in young females. JAMA, 285, 2995-3002.

Myers ER, Green S, Lipkus I (2004). Patient preferences for health states related to HPV infection: visual analog scale versus time trade-off elicitation. Abstract 542 presented at the 21st International Papillomavirus Conference, 20-27 February 2004, Mexico City, Mexico.

Paavonen J, Naud P, Salmerón J, et al (2009). Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. Lancet, 374, 301-14.

Razak NA, Mn K, Zubairi YZ, Naing NN, Zaki NM (2013). Estimating the five-year survival of cervical cancer patients treated in hospital universiti sains malaysi a. Asian Pac J Cancer Prev, 14, 825-8.

Richardson H, Kelsall G, Tellier P, et al (2003). The natural history of type-specific human papillomavirus infections in female university students. Cancer Epidemiol Biomarkers Prev, 12, 485-90.

Sanders GD, Taira AV (2003). Cost-effectiveness of a potential vaccine for human papillomavirus. Emerg Infect Dis, 9, 37-48.

Schlecht NF, Platt RW, Duarte-Franco E, et al (2003). Human papillomavirus infection and time to progression and regression of cervical intraepithelial neoplasia. J Natl Cancer Inst, 95, 1336-43.

Skinner R, Apter D, Chow SN, Wheeler C, Dubin G (2009). Cross-protection efficacy of Cervarix(tm) against oncogenic HPV types beyond HPV-16/18. Abstract no 0-29.01 presented at the 25th International Papillomavirus Conference, 08 - 14 May 2009, Malmö, Sweden.

The FUTURE II Study Group (2007). Quadrivalent Vaccine against Human Papillomavirus to Prevent High-Grade Cervical Lesions. N Engl J Med, 356, 1915-27.
Tjalma W, Paavonen J, Naud P, et al (2009). Efficacy of the HPV-16/18 AS04-adjuvanted vaccine against abnormal cytology and low-grade histopathological lesions in an oncogenic HPV-naïve population. Abstract n° A-171-0004-01446 presented at the 16th International Meeting of the European Society for Gynaecological Oncology (ESGO), 11 - 14 Oct, Belgrade, Serbia. Int J Gynecol Cancer, 19, 1008.

Van de Velde N, Brisson M, Boily MC (2007). Modeling human papillomavirus vaccine effectiveness: quantifying the impact of parameter uncertainty. Am J Epidemiol, 165, 762-75.

Villa LL (2006). Vaccines against papillomavirus infections and disease. Rev Chilena Infectol, 23, 157-63.

Woodhall SC, Jit M, Soldan K, et al (2011). The impact of genital warts: loss of quality of life and cost of treatment in eight sexual health clinics in the UK. Sex Transm Infect, 87, 458-63.

World Health Organization (WHO) (2014). Human papillomavirus vaccines: WHO position paper, October 2014. Wkly Epidemiol Rec, 89, 465-91.