Annex 18A
Model Input Parameters and Calibration

Table 18A.1 Input Parameters: Baseline Ranges

Variable	Baseline values[a]	Ranges[a]
Progression		
Normal to HPV DNA		
LR HPV	0.000100–0.010000	0.1–8
HR-other HPV	0.000100–0.010000	0.1–8
HR-16 HPV	0.000100–0.010000	0.1–8
HR-18 HPV	0.000100–0.010000	0.1–6
HPV DNA to CIN 1[b]		
LR HPV	0.004640–0.005380	0.1–6
HR-other HPV	0.004780–0.008490	0.1–6
HR-16 HPV	0.004780–0.008490	0.1–6
HR-18 HPV	0.004780–0.008490	0.1–6
HPV DNA to CIN 2,3[c]		
LR HPV	0.000037–0.000778	0–0.1
HR-other HPV	0.000184–0.003888	0–0.1
HR-16 HPV	0.000184–0.003888	0.1–1
HR-18 HPV	0.000184–0.003888	0–0.1
CIN 1 to CIN 2,3		
LR HPV	0.000037–0.000778	0.1–6
HR-other HPV	0.000184–0.003888	0.1–6
HR-16 HPV	0.000184–0.003888	0.1–6
HR-18 HPV	0.000184–0.003888	0.1–6
CIN 2,3 to local cancer[d]		
HR-other HPV	0.000015–0.006000	0.5–4
HR-16 HPV	0.000015–0.006000	0.5–6
HR-18 HPV	0.000015–0.006000	0.5–6
Local to regional invasive cancer	0.020000	—
Regional to distant invasive cancer	0.025000	—

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Table 18A.1 Input Parameters: Baseline Ranges (continued)

Variable	Baseline values[a]	Ranges[a]
Regression		
HPV DNA to normal[e]		
LR HPV	0.030500	3–8
HR-other HPV	0.030500	3–8
HR-16 HPV	0.030500	3–8
HR-18 HPV	0.030500	3–8
CIN 1 to normal[f]		
LR HPV	0.030500	0.5–6
HR-other HPV	0.030500	0.5–6
HR-16 HPV	0.030500	0.5–6
HR-18 HPV	0.030500	0.5–6
CIN 2,3 to normal[g]		
LR HPV	0.001410–0.006497	0.5–6
HR-other HPV	0.001410–0.006497	0.5–6
HR-16 HPV	0.001410–0.006497	0.5–6
HR-18 HPV	0.001410–0.006497	0.5–6
Other		
Immunity (HR HPV types only)		
HR-other HPV	0	0.0–0.5
HR-16 HPV	0	0.6–1
HR-18 HPV	0	0.6–1

Source: Goldie and others 2007.
Note: CIN = Cervical intraepithelial neoplasia; DNA = deoxyribonucleic acid; HPV = human papillomavirus; HR = high risk; LR = low risk.
a. Base case values are monthly probabilities, unless otherwise noted. A hyphenated range reported for a base case value represents age-specific probabilities. Except where noted, the ranges represent multiplier values, which are applied to baseline probabilities during calibration.
b. Although baseline rates of progression and the range of multipliers were the same among all HR HPV types, the multipliers were allowed to vary independently by type in the parameter searches.
c. A proportion of women with HPV who progress to CIN 1 transition directly to CIN 2,3.
d. Infection with high-risk HPV is considered a necessary condition for progression to invasive cancer.
e. We assumed that regression from HPV DNA to normal was equal among types and therefore the multipliers were held constant among types in the parameter searches.
f. Although baseline rates of regression and the range of multipliers were the same among all HPV types, the multipliers were allowed to vary independently by type in the parameter searches.
g. Of women with CIN 2,3, 70 percent regress to normal, 15 percent to HPV, and 15 percent to CIN 1.

Table 18A.2 Cost Parameters for Screening, Diagnosis, and Treatment and Wage Rates by Income Quintile *(2009 US$)*

	Quintile I		Quintile II		Quintile III		Quintile IV		Quintile V	
Cost parameter	Direct medical cost per woman	Women's time and OOP costs	Direct medical cost per woman	Women's time and OOP costs	Direct medical cost per woman	Women's time and OOP costs	Direct medical cost per woman	Women's time and OOP costs	Direct medical cost per woman	Women's time and OOP costs
Screening										
Cytology	7.01	2.87	7.01	2.87	7.32	2.87	7.49	2.87	7.96	2.87
VIA	2.24	2.15	2.24	2.15	2.24	2.15	2.24	2.15	2.24	2.15
HPV rapid test	7.33	2.15	7.33	2.15	7.50	2.15	7.59	2.15	7.92	2.15
Diagnosis										
Colposcopy	4.41	2.27	4.41	2.27	4.58	2.27	4.67	2.27	4.93	2.27
Biopsy	5.91		5.91		5.96		5.99		6.06	
Treatment										
LEEP	66.41	166.00	66.41	166.00	68.01	166.00	68.92	166.00	71.43	166.00
Cryotherapy	10.32	2.27	10.32	2.27						
Cold conization	293.15	178.50	293.15	178.50	293.15	178.50	367.54	253.50	367.54	253.50
Simple hysterectomy	409.48	291.00	409.48	291.00	410.60	291.00	446.63	292.00	446.63	292.00
Simple radiotherapy	290.18	252.00	290.18	252.00	292.19	252.00	384.98	252.00	384.98	252.00
Urban share of population (%)	34 (5)		34 (5)		42 (8)		47 (9)		64 (10)	
Daily wage rate	3.00		6.00		10.00		15.00		31.00	

Sources: Levin and others 2010; Shi and others 2012.
Note: Income quintiles are from lowest (I) to highest (V). Rural costs are from Shi and others (2012). Costs for urban settings and Beijing are from Levin and others (2010). Costs represent a weighted average for urban and rural for each income quintile. Numbers in parentheses indicate the percentage of women in each quintile assumed to live in or receive care in Beijing. HPV = human papillomavirus; LEEP = loop electrosurgical excision procedure; OOP = out of pocket; VIA = visual inspection with acetic acid.

Table 18A.3 Cost Parameters for Out-of-Pocket Expenses for Direct Medical, Direct Nonmedical, and Total Patient Costs by Income Quintile

(2009 US$)

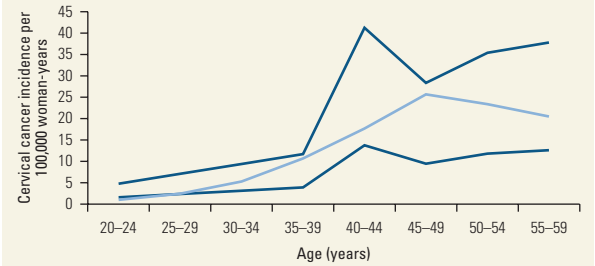
	Quintile I			Quintile II			Quintile III			Quintile IV			Quintile V		
Cost parameter	**Direct medical**	**Direct nonmedical**	**Total**	**Direct medical**	**Direct nonmedical**	**Total**	**Direct medical**	**Direct nonmedical**	**Total**	**Direct medical**	**Direct nonmedical**	**Total**	**Direct medical**	**Direct nonmedical**	**Total**
Screening															
Cytology		1.16	1.16	7.01	3.6	10.64	7.32	5.69	13.01	7.49	8.62	16.11	7.96	17.51	25.47
VIA	2.24	1.11	3.35	2.24	2.4	4.66	2.24	3.80	6.04	2.24	5.75	7.99	2.24	11.68	13.92
HPV rapid test	7.33	1.24	7.33	7.33	2.3	9.64	7.50	3.63	11.12	7.59	5.50	13.09	7.92	11.16	19.08
Diagnosis															
Colposcopy	4.41	0.00	4.41	4.41	2.6	7.00	4.58	4.07	8.65	4.67	6.16	10.83	4.93	12.51	17.44
Biopsy	5.91	110.77	5.91	5.91		5.91	5.96		5.96	5.99		5.99	6.06		6.06
Treatment															
LEEP	66.41	110.77	177.17	66.41	194.1	260.52	68.01	285.68	353.69	68.92	415.22	484.13	71.43	808.10	879.53
Cryotherapy	10.32		10.32	10.32	194.1	204.44			0.00			0.00			0.00
Cold conization	293.15	188.17	481.32	293.15		293.15	293.15	382.67	675.81	367.54	811.69	1,179.22	367.54	1,512.60	1,880.13
Simple hysterectomy	409.48	309.35	718.83	409.48	280.8	690.32	410.60	689.95	1100.55	446.63	1,007.12	1,453.75	446.63	1,906.04	2,352.67
Simple radiotherapy	290.18	269.68	559.86	290.18	490.7	780.89	292.19	633.49	925.68	384.98	902.93	1,287.91	384.98	1,720.13	2,105.11

Sources: Adapted from Levin and others 2010; Shi and others 2012.

Note: Income quintiles are from lowest (I) to highest (V). OOP direct medical costs are 35 percent of total treatment costs shown in table 18A.2. We assume 35 percent of total treatment costs are privately financed in China (WHO Global Health Observatory). OOP direct nonmedical costs are transport and waiting times for patients. Transport and waiting times obtained from Shi and others (2012) were adjusted with new estimates of average wage rates by quintile.

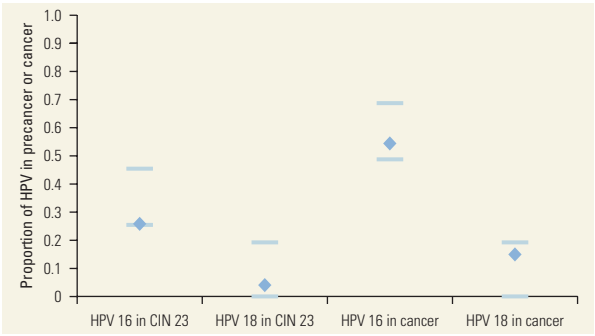
HPV = human papillomavirus; LEEP = loop electrosurgical excision procedure; OOP = out of pocket; VIA = visual inspection with acetic acid.

Figure 18A.1 Calibration Results: Cervical Cancer Incidence from Best-Fitting Parameter Set Compared with Empirical Estimates



Note: Dark blue lines depict the 95 percent confidence intervals of age-specific cervical cancer incidence in China (GLOBOCAN 2008). The light blue line represents the projected incidence of the best-fitting parameter set used in the model analysis.

Figure 18A.2 HPV 16, 18 Type Distribution from Best-Fitting Parameter Set Compared with Empirical Estimates



Note: Bars depict the 95 percent confidence intervals from empirical data on HPV 16/18 type distribution in CIN 23 and cancer (Bao and others 2008). Diamonds show the estimates projected by the best-fitting parameter set used in the model analysis. CIN = cervical intraepithelial neoplasia; HPV = human papillomavirus.

NOTES FOR FIGURES

Defining Calibration Targets

Calibration targets included type distribution within CIN categories, age-specific cancer incidence, cumulative cancer incidence, and type- and age-specific duration of HPV infections and CIN.

For each calibration target, we used the best available data sources to determine a point estimate and confidence interval. Targets were calculated using 95 percent confidence intervals of the binomial distribution in STATA/SE 9.0.

Goodness-of-Fit

The model outputs with each input parameter set were compared with the calibration targets. Model fit to the targets was evaluated by constructing a goodness-of-fit score. A composite goodness-of-fit score for each parameter set was computed by summing the log likelihood of each model outcome (Kim and others 2007). Goodness-of-fit scores followed a chi-square distribution with the number of degrees of freedom equal to the number of targets.

Input Parameter Acceptance Criterion

We determined our best-fitting parameter set as the one with the lowest goodness-of-fit score—the model-generated input parameter whose simulated model outputs were simultaneously closest to all calibration targets.

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