

Appendix: Model Inputs

Activity group	Proportion of population, %		Relative partner acquisition rate (RPAR), pc_l	Reference [23]
	males, ω_m	females, ω_f		
1 (highest)	2.56	2.56	11.29	
2	11.47	11.47	2.96	
3 (lowest)	85.97	85.97	1	

Age group	RPAR, pa_i	Mean partner acquisition rate, \bar{c}_j	
12–14	0.11	0.1	[1]
15–17	1.18	0.3	[1]
18–19	2.42	1.3	[23]
20–24	2.61		
25–29	2.55		
30–34	1.72		
35–39	1.65		
40–44	1.53		
45–49	1.38		
50–54	1.25		
55–59	1.00		
60–69	0.61	0.5	assumed
≥ 70	0.44		

	males, N_m	females, N_f
Population size	50,000	50,000

Table 1: Baseline behavioral parameter values for the sexually active population

Parameter	Estimate	Reference
Probability of transmission per partnership		[13]
From males to females	0.8	
From females to males	0.7	
mean duration of HPV infection, years		[16]
HPV 16/18, $1/(\gamma_{ki}^1 + \sum_s \theta_{ks}^1)$	1.2	
HPV 6/11, $1/(\gamma_{ki}^2 + \theta_{kg}^2 + \sum_s \theta_{ks}^2)$	0.7	
Rate of waning natural immunity, σ_{zki}^h , per year	0	
progression in the presence of HPV 16/18 per year, %		
Normal to CIN1, θ_{k1}^1	9.4	[18]
Normal to CIN2, θ_{k2}^1	5.8	[18]
Normal to CIN3, θ_{k3}^1	5.3	[18]
CIN1 to CIN2, π_{1i}^1	13.6	[15]
CIN2 to CIN3, π_{2i}^1	14	[7, 20]
CIN3 to CIS1, π_{3i}^1	42	[20, 34]
CIS1 to CIS2, π_{4i}^1	5	
CIS to LCC, π_{5i}^1	18	
LCC to RCC, π_{Li}^1	10	[11, 31, 27]
RCC to DCC, π_{Ri}^1	30	[27]
progression in the presence of HPV 6/11 per year, %		
Normal to CIN1, θ_{k1}^2	9.5	[18]
Normal to CIN2, θ_{k2}^2	1.9	[18]
CIN1 to CIN2, π_{1i}^2	0	[18]
Normal to genital warts, θ_{kg}^2	57	[36]
regression in the presence of HPV 16/18 per year, %		
CIN1 to normal/HPV, τ_{f1}^1	32.9	[15, 32]
CIN2 to normal/HPV, τ_{f2}^1	31	[20, 7, 24]
CIN2 to CIN1, τ_{f21}^1	13.3	[7]
CIN3 to normal/HPV, τ_{f3}^1	11	[20]
CIN3 to CIN1, τ_{f31}^1	3	[7, 20]
CIN3 to CIN2, τ_{f32}^1	3	[7, 20]
regression in the presence of HPV 6/11 per year, %		
CIN1 to normal/HPV, τ_{f1}^2	55.2	
CIN2 to CIN1, τ_{f21}^2	13.3	[7]
genital warts to normal/HPV, τ_{gk}^2	87.5	[36]
hysterectomy rate, % per year, Δ_i		[21]
15–24 years	0.02	
25–29 years	0.26	
30–34 years	0.53	
35–39 years	0.89	
40–44 years	1.17	
45–54 years	0.99	
≥ 55 years	0.36	

Table 2: Baseline biological parameter values for the HPV and disease compartments

Parameter	Estimate	Reference
		[33]
age-specific cervical cancer mortality rates, per year, %		
for LCC, χ_L		
15–29 years	0.7	
30–39 years	0.6	
40–49 years	0.8	
50–59 years	1.9	
60–69 years	4.2	
≥ 70 years	11.6	
for RCC, χ_R		
15–29 years	13.4	
30–39 years	8.9	
40–49 years	11.0	
50–59 years	10.1	
60–69 years	17.6	
≥ 70 years	28.6	
for DCC, χ_D		
15–29 years	42.9	
30–39 years	41.0	
40–49 years	46.7	
50–59 years	52.7	
60–69 years	54.6	
≥ 70 years	70.3	

Table 3: Annual age-specific cervical cancer mortality rates, 1997–2002

Parameter	Estimate	Reference
Routine cervical screening, $cover_i$, % per year		[17]
10–14 years	0.6	
15–19 years	21.0	
20–24 years	44.8	
25–29 years	61.6	
30–34 years	54.9	
35–39 years	50.5	
40–44 years	48.1	
45–49 years	49.1	
50–54 years	51.1	
55–59 years	46.7	
60–64 years	42.5	
65–69 years	38.9	
70–74 years	29.6	
75–79 years	20.1	
80–84 years	11.1	
85+	5.5	
Females never screened, ϱ_1 , %	5	
Liquid-based cytology sensitivity, $papsn_s$, %		
for CIN1	28	[3]
for \geq CIN2/3	59	[3]
Liquid-based cytology specificity, $papsps_s$, %	94	[3, 5]
Colposcopy sensitivity, $colpsn_s$, %	96	[26]
Colposcopy specificity, $colpsp_s$, %	48	[26]
Genital wart patients seeking physician care, $1 - \theta_{gs}$, %	75	
Symptoms recognition, %		[4]
LCC, $recog_L$	3.8	
RCC, $recog_R$	18	
DCC, $recog_D$	90	
Cure rate with treatment per year, %		
for CIN1, $cure_1$	96	[9]
for CIN2, Γ_2	92	[9]
for CIN3, Γ_3	92	[9]
for LCC, Ω_L	92	[30]
for RCC, Ω_R	53	[30]
for DCC, Ω_D	17	[30]
Persistence of HPV after treatment for CIN, ψ_s , %	34	[6]

Table 4: Cervical cytology screening and colposcopy characteristics and rates of cure and symptom recognition

Condition	Estimate		Reference
	females	males	
Genital warts, qgw_k	0.91	0.91	[28]
CIN1, $qcin_1$	0.91		[28]
CIN2, $qcin_2$	0.87		[28]
CIN3, $qcin_3$	0.87		[28]
LCC, qcc_L	0.76		[28]
RCC, qcc_R	0.67		[28]
DCC, qcc_D	0.48		[10]
Cancer survivors, $qccs$	0.76		[35]
No condition, qki			
12–17 years	0.93	0.93	[10]
18–34 years	0.91	0.92	[10]
35–44 years	0.89	0.90	[10]
45–54 years	0.86	0.87	[10]
55–64 years	0.80	0.81	[10]
65–74 years	0.78	0.76	[10]
≥ 75 years	0.70	0.69	[10]

Table 5: Quality of life weights

Condition	Estimate		Reference
	females	males	
cytology test, scn	\$99		[25]
colposcopy, $colp$	\$165		[25]
colposcopy and biopsy, $biopsy$	\$318		[25]
genital warts, cgw_k	\$489	\$489	[14]
CIN1, $ctcin_1$	\$1,554		[22]
CIN2, $ctcin_2$	\$3,483		[22]
CIN3/CIS, $ctcin_3$	\$3,483		[22]
LCC, $ctcc_L$	\$26,470		[22]
RCC, $ctcc_R$	\$28,330		[22]
DCC, $ctcc_D$	\$45,376		[22]

Table 6: Cost of screening, diagnosis, and treatment

References

- [1] Abma J.C., Sonenstein F.L. Sexual Activity and Contraceptive Practices Among Teenagers in the United States, 1988 and 1995. National Center for Health Statistics. *Vital Health Stat* 2001; 23(21):1–79.
- [2] Aoyama, C., Peters, J., Senadheera, S., et al., 1998. Uterine cervical dysplasia and cancer: identification of c-myc status by quantitative polymerase chain reaction. *Diagn. Mol. Pathol.* 7, 324–330.
- [3] Bigras, G., de Marval, F., 2005. The probability for a Pap test to be abnormal is directly proportional to HPV viral load: results from a Swiss study comparing HPV testing and liquid-based cytology to detect cervical cancer precursors in 13,842 women. *Br. J. Cancer* 93, 575–581.
- [4] Chesson, H.W., Blandford, J.M., Gift, T.L., et al., 2004. The estimated direct medical cost of sexually transmitted diseases among American youth, 2000. *Perspect. Sex. Reprod. Health* 36, 11–19.
- [5] Coste, J., Cochand-Priollet, B., De Cremoux, P., et al., 2003. Cross sectional study of conventional cervical smear, monolayer cytology, and human papillomavirus DNA testing for cervical cancer screening. *BMJ* 326, 733.
- [6] Cruickshank, M.E., Sharp, L., Chambers, G., et al., 2002. Persistent infection with human papillomavirus following the successful treatment of high grade cervical intraepithelial neoplasia. *BJOG* 109, 579–581.
- [7] De Aloysio, D., Miliffi, L., Iannicelli, T., et al., 1994. Intramuscular interferon-beta treatment of cervical intraepithelial neoplasia II associated with human papillomavirus infection. *Acta. Obstet. Gynecol. Scand.* 73, 420–424.
- [8] Evans, M.F., Mount, S.L., Beatty, B.G., et al., 2002. Biotinyl-tyramide-based in situ hybridization signal patterns distinguish human papillomavirus type and grade of cervical intraepithelial neoplasia. *Mod. Pathol.* 15, 1339–1347.
- [9] Flannelly, G., Langhan, H., Jandial, L., Mana, E., Campbell, M., Kitchener, H., 1997. A study of treatment failures following large loop excision of the transformation zone for the treatment of cervical intraepithelial neoplasia. *Br. J. Obstet. Gynaecol.* 104, 718–22.

- [10] Gold M, Franks P, McCoy K, Fryback D. Toward consistency in cost-utilities analysis. *Med care* 1998; 36:778–792.
- [11] Goldie SJ, Kohli M, Grima D, Weinstein MC, Wright TC, Bosch FX, Franco E. Projected Clinical Benefits and Cost-Effectiveness of a Human Papillomavirus 16/18 Vaccine. *Journal of the National Cancer Institute* 2004; 96: 604–615.
- [12] Hoyer, H., Scheungraber, C., Kuehne-Heid, R., et al., 2005. Cumulative 5-year diagnoses of CIN2, CIN3 or cervical cancer after concurrent high-risk HPV and cytology testing in a primary screening setting. *Int. J. Cancer* 116, 136–143.
- [13] Hughes JP, Garnett GP, Koutsky LA. The theoretical population level impact of a prophylactic human papilloma virus vaccine. *Epidemiology* 2002; 13:631–639.
- [14] Insinga RP, Dasbach EJ, Myers ER. The health and economic burden of genital warts in a set of private U.S. Health Plans. *Clin Infect Dis* 2003; 36:1397–1403.
- [15] Insinga, R.P., 2007. The natural history of low-grade cervical intraepithelial neoplasia. Manuscript in preparation.
- [16] Insinga, R.P., Dasbach, E. J., Elbasha, E.H. , Liaw, K-L, Barr E, 2007. Incidence and duration of cervical human papillomavirus 6, 11, 16, and 18 infections in young women: An evaluation from multiple analytic perspectives. *Cancer Epidemiol Biomarkers Prev* 16(4):709–15.
- [17] Insinga, R.P., Glass, A.G., Rush, B.B., 2004. Pap screening in a U.S. health plan. *Cancer Epidemiol. Biomarkers Prev.* 13, 355–360.
- [18] Insinga, Ralph P; Dasbach, Erik J; Elbasha, Elamin H, et al. Progression and regression of incident cervical HPV 6, 11, 16 and 18 infections in young women. *Infect. Agent. Cancer* 2007;2:15.
- [19] Isacson, C., Kessis, T.D., Hedrick, L., et al., 1996. Both cell proliferation and apoptosis increase with lesion grade in cervical neoplasia but do not correlate with human papillomavirus type. *Cancer Res.* 56, 669–674.
- [20] Kataja, V., Syrjanen, K., Mantyjarvi, R., et al., 1989. Prospective follow-up of cervical HPV infections: life table analysis of histopathological, cytological and colposcopic data. *Eur. J. Epidemiol.* 5, 1–7.

- [21] Keshavarz, H., Hillis, S.D., Kieke, B.A., et al., 2002. Hysterectomy surveillance-United States, 1994-1999. *MMWR CDC Surveill. Summ.* 51, 1–8.
- [22] Kim J, Wright T, Goldie S. Cost-effectiveness of alternative triage strategies for atypical squamous cells of undetermined significance. *JAMA* 2002;287:2382–90.
- [23] Lauman E, Gagnon J, Michael R, Michaels S. *The social organization of sexuality*. Chicago, IL: University of Chicago Press, 1994.
- [24] Matsumoto, K., Yasugi, T., Oki, A., et al., 2006. IgG antibodies to HPV16, 52, 58 and 6 L1-capsids and spontaneous regression of cervical intraepithelial neoplasia. *Cancer Lett.* 231, 309–313.
- [25] Medstat, 2001. MarketScan R database, Thomson Medstat. Ann Arbor, MI. Rockville, MD: Agency for Health Care Policy and Research. February 1999. Available: <http://www.ahrq.gov/clinic/epcsums/cervsumm.htm>.
- [26] Mitchell, M.F., Schottenfeld, D., Tortolero Luna, G., Cantor, S.B., Richards Kortum, R., 1998. Colposcopy for the diagnosis of squamous intraepithelial lesions: a meta analysis. *Obstet. Gynecol.* 91, 626–31.
- [27] Myers E, McCrory D, Nanda K, Bastian L, Matchar D. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. *Am J Epidemiol* 2000; 151:1158–71.
- [28] Myers E, Green S, Lipkus I. Patient preferences for health states related to HPV infection: visual analogue scales vs. time trade-off elicitation. *Proceedings of the 21st International Papillomavirus Conference*, 390.2 2004. Mexico City, Mexico.
- [29] Quade, B.J., Park, J.J., Crum, C.P., et al., 1998. In vivo cyclin E expression as a marker for early cervical neoplasia. *Mod Pathol* 11, 1238–1246.
- [30] Ries, L., Eisner, M., Kosary, C., et al., 2005. SEER cancer statistics review, 1975–2002. Bethesda, MD, National Cancer Institute, http://seer.cancer.gov/csr/1975_2002/.
- [31] Sanders GD, Taira AV. Cost Effectiveness of a Potential Vaccine for Human Papillomavirus. *Emerging Infectious Diseases* 2003. 9:37–48.
- [32] Sastre-Garau, X., Cartier, I., Jourdan-Da Silva, N., et al., 2004. Regression of low-grade cervical intraepithelial neoplasia in patients with HLA-DRB1*13 genotype. *Obstet. Gynecol.* 104, 751–755.

- [33] Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Survival - SEER 9 Regs Public-Use, Nov 2004 Sub (1973-2002), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2005, based on the November 2004 submission.
- [34] Westergaard, L., Norgaard, M., 1981. Severe cervical dysplasia. Control by biopsies or primary conization? A comparative study. *Acta Obstet. Gynecol.Scand.* 60, 549–554.
- [35] Wenzel L, DeAlba I, Habbal R, Kluhsman BC, Fairclough D, et al. Quality of life in long-term cervical cancer survivors. *Gynecol Oncol* 2005; 97(2): 310–7.
- [36] Winer RL, Kiviat NB, Hughes JP, Adam DE, Lee SK, et al. Development and duration of human papillomavirus lesions, after initial infection. *J Infect Dis* 2005; 191: 731–8.