

Supplementary Table 1: Sample size and proportion of women sampled from the state-wide population, based on age and cytology for December 2007- April 2009. Sample restricted to women 15-75 years.

Age (years)	Cytology	Sample (N)	Ratio (%) (Sampling)	Number of screened women in the state-wide population
>30	Negative	10 351	4.89 (20.44)	211 563
	Abnormal	6590	63.7 (1.57)	10 334
≤30	Negative	22 905	24.3 (4.11)	94 165
	Abnormal	7274	58.8 (1.70)	12 365
Total		47 120		328 427

Supplementary Table 2: High-risk (hr) HPV genotype-specific Positive Predictive Values (PPV) and hierarchical ranking by PPV for CIN2+ detected within 3 years of the enrolment cytology, weighted to the state-wide population.

hrHPV type	Individual hrHPV type	For the new hrHPV type				Cumulative				
	PPV (%) (95% CI)	N at risk	Positive		PPV (%)	Positive		PPV (%)	Sensitivity	Specificity
			CIN2+	HPV		CIN2+	HPV			
16	11.87 (11.28, 12.47)	328 427	1359	11 445	11.87	1359	11 445	11.87	39.52	96.90
33	10.09 (8.60, 11.58)	316 981	108	1360	7.91	1467	12 805	11.45	42.65	96.51
31	8.20 (7.50, 8.90)	315 622	350	5139	6.80	1816	17 944	10.12	52.81	95.04
35	6.37 (5.48, 7.26)	310 483	130	2365	5.51	1946	20 308	9.58	56.60	94.35
18	6.25 (5.49, 7.00)	308 118	148	2930	5.04	2094	23 238	9.01	60.90	93.49
58	6.04 (5.30, 6.79)	305 189	114	2860	4.00	2208	26 098	8.46	64.23	92.65
51	5.24 (4.74, 5.75)	302 329	188	5543	3.39	2396	31 640	7.57	69.69	91.00
45	4.71 (4.01, 5.42)	296 786	58	2465	2.35	2454	34 106	7.20	71.37	90.26
39	4.85 (4.34, 5.35)	294 321	103	4638	2.21	2557	38 743	6.60	74.35	88.87
52	4.76 (4.23, 5.28)	289 683	76	4088	1.85	2632	42 831	6.15	76.55	87.63
59	3.76 (3.31, 4.21)	285 595	72	4008	1.80	2705	46 840	5.77	78.65	86.42
56	3.41 (2.86, 3.96)	281 587	23	2171	1.04	2727	49 011	5.56	79.31	85.76
68	3.37 (2.68, 4.05)	279 416	9	1462	0.61	2736	50 473	5.42	79.57	85.31

CI: Confidence Interval

For example, the highest ranked HPV type was the genotype with the highest univariate PPV. All co-infections with this HPV type were then excluded from the subsequent analysis, and the HPV type with the next highest PPV was identified. This was repeated for all 13 hrHPV types.

Supplementary Table 3a: High-risk (hr) HPV genotype-specific Positive Predictive Values (PPV) and hierarchical ranking by PPV for CIN3+ detected within 3 years of the enrolment cytology for women ≤ 30 years, weighted to the state-wide population.

hrHPV type	Individual hrHPV type	For the new hrHPV type				Cumulative				
	PPV (%) (95% CI)	N at risk	Positive		PPV (%)	Positive		PPV (%)	Sensitivity	Specificity
			CIN3+	HPV		CIN3+	HPV			
16	7.46 (6.87, 8.05)	106 530	568	7622	7.46	568	7622	7.46	60.08	93.32
33	5.76 (4.31, 7.21)	98 908	29	797	3.68	598	8419	7.10	63.18	92.59
31	4.18 (3.55, 4.82)	98 111	97	3082	3.15	695	11 501	6.04	73.45	89.77
45	3.47 (2.68, 4.26)	95 029	39	1575	2.49	734	13 076	5.61	77.60	88.31
35	2.78 (1.99, 3.58)	93 454	20	1166	1.75	754	14 242	5.30	79.76	87.23
52	2.74 (2.23, 3.25)	92 288	37	2869	1.29	792	17 111	4.63	83.69	84.54
58	2.18 (1.63, 2.73)	89 419	22	1841	1.20	814	18 953	4.29	86.02	82.82
18	2.02 (1.47, 2.56)	87 577	14	1441	0.94	827	20 393	4.06	87.46	81.47
59	1.71 (1.34, 2.09)	86 136	21	2702	0.77	848	23 095	3.67	89.66	78.93
51	1.70 (1.35, 2.05)	83 434	15	2850	0.53	863	25 945	3.33	91.25	76.24
39	1.99 (1.59, 2.39)	80 585	8	2366	0.32	871	28 311	3.08	92.04	74.01
56	1.38 (0.94, 1.83)	78 219	3	1102	0.31	874	29 413	2.97	92.40	72.97
68	1.08 (0.54, 1.61)	77 116	0	547	0.00	874	29 961	2.92	92.40	72.45

CI: Confidence Interval

For example, the highest ranked HPV type was the genotype with the highest univariate PPV. All co-infections with this HPV type were then excluded from the subsequent analysis, and the HPV type with the next highest PPV was identified. This was repeated for all 13 hrHPV types.

Supplementary Table 3b: High-risk (hr) HPV genotype-specific Positive Predictive Values (PPV) and hierarchical ranking by PPV for CIN3+ detected within 3 years of the enrolment cytology for women >30 years, weighted to the state-wide population.

hrHPV type	Individual hrHPV type	For the new hrHPV type				Cumulative				
	PPV (%) (95% CI)	N at risk	Positive		PPV (%)	Positive		PPV (%)	Sensitivity	Specificity
			CIN3+	HPV		CIN3+	HPV			
16	6.03 (5.28, 6.79)	221 897	231	3823	6.03	231	3823	6.03	43.60	98.38
33	3.53 (2.02, 5.03)	218 074	16	563	2.79	246	4386	5.62	46.57	98.13
18	2.24 (1.47, 3.02)	217 511	28	1282	2.20	275	5668	4.84	51.90	97.56
31	2.24 (1.62, 2.86)	216 229	39	2001	1.96	314	7669	4.09	59.32	96.68
58	2.39 (1.55, 3.24)	214 228	17	1086	1.59	331	8754	3.78	62.58	96.19
51	1.80 (1.26, 2.33)	213 143	28	2065	1.37	359	10 819	3.32	67.93	95.27
59	1.50 (1.01, 1.98)	211 078	27	1963	1.36	386	12 783	3.02	72.98	94.40
52	1.33 (0.87, 1.80)	209 114	17	1966	0.88	403	14 749	2.73	76.24	93.52
35	1.22 (0.62, 1.82)	207 148	6	944	0.66	409	15 693	2.61	77.42	93.10
39	1.11 (0.68, 1.55)	206 204	9	1757	0.54	419	17 451	2.40	79.20	92.31
45	1.09 (0.55, 1.63)	204 446	5	1078	0.44	424	18 529	2.29	80.09	91.82
68	0.87 (0.36, 1.39)	203 368	2	920	0.17	425	19 448	2.19	80.39	91.41
56	0.31 (0.03, 0.60)	202 449	0	1064	0.00	425	20 512	2.07	80.39	90.93

CI: Confidence Interval

For example, the highest ranked HPV type was the genotype with the highest univariate PPV. All co-infections with this HPV type were then excluded from the subsequent analysis, and the HPV type with the next highest PPV was identified. This was repeated for all 13 hrHPV types.

Supplementary Table 4: Hierarchical odds ratios for CIN2+ for high-risk (hr) HPV genotypes and for different viral load groups (high, intermediate [Inter], low) ordered by the genotype hierarchy and weighted to the state-wide population of women.

HPV type	Viral load (N, %)	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
<i>Any hrHPV^a</i>	<i>High (18 226, 5.6)</i>	40.36 (31.69, 51.39)	1.1E-195	4.20 (3.34, 5.28)	1.4E-34	2.19 (1.84, 2.60)	7.4E-19
	<i>Inter (13 353, 4.1)</i>	18.42 (14.04, 24.17)	1.0E-97	1.92 (1.48, 2.49)	9.6E-07	<i>ref</i>	
	<i>Low (18 894, 5.8)</i>	9.61 (7.05, 13.11)	2.3E-46	<i>ref</i>			
	<i>Negative (277 954, 84.6)</i>	<i>ref</i>					
	<i>P-value (trend)</i>	1.9E-293		8.0E-41			
16	High (6171, 1.9)	32.40 (27.84, 37.70)	<3.8E-442	5.28 (3.27, 8.52)	1E-11	3.02 (2.23, 4.10)	1.7E-12
	Inter (2431, 0.7)	10.72 (7.92, 14.50)	3.2E-53	1.75 (1.01, 3.01)	0.05	<i>ref</i>	
	Low (2844, 0.9)	6.14 (3.82, 9.87)	7.3E-14	<i>ref</i>			
	Negative (316 981, 96.5)	<i>ref</i>					
	<i>P-value (trend)</i>	<1.3E-458		5.9E-16			
33	High (564, 0.2)	18.25 (11.39, 29.23)	1.6E-33	2.48 (1.10, 5.58)	0.03	1.10 (0.46, 2.67)	0.82
	Inter (287, 0.1)	16.52 (7.75, 35.19)	3.7E-13	2.24 (0.82, 6.14)	0.12	<i>ref</i>	
	Low (509, 0.2)	7.37 (3.75, 14.49)	7.0E-09	<i>ref</i>			
	Negative (315 622, 96.1)	<i>ref</i>					
	<i>P-value (trend)</i>	6.6E-49		0.03			
31	High (781, 0.2)	22.96 (12.85, 41.05)	4.2E-26	2.84 (1.48, 5.44)	2E-03	1.23 (0.66, 2.31)	0.52
	Inter (1807, 0.6)	18.67 (13.80, 25.27)	8.2E-80	2.31 (1.50, 3.55)	2E-04	<i>ref</i>	
	Low (52551, 0.8)	8.10 (5.69, 11.51)	3.0E-31	<i>ref</i>			
	Negative (310 483, 94.5)	<i>ref</i>					
	<i>P-value (trend)</i>	7.7E-98		2.1E-04			
35	High (354, 0.1)	23.09 (13.21, 40.35)	3.2E-28	2.99 (1.37, 6.55)	6E-03	1.75 (0.87, 3.52)	0.12
	Inter (902, 0.3)	13.19 (8.38, 20.76)	8.7E-29	1.71 (0.84, 3.49)	0.14	<i>ref</i>	
	Low (1109, 0.3)	7.72 (4.33, 13.76)	4.2E-12	<i>ref</i>			
	Negative (308 118, 92.9)	<i>ref</i>					
	<i>P-value (trend)</i>	3.4E-60		0.01			

Supplementary Table 4: Continued.

HPV type	Viral load (N, %)	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
18	High (1458, 0.4)	18.86 (13.38, 26.58)	7.2E-63	3.95 (1.77, 8.83)	8.4E-04	2.86 (1.40, 5.86)	4.1E-03
	Inter (641, 0.2)	6.59 (3.40, 12.79)	2.5E-08	1.38 (0.51, 3.70)	0.52	<i>ref</i>	
	Low (830, 0.3)	4.78 (2.25, 10.14)	4.7E-05	<i>ref</i>			
	Negative (305 189, 92.9)	<i>ref</i>					
	<i>P-value (trend)</i>	1.2E-68		2.4E-04			
58	High (1483, 0.5)	16.19 (11.47, 22.86)	3.1E-56	5.54 (1.77, 17.38)	3.4E-03	2.92 (1.31, 6.52)	0.01
	Inter (595, 0.2)	5.55 (2.60, 11.85)	9.4E-06	1.90 (0.50, 7.19)	0.34	<i>ref</i>	
	Low (781, 0.2)	2.92 (0.96, 8.87)	0.06	<i>ref</i>			
	Negative (302 329, 92.1)	<i>ref</i>					
	<i>P-value (trend)</i>	3.8E-58		1.0E-03			
51	High (1063, 0.3)	13.37 (8.74, 20.46)	6.9E-33	2.00 (0.88, 4.55)	0.10	1.02 (0.50, 2.12)	0.95
	Inter (1755, 0.5)	13.05 (6.92, 24.62)	2.2E-15	1.95 (0.75, 5.04)	0.17	<i>ref</i>	
	Low (2725, 0.8)	6.70 (3.19, 14.05)	4.8E-07	<i>ref</i>			
	Negative (296 786, 90.4)	<i>ref</i>					
	<i>P-value (trend)</i>	1.6E-45		0.06			
45	High (873, 0.3)	10.44 (6.10, 17.87)	1.2E-17	2.62 (0.79, 8.69)	0.11	1.45 (0.54, 3.91)	0.46
	Inter (710, 0.2)	7.18 (3.02, 17.08)	8.1E-06	1.80 (0.45, 7.20)	0.40	<i>ref</i>	
	Low (882, 0.3)	3.98 (1.32, 11.98)	1.4E-02	<i>ref</i>			
	Negative (294 321, 89.6)	<i>ref</i>					
	<i>P-value (trend)</i>	1.1E-22		0.09			
39	High (1157, 0.4)	7.07 (4.03, 12.39)	9.2E-12	1.06 (0.36, 3.11)	0.91	0.76 (0.35, 1.63)	0.47
	Inter (1124, 0.3)	9.36 (5.20, 16.83)	8.5E-14	1.41 (0.47, 4.18)	0.54	<i>ref</i>	
	Low (2356, 0.7)	6.64 (2.57, 17.15)	9.1E-05	<i>ref</i>			
	Negative (289 683, 88.2)	<i>ref</i>					
	<i>P-value (trend)</i>	1.2E-25		0.83			
52	High (1202, 0.4)	16.93 (10.54, 27.19)	1.4E-31	12.00 (4.06, 35.50)	7.8E-06	4.08 (1.61, 10.36)	3.2E-03
	Inter (1210, 0.4)	4.15 (1.77, 9.72)	1.0E-03	2.94 (0.80, 10.76)	0.10	<i>ref</i>	
	Low (1677, 0.5)	1.41 (0.51, 3.90)	0.51	<i>ref</i>			
	Negative (285 595, 87.0)	<i>ref</i>					
	<i>P-value (trend)</i>	2.6E-29		2.3E-06			

Supplementary Table 4: Continued.

HPV type	Viral load (N, %)	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
59	High (1779, 0.5)	11.03 (4.46, 27.24)	2.0E-07	3.08 (0.77, 12.35)	0.11	2.61 (0.70, 9.81)	0.15
	Inter (976, 0.3)	4.22 (1.53, 11.64)	5.4E-03	1.18 (0.27, 5.11)	0.83	<i>ref</i>	
	Low (1254, 0.4)	3.58 (1.19, 10.75)	0.02	<i>ref</i>			
	Negative (281 587, 85.7)	<i>ref</i>					
	<i>P-value (trend)</i>	1.2E-08		0.11			
56	High (750, 0.2)	5.26 (2.23, 12.41)	1.5E-04	7.68 (0.90, 65.67)	0.06	0.54 (0.14, 1.98)	0.35
	Inter (446, 0.1)	9.82 (3.52, 27.41)	1.3E-05	14.35 (1.56, 132.00)	0.02	<i>ref</i>	
	Low (975, 0.3)	0.68 (0.09, 4.97)	0.71	<i>ref</i>			
	Negative (279 416, 85.1)	<i>ref</i>					
	<i>P-value (trend)</i>	2.3E-07		0.02			
68	High (591, 0.2)	3.26 (0.99, 10.67)	0.05	0.80 (0.08, 8.12)	0.85	-	-
	Inter (469, 0.1)	-		-			
	Low (402, 0.1)	4.08 (0.55, 30.28)	0.17	<i>ref</i>			
	Negative (277 954, 84.6)	<i>ref</i>					
	<i>P-value (trend)</i>	0.09		0.93			

Multiple HPV infections with types ranked higher in the hierarchy are excluded.

Separate analyses are shown with low and intermediate viral loads as the reference category.

*Highest ranked hrHPV type per woman

OR: Odds Ratio, CI: Confidence Interval

Supplementary Table 5: Hierarchical ranking based on high-risk (hr) HPV genotype and viral load (high, intermediate [Inter], low) Positive Predictive Values (PPV) for CIN3+ compared with hierarchical PPV values (from Table 4) based on hrHPV genotype alone. All data weighted to the state-wide population level.

Category		CIN3+		
		Hierarchy based on hrHPV and viral load		From Table 4 (genotype alone)
hrHPV	Viral load	N	PPV (%)	PPV (%)
16	High	6171	10.56	10.56
33	Inter	304	6.36	6.20
33	High	599	4.27	3.93
31	Inter	1908	4.09	4.32
16	Inter	2353	3.48	3.58
52	High	1663	3.07	2.55
35	High	393	2.53	2.50
58	High	1801	2.45	2.20
18	High	1519	2.25	2.52
31	High	718	2.16	1.77
16	Low	2572	1.98	2.11
45	Low	948	1.84	1.25
31	Low	2449	1.62	1.75
35	Inter	811	1.64	1.97
39	High	2427	1.35	0.83
45	High	896	1.36	1.07
45	Inter	750	1.23	1.23
39	Inter	1203	1.23	0.56
51	Low	2540	1.07	1.11
18	Inter	590	1.09	0.95
51	High	996	0.98	0.55
39	High	1156	0.85	0.83
59	Inter	1118	0.66	0.65
51	Inter	1506	0.65	0.78
59	Low	1341	0.56	0.42
56	High	807	0.42	0.45
33	Low	407	0.42	1.00
52	Inter	1175	0.27	0.84
68	High	642	0.24	0.27
18	Low	682	0.23	1.25
52	Low	1651	0.20	0.26
35	Low	803	0.20	0.85
39	Low	2148	0.15	0.15
58	Inter	493	0.00	0.29
58	Low	656	0.00	0.22
56	Inter	440	0.00	0.00
56	Low	1000	0.00	0.00
68	Inter	471	0.00	0.00
68	Low	443	0.00	0.00

Table gives number of women (N) within each category with no infections in categories higher in the hierarchy.

For example, the PPV for CIN3+ for a woman with an intermediate viral load of HPV33 was 6.36, given she did not have high viral load of HPV16. In comparison (Table 4), the PPV for CIN3+ if a woman had intermediate viral load of HPV33 was 6.20, given she had no HPV16 infection (regardless of viral load).