

Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: A meta-analysis update

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Data on human papillomavirus (HPV) type distribution in invasive and pre-invasive cervical cancer is essential to predict the future impact of HPV16/18 vaccines and HPV-based screening tests. A meta-analysis of HPV type distribution in invasive cervical cancer (ICC) and high-grade squamous intraepithelial lesions (HSIL) identified a total of 14,595 and 7,094 cases, respectively. In ICC, HPV16 was the most common, and HPV18 the second most common, type in all continents. Combined HPV16/18 prevalence among ICC cases was slightly higher in Europe, North America and Australia (74–77%) than in Africa, Asia and South/Central America (65–70%). The next most common HPV types were the same in each continent, namely HPV31, 33, 35, 45, 52 and 58, although their relative importance differed somewhat by region. HPV18 was significantly more prevalent in adeno/adenosquamous carcinoma than in squamous cell carcinoma, with the reverse being true for HPV16, 31, 33, 52 and 58. Among HSIL cases, HPV16/18 prevalence was 52%. However, HPV 16, 18 and 45 were significantly under-represented, and other high-risk HPV types significantly over-represented in HSIL compared to ICC, suggesting differences in type-specific risks for progression. Data on HPV-typed ICC and HSIL cases were particularly scarce from large regions of Africa and Central Asia.

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Data on human papillomavirus (HPV) type distribution in women with invasive cervical cancer (ICC) and its precursor lesions are essential to predict the potential worldwide impact of new prophylactic vaccines against HPV16/18,^{1,2} as well as to determine priorities for the inclusion of HPV types in future HPV vaccines and HPV-based screening tests.

A standardised pooled analysis of 3,607 ICC cases³ and a wider meta-analysis of 10,058 ICC cases⁴ both confirmed that a majority of worldwide ICC cases are associated with HPV16/18. They also suggested some geographical variation in the importance of specific HPV types,^{3,4} although data were limited or missing from many regions in Africa and Asia.

A further meta-analysis in 4,338 high-grade squamous intraepithelial lesions (HSIL) showed that the most common HPV types in HSIL were broadly similar, but not identical, to those in ICC.⁵

The purpose of the present publication is to update previous meta-analyses of HPV type distribution in ICC and HSIL with studies published between January 2002 and January 2006, including many from previously under-studied regions, and to identify remaining worldwide epidemiological data gaps prior to HPV vaccine implementation.

Material and methods

The detailed methods used for this meta-analysis of type-specific HPV prevalence have been reported previously, and are similar for both ICC and HSIL.^{4,5} In brief, Medline was employed to search for citations published from January 2002 to January 2006

using the following MeSH terms: “cervical cancer”, “cervical intraepithelial neoplasia”, “HPV”, “human”, “female” and “polymerase chain reaction”. Additional relevant references cited in retrieved articles were also evaluated. Included studies had to meet all of the following criteria: (i) use of polymerase chain reaction (PCR)-based technology to detect HPV DNA, (ii) inclusion of at least 20 cases of ICC or HSIL and (iii) reporting of type-specific prevalence for at least one HPV type other than 6, 11, 16 and 18.

For the purposes of this study, ICC refers both to squamous cell carcinoma (SCC)/unspecified histology (85% of included cases) and adeno/adenosquamous carcinoma (ADC, 15%). HSIL refers both to cytologically-detected lesions as classified by the Bethesda system (44% of included cases), and those reported as histologically diagnosed cervical intraepithelial neoplasia (CIN)2 (17%), CIN3 (37%), or carcinoma *in situ* (2%).

For each included study, the following key information was extracted: country of sample; sample size; distribution of cancer cases by histological type (SCC/unspecified or ADC), HPV DNA source (fresh/fixed biopsies or exfoliated cells), PCR primers used to detect HPV-positive samples, and type-specific and overall prevalence of HPV DNA. These data are presented study by study in the Appendices. Studies were additionally classified into 17 geographical regions.

Crude type-specific prevalence is presented for 19 HPV types, including the 18 most common HPV types as identified by the previous ICC meta-analysis,⁴ namely HPV6, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 70, 73 and 82. HPV11 was also considered on account of its inclusion in currently available quadrivalent HPV vaccines.² Each HPV type was evaluated independently of all others. All studies provided information on HPV16, but for other types, prevalence was estimated only among those studies testing for the HPV type in question, and thus denominators of prevalence estimates vary by type. Type-specific prevalence thus includes that in either single- or multiple-type HPV infections.

Statistical analysis

Type-specific HPV prevalence was compared between HSIL and SCC by prevalence ratios, adjusted for continent (Africa, Asia, Europe, North America, Oceania, South/Central America), with corresponding 95% confidence intervals (CIs).

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TABLE I – GEOGRAPHIC DISTRIBUTION OF STUDIES AND CASES WITH TYPE SPECIFIC HUMAN PAPILLOMAVIRUS DNA TYPING FOR INVASIVE CERVICAL CARCINOMA (ICC) AND HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS (HSIL)

CONTINENT	ICC		HSIL		Countries represented
	N studies	N cases	N studies	N cases	
Africa	13	1,339	5	296	Algeria, ¹ Benin, Ethiopia, ² Guinea, Ivory Coast, ³ Kenya, ³ Mali, Morocco, Mozambique, ² Senegal, ¹ South Africa, ¹ Tanzania, Uganda, Zimbabwe ²
Asia	51	5,652	22	1,364	China, ¹ India, ¹ Indonesia, ¹ Japan, ¹ South Korea, ¹ Malaysia, Philippines, Taiwan, ¹ Thailand, ¹ Iran ²
Europe	41	4,373	37	3,494	Austria, ¹ Belgium, ¹ Croatia, ³ Czech Republic, Denmark, Finland, France, Germany, Greece, Greenland, The Netherlands, ¹ Hungary, Ireland, Italy, ¹ Latvia, ² Lithuania, ² Norway, Poland, ¹ Portugal, ² Russia, Sweden, ¹ UK
North America	13	1,354	10	1,059	Canada, ¹ USA ¹
Oceania	5	450	1	48	Australia ¹
South/Central America	13	1,427	11	833	Argentina, ¹ Bolivia, Brazil, ¹ Chile, Colombia, Costa Rica, ¹ Cuba, Honduras, Jamaica, ³ Mexico, Panama, Paraguay, Peru
Total	130 ⁴	14,595	85 ⁴	7,094	

¹Country for which additional ICC cases have been gained since Clifford *et al.*, 2003 [ref. 4].-²Country not previously represented with ICC cases in Clifford *et al.*, 2003 [ref. 4].-³Country for which HSIL data only is available.-⁴Continents do not add up to total due to multi-centric studies.

Results

One hundred thirty ICC and 85 HSIL studies met inclusion criteria, including a total of 14,595 ICC and 7,094 HSIL cases (Table I). This constituted a gain of 4,537 ICC and 2,756 HSIL cases from previous meta-analyses.^{4,5} The proportional gain in cases was greatest for Africa (from 609 to 1,339 ICC cases) and Asia (from 3,091 to 5,652 ICC cases, Table I). Thirty-eight percent of ICC cases came from Asia, 30% from Europe, 10% from South/Central America, 9% from North America, 9% from Africa and 3% from Oceania. The equivalent regional proportions were 19%, 49%, 12%, 15%, 4% and 1%, respectively, for HSIL cases (Table I).

Overall HPV prevalence in ICC was 87%, ranging from 86% to 94% by region. The 8 most common HPV types in ICC are shown by continent in Figure 1a. HPV16 was the most common type (ranging from 52% in Asia to 58% in Europe) and HPV18 the second most common type (ranging from 13% in South/Central America to 22% in North America) in ICC cases from all continents studied. HPV16/18 prevalence was thus 70% overall, and varied from 65% in South/Central America to 76% in North America. The next most common HPV types in ICC were also the same in each continent, namely HPV31, 33, 35, 45, 52 and 58 (with the slight exception of Europe, where HPV56 was the eighth most common type instead of HPV52), although their relative importance differed somewhat by continent. HPV58 and 52 prevalence was notably higher in ICC cases from Asia (5.6% and 3.8%, respectively). HPV types other than these 8 accounted individually for no more than 2% of ICC cases from any continent. Appendix I summarises the prevalence of the 19 most common types and the prevalence of multiple infections in ICC (although the frequency of multiple infections depends largely on the number of HPV types tested for within a given study).

The breakdown of HPV type-specific prevalence data by histological type of ICC was available for 9,494 SCC and 1,949 ADC cases. Among these cases, overall HPV positivity was higher in SCC (90%) than in ADC (85%). The 8 most common HPV types in ICC are compared by histological type in Figure 2. HPV16 was significantly under-represented in ADC (33%) compared with SCC cases (55%), as were HPV31, 33, 52 and 58. Conversely, HPV18 was significantly over-represented in ADC (37%) compared with SCC (13%).

Overall HPV prevalence in HSIL was 85%, ranging from 78% in Asia to 88% in Europe. Combined HPV16/18 prevalence in all HSIL cases was 52%. Overall, the 8 most common HPV types in

HSIL (Fig. 1b) were largely similar to those in cervical cancer (Fig. 1a), except for a noticeable absence of HPV45. HPV16 was the predominant type in HSIL from all continents studied, varying from 34% in Asia to 52% in Europe. The prevalence of the 19 most common types and multiple infections (see note on multiple infection prevalence above) in HSIL is summarised by study and by region in Appendix II.

HPV type-specific prevalence among 7,094 HSIL cases was formally compared with that among 9,494 SCC cases using prevalence ratios (Table II). HPV16 was significantly less prevalent in HSIL (45.3%) than in SCC (55.2%) (SCC:HSIL prevalence ratio 1.30, 95% CI: 1.26–1.34), as were both HPV18 (1.76, 95% CI: 1.58–1.95) and HPV45 (1.54, 95% CI: 1.20–1.98). Conversely, HPV types 31, 33, 35, 39, 52, 56, 58, 68 and 73 were each 2- to 3-fold more prevalent in HSIL than ICC, and HPV types 6, 11, 51, 66, 70, and 82 were 5- to 10-fold more prevalent in HSIL than ICC.

Figure 3 maps the availability of HPV-typed ICC and HSIL cases by country, and highlights the limited amount of ICC and HSIL data from most countries in Africa, Central/Eastern Europe, and Western and South-Central Asia. No data were available from Melanesia/Micronesia/Polynesia, and were very limited for the Caribbean.

Discussion

This present study represents a 50% gain in information on HPV type distribution in ICC over a previous meta-analysis.⁴ This gain in information was particularly high for Africa and Asia, making overall estimates of HPV type distribution from these continents more robust and representative than before. Overall, 70% of ICC cases were associated with either HPV16 (55%) or 18 (15%) infection. The 6 next most common types, namely HPV31, 33, 35, 45, 52 and 58 accounted for an additional 18% of cases.

Whilst these overall findings are similar to previous estimates,³⁻⁵ interpretations by continent have altered somewhat. With the accumulation of additional published data, differences by continent became less pronounced than those noted in previous analyses,³⁻⁵ with the estimates for the proportion of ICC cases attributable to HPV16/18 in Africa, Asia and South/Central America all increasing from the previously reported 59–64%.⁴ However, the most relevant variation by continent in HPV type distribution noted by the previous meta-analysis⁴ remained evident, namely that although HPV16/18 are the most common types in ICC from all continents, the

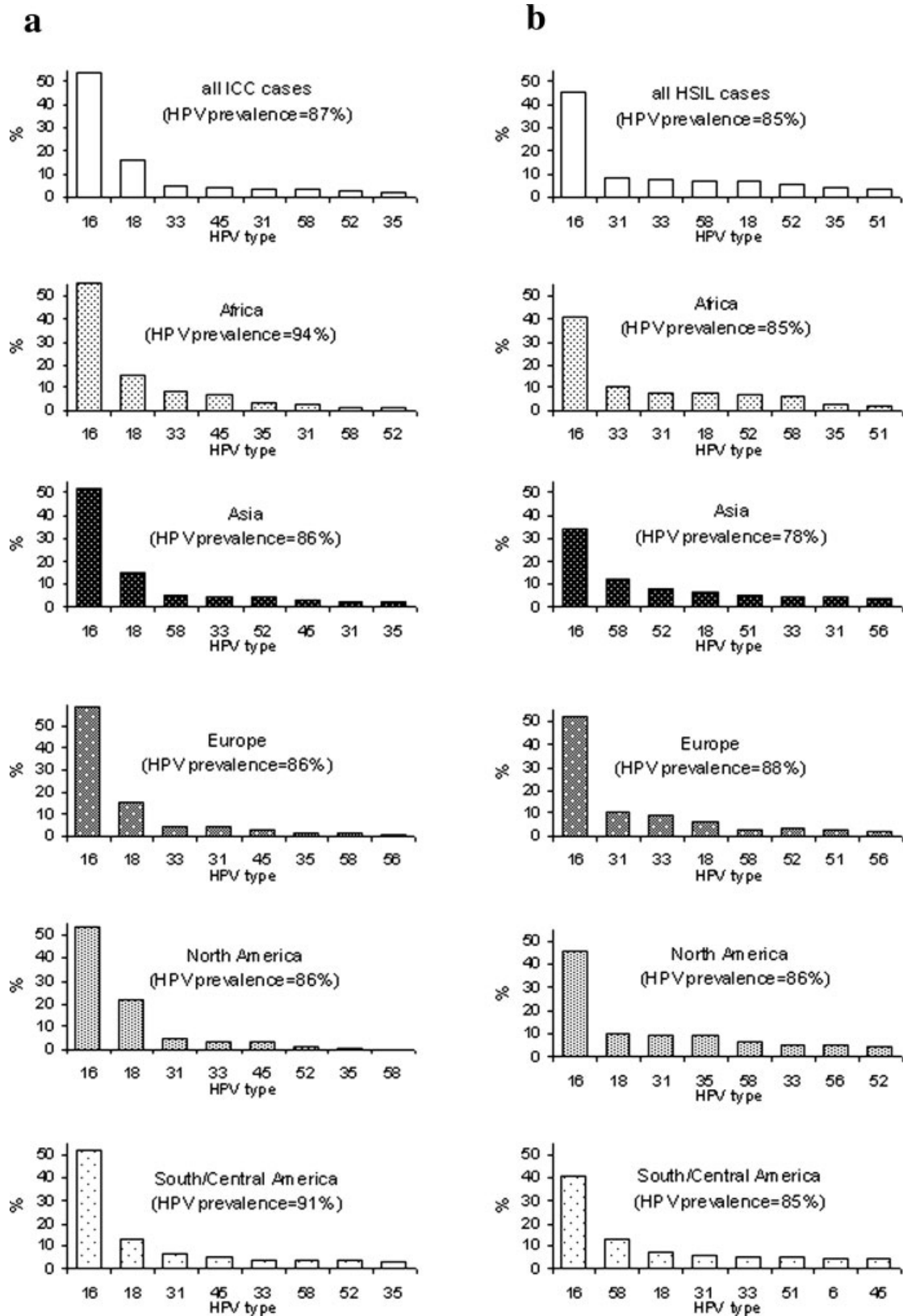


FIGURE 1 – Type-specific prevalence of human papillomavirus (HPV) infection in (a) invasive cervical cancer (ICC) cases and (b) high-grade squamous epithelial lesions (HSIL), stratified by continent. Type-specific prevalence for Oceania are presented in Appendices only. HPV types tested for in less than 200 cases are presented in Appendices only.

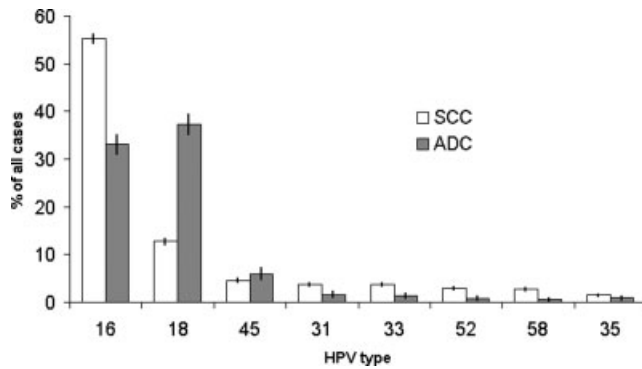


FIGURE 2 – Comparison of type-specific prevalence of human papillomavirus (HPV) infection in 9,494 squamous cell carcinoma (SCC) cases and 1,949 adeno/adenosquamous carcinoma (ADC) cases.

HPV16/18 proportion is higher in Europe, North America and Oceania (74–77%) than in Africa, Asia and South/Central America (65–70%).

An additional effect of the gain in data from less developed countries is that the 6 most important types in ICC after HPV16/18, namely HPV31, 33, 35, 45, 52 and 58, now appear to be the same in all continents. The consistency in the 8 most common types is therefore clearer than in previous estimates,^{3,4} likely due to a reduction in random fluctuation. Future generations of prophylactic vaccines would benefit by including high-risk types other than 16 and 18. However, if it is not possible to include all 6 additional types in next generation vaccines for ICC prevention, then there do remain some differences by continent in the priorities for HPV types. In particular, the prevalence of HPV58 and 52 is relatively high in ICC from Asia. This pattern was also seen in HSIL, and from a previous meta-analysis of low-grade squamous intraepithelial lesions.⁷

Data on HSIL have greatly increased since a previous report⁵ and the 8 most common HPV types in HSIL were broadly similar to those in ICC. However, the HSIL data from less-developed countries remain scarce as HSIL detection requires active cervical screening, which is rare in such settings. Despite these limitations, it is clear that HPV type distribution in HSIL is not entirely representative of that in ICC. In agreement with similar previous reports,^{5,8} HPV types 16, 18 and 45 were significantly over-represented in ICC compared to HSIL, and all other high-risk types were significantly under-represented, suggesting type-specific differences in propensity to progress from HSIL to cancer. Alternatively, HPV18-positive HSIL may be preferentially missed by cervical screening programmes.⁹ Thus, whilst data on HPV type distribution in HSIL is relevant to predicting the impact of HPV16/18 vaccines on reducing screen-detected HSIL, it underestimates the impact on ICC.

Limitations associated with cross-sectional meta-analyses of HPV type-specific prevalence include variation in HPV type-specific sensitivity of different PCR protocols used in the included studies,¹⁰ the fact that many studies did not type for a broad range of HPV types, and the lack of standardisation of cytohistological diagnoses across studies. Thus, the observed overall HPV DNA prevalence of 87% in ICC is lower than the 99.7% found by gold standard HPV detection techniques.¹¹ Furthermore, type-specific prevalence estimates include those in both single- and multiple-type HPV infections. This means that multiple infections count at least twice when summing the prevalence for more than one type, and that some types, *e.g.*, HPV6 and 11, may exist exclusively in multiple infections. These limitations have been previously described in detail.⁴

TABLE II – COMPARISON OF HUMAN PAPILLOMAVIRUS (HPV) TYPE DISTRIBUTION IN SQUAMOUS CELL CARCINOMA (SCC) VERSUS HIGH-GRADE INTRAEPITHELIAL LESIONS (HSIL)

HPV type	SCC		HSIL		SCC vs HSIL Prevalence ratio ² (95% CI)
	N	% HPV positive ¹	N	% HPV positive ¹	
Any	9,494	89.7	7,094	84.9	1.06 (1.05–1.07)
16	9,494	55.2	7,094	45.3	1.30 (1.26–1.34)
18	9,402	12.8	6,978	6.9	1.76 (1.58–1.95)
45	6,215	4.6	3,726	2.3	1.54 (1.20–1.98)
31	7,565	3.8	6,282	8.6	0.53 (0.45–0.61)
33	8,803	3.7	6,418	7.3	0.52 (0.45–0.60)
52	6,431	2.9	3,945	5.1	0.44 (0.36–0.54)
58	6,873	2.8	4,181	7.0	0.30 (0.25–0.35)
35	6,982	1.5	4,739	3.8	0.38 (0.29–0.49)
59	5,160	1.1	2,933	0.8	0.88 (0.53–1.47)
51	5,706	1.0	3,509	3.6	0.21 (0.15–0.30)
56	5,605	1.0	3,465	2.9	0.29 (0.20–0.42)
39	5,578	0.9	3,067	2.0	0.40 (0.27–0.60)
68	5,224	0.5	2,563	1.1	0.44 (0.24–0.82)
6	7,523	0.5	3,728	2.2	0.17 (0.11–0.25)
66	5,427	0.4	2,840	1.9	0.20 (0.12–0.34)
73	4,717	0.4	1,464	1.8	0.45 (0.23–0.87)
70	4,925	0.1	1,105	1.3	0.11 (0.04–0.29)
82	4,776	0.1	1,183	1.2	0.06 (0.02–0.18)
11	6,874	0.1	3,762	1.3	0.09 (0.05–0.18)

¹Type-specific prevalence includes that in single or multiple infections. ²Prevalence ratio adjusted for continent. CI = confidence interval.

We assumed that the proportion of ADC in the included studies, which varied from 4% in Africa to 32% in North America, was representative of underlying ICC in the continent. Previously identified differences in HPV type distribution by histology, namely HPV16 being more prevalent in SCC than in ADC and HPV18 being more prevalent in ADC than in SCC,⁴ were clearly apparent from this analysis. Differences by histological type may contribute to some of the heterogeneity in HPV type distribution by continent and also to some of the differences between ICC and HSIL, given that HSIL, but not ICC, includes, by definition, only squamous cell lesions.

Although this study is the broadest summary of HPV type distribution in ICC and HSIL worldwide to date, the cases included in the overall estimates were far from being geographically representative of the worldwide cervical cancer burden. More than half of all HPV-typed ICC cases came from North America, Eastern Asia and Northern Europe alone. Data were relatively scarce from South-Central Asia, including India, where approximately one-quarter of all worldwide cervical cancer occurs.⁶ Furthermore, while data has increased for Africa as a whole, they remained missing for vast regions of the continent, where cervical cancer incidence rates are estimated to be among the world's highest.⁶

As more data are accumulated, it is reassuring to observe that HPV16/18 account for at least two-thirds of ICC in all continents, suggesting that it is not essential to collect data from every country. On the other hand, local decision makers may seek assurance of the relevance of a HPV16/18 vaccine to their local ICC burden, especially as data aggregation may also mask some intra-continental heterogeneity. In Asia for example, the proportion of ICC due to HPV16/18 in the few studies from South-Central Asia appears as high as that in Europe and North America, but is lower in the studies from Eastern Asia. For the comparison of smaller geographical groupings, HPV type-specific information is given for individual studies and by region in the Appendices.

In summary, this meta-analysis suggests that a prophylactic vaccine against HPV16/18 has the potential to prevent more than two-thirds of worldwide ICC and half of HSIL. These pro-

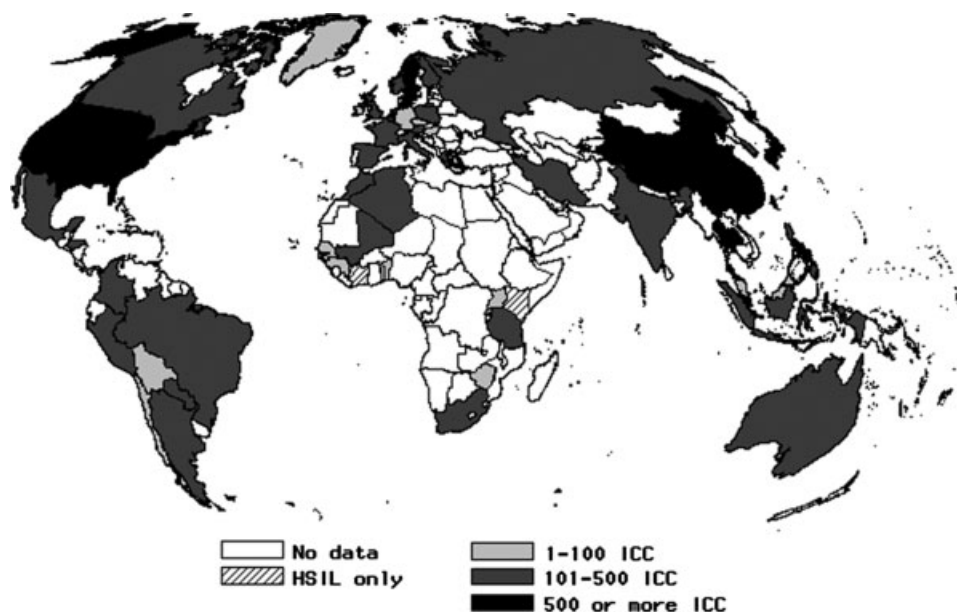


FIGURE 3 – Global distribution of invasive cervical cancer (ICC) cases with available human papillomavirus DNA typing data. HSIL = high-grade squamous epithelial lesions.

portions may be even higher if cross-protection against other high-risk HPV type infections, as recently reported for one of the two HPV16/18 vaccine candidates,¹ also proves to be relevant for preventing cancer and HSIL associated with these types.

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(See Appendices I and II on next page)

APPENDIX I. TYPE-SPECIFIC HUMAN PAPILLOMAVIRUS (HPV) PREVALENCE AMONG WOMEN WITH INVASIVE CERVICAL CANCER, BY STUDY AND REGION

First author	Reference	Country	HPV DNA source	PCR primers used	N cases	SCC ¹	ADC	HPV prevalence (% of all cases tested)														Multiple infections					
								any	16	18	33	45	31	58	52	35	59	56	39	51	6		68	73	66	11	70
AFRICA																											
Eastern Africa																											
Faiza B	Ethiopia Med J, 2005	Ethiopia	fixed biopsies	TS-PCR	163	153	10	96.9	71.8	18.4	18.4	1.8	0.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.3	
Naudier P	J Gen Virol, 2004	Mozambique	fresh + frozen biopsies	MY09/11, GP5+6+	72	71	1	97.2	55.6	28.4	9.7	23.6	2.8	1.4	1.4	19.4	1.4	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	33.3
Western Africa																											
Bosch FX	JNCI, 1995	Tanzania	fresh biopsies	MY09/11	49	44	5	100.0	44.9	30.6	2.0	10.2	2.0	0.0	4.1	0.0	0.0	0.0	2.0	0.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0
Mer Meulen J	Int J Cancer, 1992	Tanzania	fresh biopsies	GP5/6	53	53	0	88.7	37.7	32.1	1.9	5.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bosch FX	JNCI, 1995	Uganda	fresh biopsies	MY09/11	43	41	2	97.7	58.1	18.6	4.7	4.7	2.3	0.0	0.0	0.0	0.0	9.3	0.0	2.3	0.0	0.0	0.0	0.0	0.0	0.0	2.3
Stanczuk GA	Acta Obstet Gynecol Scand, 2003	Zimbabwe	Exfoliated cells	Degenerate nested primers	98	95	3	96.9	61.2	18.4	38.8	0.0	4.1	1.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	25.5
Regional subtotal																											
					478	457	21	96.4	59.4	22.4	15.6	6.3	2.5	0.7	1.2	4.7	0.4	3.1	0.0	0.8	0.0	1.2	1.1	0.6	0.0	1.1	16.8
Northern Africa																											
JNCI, 1995	Algeria	fresh biopsies	MY09/11	12	10	2	75.0	33.3	41.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Hannouss D	Int J Cancer, 2005	Algeria	biopsies + exfoliated cells	GP5+6+	171	159	12	97.7	61.4	15.8	3.5	6.4	2.3	0.6	4.1	1.2	1.8	2.3	1.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	9.9
Regional subtotal																											
					152	139	13	94.7	58.6	8.6	0.7	5.3	2.6	0.0	1.3	0.7	2.0	0.0	0.0	0.0	0.7	0.0	0.0	0.0	0.0	0.0	7.9
Southern Africa																											
Kay P	J Med Virol, 2003	South Africa	fresh biopsies	L1 PCR	50	50	0	94.0	82.0	10.0	10.0	2.0	2.0	0.0	2.0	2.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	16.0
Pegoraro RJ	Int J Gynecol Cancer, 2002	South Africa	fresh biopsies	MY09/11	190	190	0	98.4	46.8	14.2	10.0	4.7	1.1	1.1	1.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Williamson AL	J Med Virol, 1994	South Africa	fresh biopsies	MY09/11	68	60	8	80.9	45.6	1.5	5.9	1.5	5.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.9
Regional subtotal																											
					308	300	8	93.8	52.2	10.7	9.1	3.2	4.2	1.3	0.9	1.7	2.0	0.0	0.0	0.0	0.0	2.0	0.0	0.0	0.0	0.0	10.2
Western Africa																											
JNCI, 1995	Benin	fresh biopsies	MY09/11	6	6	0	83.3	50.0	16.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bosch FX	JNCI, 1995	Guinea	fresh biopsies	MY09/11	18	17	1	100.0	38.9	5.6	0.0	33.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bosch FX	Int J Epidemiol, 2002	Mali	fresh biopsies	GP5+6+	65	65	0	96.9	47.7	12.3	1.5	10.8	0.0	3.1	0.0	1.5	0.0	0.0	6.2	0.0	6.2	0.0	0.0	0.0	0.0	0.0	10.8
Bosch FX	JNCI, 1995	Mali	fresh biopsies	MY09/11	58	57	1	91.4	34.5	13.8	0.0	19.0	6.9	8.6	3.4	5.2	0.0	1.7	1.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Lin P	Cancer Epidemiol Biomark Prev, 2001	Senegal	exfoliated cells	MY09/11 + HMB01	51	51	0	64.7	37.3	7.8	5.9	9.8	0.0	2.0	3.9	2.0	0.0	2.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Xi LF	Int J Cancer, 2003	Senegal	exfoliated cells	MY09/11	20	20	0	85.0	35.0	5.0	0.0	10.0	15.0	5.0	2.3	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Regional subtotal																											
					218	216	2	85.9	39.9	10.5	2.3	13.3	2.8	5.1	2.3	2.3	0.0	0.5	1.8	0.9	0.0	0.0	0.0	0.0	0.0	0.0	10.8
AFRICA TOTAL																											
					1,339	1,281	58	93.9	54.5	15.5	7.6	6.6	2.5	1.5	1.2	2.9	0.8	1.1	0.8	0.9	0.4	0.7	0.9	0.9	0.0	0.0	12.4
ASIA																											
Eastern Asia																											
Gao YE	Sheng Wu Hua Xue Yu Sheng Wu Ji Xue Bao, 2003	China	fresh biopsies	GP5+6+	65	65	0	87.7	40.0	20.0	3.1	6.2	15.4	3.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	10.8
Huang S	Int J Cancer, 1997	China	fresh biopsies	MY09/11	40	35	5	87.5	27.5	30.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	32.5
Lin QQ	Int J Cancer, 1998	China	fresh + fixed biopsies	MY09/11, GP5+6+	77	72	5	93.5	48.1	5.2	3.9	1.3	2.6	16.2	5.2	0.0	2.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Liu J	Gynecol Oncol, 2004	China	fresh + fixed biopsies	MY09/11, GP5+6+	106	94	12	83.0	50.0	9.4	9.0	2.8	2.8	5.7	0.0	0.9	5.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Lo KWK	Gynecol Obstet Invest, 2001	China	fresh biopsies	MY09/11	121	107	14	78.5	48.8	11.6	5.0	0.0	0.8	6.6	0.8	0.0	0.0	0.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Lo KWK	Int J Cancer, 2002	China	fresh biopsies	MY09/11, GP5+6+	809	731	78	83.7	66.9	6.3	1.5	0.4	0.6	3.2	2.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4
Peng H	Int J Cancer, 1991	China	exfoliated cells	TS-PCR only	101	92	9	34.7	31.7	3.0	3.0	2.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Stephen AL	Int J Cancer, 2000	China	fixed biopsies	GP5+6+ of TS-PCR neg samples only	34	24	10	88.2	61.8	8.8	2.9	2.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Wu Y	J Clin Virol, 2006	China	exfoliated cells	MY09/11, GP5+6+	152	152	0	100.0	79.6	2.6	3.9	1.3	5.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0
Yu MY	Int J Cancer, 2003	China	fixed biopsies	TS-PCR only	50	33	17	96.0	70.0	16.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Asato T	J Infect Dis, 2004	Japan	exfoliated cells	L1C1C2	356	356	0	87.4	37.1	6.7	7.9	0.3	5.3	7.0	6.2	3.7	1.1	2.0	0.0	1.1	0.0	0.8	0.3	0.8	0.0	0.6	0.3
Fujinaga Y	J Gen Virol, 1991	Japan	fresh biopsies	pU-1Mpu-2R	39	39	0	84.6	48.7	12.8	5.1	7.7	2.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	7.7
Harima Y	Int J Radiat Oncol Biol Phys, 2002	Japan	fresh biopsies	pU-1Mpu-2R	84	79	5	76.2	26.2	4.8	2.4	7.1	2.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2
Ishikawa H	Cancer, 2001	Japan	fresh biopsies	TS-PCR only	52	52	0	76.9	53.8	23.1	1.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.9
Kanao H	Cancer Lett, 2004	Japan	fresh biopsies	pU-1Mpu-2R	25	25	0	84.0	32.0	26.0	8.0	4.0	12.0	16.0	4.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	20.0
Kashihara K	Acta Pathol, Japan, 1992	Japan	fixed biopsies	L1C1C2	83	68	15	58.1	41.9	6.5	1.1	0.0	0.0	3.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Maki H	Jpn J Cancer Res, 1991	Japan	biopsies	L1 PCR	29	29	0	82.8	44.8	20.7	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9	6.9
Nakagawa H	Anticancer Res, 2002	Japan	exfoliated cells	L1C1C2/C3	28	19	9	75.0	39.3	21.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.4
Nakagawa S	Cancer, 1996	Japan	fresh biopsies	L1C1C2 + C2M	146	116	30	88.4	37.7	18.5	6.2	0.7	2.1	8.2	10.3	2.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Nawa A	Cancer, 1995	Japan	fresh + fixed biopsies	ESG1C2	23	23	0	87.0	73.9	13.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7
Saito J	Gynecol Obstet Invest, 2000	Japan	fixed biops																								

APPENDIX II. TYPE-SPECIFIC HUMAN PAPILLOMAVIRUS (HPV) PREVALENCE AMONG WOMEN WITH HIGH-GRADE CERVICAL INTRAEPITHELIAL LESIONS, BY STUDY AND REGION

First author	Reference	Country	HPV DNA source	PCR primers used	N cases	CINII	CINIII	CIS	HSIL	HPV prevalence (% of all cases tested)														Multiple infections				
										any	16	18	33	45	31	58	52	35	59	56	39	51	6		68	73	66	11
AFRICA																												
Eastern Africa																												
'de Vries	Sex Transm Dis, 2003	Kenya	exfoliated cells	SPF 10	29	0	0	0	0	29	96.6	34.5	3.4	3.4	6.9	6.9	24.1	17.2	0.0	3.4	0.0	10.3	0.0	6.9	10.3	0.0	0.0	
Regional subtotal																												
					29	0	0	0	0	29	96.6	34.5	3.4	3.4	6.9	6.9	24.1	17.2	0.0	3.4	0.0	10.3	0.0	6.9	10.3	0.0	0.0	
Southern Africa																												
Kay P	J Med Virol, 2003	South Africa	fixed biopsies	L1 primers	129	0	0	0	0	129	88.4	56.6	1.6	14.0	0.0	10.9	3.1	3.9	2.3	0.0	0.0	0.0	0.0	0.0	0.0	0.8	12.4	
Regional subtotal																												
					129	0	0	0	0	129	88.4	56.6	1.6	14.0	0.0	10.9	3.1	3.9	2.3	0.0	0.0	0.0	0.0	0.0	0.8	12.4		
Western Africa																												
'La Roche	Int J Cancer, 1998	Ivory Coast	exfoliated cells	MY09/11	49	0	0	0	0	49	77.6	30.6	10.2	8.2	0.0	6.1	8.2	4.1	0.0	4.1	0.0	0.0	0.0	2.0	0.0	0.0	8.2	
Chabaud M	J Med Virol, 1996	Senegal	exfoliated cells	TS-PCR only	23	0	0	0	0	23	95.7	43.5	47.8	4.3	8.7	0.0	0.0	0.0	0.0	0.0	0.0	21.7	4.3	0.0	0.0	17.4	0.0	
Xi LF	Int J Cancer, 2003	Senegal	exfoliated cells	MY09/11	66	0	0	0	0	66	75.8	19.7	4.5	9.1	0.0	4.5	12.1	9.1	1.5	0.0	1.5	4.5	1.5	0.0	0.0	3.0	3.0	
Regional subtotal																												
					138	0	0	0	0	138	79.9	27.5	13.7	8.0	1.5	4.3	8.7	5.8	0.7	0.0	2.6	0.9	2.6	4.3	1.4	0.0	8.2	
AFRICA TOTAL																												
					296	0	0	0	0	296	85.2	40.9	7.4	10.2	1.4	7.4	6.1	6.8	3.0	0.0	2.8	0.7	2.2	3.6	2.4	0.0	5.2	
ASIA																												
Eastern Asia																												
'Chan MKM	Gynecol Oncol, 1996	China	exfoliated cells	MY09/11	45	10	35	0	0	55.6	24.4	8.9	4.4	0.0	0.0	0.0	11.2	1.1	0.0	0.0	1.1	0.0	0.0	0.0	0.0	2.2	2.2	
'Chen PKS	J Med Virol, 1999	China	exfoliated cells	MY09/11	89	29	60	0	0	58.4	25.8	4.5	6.7	0.0	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.2	0.0	
'Wu CH	Sex Transm Dis, 1994	China	fresh biopsies	TS-PCR only	34	13	15	6	0	76.5	35.3	20.6	5.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.2	8.8	0.0	0.0	20.6	0.0	
Ichimura H	Int J Clin Oncol, 2003	Japan	exfoliated cells	L1 primers	31	2	29	0	0	93.5	41.9	3.2	0.0	3.2	9.7	16.1	3.2	0.0	0.0	0.0	0.0	3.2	0.0	0.0	0.0	3.2	3.2	
'Nagai Y	Gynecol Oncol, 2000	Japan	exfoliated cells	L1 primers	58	0	58	0	0	96.6	37.9	3.4	15.5	8.6	6.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	8.6
Niwa K	Oncol Rep, 2003	Japan	exfoliated cells	L1 primers	22	4	5	13	0	95.5	36.4	4.5	0.0	0.0	4.5	22.7	4.5	4.5	0.0	4.5	0.0	4.5	0.0	0.0	0.0	0.0	4.5	
'Sasagawa T	Cancer Epidemiol Biomarkers Prev, 2001	Japan	exfoliated cells	LCR-E7	137	0	0	0	137	91.2	35.8	2.2	2.2	2.2	9.5	13.1	10.9	2.9	0.0	5.8	0.0	7.3	0.7	0.0	0.0	0.7	0.0	
Tsuda H	Gynecol Oncol, 2003	Japan	fixed biopsies	L1 PCR	26	14	12	0	0	73.1	11.5	3.8	0.0	0.0	15.4	15.4	0.0	0.0	0.0	11.5	0.0	15.4	0.0	0.0	0.0	0.0	0.0	3.8
Yoshida T	Cancer, 2004	Japan	exfoliated cells	L1 primers	33	0	0	0	0	33	93.9	33.3	0.0	6.1	9.1	0.0	6.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
'Yoshikawa H	Int J Cancer, 1999	Japan	biopsies	L1 primers	31	0	0	0	20	11	90.3	38.7	9.7	12.9	6.5	3.2	12.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
An HJ	Cancer, 2003	South Korea	exfoliated cells	TS-PCR only	151	0	0	0	0	151	96.0	55.0	6.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.8	5.6	0.0	0.0	0.0	0.0	0.0
Cho NH	Ann J Obstet Gynecol, 2003	South Korea	exfoliated cells	GP5+6+	72	0	0	0	72	83.3	51.4	9.7	2.8	1.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.8	5.6	0.0	0.0	0.0	0.0	0.0
Hwang TS	Gynecol Oncol, 2003	South Korea	exfoliated cells	GR5+6+	73	22	51	0	0	80.8	24.7	4.1	11.0	0.0	12.3	13.7	4.1	6.8	0.0	1.4	2.7	4.1	0.0	0.0	2.7	0.0	0.0	12.5
Kim CJ	Gynecol Oncol, 2003	South Korea	exfoliated cells	L1 primers	40	7	10	23	0	97.5	52.5	12.5	7.5	0.0	2.5	17.5	2.5	7.5	0.0	7.5	2.5	5.0	0.0	7.7	0.0	0.0	0.0	0.0
'Oh YI	Gynecol Oncol, 2001	South Korea	exfoliated cells	pL1/M1/L2R	42	0	0	0	42	73.8	40.5	7.1	19.0	7.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ho CM	Gynecol Oncol, 2005	Taiwan	exfoliated cells	MY11/GP6+	97	0	0	0	0	97	83.5	18.8	7.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	29.9
'Lai HC	Int J Cancer, 2003	Taiwan	exfoliated cells	MY09/11	131	0	0	0	0	131	88.0	27.5	1.5	4.6	10.7	12.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.1	
Lin H	Gynecol Oncol, 2005	Taiwan	exfoliated cells	MY09/11	20	0	0	0	20	85.0	35.0	10.0	10.0	0.0	0.0	5.0	10.0	5.0	0.0	0.0	0.0	5.0	5.0	0.0	0.0	0.0	0.0	
Regional subtotal																												
					1,132	101	275	62	694	81.3	35.4	5.7	6.4	0.9	5.4	12.2	9.5	3.3	0.0	3.6	1.2	5.1	0.7	1.1	0.0	0.7	1.5	
South-Central Asia																												
Nagpal JK	Eur J Clin Invest, 2002	India	fresh biopsies	MY09/11	25	0	0	0	0	25	64.0	48.0	8.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Regional subtotal																												
					25	0	0	0	0	25	64.0	48.0	8.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
South-Eastern Asia																												
Bhattrakosol P	J Med Assoc Thai, 2002	Thailand	fixed biopsies	MY09/11	146	38	108	0	0	65.1	24.7	9.6	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	12.4
'Eklaksananan T	J Obstet Gynecol Res, 2001	Thailand	exfoliated cells	E1 primers	40	10	4	26	0	30.0	7.5	15.0	2.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
'Lumpaboon T	Southeast Asian J Trop Med Public Health, 2000	Thailand	fixed biopsies	MY09/11	21	0	21	0	0	100.0	33.3	14.3	4.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.8	0.0	
Regional subtotal																												
					207	48	133	26	0	61.9	22.2	11.1	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.7	12.4	
ASIA TOTAL																												
					1,364	149	408	88	719	78.0	33.7	6.6	5.9	0.9	5.4	12.2	9.5	3.3	0.0	3.6	1.2	5.1	0.8	1.1	0.0	0.7	1.5	

APPENDIX II. TYPE-SPECIFIC HUMAN PAPILLOMAVIRUS (HPV) PREVALENCE AMONG WOMEN WITH HIGH-GRADE CERVICAL INTRAEPITHELIAL LESIONS, BY STUDY AND REGION (CONT.)

First author	Reference	Country	HPV DNA source	PCR primers used	N cases	CINII	CINIII	CIS	HSIL	HPV prevalence (% of all cases tested)														Multiple Infections						
										any	16	18	33	45	31	58	52	35	59	56	39	51	6		68	73	66	11	70	82
EUROPE																														
Central/Eastern Europe																														
Tachazy R	Hum Genet, 1999	Czech Republic	exfoliated cells	MY09/11	88	0	0	0	86	58.0	43.2	5.7	6.8	3.4	1.1	0.0	1.1	0.0	0.0	0.0	0.0	0.0	0.0	1.1	0.0	9.1				
Szoke K	J Med Virol, 2003	Hungary	exfoliated cells	MY09/11	75	31	19	25	0	96.0	57.3	4.0	6.7	1.3	5.3	0.0	1.3	1.3	0.0	0.0	0.0	0.0	0.0	1.3	1.3	0.0	6.7			
Regional subtotal																														
					163	31	19	25	86	75.5	49.7	4.9	6.8	2.4	3.0	0.0	1.2	0.6	1.1	1.2	0.0	0.0	0.0	1.1	1.2	0.0	8.0			
Northern Europe																														
'Sebbelov	Res Virol, 1994	Denmark	fixed biopsies	GP5+6+	34	0	0	0	0	91.2	85.3	0.0	29.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	7.5			
'Sabbey	Res Virol, 1994	Greenland	fixed biopsies	GP5+6+	30	0	0	0	0	63.3	70.0	3.3	10.0	0.0	6.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	17.0			
Buller D	J Pathol, 2000	Ireland	fixed biopsies	TS-PCR only	27	0	0	0	0	85.2	70.4	3.7	3.7	0.0	3.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0			
Murphy N	J Clin Pathol, 2003	Ireland	fixed biopsies	L1 PCR	64	28	36	0	0	90.6	78.1	7.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0			
'O'Leary JJ	J Clin Pathol, 1998	Ireland	fixed biopsies	GP5+6+	29	0	0	0	0	95.0	95.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0			
Gudleviciene Z	Medicina (Kaunas), 2005	Lithuania	exfoliated cells	TS-PCR only	20	0	0	0	29	79.3	48.3	6.9			3.4											0.0	0.0			
Kraus I	Br J Cancer, 2004	Norway	fresh biopsies	GP5+6+	67	30	37	0	0	79.1	49.3	6.0	10.4	4.5	9.0	1.5	1.5	1.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	7.5			
Andersson S	Br J Cancer, 2005	Sweden	fixed biopsies	"Quantovir" tip*	115	60	56	0	0	82.9	37.1	7.3	10.4		5.2												0.6			
'Aalanson M	Hum Pathol, 1999	Sweden	exfoliated cells	MY09/11	164	89	95	0	0	82.9	35.4	7.3	10.4		7.3												0.6			
'Zerbini M	Histopathol, 1996	Sweden	fixed biopsies	GP5+6+	53	53	0	0	0	85.1	50.5	9.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0			
'Arends MJ	Histopathol, 1993	United Kingdom	fixed biopsies	TS-PCR only	40	20	0	0	0	65.0	10.0	10.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0			
'Cusson KS	J Clin Pathol, 2004	United Kingdom	exfoliated cells	GP5+6+	84	0	0	0	94	93.0	48.9	11.7	7.4	9.6	18.0	5.3	8.5	3.2	3.2	2.1	3.2	6.4	0.0	0.0	0.0	0.0	0.0			
'Cuzick J	Br J Cancer, 1994	United Kingdom	exfoliated cells	TS-PCR only	73	12	61	0	0	91.9	63.0	20.5	16.4		26.0												45.7			
'Giannoudis A	Int J Cancer, 1999	United Kingdom	fixed biopsies	GP5+6+	118	31	87	0	0	100.0	68.6	4.2	11.0	0.0	14.4	3.4	0.8	2.5	0.0	0.0	0.0	0.8	2.5	0.0	0.0	0.0	0.0	11.9		
'Herrington CS	Br J Cancer, 1995	United Kingdom	exfoliated cells	MY09/11	38	12	26	0	0	92.1	52.6	7.9	7.9		15.8												0.0			
Regional subtotal																														
					1,017	317	577	0	123	85.1	64.2	8.1	9.5	3.1	9.9	3.0	2.4	2.7	1.4	1.2	3.0	2.9	1.3	0.9	10.6	2.5	0.5	0.0	1.1	14.8
Southern Europe																														
Grace M	J Clin Microbiol, 2004	Croatia	exfoliated cells	L1 primers	158	79	79	0	0	75.3	20.2	0.0	6.3		9.5													0.0		
'Labropoulou V	Sex Transm Dis, 1997	Greece	fresh biopsies	MY09/11	50	0	0	0	50	88.0	36.0	12.0	6.0	6.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
'Paraskovalis E	Gynecol Oncol, 2001	Greece	exfoliated cells	MY09/11	28	0	0	0	28	89.3	35.7	7.1	14.3	3.6	25.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
'Lacort	Pathologica, 2000	Italy	fixed biopsies	GP5+6+	38	19	17	0	0	100.0	50.0	8.3			2.8													0.0		
'Zerbini M	J Clin Pathol, 2001	Italy	exfoliated cells	MY09/11	89	0	0	0	89	79.8	50.6	3.4	9.0	2.2	7.9													0.0		
'Medeiros R	Eur J Cancer Prev, 2005	Portugal	fixed biopsies	MY09/11	132	22	110	0	0	91.7	74.2	0.8																5.6		
'Bosch FX	Cancer Epidemiol Biomarkers Prev, 1993	Spain	exfoliated cells	GP5+6+ MY09/11	157	0	157	0	0	70.7	49.0	0.6	5.7		1.3													3.8		
Regional subtotal																														
					650	120	363	0	167	81.1	45.8	2.5	7.0	1.8	6.8	0.0	0.9	1.1	0.0	1.8	0.0	2.6	0.6	0.0	2.8	0.0	0.0	0.0	3.6	
Western Europe																														
'Baay HFD	Eur J Gynecol Oncol, 2001	Belgium	fixed biopsies	GP5+6+	97	42	55	0	0	82.5	56.7	6.2	6.2	0.0	6.2	2.1	2.1	0.0	2.1	0.0	2.1	0.0	1.0	0.0	1.0	0.0	0.0	0.0	4.1	
Beaens E	Cytovathol, 2005	Belgium	exfoliated cells	SPF 10	123	0	0	0	123	88.6	43.1	4.1	6.5	3.3	9.8	11.4	3.3	0.8	4.9	6.5	10.6	0.8	4.1	5.7	0.0	3.3	16.4			
Dequidt CE	Br J Cancer, 2003	Belgium	exfoliated cells	MY09/11	134	0	0	0	134	98.5	50.0	5.2	20.9	1.5	6.7	0.0	3.0	17.9	0.0	3.0	5.2	0.0	0.7	0.0	0.0	0.0	0.0	0.0		
'Bergann C	Am J Surg Pathol, 1992	France	fresh biopsies	L1 primers	53	0	0	0	53	92.5	56.6	3.6	1.9	0.0	1.9	0.0	3.8	3.8	0.0	1.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0		
'Merkebach-Bruse S	Diagn Mol Pathol, 1999	Germany	fixed biopsies	GP5+6+	88	21	67	0	0	78.4	61.4	1.1	1.1		3.4													1.1		
'Meyer T	Int J Gynecol Cancer, 2001	Germany	fresh biopsies	MY09/11	288	0	0	0	288	94.4	46.2	6.6	9.4	1.4	13.2	1.7	5.6	3.1	0.7	1.4	1.4	1.0	2.4	0.3	3.8	2.1	1.0	0.0		
'Nindl I	Int J Gynecol Pathol, 1997	Germany	exfoliated cells	GP5+6+	85	0	0	0	85	83.5	36.5	2.4	12.9		5.9													4.7		
'Nindl I	J Clin Pathol, 1999	Germany	exfoliated cells	GP5+6+	65	31	34	0	0	87.7	56.9	6.2	7.7	1.5	18.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
Bekkers RL	Br J Cancer, 2003	The Netherlands	biopsies	SPF 10	90	18	36	36	0	100.0	54.4	7.8	3.3	16.7														12.3		
'Bollen LJM	Sex Transm Dis, 1997	The Netherlands	exfoliated cells	CpI/CPiG	91	24	64	0	3	97.8	36.3	4.4	5.5	4.4	18.7	7.7	2.2	4.4	1.1	4.4	1.1	3.3	0.4	0.4	0.4	0.4	0.4	1.1		
Bulkmaans NWJ	Int J Cancer, 2005	The Netherlands	fresh biopsies	GP5+6+	225	50	175	0	0	100.0	63.6	4.9	7.6	1.8	8.9	6.2	4.4	2.2	0.0	1.3	0.9	3.6	0.0	0.0	0.0	0.0	0.0	0.0		
'Cornelissen MTE	Virohows Arch B Cell Pathol Incl Mol Pathol, 1992	The Netherlands	fixed biopsies	MY09/11	89	16	73	0	0	88.8	52.8	6.7	5.6		12.4													17.8		
'Reesink-Peters N	Eur J Obstet Gynecol Reprod Biol, 2001	The Netherlands	exfoliated cells	SPF 10	216	44	172	0	0	97.7	56.9	13.9	11.6		19.4													27.8		
van Duin M	Int J Cancer, 2003	The Netherlands	fresh and fixed biopsies	GP5+6+	20	0	20	0	0	100.0	65.0	0.0	0.0	0.0	20.0	5.0	10.0	0.0	0.0	0.0	0.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0	10.0	
Regional subtotal																														
					1,664	246	696	36	686	93.3	52.2	6.3	8.8	1.9	11.4	3.5	4.7	4.7	0.3	2.7	1.8	3.4	1.2	0.9	2.7	1.7	0.5	1.7	0.0	15.7
EUROPE TOTAL																														
					3,494	714	1,655	61	1,064	87.8	51.5	6.0	8.6	2.2	9.8	2.9	3.6	3.4	0.4	2.2	1.9	3.0	1.1	0.8	3.5	1.5	0.4	1.0	0.3	13.0

