Oral Human Papillomavirus in Healthy Individuals: A Systematic Review of the Literature

Aimée R. Kreimer, PHD, Rohini K. Bhatia,* Andrea L. Messeguer, MD,† Paula González, MD,† Rolando Herrero, MD,† and Anna R. Giuliano, PHD‡*

Background: Human papillomavirus type 16 (HPV16) is a common infection in the anogenital tract. HPV16 DNA detected in oral specimens has recently been identified as a risk factor for some oropharyngeal cancers. The reported prevalence of oral HPV infection from individual studies is highly variable.

Methods: We systematically reviewed and abstracted data from published studies (n = 18) that detected oral HPV DNA in 4581 cancer-free subjects to determine the pooled prevalence (and 95% confidence intervals [CI]) of HPV16, carcinogenic HPV, and any HPV.

Results: 1.3% (95% CI: 1.0–1.7%) of 3977 healthy subjects had oral HPV16, 3.5% (95% CI: 3.0–4.1) of 4441 subjects had carcinogenic HPV, and 4.5% (95% CI: 3.9–5.1) of 4070 subjects were positive for any HPV. Oral HPV16 accounted for 28% of all HPV detected in the oral region. Men (47 of 1017) and women (117 of 3690) had nearly exactly the same prevalence of any oral HPV detected (4.6% vs. 4.4%, respectively).

Conclusions: HPV-16, a common anogenital infection, was rarely detected in oral specimens. However, a small but noteworthy proportion of healthy individuals have oral HPV infections with types known to cause cancer in the oral region.

Infection with human papillomavirus (HPV) is a necessary cause of cervical cancers worldwide, and is increasingly recognized as an important cause of a subset of other anogenital cancers, including some vaginal, vulvar, penile, and anal cancers.[1] HPV is also associated with a subset of head and neck cancers occurring specifically in the oropharynx.[1] HPV type 16 (HPV16), the most prevalent of the approximately 13 cancer-associated types in cervical cancer, is also the most common type present in HPV-positive oropharyngeal cancers (of which, approximately 90% are positive for HPV16).[2,3]

Recent case-control data suggest that detection of prevalent HPV16 infection in oral exfoliated cells increased the odds of oropharyngeal cancer more than 13 fold.[3] There is limited information about the natural history of oral HPV infection, but since oral HPV16 infection is associated with this cancer, it is important to estimate the proportion of healthy individuals with oral HPV infection. The aim of this work was to review existent literature to estimate the prevalence of HPV DNA detected in oral specimens collected from cancer-free individuals.

*National Cancer Institute, National Institutes of Health, Bethesda, MD; †Proyecto Epidemiológico Guanacaste, Fundación INCIENSA, San José, Costa Rica; and ‡H. Lee Moffitt Cancer Center, Tampa, FL

The authors thank Amanda Hansborough for her help in collecting the articles and preparing the tables for publication.

Correspondence: Aimee Kreimer. 6120 Executive Blvd., EPS/7084, Rockville, MD 20852. E-mail: kreimera@mail.nih.gov.

Received for publication July 30, 2009, and accepted October 21, 2009.
DOI: 10.1097/OLQ.0b013e3181c94a3b

Copyright © 2010 American Sexually Transmitted Diseases Association
All rights reserved.

MATERIALS AND METHODS

Study Selection

The National Institutes of Health "PubMed" search engine was employed to search for citations published from January 1997 to June 2009, using the keywords "Papillomavirus" and "Oral" and limiting to English publications in humans. Using these terms, we identified 729 manuscripts. After reviewing their titles and abstracts for relevance, we identified 47 studies that appeared to evaluate HPV DNA in oral specimens collected from healthy individuals. We excluded studies that focused on individuals with precancerous lesions (n = 12) and studies of immunosuppressed populations (renal transplant or HIV-positive) (n = 1); although if a study included HIV-negative and HIV-positive individuals and HPV data were provided stratified by group, we utilized available data. We also excluded case-control studies, commentaries and systematic reviews (n = 11), studies that focused exclusively on infants/children (n = 2), studies with HPV test results on less than 50 people (n = 4), and studies that did not use DNA-based testing methods on oral specimens (i.e., serologic assays and secretory immunoglobulin) (n = 1). Using these criteria, 16 manuscripts were identified; two additional manuscripts were identified from manuscript references for a total of 18 manuscripts included in the final data abstraction. Informed consent was assumed to have been obtained by the individual studies from their respective subjects.

Data Abstraction

Data were abstracted (by A.R.K. and R.K.B.) and confirmed (by P.G. and A.L.M.) on the following variables: first and last author, year of publication, country, population, year of data collection, sample size, age of population, gender distribution, oral specimen collection method, laboratory methods for DNA extraction and HPV detection, as well as HPV types detected, and are presented in Table 1.

The HPV prevalence of overall, carcinogenic, and HPV16 was abstracted from each study when available. If information was missing from the publication, the author was contacted to obtain additional details and data when available.

Statistical Analyses

Overall HPV prevalence was defined as persons testing positive for any oral HPV type, divided by the total healthy population tested for HPV. Carcinogenic HPV, defined as HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66,[1] and

Copyright © by the American Sexually Transmitted Diseases Association. Unauthorized reproduction of this article is prohibited.

TABLE 1. Studies That Investigated Oral HPV Infection in Cancer-Free Populations

Reference	Country	Study Population (Year of Data Collection)	Sample Size (Restricted to β Globin Positive)	Age	Gender	Oral Specimen Collection Method and Anatomic Site	Specimen Processing Method/DNA Extraction	HPV Detection Method	HPV16 Prevalence N (%)	Carcinogenic HPV Prevalence N (%)	Any HPV Prevalence N (%)	HPV Types Detected	
												C	NC
Canadas et al[4]	Spain	Female sex workers who attended a dermatology or sexually transmitted disease (–)	188	19–49	188 women	Toothbrush on the oral cavity	Protinease K	MY09/11	4 (2.1)	4 (2.1)	15 (8.0)	16, 18	6, 11
Coutlée et al[5]	Canada	STD and endoscopy clinics HIV negative women (1994)	114	16–60 age matched to HIV+ individuals	73 men, 36 women	Cytobrush of cheeks, hard palate, dorsum of the tongue	Protinease K	MY09/11	2 (1.8)	3 (2.6)	3 (2.6)	16, 35	None
D'Souza et al[6]	USA	College-aged men (2007)	210	18–23	210 men	Oral rinse and gargle	Puregene-based protocol (Qiagen)	PGMY09/11 and Roche line-blot hybridization	1 (0.5)	5 (2.4)	6 (2.9)	16, 35, 39, 51, 66	84
do Sacramento et al[7]	Brazil	Individuals who underwent surgery (–)	50	16–52	21 men, 29 women	Scraped 4 separate sites in oropharynx: right and left palatine tonsils, soft palate, base of the tongue, and wall of the pharynx	—*	MY09/11	1 (2.0)	3 (6.0)	7 (14.0)	16, 18, 52	61
Fakhry et al[8]	USA	HIV-women in Women's Interagency HIV Study Cohort (WIHS) (2004)	78	40 (mean)	78 women	Oral rinse and gargle	Puregene DNA purification kit	PGMY	—	3 (3.8)	7 (9.0)	—	—
Giraldo et al[9]	Brazil	Outpatient clinic at the Women's Health Center at the State University of Campinas (with and without confirmed genital lesions) (2001–2002)	140	18–45	140 women	Swab—hard palate and cheeks	Protinease K	MY09/11	—	—	29 (20.7)	—	—
Kreimer et al[10]	USA	Average and high risk subjects (2000–2001)	396	18–85	231 men, 165 women	Tonsil brush, oral rinse and gargle	Protinease K	PGMY	5 (1.3)	17 (4.5)	30 (7.6)	16, 18, 35, 39, 52, 56, 59	55, 61, 62, 64, 67, 71, 72, 73, 81, 82, 83, 84, 89
Kujan et al[11]	UK	Dental students (–)	50	18+	26 men, 24 women	Two brushes: (1) cervex brush -each side of buccal mucosa and (2) cytobrush-lateral border of the tongue	Roche MagNA Pure System	Digene HC2 assay and Roche Amplification	—	4 (8)-Roche kit	0 (0)-HC2 assay 4 (8) - Roche kit	—	—
Kurose et al[12]	Japan	Healthy dental clinic visitors (2000–2002)	662	3–85	277 men, 385 women	Cytobrush inside of the cheek	Puregene DNA Isolation kit	MY09/11 and sequence analysis	1 (0.2)	1 (0.2)	4 (0.6)	16	12, 53, 71
Lambropoulos et al[13]	Greece	Healthy population (1994–1996)	169	14–85	76 men, 93 women	Cytobrush from the buccal mucosa	Protinease K	MY09/11-but probed for 16, 18, 33, 6, 11 only	4 (2.4)	4 (2.4)	16 (9.5)	16	6, 11

(*Continues*)

Copyright © by the American Sexually Transmitted Diseases Association. Unauthorized reproduction of this article is prohibited.

TABLE 1. (Continued)

Reference	Country	Study Population (Year of Data Collection)	Sample Size (Restricted to β Globin Positive)	Age	Gender	Oral Specimen Collection Method and Anatomic Site	Specimen Processing Method/DNA Extraction	HPV Detection Method	HPV16 Prevalence N (%)	Carcinogenic HPV Prevalence N (%)	Any HPV Prevalence N (%)	HPV Types Detected	
												C	NC
Marais et al[14]	South Africa	Dental clinic visitors (2003)	194	13–61	83 men, 111 women	Cervibrush (Digene) on both cheeks	QiAmp DNA mini kit (Qiagen)	Roche Line Blot	1 (0.3)	2 (1.0)	8 (4.1)	16, 31	11, 13, 32, 72
Montaldo et al[15]	Sardinia	Recruited from surgery department (2007)	164	4–77	69 men, 95 women	Saliva samples	Protinease K and Qiaquick Purification PCR Kit (Qiagen)	MY09/11 and GP5 + N/MY09	23 (14)	30 (18.3)	—	16, 31	None
Ragin et al[16]	Tobago	Healthy women from general population (2004)	212	18–65	212 women	Mouthwash and gargle	Puregene DNA purification kit	Linear Array-PGMY and GP5+/6+	2 (0.9)	4 (1.9)	14 (6.6)	16, 31, 66	32, 62, 72
Rintala et al[17]	Finland	Pregnant women and their spouses (–)	347	25.5 mean for women 28.8 mean for men	131 men, 216 women	Brush of oral mucosa	Protinease K	MY09/11 and GP5+/6+	—	57 (16.0)	—	—	—
Smith et al[18]	USA	Pregnant women and male partners (1997–2000)	645	18–45	68 men, 577 women	Oral rinse with normal saline	Protinease K	MY09/11	3 (0.5)	10 (1.6)	18 (2.8)	16, 31, 39	6, 11, 68, 70
Smith et al[19]	USA	Adolescents—family medicine clinic, university students health center, and a sorority (1998–2000)	336	16–20	101 men, 235 women	Oral rinse with sterile water	QIAamp DNA mini kit (Qiagen)	MY09/11	—	4 (1.2)	11 (3.3)	16, 18, 56, 58, 66	6, 11, 70
Summersgill et al[20]	USA	Outpatient clinics at University of Iowa Health Care (1996–1997)	97	13–20	—	Oral rinse with normal saline	Protinease K	MY09/11	3 (3.1)	3 (3.1)	5 (5.2)	16	6
Winer et al[21]	USA	Female students at Washington State University (1990–1997)	529	18–20	529 women	Toothbrush samples of buccal mucosa	Dot-blot hybridization	PGMY09/11 and HMB01	1 (0.2)	1 (0.2)†	5 (1.0)	16, 31/33/35/39	40/42/53/54

—, Cells were left blank if the data were not provided in the manuscript.
*Author quotes the method from Sambrook 1989, however, upon further investigation, additional information was not obtainable.
†An additional carcinogenic HPV-type may have been found, but we were unable to determine this due to the use of mixed probe methods.
C indicates carcinogenic; HPV, human papillomavirus; NC, noncarcinogenic.

Copyright © by the American Sexually Transmitted Diseases Association. Unauthorized reproduction of this article is prohibited.

HPV16 alone were measured only among those tested for the specific HPV type in question, and therefore, the sample size and number of contributing studies varied between analyses. Composite estimates (percent prevalence) and exact binomial 95% confidence intervals (CI) were calculated.

To begin to look at oral HPV by world region, we stratified by economic status using the definition put forth by the United Nations Public Administration Network.[22] The following countries or regions were considered developed: Europe (excluding the east European transition economies), Canada, the United States of America, Japan, Australia, and New Zealand.

Categorizations were also made based on the study population to determine if the 'healthiness' of the population influenced the findings. Specifically, healthier populations "low-risk," such as those from dental clinics and the general population, were compared to higher-risk groups "high-risk," such as female sex workers. An unknown risk category was used for studies with mixed populations or for those whose 'riskiness' could not be determined.

Evaluating the age-specific oral HPV distribution and comparing oral HPV prevalence among men and women were aims of this work. While most of the studies provided data on any HPV prevalence stratified by gender, many did not provide data in a manner that could be used for the age-analysis. The raw data from individual studies is displayed in tabular format (Table 1) and a gender-stratified analysis of any HPV was conducted.

Although understanding the influences of methods of specimen collection and laboratory analysis (specifically DNA extraction and HPV testing methods) is important for comparing results between studies, such methods work is best conducted within individual studies using head-to-head comparisons, as have been previously published.[10,23]

The relationship between study sample size and oral HPV prevalence was evaluated. We tested for heterogeneity between studies using the I^2 statistic, which represents the approximate proportion of total variability in point estimates that can be attributed to heterogeneity.[24] Formal testing using both the Begg and Mazumdar[25] and Egger et al[26] tests indicated publication bias was present ($P = 0.04$ and $P < 0.001$, respectively).

RESULTS

Eighteen studies including 4581 healthy individuals were identified and are presented in the Table 1. 1.3% (95% CI: 1.0%–1.7%) of 3977 healthy subjects had oral HPV16, 3.5% (95% CI: 3.0–4.1) of 4441 subjects had carcinogenic HPV, and 4.5% (95% CI: 3.9–5.1) of 4070 subjects were positive for any HPV (Table 2). HPV16 accounted for 28.0% (51/182) of all HPV infections detected in the oral region amongst individuals (and 32.9% [51/155] of carcinogenic HPV infections). Other carcinogenic types detected included: HPV 18, 31, 35, 39, 52, 56, 58, and 66.

Studies that occurred in developing nations (n = 4) had a greater prevalence of HPV16 compared to those from developed nations (n = 12) (4.3% vs. 0.7%, respectively); similar patterns were observed for carcinogenic and any HPV detected (Table 2).

By risk strata, studies (n = 6) that recruited lower-risk populations, such as people from the general population or college students, had a lower HPV16 prevalence (0.4%) compared to the unknown (n = 5) and higher (n = 2) risk categories (4.1% vs. 2.1%, respectively); a similar trend was observed for any HPV. An anomaly was noted for carcinogenic HPV, where low and high risk populations had similar prevalence of

TABLE 2. Global Prevalence of Oral HPV16, Carcinogenic HPV, and any HPV Detected Among Healthy Individuals, by Economic and Health Status

	HPV-16				Carcinogenic				All HPV			
	No. Studies	No. Individuals	HPV+ (n)	HPV Prevalence % (95% CI)	No. Studies	No. Individuals	HPV+ (n)	HPV Prevalence % (95% CI)	No. Studies	No. Individuals	HPV+ (n)	HPV Prevalence % (95% CI)
Global estimate	13	3977	51	1.3 (1.0–1.7)	17	4441	155	3.5 (3.0–4.1)	16	4070	182	4.5 (3.9–5.1)
Economic status												
Developed nations	9	3357	24	0.7 (0.5–1.1)	13	3357	116	3.5 (2.9–4.1)	12	3474	124	3.6 (3.0–4.2)
Developing nations	4	620	27	4.3 (2.9–6.3)	4	1084	39	3.6 (2.6–4.9)	4	796	58	7.3 (5.6–9.3)
Risk												
High-risk*	2	188	4	2.1 (0.6–5.4)	2	266	7	2.6 (1.1–5.3)	2	266	22	8.3 (5.3–12.3)
Unknown-risk†	5	821	34	4.1 (2.9–5.7)	5	821	56	6.8 (5.2–8.8)	5	797	74	9.2 (7.4–11.5)
Low-risk‡	6	2968	13	0.4 (0.2–0.7)	10	3354	92	2.7 (2.2–3.3)	9	3007	86	2.9 (2.3–3.5)

*High-risk includes publications by Canadas et al[4] and Fakhry et al.[8]
†Unknown-risk includes publications by Coutlee et al,[5] do Sacramento et al,[7] Giraldo et al,[9] Kreimer et al,[10] Montaldo et al,[15] and Summersgill et al.[20]
‡Low-risk includes publications by D'Souza et al,[23] Kujan et al,[11] Kurose et al,[12] Lambropoulous et al,[13] Marais et al,[14] Ragin et al,[16] Rintala et al,[17] Smith et al,[18] Smith et al,[19] and Winer et al.[21]
95% CI indicates 95 percent confidence interval.

Copyright © by the American Sexually Transmitted Diseases Association. Unauthorized reproduction of this article is prohibited.

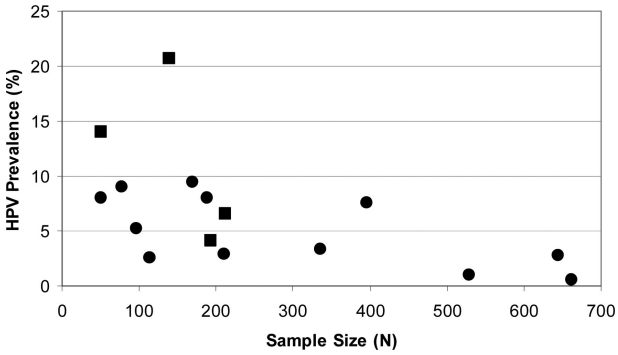

Figure 1. Human papillomavirus prevalence by study sample size, stratified by economic status. Developing countries are indicated by squares and developed countries are indicated by circles.

oral HPV (2.7% vs. 2.6% respectively). For all categorizations of HPV, studies of individuals of unknown risk had the highest oral HPV prevalence (Table 2).

Thirteen studies provided oral HPV data stratified by gender. Men (47 of 1017) and women (117 of 3690) had similar prevalence of any oral HPV detected (4.6% vs. 4.4%, respectively).

The relationship between any HPV prevalence and study size was assessed (Fig. 1). The majority of studies had around 100 to 200 individuals and showed broad variation in detection of any HPV (ranging from 2.6%–20.7%). The long right tail showed that six studies included over 200 people; the largest study had a sample size of 662 people. These larger studies tended to show overall HPV prevalence lower than the average (Fig. 1). By economic status, the few studies that occurred in developing countries tended to be smaller (all but one had less than 200 individuals).

Significant heterogeneity was present between studies: I^2 for HPV16 of 89.3%, for carcinogenic HPV of 92.1%, and for overall HPV of 88.7% (all $P < 0.001$).

DISCUSSION

HPV16 infection has been established as a cause for a subset of oropharyngeal cancers[1,3]; therefore, quantitating the prevalence of oral HPV16 among healthy individuals is important. The present review included 18 studies that investigated HPV DNA, as measured by PCR-based assays, in over 4500 oral specimens collected from healthy individuals: more than one percent had HPV16 detected in their oral region. HPV16 accounted for 28% of all HPV infections detected in the oral region amongst individuals. Correspondingly, HPV16 accounts for approximately 25% of cervical infections detected among cytologically normal woman.[27] Paradoxically, the proportion of HPV16 to all HPV types detected appears similar in the oral and cervical regions yet HPV16 causes a greater proportion of HPV-associated oropharyngeal cancers (approximately 90%)[2,3] compared to cervical cancers (approximately 50%).[28] While detection of oral HPV DNA does not translate to productive HPV infection, these data argue for large, well-designed studies that aim to understand the natural history and epidemiology of oral HPV infection. Given that HPV persistence is necessary for cervical cancer development,[29] it is likely important for the oral region as well. Further, as differences were observed in the prevalence between nations with differing economic statuses, inclusion and comparison of multiple countries within one study will help determine if these differences are real or due to differences in study methodology.

To obtain an estimate of the burden of oral HPV infection in the general population, we focused on studies of healthy adults and chose to exclude certain populations. For instance, healthy controls from case-control studies were excluded because more than half of the control populations from these studies were recruited from either a hospital or clinic based setting and were typically matched to the case-distribution by at least age and gender, thereby potentially skewing results towards older ages and male gender, given the distribution of head and neck cancers. Additionally, studies conducted exclusively among children were excluded as the route of transmission is in most instances nonsexual, and the prevalence may accordingly differ as well. While our work is not necessarily generalizable to the population at large, especially considering the inclusion of higher-risk populations such as female sex workers and STD clinic attendees, we wanted to avoid further skewing the work in known ways. Lastly, because we restricted to healthy adults, we excluded populations at increased risk of infection, including HIV-positive, renal transplant patients, and cancer patients. Each of these special populations is of interest and warrants further investigation.

The methods employed in these studies were heterogeneous. Sources of variability between studies that we were unable to address with the current review included method of specimen collection and processing methods. In fact, inadequate sample purification due to PCR inhibition has been shown to importantly underestimate the prevalence of oral HPV infection.[23] In addition, studies of oral HPV among cancer-free people have been, with rare exception, small (less than 200 cases); the HPV prevalence seemed to be inversely proportional to the study sample size. Hence, this work appeared to be susceptible to publication bias, in which certain studies may have been published because of higher oral HPV prevalence.

We determined from existing studies that a small but significant proportion of healthy individuals have HPV types detected in their oral region that are known to cause cancer in the oral region. While the fraction of these infections in healthy people that will lead to cancer will be small, HPV16 appears to cause approximately 40% to 60% of oropharynx cancers.[3,30] There theoretically exists the possibility that the prophylactic HPV16 vaccine could be protective in this context. While a direct evaluation of vaccine efficacy against oral HPV16 infection remains necessary because there are no published data on this topic, if the HPV vaccine protects against oral HPV infections akin to the near complete efficacy observed for cervical infections among HPV naïve women,[31,32] a percentage of oropharynx cancers could be prevented. Little is known about transmission and natural history of oral HPV infections, but prophylactic vaccines directed against oral HPV16 would need to be administered before exposure and would need to provide long-term protection. However, before any programmatic vaccine implementation, cost-effectiveness analyses are necessary and should aid in the decision of whether to promote vaccination to protect against some oropharyngeal cancers.

Prevention of even a subset of head and neck cancers is important, and is highlighted by recent data suggesting that the incidence of oropharynx cancer is increasing and may be due to changes in HPV endemicity.[33] Prospective, epidemiologic studies that focus on the age-specific and type-specific oral HPV distribution, oral HPV prevalence by gender, and evaluation of rates of oral HPV incidence and persistence will be an important next step in understanding the natural history of oral

Copyright © by the American Sexually Transmitted Diseases Association. Unauthorized reproduction of this article is prohibited.

HPV and in the evaluation of population benefit if the vaccine is effective.

REFERENCES

1. Cogliano V, Baan R, Straif K, et al. Carcinogenicity of human papillomaviruses. Lancet Oncol 2005; 6:204.
2. Kreimer AR, Clifford GM, Boyle P, et al. Human papillomavirus types in head and neck squamous cell carcinomas worldwide: A systematic review. Cancer Epidemiol Biomarkers Prev 2005; 14:467–475.
3. D'Souza G, Kreimer AR, Viscidi R, et al. Case-control study of human papillomavirus and oropharyngeal cancer. N Engl J Med 2007; 356:1944–1956.
4. Canadas MP, Bosch FX, Junquera ML, et al. Concordance of prevalence of human papillomavirus DNA in anogenital and oral infections in a high-risk population. J Clin Microbiol 2004; 42: 1330–1332.
5. Coutlee F, Trottier AM, Ghattas G, et al. Risk factors for oral human papillomavirus in adults infected and not infected with human immunodeficiency virus. Sex Transm Dis 1997; 24:23–31.
6. D'Souza G, Agrawal Y, Halpern J, et al. Oral sexual behaviors associated with prevalent oral human papillomavirus infection. J Infect Dis 2009; 199:1263–1269.
7. do Sacramento PR, Babeto E, Colombo J, et al. The prevalence of human papillomavirus in the oropharynx in healthy individuals in a Brazilian population. J Med Virol 2006; 78:614–618.
8. Fakhry C, D'Souza G, Sugar E, et al. Relationship between prevalent oral and cervical human papillomavirus infections in human immunodeficiency virus-positive and -negative women. J Clin Microbiol 2006; 44:4479–4485.
9. Giraldo P, Goncalves AK, Pereira SA, et al. Human papillomavirus in the oral mucosa of women with genital human papillomavirus lesions. Eur J Obstet Gynecol Reprod Biol 2006; 126: 104–106.
10. Kreimer AR, Alberg AJ, Daniel R, et al. Oral human papillomavirus infection in adults is associated with sexual behavior and HIV serostatus. J Infect Dis 2004; 189:686–698.
11. Kujan O, Desai M, Sargent A, et al. Potential applications of oral brush cytology with liquid-based technology: Results from a cohort of normal oral mucosa. Oral Oncol 2006; 42:810–818.
12. Kurose K, Terai M, Soedarsono N, et al. Low prevalence of HPV infection and its natural history in normal oral mucosa among volunteers on Miyako Island, Japan. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004; 98:91–96.
13. Lambropoulos AF, Dimitrakopoulos J, Frangoulides E, et al. Incidence of human papillomavirus 6, 11, 16, 18 and 33 in normal oral mucosa of a Greek population. Eur J Oral Sci 1997; 105: 294–297.
14. Marais DJ, Sampson C, Jeftha A, et al. More men than women make mucosal IgA antibodies to human papillomavirus type 16 (HPV-16) and HPV-18: A study of oral HPV and oral HPV antibodies in a normal healthy population. BMC Infect Dis 2006; 6:95.
15. Montaldo C, Mastinu A, Quartuccio M, et al. Detection and genotyping of human papillomavirus DNA in samples from healthy Sardinian patients: A preliminary study. J Oral Pathol Med 2007; 36:482–487.
16. Ragin CC, Wheeler VW, Wilson JB, et al. Distinct distribution of HPV types among cancer-free Afro-Caribbean women from Tobago. Biomarkers 2007; 12:510–522.
17. Rintala M, Grenman S, Puranen M, et al. Natural history of oral papillomavirus infections in spouses: A prospective Finnish HPV Family Study. J Clin Virol 2006; 35:89–94.
18. Smith EM, Ritchie JM, Yankowitz J, et al. HPV prevalence and concordance in the cervix and oral cavity of pregnant women. Infect Dis Obstet Gynecol 2004; 12:45–56.
19. Smith EM, Swarnavel S, Ritchie JM, et al. Prevalence of human papillomavirus in the oral cavity/oropharynx in a large population of children and adolescents. Pediatr Infect Dis J 2007; 26:836–840.
20. Summersgill KF, Smith EM, Levy BT, et al. Human papillomavirus in the oral cavities of children and adolescents. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001; 91:62–69.
21. Winer RL, Lee SK, Hughes JP, et al. Genital human papillomavirus infection: Incidence and risk factors in a cohort of female university students. Am J Epidemiol 2003; 157:218–226.
22. United Nations Public Administration Network. List of country groupings and sub-groupings for the analytical studies of the United Nations World Economic Survey and other UN reports. Available at: http://unpan1.un.org/intradoc/groups/public/documents/un/unpan008092.pdf. Accessed 07 July 2009.
23. D'Souza G, Sugar E, Ruby W, et al. Analysis of the effect of DNA purification on detection of human papillomavirus in oral rinse samples by PCR. J Clin Microbiol 2005; 43:5526–5535.
24. Higgins JP. Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. Int J Epidemiol 2008; 37:1158–1160.
25. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994; 50:1088–1101.
26. Egger M, Smith GD, Schneider M, et al. Bias inmeta-analysis detected by a simple, graphical test. Br Med J 1997; 315:629–634.
27. de Sanjose S, Diaz M, Castellsague X, et al. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: A meta-analysis. Lancet Infect Dis 2007; 7:453–459.
28. Munoz N, Bosch FX, de Sanjose S, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med 2003; 348:518–527.
29. Koshiol J, Lindsay L, Pimenta JM, et al. Persistent human papillomavirus infection and cervical neoplasia: A systematic review and meta-analysis. Am J Epidemiol 2008; 168:123–137.
30. Zumbach K, Hoffmann M, Kahn T, et al. Antibodies against oncoproteins E6 and E7 of human papillomavirus types 16 and 18 in patients with head-and-neck squamous-cell carcinoma. Int J Cancer 2000; 85:815–818.
31. Mao C, Koutsky LA, Ault KA, et al. Efficacy of human papillomavirus-16 vaccine to prevent cervical intraepithelial neoplasia: A randomized controlled trial. Obstet Gynecol 2006; 107:18–27.
32. Harper DM, Franco EL, Wheeler CM, et al. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: Follow-up from a randomised control trial. Lancet 2006; 367:1247–1255.
33. Sturgis EM, Cinciripini PM. Trends in head and neck cancer incidence in relation to smoking prevalence: An emerging epidemic of human papillomavirus-associated cancers? Cancer 2007; 110:1429–1435.

Copyright © by the American Sexually Transmitted Diseases Association. Unauthorized reproduction of this article is prohibited.