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Review article

Age-Specific Prevalence of Human Papillomavirus Infection in Males: A Global Review

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A B S T R A C T

Purpose: Global data on age-specific prevalence of human papillomavirus (HPV) infection in males, especially for oncogenic HPV types 16 and 18, are essential for future efforts to prevent HPV-related diseases, including expanded access to HPV prophylactic vaccines for boys and young men.
Methods: A systematic review of peer-reviewed publications was conducted to summarize worldwide data on genital HPV-DNA prevalence in men. Studies using polymerase chain reaction or hybrid capture detection assays were included.
Results: Approximately 6,600 abstracts were identified. Of them, 64 reported age-specific HPV prevalence and were included in the review. Of these, 38 were from populations at high risk of HPV infections, such as sexually transmitted infection clinic attendees, human immunodeficiency virus-positive males, and male partners of women with HPV infection or abnormal cytology. The largest proportions of studies were from Europe (38%) and North America (25%), with smaller proportions from Central and South America (19%), Asia (11%), and Africa (5%). Across all regions, data on HPV prevalence were generally limited to men >18 years of age. HPV prevalence was high among sexually active men in all regions but with considerable variation, from 1% to 84% among low-risk men and from 2% to 93% among high-risk men. Peak HPV prevalence spanned a wide range of ages and was generally not concentrated in the younger age groups. Age-specific prevalence curves were relatively flat or declined only slightly following peak prevalence.
Conclusions: Genital HPV infection in men varies widely, both between and within high- and low-risk groups and by geographic region. Compared with that in women, HPV prevalence in men seems to peak at slightly older ages and remains constant or decreases slightly with increasing age, suggesting persistent HPV infection or a higher rate of reinfection.

The development of effective prophylactic vaccines against human papillomavirus (HPV) types 16 and 18 [1,2] has significantly advanced the prevention of invasive cervical cancer, the second most common cancer in women worldwide [3]. Subsequently, there has been increasing interest in extending HPV vaccination to men [4–6], in whom genital warts and oropharyngeal, anal, and penile cancers are also manifestations of HPV infection [7–10]. In October 2009, the US Food and Drug Administration approved use of the quadrivalent HPV vaccine (Gardasil; Merck & Co., Inc., Whitehouse Station, NJ) in males aged 9–26 years for prevention of genital warts [11,12].

HPV is one of the most common sexually transmitted infections (STIs) worldwide [13], yet prevalence estimates in males vary widely. Among males who report no previous sexual activ-

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ity, the detection of HPV from anogenital swab samples is negligible [14,15]. A wide range of HPV prevalence in sexually active males has been reported [2,16], which varied with regard to geographic area, anatomical site, and sampling method. Several groups at higher risk of HPV infection have been identified, including men with multiple sex partners [17,18] and men who are infected with human immunodeficiency virus (HIV) [19,20].

Compared with the global data available on HPV in women [21], there are limited data on population-based samples of men from different geographic areas. The extent to which HPV infection in males varies by age, country, region within country, and population subgroup is largely unexplored. To compare HPV prevalence between geographic areas or countries, data on age-specific or age-adjusted prevalence using sensitive HPV detection methods are needed. Global data on age-specific prevalence, especially for oncogenic HPV types, are essential for future efforts to prevent HPV-related diseases in men and their sexual partners.

This review summarizes the available published data on the prevalence of HPV-DNA in men, based on highly sensitive detection techniques and associated HPV prevalence curves by age for different populations throughout the world.

Methods

Material reviewed

A systematic search via PubMed of literature published from January 1, 1989, through June 30, 2009, identified approximately 6,600 abstracts concerning HPV and men. Key search words included *papillomavirus*, *human*, *polymerase chain reaction* (PCR), *hybrid capture* (HC), and *viral DNA*. The literature search was restricted to peer-reviewed articles providing a clear description of PCR or HC methodology for detection of HPV infection. Studies using relatively less sensitive detection methods (i.e., in situ hybridization) or the detection of HPV serum antibodies were excluded. Studies were limited to those that provided data on age; sample sizes were at least 20 per age group; and age groups were combined when necessary. There were no language restrictions. Articles were reviewed in full if abstracts indicated fulfilling these criteria. Reference lists of included articles were also checked for eligible articles. Conference abstracts and other unpublished manuscripts were excluded.

Data extraction and analysis

For each study, we extracted the following: first author, publication journal, and date; country and city of study; dates of sample collection; HPV detection methodology (e.g., PCR primers or HC–II); anatomical site and method of sample collection; population description (e.g., national survey, STI clinic attendees); mean or median age of sample, with range when available; sample size; and prevalence of HPV in the total population sample. We report overall prevalence of all HPV types measured in a sample; whenever available we also report prevalences of high-risk types, low-risk types, HPV-16, and HPV-18. Because HPV prevalence was measured differently across studies and was dependent on the particular laboratory assay used (e.g., HC–II, PCR-overall, type-specific), we provide details of the HPV detection assay used in each study in the tables. High-risk populations were defined as having a greater risk of acquiring genital HPV infection, such as STI clinic attendees, HIV-positive males, and male partners of women with HPV infection or abnormal cytology; all others were classified as "low-risk" populations [22]. When published results were presented only graphically, prevalence was estimated from these graphical representations. In cases when age-stratified sample sizes were not available, overall HPV prevalence was reported, for which a sample size was available with the mean or median age. For articles presenting data on HPV prevalence for both PCR and HC, all results were presented in the tables, although only PCR results were presented in the figures. A smoothed prevalence curve was estimated among low-risk Central/South American populations and is shown in the inset on Figure 1; we were unable to estimate a smoothed prevalence curve for high-risk populations because there were no more than two studies that reported prevalences in any region. For quality control, 80% of data were entered twice by two independent data abstractors, and discordant results

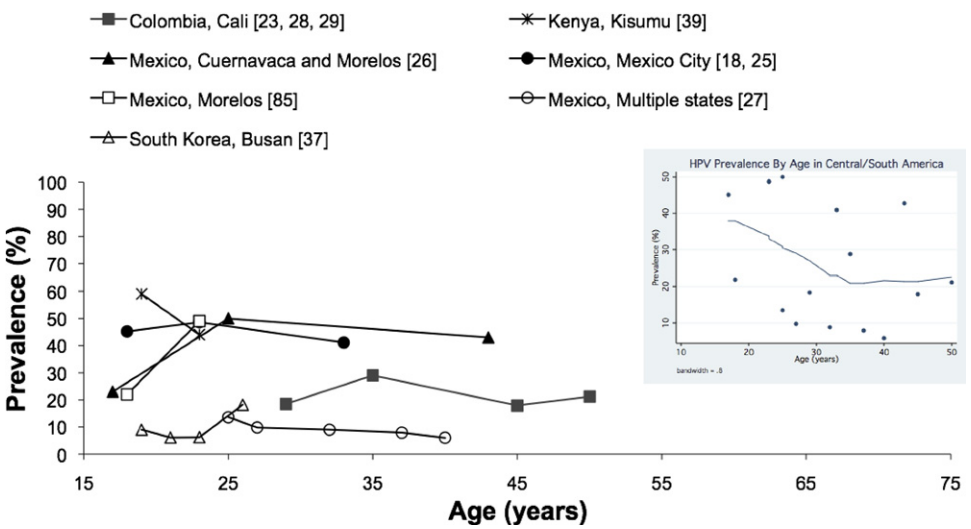

Figure 1. HPV prevalence by age for low-risk male population by country, city, and study. For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.

were resolved by consensus. When studies presented data on HPV with the same population in multiple publications, the largest publication was chosen, and references to all corresponding publications were included with data tables for that particular study. Where HPV data are defined in the tables for individuals within an age group, the mean of the age range was used for graphical representation of data points.

Results

Twenty-six studies on low-risk male populations and 36 studies on high-risk male populations were selected for the review, including HPV-DNA prevalence data from more than 14,800 men in 23 countries. HPV prevalence was generally high among sexually active men but with considerable variation, that is, from 1% to 84% among low-risk men and from 2% to 93% among high-risk men. Observed prevalence varied within and across regions. The results of both low- and high-risk populations varied. Results are presented separately for low- and high-risk populations in Tables 1 and 2, respectively. Within each geographic area, studies were arranged alphabetically by country and then by region or state within the country. HPV positivity was determined in exfoliated cells obtained by cytology brush or swab, predominately from the coronal sulcus, glans, prepuce, shaft, urethra, scrotum, perianal area, and anus. Similarly, most studies in the present review for both high- and low-risk groups collected exfoliated cells from these anatomical sites (often with additional exfoliated cell sampling). Fewer than 10% of studies used semen or urine.

Overall age-specific HPV prevalence

A worldwide study of men in Brazil, Columbia, Thailand, the Philippines, and Spain, with a median age of approximately 46 years (range: 19–82 years), reported an overall HPV prevalence of 16% [24,91]. HPV prevalence was 16% in men aged <30 years and was 15% in those aged 40–49 years. For men aged 50 and older, HPV prevalence increased to 19%.

Low-risk Central and South American populations. Among seven studies conducted in Central and South America, five were conducted in Mexico, where the observed overall prevalence varied widely (6%–50%). Soldiers in Mexico City (mean age: 23 years) [18] and Morelos (mean age: 24 years) [29] had overall HPV prevalence of 45% and 46%, respectively. Peak prevalence among soldiers aged 21–24 years was 49% in Mexico City [18]. Males in Cuernavaca and Morelos, Mexico (mean age: 29 years) had an overall prevalence of 43% and a similar peak prevalence of 50% in those aged 20–29 years (Figure 1) [28]. These studies had much higher prevalence rates than of men attending vasectomy clinics in Mexico (mean age: 30 years), who had an overall HPV prevalence of 9% and a peak prevalence of 14% in males under 25 years of age [27]. Prevalence of HPV-16 and HPV-18 also varied between studies. Soldiers in Mexico City (mean age: 23 years) had HPV-16 and HPV-18 prevalences of 6% and 4% [18,29], respectively, accounting for 8%–13% of overall HPV prevalence, whereas men attending vasectomy clinics (mean age: 34 years) had HPV-16 and HPV-18 prevalences of .8% and .5%, accounting for 6%–9% of overall HPV prevalence [27]. A study of male partners of women without a previous diagnosis of HPV infection or abnormal cervical cytology in Cali, Columbia (mean age: 46 years) [25,26] reported an overall prevalence of 29% and an HPV-16 prevalence of 2% [25,26]. The highest HPV prevalence in the region was reported in a sample of university students (mean age: 23 years) in Temuco, Chile, with an overall HPV prevalence of 84%, that is, HPV-16 prevalence was 45% and HPV-18, 9% [23].

Low-risk North American populations. Five low-risk populations of men were reported in North America. Male university students from Hawaii (mean age: 29 years), Tampa, FL (no mean/median age reported), Tucson, AZ (no mean/median age reported), and Seattle, WA (mean age: 20 years), sampled at multiple anatomical sites, had overall HPV prevalences between 26% and 65% [2,32,35,36]. In addition, the prevalences of HPV-16 and HPV-18 among university students ranged between 5% and 11%, and 2% and 3%, respectively. In contrast, semen samples from volunteers without a previous or current diagnosis of HPV infection in Saskatchewan, Canada (median age: 27 years) showed overall HPV prevalence of 8% [31].

Low-risk Asian populations. Lower overall HPV prevalence was observed in four Asian low-risk male populations compared with data on low-risk men from other regions. Overall HPV prevalence peaked at 8% and 9% for men without a previous diagnosis of HPV infection or current visible genital warts in Japan (mean age: 23 years) [38,39] and South Korea (mean age: 22 years) [40], respectively. In South Korea, the prevalence of both HPV-16 and HPV-18 was .5%. Husbands of women without a previous diagnosis of HPV infection or abnormal cervical cytology (mean age: 47 years) from an unspecified Indian city had an overall HPV prevalence of 27% and an HPV-16 prevalence of 3% [37]. This higher observed HPV prevalence in South Asia was consistent with overall prevalences previously reported in some female studies in India [21].

Low-risk African populations. Three studies reported high HPV prevalences among males in Africa. Two studies in Kenya reported overall prevalences of HPV: 54% among men aged 17–25 and 58% among men aged 18–63 [48,19]. The second study also reported high prevalences of HPV-16 (12%) and HPV-18 (7%) among a sample of Kenyan men with a wide age range. In a South African sample (no mean/median age reported), researchers found a prevalence of high-risk HPV types of 19% [50].

Low-risk European populations. In Europe, prevalence was lower than in Africa and intermediate compared with Asia. The highest prevalence was observed in soldiers from Copenhagen, Denmark (mean age: 20 years), who had an overall HPV prevalence of 34% and an HPV-16 prevalence of 6% [17]. Military conscripts in Finland (mean age: 20 years) [41] and Sweden (mean age: 21 years) [47] had overall HPV prevalences of approximately 9%. "Clinically healthy" males in Turku, Finland, undergoing vasectomy (mean age: 40 years) had an overall HPV prevalence of 19% and HPV-16 prevalence of 11% [42–44]. This differed from low-risk males in Italy (mean age: 60 years) [45] and Spain (mean age: 45 years) [24–26], who had overall HPV prevalences of 9% and 4%, respectively, and HPV-16 prevalences of 4% and .6%, respectively.

High-risk Central and South American populations. In Central and South America, all high-risk populations were male partners of HPV-DNA-positive women or women with cervical intraepithelial neoplasia (CIN) or cervical cancer. In South America, overall HPV prevalence varied greatly between populations, from 70%

Table 1
HPV prevalence estimates in men from low-risk populations by continent, country, and study year[a]

Study location, dates, reference	Assay	Site of specimen	Group tested	Mean or median age, years (range)	Sample size	Prevalence (%)				
						Overall HPV	High-risk HPV types	Low-risk HPV types	HPV-16	HPV-18
Central/South America										
Chile, Temuco, no dates reported [23]	GP5+/6+ PCR	Shaft, coronal sulcus	University students	22.8 (20–51)	61	84			45	9
Colombia, California, 1985–1987 [24–26]	MY09/11+ HMB01	Coronal sulcus. Distal and intrameatal urethra, glans—wet swab	Partners of women with normal cytology	46.0	132	29.0	8.3	5.5	2.3	
				≤29	27	18.5				
				30–39	62	29.0				
				40–49	67	17.9				
				≥50	85	21.2				
Mexico, multiple cities, 2003–2004 [27]	L1 PCR with biotinylated primers	Coronal sulcus, glans, meatus, scrotum, shaft—wet brush	Men attending vasectomy clinics	34.0	799	8.7	6.0	4.2	.8	.5
				<25	66	13.6	10.6			
				25–29	183	9.8	7.7			
				30–34	212	9.0	5.2			
				35–39	152	7.9	4.6			
				≥40	166	6.0	4.8			
Mexico, Cuernavaca and Morelos, 1998 [28]	GP5+/6+	Coronal sulcus and urethra—swab	Sexually active males (automobile industry workers and college students)	29.3 (14–55)	96	42.7	19.8	17.7		
				<20		23.0				
				20–29		50.0				
				≥30		43.0				
Mexico, Mexico City, 2000–2003 [18, 29]	BGH20/BPCO4	Coronal sulcus, scrotum, and shaft—swab/brush urethra, and urethral meatus—swab	Soldiers	23 (16–40)	1,030	44.6	34.8	23.9	6.0	3.7
				<21	385	45.2				
				21–24	286	48.6				
				>24	353	41.1				
Mexico, no city reported, 2001–2002 [29]	MY09/11, L1	Coronal sulcus, glans, scrotum, shaft, tip—wet brush and/distal urethra—wet swab, or meatus urethralis—swab	Soldiers	24.0 (16–50)	582	46.4			5.5	4.0[b]
Mexico, Morelos, 2000–2001 [30]	HCII	Glans and prepuce—swab	University students	18−~26	71		8.5			
				16–20	22		9.1			
				≥21	49		8.2			
North America										
Canada, Saskatchewan[d] [31]	MY09/11	Semen	Volunteers with no prior or current HPV infection	27[d] (20–41)	40	8.0				
USA, Florida (Tampa) and Arizona (Tucson), 2003–2006 [32–34]	PGMY 09/11	Glans/coronal sulcus, shaft, scrotum, perianal area, anus—wet swab	Heterosexual men (general public, college students, military, STD clinic attendees)	No mean/ median age reported (18–40)	463	65.4	29.2	36.3	11.4	1.9
USA, Hawaii, no city reported, 2004–2005 [35]	MY09/11+ HMB01	Coronal sulcus, glans, shaft—wet swab	University students—physician collected sample	28.5 (18–63)	385	41.3			7.2[b]	2.5[b]
			University students—self-collected sample	28.5 (18–63)	418	42.8			7.5[b]	1.5[b]
USA, Washington, Seattle, 2000–2002 [36]	MY09/11+ HMB01	Glans, prepuce, scrotum, shaft—emery paper, wet swab	University students	20.5 (18–25)	317	32.8				
USA, Washington, Seattle, 2003–2006 [2]	QIAamp	Glans, shaft, scrotum—emery paper, wet swab	University students	19.4 (18–20)	240	25.8	20.0	13.3	5.4	2.5

Table 1
Continued

Study location, dates, reference	Assay	Site of specimen	Group tested	Mean or median age, years (range)	Sample size	Prevalence (%)				
						Overall HPV	High-risk HPV types	Low-risk HPV types	HPV-16	HPV-18
Asia										
India, no city reported[c] [37]	L1	Coronal sulcus, distal and intrameatal urethra, glans—wet swab, urine	Husbands of women with normal cytology	46.9	30	26.7			3.3	
Japan, multiple cities[c] [38]	HC II (Digene)	Coronal sulcus, glans, prepuce—self-sampled wet swab	University students with no visible genital warts	22[d] (18–35)	75	1.3	1.3	.0		
Japan, Sapparo[d] [39]	HC II (Digene)	Coronal sulcus, glans, inner prepuce—self-sampled wet swab	University students with no visible genital warts	22.5 (18–35)	150	8.0	8.0	.1		
South Korea, Busan, 2002 [40]	Type-specific PCR (6, 11, 16, 18, 31, 33–35, 39, 40, 42–45, 51–54, 56, 68, 59, 66, 68, 73, 70, 74)	Coronal sulcus, glans, scrotum, and tip—wet brush, urethra—wet swab	University students	22 (18–28) ≤19 20–21 22–23 ≥24	381 100 49 177 55	8.7 9.0 6.1 6.2 18.2	4.5	3.7	.5	.5
Europe										
Denmark, Copenhagen, 1998 [17]	GP5+/6+	Coronal sulcus, and glans—wet swab	Soldiers	20.3 (18–29)	337	33.8			5.6	
Finland, Kontioranta, Ylamylly and Kuopio, 1992 [41]	MY09/11	Coronal sulcus, glans, meatus prepuce, urethral meatus—brush	Military conscripts	19.8	175	9.1				
Finland, Turku, 1998–2000, [42,43]	MY09/11, GP5+/6+	Distal urethra—brush	Husbands of third trimester pregnant women	28.1 (19–43)	76	16.0				
Finland, Turku, 1998–1999 [44]	MY09/11, GP5+/6+	Vas deferens—biopsy	"Clinically healthy" males undergoing vasectomy	40.3 (33–49)	27	18.5		7.4 (6.11)	11.1	
Italy, Catania, and Rome[c] [45]	MY09/11, GP5+/6+	Penile mucosa—brush	Hospital based controls attending clinic for nongenital complaints	59.5 (27–79)	46	8.7			4.3	
Spain (nine provinces), 1985–1987 [24,25,46]	MY09/11, HMB01	Coronal sulcus, glans, distal and intrameatal urethra—wet swab	Partners of women with normal cytology	45.4	171	3.5	2.3	1.2	.6	
Sweden, no city reported, 1991 [47]	Type-specific PCR (6, 11, 16, 18, 33)	Urethra—wet brush	Military conscripts	21 (20–23)	138	8.7			3.6	
Africa										
Kenya, Kisumu, 2002–2005 [48]	GP5+/6+ PCR	Glans/coronal sulcus, urethra—wet swab	Sexually active male participants in clinical trial of circumcision	22 (17–25) <21 ≥21	98 44 59	54				
Kenya, Kisumu[c] [49]	QIAamp DNA	Coronal sulcus, shaft, scrotum, perianal—wet swab	Fishermen along Lake Victoria short	31.3 (18–63)	250	57.6	42.4	43.2	12.4	6.8
South Africa, Orange Farm, 2002–2004 [50]	Roche Amplicor HPV test	Urethral swab	Men enrolled in trial of male circumcision	No mean/median age reported (18–24)	1,264		18.5			

HC = hybrid capture; HPV = human papillomavirus; PCR = polymerase chain reaction; STD = sexually transmitted disease; DNA = deoxyribonucleic acid.
[a] Low-risk populations exclude male STI clinic attendees, HIV positive males, and male partners of women with HPV infection or abnormal cytology.
[b] Estimate via calculation or graph.
[c] Date of sample collection was not specified.
[d] Median.

Table 2
HPV prevalence estimates in men from high-risk populations by continent, country and study year[a]

Study location, dates, reference	Assay	Site of specimen	Group tested	Mean or median age, years (range)	Sample size	Prevalence (%)				
						Overall HPV	High-risk HPV types	Low-risk HPV types	HPV-16	HPV-18
Central/South America										
Argentina, La Plata, 2004 [51]	MY09/11 + GP5+/6+	Voided urine	Men whose female partners are HPV positive	31 (17–71)	112	68.8			16.1	2.7
Brazil, Caxias do Sul, 2003–2004 [52]	L1, MY09/11	Prepuce, preglans, shaft, urethral canal—brush	Partners of women with CIN	31.7[b] (18–59)	99	54.5			2.0	
				18–29	49	55.1				
				30–39	25	64.0				
				40–59	25	40.0				
Brazil, no city reported, 1997–2000 [53]	HCII (Digene)	Anus, distal urethra, glans, prepuce, and scrotum—wet brush	Partners of HPV-positive women	31 (19–53)	50	70.0	32.0	14.0		
Colombia, California, 1985–1987 [25, 26]	MY09/11 + HMB01	Coronal sulcus, distal and intrameatal urethra, glans—wet swab	Partners of women with cervical cancer	45.2	109	25.7	12.8	4.6	5.5	
Mexico, Mexico City, 1997–1998 [54]	L1	Urethra—swab	Partners of women with CIN	33.3[c] (17–64)	187	2.0				
North America										
Canada, British Columbia, Vancouver[d] [55]	Roche Amplicor HPV test	Shaft, scrotum—emery paper, wet swab	Heterosexual men attending provincial STD clinic	29 (16–69)	262	62.6	24.0		18.7	8.4
Canada, Ontario, Toronto, 2001–2005 [56]	PGMY09/11	Anus—swab	HIV positive MSM participants in TRACE study	44 (38–50)	224	93	79			
USA (13 cities)[d] [57]	MY09/11 + HMB01	Anus—wet swab	High-risk adolescent boys in REACH cohort	(13–18)	83	44.6	20.5	27.7	6.0	.0
USA, Massachusetts (Boston), Colorado (Denver), New York (NY), California (San Francisco), 1999–2001 [58]	MY09/11	Anus—wet swab	HIV negative MSM in EXPLORE cohort	37[c] (18–89)	1218	57	26	26	12	
				<25	98	51	16	28		
				25–29	167	54	25	29		
				30–34	271	61	30	28		
				35–39	273	59	26	31		
				40–44	180	54	26	22		
				45–49	125	58	23	22		
				50–54	53	57	26	13		
				≥50	51	53	22	22		

Table 2
Continued

Study location, dates, reference	Assay	Site of specimen	Group tested	Mean or median age, years (range)	Sample size	Prevalence (%)				
						Overall HPV	High-risk HPV types	Low-risk HPV types	HPV-16	HPV-18
USA, Arizona, Tucson, 2000–2001 [59, 60]	MY09/11	Coronal sulcus, glans, and urethra—wet swab	STI clinic attendees	30.9 (18–70)	393	28.2	12.0	14.8	2.3	1.0
				18–24	125	33.6				
				25–29	96	19.8				
				30–39	88	25.0				
				40–70	83	32.5				
USA, California, San Francisco, 1991–1994 [19, 61]	MY09/11	Anus—swab	HIV± homosexual or bisexual men	43.2[b] (24–73)	489	80.0				
			HIV+ homosexual or bisexual men	42 (24–64)	289	93.1			38.0	28.0
			HIV− homosexual or bisexual men	45 (26–73)	200	61.0			19.0	3.0
USA, California, San-Francisco, 2004 [62]	PCR	Anus—wet swab	Subsample of MSM participants in Urban men's Health Study	44 (24–73)	125					
			HIV+ homosexual or bisexual men		38	88.0	72.0			
			HIV− homosexual or bisexual men		87	57.0	34.0			
USA, California, San–Francisco, 1990–1991 [63]	MY09/11	Anus—swab	HIV+ homosexual or bisexual men with CDC group IV disease	41 (24–66)	118	93.2			48.0[b]	25.0[b]
USA, Indiana, Indianapolis, 2002 [64]	Type-specific PCR (6,11)	Glans, inguinal skin, perianal area and perineum scrotum, and shaft—dry swab	STI clinic attendees with no history of genital warts	(18–50)	20			10.0		
USA, New York, Washington, DC, 1982 [65]	Type-specific PCR (6, 11, 16, 18, 31, 33, 35)	Anus—wet swab	HIV± homosexual men	40.6[b]	105	39.0			7.6	
USA, Washington, Seattle, 1989–1997 [20, 66, 67]	MY09/11	Anus—dry swab	HIV+ homosexual men presenting at AIDS prevention project	28.0	322	91.6	55.9	49.1	51.8	
			HIV-homosexual men presenting at AIDS prevention project	29.0	287	65.9	28.9	36.2	38.2	
USA, Washington, Seattle, 1991–1992 [68]	MY09/11	Penis—swab	STI clinic attendees	28.7	50	62.5			17.0[b]	
Asia										
China, Hangzhou, 2003–2004 [69]	MY09/11	Urethral meatus—swab	STI clinic attendees	28.5 (18–70)	305	13.8	4.3	8.5	2.3	1.0
				18–29	124	16.1				
				30–39	134	12.7				
				40–70	47	10.6				
India, no city reported[d] [37]	L1 consensus primers and type specific PCR (16, 18)	Coronal sulcus, glans, intrameatal urethra—wet swab urine	Partners of women with cervical cancer	46.4	30	66.7			30	

Table 2
Continued

Study location, dates, reference	Assay	Site of specimen	Group tested	Mean or median age, years (range)	Sample size	Prevalence (%)				
						Overall HPV	High-risk HPV types	Low-risk HPV types	HPV-16	HPV-18
Japan, multiple cities[d] [38]	HC II (Digene)	Coronal sulcus, glans, prepuce—wet swab	Patients with urethritis	28 (17–49)	130	18.5	15.4	9.2		
Europe										
Denmark, Copenhagen, 1993 [70, 71]	GP5+/6+ type-specific PCR (6, 11, 16, 18, 31, 33)	Coronal sulcus, glans, perianal area, scrotum, and shaft—wet swab	STI clinic attendees	31.9 (≥18)[b]	198	44.9	12.6	9.1	6.6	3.5
				18–24	44	47.7				
				25–29	63	52.4				
				30–39	66	37.9				
				≥40	25	40.0				
				18–24	30		23.3	20.7		
				25–34	68		22.1	15.9		
				≥35	36		8.3	5.7		
England, London, 1990 [72] [2436]	GP5+/6+	Urethra—swab	Men infected with gonorrhea	26.7 (17–55.6)	100	18.0	15.0 (16, 18, 31, 33)		6.0	8.0
France, Paris[d] [73]	Type-specific PCR (6, 11, 42, 16, 18, 33)	Semen	Men with normal peniscopy whose female partners have genital HPV lesions	29 (19–42)[b]	46	2.2		2.2		
France, Paris[d] [74]	Type-specific PCR (6, 11, 42, 16, 18, 33)	Meatal urethra—brush	Men with normal peniscopy whose female partners have genital HPV lesions	30	34	14.7			2.9	
Greenland, Nuuk[d] [70]	Type-specific PCR (6, 11, 16, 18, 31, 33)	External genital area – wet swab	STI clinic attendees	30.2 (18–58)	88	48			7	
Italy, Palermo, 2003–2005 [75]	LiPA, GP5+/6+, MY09/11	Coronal sulcus, frenulum, glans, prepuce, shaft—dry swab, urethra—wet brush, semen	Partners of HPV-positive women	36.7 (23–58)	50	72.0	62.0	36.0	8.0	
Italy, Rome, 2004–2006 [76]	PCR	Coronal sulcus, urethra, prepuce, shaft—cytobrush	Male partners of women with CIN and/or positive HPV	37.6 (20–61)	71	35	31	4	12.7	4.2
The Netherlands, Amsterdam, 1989–1990 [77, 78]	Type-specific PCR (6/11, 16, 18, and 33)	Anus, coronal sulcus, rectum, urethra—swab	STI clinic attendees	38 (≥18)	65	16.9			4.6	10.8
The Netherlands, Amsterdam and Dordrecht, 1995–2002 [79–83]	GP5+/6+	Corona, frenulum, glans, inner prepuce and sulcus—brush	Men visiting department of dermatology for non-STI complaints	46.1 (22.8–73.2)	83	25.3	19.3	12.0	4.8	2.4
			Partners of women with dyskaryosis and/or CIN	37.6 (22.5–57.7)	181	72.9	58.6	27.1	34.8	3.9
The Netherlands, Rotterdam, 1999–2000 [84]	Type-specific PCR (6, 11, 16, 18, 26, 31, 33) and PCR reverse hybridization (6, 11, 16, 18, 26, 31, 33, 34, 35, 39, 40, 42–45, 51-54, 56, 58, 59, 66, 68, 70, 74)	Perianal area—dry swab	HIV± MSM	43	258	34.9			9.1	3.7

Table 2
Continued

Study location, dates, reference	Assay	Site of specimen	Group tested	Mean or median age, years (range)	Sample size	Prevalence (%)				
						Overall HPV	High-risk HPV types	Low-risk HPV types	HPV-16	HPV-18
Spain, (nine provinces), 1985–1987 [24,25,46]	MY09/11 +HMB01	Coronal sulcus, glans, distal and intrameatal urethra—wet swab	Partners of women with cervical cancer	44.7	183	17.5	15.8	2.2	4.9	
			Partners of women with cervical cancer and control women	≤29	28	14.3				
				30–39	128	10.2				
				40–49	92	12.0				
				≥50	106	9.4				
Spain, Barcelona, 2005 [85]	MY09/11 (6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68)	Anus, coronal sulcus, distal urethra, and glands—brush	HIV+ men	42	74	78 (Anal) 36 (Penile)				
Sweden, Göteborg[d] [86]	MY09/11, GP5+/6+	Glans and prepuce—brush	STI clinic attendees	31 (19–67)	20	25.0				
Sweden, Göteborg, 1995–1996 [87]	MY09/11	Anal—swab	HIV± STI clinic attendees	34.5[b] (26–62)	30	76.7			26.7	
Sweden, Stockholm, 1999 [88]	GP5+/6+	Coronal sulcus, glans, prepuce—brush	STI clinic attendees	27.1 (18–54)	235	13.2			2.6	1.7
Sweden, Stockholm[d] [89]	Type-specific PCR (6, 11, 16)	Coronal sulcus, meatal urethra, and prepuce—brush/swab	Men with no prior history of genital warts attending an STI clinic	28 (17–58)	135	50			13	
Sweden, Uppsala, 1991–1992 [90]	MY09/11 and GP5+/6+	Coronal sulcus, glans, preputium, and shaft—swab	STI clinic attendees	25 (20–53)	65	29.2				
Worldwide: Brazil, Colombia, Thailand, Philippines, Spain, 1985–1993 [24, 91]	MY09/11, GP5+/6+	Coronal sulcus, glans, and urethra—wet swab	Partners of women with CIN III, ICC or controls from a multicenter study	46[b] (19–82)	1,143	16.0			3.9	.8
				<30	73	16.4				
				30–39	294	15.3				
				40–49	314	14.7				
				50–59	260	16.2				
				60	202	18.8				

CIN = cervical intraepithelial neoplasia; HC = hybrid capture; HPV = human papillomavirus; ICC; MSM = men who have sex with men; PCR = polymerase chain reaction; STI = sexually transmitted infection; TRACE = Toronto Research for Anal Cancer Evaluation; REACH = Reaching for Excellence in Adolescent Care and Health; AIDS = acquired immune deficiency syndrome; EXPLORE = HIV Prevention Trials Network EXPLORE Study.

[a] High-risk populations include male STI clinic attendees, HIV positive males, and male partners of women with HPV infection or abnormal cytology.

[b] Estimate via calculation or graph.

[c] Median.

[d] Date of sample collection was not specified.

and 69% in male partners of HPV-positive women in Sao Paulo (mean age: 31 years) [53] and La Plata, Argentina (mean age: 31 years) [51], respectively, to 26% in partners of women with cervical cancer in Cali, Colombia (mean age: 45 years) [25,26]. Relatively high HPV-16 and HPV-18 prevalences were observed in La Plata (16% and 2.7%, respectively) [51]. Age-specific prevalence in male partners of women with CIN from Caxias do Sul, Brazil, ranging in age from 18 to 59 years, showed a peak prevalence of 64% in those aged 30–39 years [52]. The only high-risk population in Central America consisted of partners of women with CIN from Mexico City (median age: 33 years), who had a low overall HPV prevalence (2%) in urethral swabs among participating men [54].

High-risk North American populations. Twelve studies reported HPV prevalence among high-risk populations in North America, 10 of which were from the United States (Table 2). HIV-positive men who have sex with men (MSM) showed the highest prevalences. In San Francisco, HIV-positive MSM (mean age: 42 years) and HIV-negative MSM (mean age: 45 years) had overall anal HPV prevalences of 93% and 61%, respectively [19,61,63]. In Toronto, Canada, overall HPV prevalence among HIV-positive men (mean age: 44 years) was 93% [56]. In Seattle, HIV-positive MSM (mean age: 28 years) and HIV-negative MSM (mean age: 29 years) had overall prevalences of 92% and 66%, respectively [20,66,67]. Anal samples from young males in the Reaching for Excellence in Adolescent Care and Health [REACH] cohort (13–18 years of age), drawn from 13 cities in the United States, had an overall and HPV-16 prevalence of 45% and 6.0%, respectively [57]. HIV-negative MSM in the EXPLORE cohort (mean age: 37 years) had an overall anal HPV prevalence of 57% [58]. In this cohort, all age groups (ranging from 18–25 years of age to 50–89 years of age) showed stable prevalences >50%, with a peak prevalence of 61% in those aged 30–34 years [58].

Penile samples from male STI clinic attendees in Seattle (mean age: 29 years) and Vancouver (mean age: 29 years) both had an overall HPV prevalence of 63% [55,68]. This was higher than STI clinic attendees in Tucson (mean age: 31 years), who had an overall HPV prevalence of 28% and more of a U-shaped HPV age-specific prevalence [59,60]. Peak HPV prevalence was approximately 34% in males 18–24 years of age and decreased to 20% and 25% in those aged 25–29 years and 30–39 years, respectively, before increasing to an overall prevalence of 33% in males 40–70 years of age [59,60].

High-risk Asian populations. Only three high-risk populations were reported in Asia (Table 2). Similar to lower overall HPV prevalences observed in other Asian populations [21], STI clinic attendees in Hangzhou, China (mean age: 29 years) [69] and urethritis patients in Japan (mean age: 28 years) [38] had overall HPV prevalences of approximately 14% and 19%, respectively. Age-specific prevalence of HPV in Hangzhou males showed a peak prevalence of 16% in those aged 18–29 years, decreasing to approximately 11% in those aged 40–70 years [69]. In contrast, husbands of women with cervical cancer in India (mean age: 46 years) had an overall HPV prevalence of 67% and an HPV-16 prevalence of 30% [37].

High-risk European populations. Eighteen high-risk studies were conducted in Europe (Table 2). Partners of HPV-positive women in Palermo, Italy (mean age: 37 years) had an overall HPV prevalence of 72% and an HPV-16 prevalence of 8% [75]. Similar results were found for male partners of women with CIN in Rome, Italy (mean age: 37 years), in whom overall HPV prevalence was 71% and HPV-16 prevalence was 13% [76]. These prevalences were more than three times as high as the overall and HPV-16 prevalences (15% and 2.9%, respectively) observed in Parisian males (mean age: 30 years) whose female partners had genital HPV lesions [74]. Male partners of women with abnormal cytology in the Netherlands (mean age: 38 years) had an overall HPV prevalence of 73% and HPV-16 and HPV-18 prevalences of 35% and 3.9%, respectively [79,80]. HIV-positive men in Barcelona, Spain (mean age: 42 years) had overall penile and anal HPV prevalences of 36% and 78%, respectively [85]. Male partners of cervical cancer patients throughout Spain (mean age: 45 years) had an overall and HPV-16-specific penile prevalence of approximately 18% and 4.9%, respectively [4,25,46].

STI clinic attendees in Nuuk, Greenland (mean age: 30 years) had an overall penile HPV prevalence of 48% and an HPV-16 prevalence of 7% [70]. Anal swabs from STI clinic attendees, with and without HIV, in Göteborg, Sweden (mean age: 35 years) had an overall HPV prevalence of 77% and an HPV-16/18 prevalence of 27% [87]. This was higher than other Swedish studies from STI clinic attendees in Göteborg (mean age: 31 years) [86], Stockholm (mean age: 27 years) [88], and Uppsala (mean age: 25 years) [90], who had overall penile HPV prevalences of 25%, 13%, and 29%, respectively. An earlier study of STI clinic attendees in Stockholm (mean age: 28 years) [89] reported an overall HPV prevalence of 50% and an HPV-16 prevalence of 13% in men without a history of, or contact with, condylomata. In London, England, men infected with gonorrhea (mean age: 27 years) had HPV-16 and HPV-18 type-specific prevalences of 6.0% and 8.0%, respectively [72]. These studies showed no HPV prevalence peak in younger age groups, in contrast to trends observed in females [21].

Discussion

This represents, to our knowledge, the largest literature review of HPV prevalence in men worldwide. HPV prevalence was high among sexually active men but with considerable variation depending on age, country, and region. Peak HPV prevalence spanned a wide range of ages and was generally not concentrated in the younger age groups. Overall HPV prevalence did not change greatly among men in both low- and high-risk groups from age 20 to at least 50 years of age. Few data on HPV-16/18 prevalence are available among young men (age range: 9–18 years) for whom current HPV prophylactic vaccines are approved. These data would be useful to estimate the proportion of young men negative for both HPV-16/18, and thus who may obtain optimal benefits from HPV vaccination. Our review shows that risk of HPV infection is generally high for most males in many geographic areas, with comparable prevalence in both low- and high-risk populations. This finding supports efforts to extend HPV vaccination to boys and young men.

A previous systematic review summarizing HPV prevalence studies in males included studies with and without reported age, as well as overall, high-risk, low-risk, and other type-specific HPV prevalence groupings [92]. In the present review, we include age-specific data updated to 2009 stratified by continent/region and city. In addition to reporting overall, high-risk, and low-risk HPV prevalence, we also report HPV-16 and HPV-18 prevalence, the oncogenic HPV types that are currently targeted by HPV vaccines [4,93]. Our analysis was limited to studies providing some indication of the age of the surveyed population.

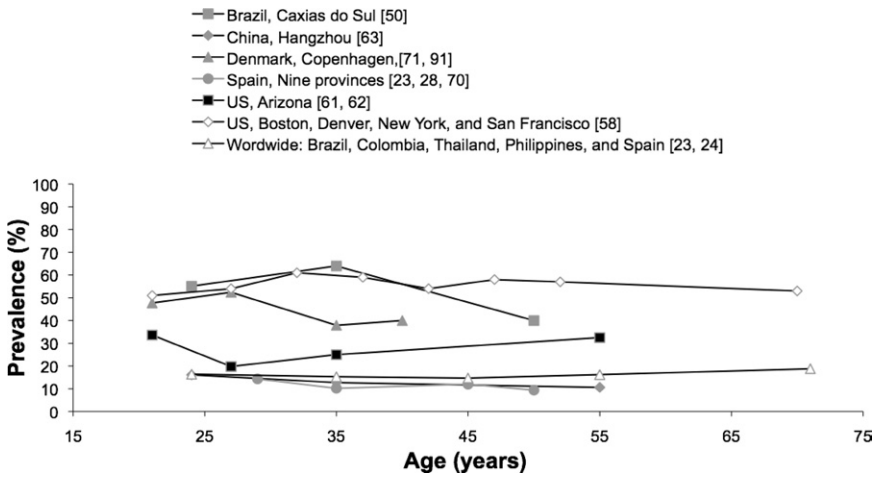

Figure 2. HPV prevalence by age for high-risk male population by country, city, and study.

Further, age-specific prevalence data reported in Tables 1 and 2 and presented graphically in Figures 1 and 2 facilitate discerning patterns of HPV trends by age.

Similar to a previous systematic review, this review showed high HPV prevalence among sexually active men in all world regions, reflecting higher probability of newly acquired infections at younger ages. Given heterogeneity in laboratory assays used for HPV infection detection, populations surveyed, and the observed variation in HPV positivity across the different publications, we have chosen not to present a summary estimate for overall HPV prevalence for geographic regions or for specific age groups [94]. Instead, we provide age- and country-specific data on penile HPV infection in both high- and low-risk groups, allowing for the examination of age-specific prevalence trends within a particular region or a population subgroup of interest.

Compared with HPV prevalence studies among females, data from studies of men were more frequently limited to higher-risk populations rather than representative population-based samples. In men, peak HPV prevalence spanned a wide range of ages and was generally not concentrated in younger age groups. In contrast to results for females, age-specific prevalence curves were relatively flat with age or declined only slightly with post-peak prevalence. These data suggest that men may have the potential for longer-term persistence of HPV infection or a higher rate of reinfection. At present, available methods to detect HPV serum antibodies cannot reliably measure cumulative exposure to HPV because of their relatively low sensitivity [95].

Sampling methods and anatomical sites used for HPV-DNA detection varied across different studies and may contribute to observed differences among men in different geographic regions. Previous reports have shown an increase in HPV-DNA detection when multiple anatomical sites were sampled [36,96]. Current recommendations include sampling the penile shaft, glans penis, and coronal sulcus; scrotal, perianal, or anal samples could also be used to optimize HPV detection [96].

Comparisons of HPV prevalence by region or country are also hampered by differences among study populations surveyed, laboratory methods used, and the variation in HPV types detected (i.e., overall HPV positivity, high-risk HPV types, low-risk HPV types, or type-specific positivity). To reduce possible underestimation of overall or type-specific prevalence, study criteria included the detection of HPV PCR or HC–II (Digene Corporation; Digene Corp., Gaithersburg, MD) detection assays. Although these assays have been shown to have a relative higher sensitivity for HPV detection than earlier detection assays, the sensitivity of HPV-DNA detection presented here may not have been optimal if chosen type-specific PCR primers included typing for only a relatively small number of HPV types or if there was underdetection of HPV due to laboratory testing procedures. Across geographic regions, HPV-DNA was generally detected using GP5+/6+, MY09/11, HC–II, or type-specific PCR primer systems, except in Japan, where a larger proportion of studies used L1 primers for HPV detection. To our knowledge, this systematic review of HPV prevalence in men represents the largest, to date, with a comprehensive investigation of HPV-DNA prevalence in all major geographic regions. For quality assurance, data were extracted and double-checked by independent abstractors.

Among study limitations, type-specific data for carcinogenic HPV types other than 16 and 18 (e.g., HPV-45, -31, -33, -52, -58, etc.) were not included. HPV prevalence estimates are also largely limited to sexually active men. Thus, prevalence results for low-risk populations may not entirely reflect those of the general population. Further, our review is limited to cross-sectional prevalence, rather than the ascertainment of persistent HPV infection, which has been shown to be highly predictive of future risk of high-grade cervical neoplasia or cancer [97–99] in women, and likely represents a higher probability of male-to-female sexual transmission.

Conclusions

Age-specific HPV prevalence data in males are essential in understanding HPV trends in all major world regions. Compared with females, there are fewer population-based studies on HPV prevalence in males throughout the world [21], and many regions, such as Africa, have few available data. Data reported here suggest a more stable HPV prevalence in men by age than in women.

Despite different techniques and collection methods, age-stratified data on HPV-16 and HPV-18 (included in current HPV prophylactic vaccines) show similar age-related trends across major regions. HPV-18 is typically less prevalent than HPV-16, and prevalence differs notably by geographic region. Further data are needed for all age groups among population-based samples, particularly male adolescents. Nevertheless, given the gen-

erally high prevalence of HPV in both low- and high-risk men in many geographic areas, the need for universal HPV vaccination of males in early adolescence seems warranted.

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