Preventive Medicine 123 (2019) 288–298

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Multisite HPV infections in the United States (NHANES 2003–2014): An overview and synthesis

Andrew F. Brouwer[a,*], Marisa C. Eisenberg[a], Thomas E. Carey[b], Rafael Meza[a]

[a] Department of Epidemiology, University of Michigan, 1415 Washington Heights, Ann Arbor, MI 48109, United States
[b] Department of Otolaryngology/Head & Neck Surgery, University of Michigan, 1500 E. Medical Center Dr., Ann Arbor 48109, United States

ARTICLE INFO

Keywords:
Human papillomavirus
Prevalence
Multisite
Concordant infection
NHANES
Vaccine efficacy

ABSTRACT

HPV is the most common sexually transmitted infection in the U.S., infecting both anogenital and oral sites. Nationally representative data are collected through the National Health and Nutrition Examination Survey (NHANES). However, changing designations of HPV genotypes as high or low risk and varying underlying populations as new results are reported have made direct comparison of results difficult. We reanalyzed HPV data from NHANES derived from self-collected cervicovaginal swabs (women ages 18–59, 2003–14), penile swabs (men ages 18–59, 2013–14), and oral rinses (men and women ages 18–69, 2009–14), using consistent populations and definitions across NHANES cycles. These data strengthen our understanding of age trends in HPV prevalence: cervicovaginal prevalence decreases with age, penile prevalence increases with age, and oral prevalence is bimodal but with an earlier first peak in women. There is strong evidence for reduced prevalence of vaccine genotypes (6, 11, 16, 18) in vaccinated men and women (ages 18–24) at both genital (RR 0.2 (0.1–0.3) in women and 0.7 (0.1–5.4) in men) and oral sites (RR 0.1 (0.0–1.3) in women; no infections detected in vaccinated men). A more complete picture of the burden of HPV in the U.S. is emerging, including evidence for reduced HPV genital and oral prevalence in vaccinated individuals.

1. Introduction

The human papillomavirus (HPV) is the causal agent for nearly every cervical cancer, 90% of anal cancers, 60% of cancers at certain oral sites, and 40% of penile, vaginal, and vulvar cancers (Jemal et al., 2013). The appreciation of HPV's role in cervical cancer, and the importance of genotypes 16 and 18 in particular, led to the surveillance of cervicovaginal HPV in women in the United States in the National Health and Nutrition Examination Survey (NHANES), beginning in the 2003–2004 survey eNCHS, Dunne2007. A growing appreciation for HPV's role in oral and male cancers (Gillison et al., 2012a; Jemal et al., 2013; Kreimer, 2014) led to the introduction of oral HPV testing in both men and women in NHANES starting in 2009–10 (Gillison et al., 2012b). Testing for penile HPV began in 2013–2014 (Gargano et al., 2017; Han et al., 2017), which allows for a more complete assessment of the epidemiology of HPV at the U.S. population level. However, many previous prevalence estimates are not directly comparable because they use different subsamples of the data (different age ranges in particular) or different classifications of HPV genotypes as high-risk.

Although HPV is the most common sexually transmitted infection in the U.S. (Satterwhite et al., 2013), not all genotypes rate the same level of concern. Indeed, many strains have very low oncogenic potential, are asymptomatic, and clear within a few years (Franco et al., 1999; Giuliano et al., 2011a; Ho and Bierman, 1998; Kreimer et al., 2013; Molano et al., 2003; Moscicki et al., 2012). Studies have tested for different sets of genotypes and have different classifications of high- vs. low-risk genotypes, further confusing the picture, making comparisons between studies difficult, and undermining our abilities to understand implications for future cancer burden. In Table 1, we compare HPV genotype designation and population of interest for previous NHANES analyses; this table is not an exhaustive list of all studies that have used HPV data from NHANES but rather those focused on reporting new prevalence data.

The heterogeneity in age-ranges and variability in high-risk genotype classification across these studies make it hard to directly compare results across the literature. In this study, we use the 2012 International Agency for Research on Cancer (IARC) classification of risk potential (Bouvard et al., 2009; International Agency for Research on Cancer, 2012) consistently across years and infection site. Group 1 genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59) are known to have oncogenic potential, Group 2A genotypes (68) are probably oncogenic, and Group 2B genotypes (26, 30, 34, 53, 66, 67, 69, 70, 73, 82, 85, 97)

* Corresponding author.
E-mail address: brouweaf@umich.edu (A.F. Brouwer).

https://doi.org/10.1016/j.ypmed.2019.03.040
Received 24 September 2018; Received in revised form 21 March 2019; Accepted 28 March 2019
Available online 05 April 2019

Table 1
Previous analyses of HPV outcomes in NHANES. Previous analyses have considered different underlying populations and different classifications of HPV genotypes. Note that genotypes 55, 64, and IS39 are now classified as subtypes of 44, 34, and 82, respectively. All studies used data from the full 37 genotype assay except where denoted by *, indicating only a subset of genotypes were considered.

Reference	Outcome	Age range	High-risk (HR) genotypes	Low-risk (LR) genotypes
(Dunne et al., 2007)	Cervicovaginal prevalence 2003–04	14–59	16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82, 85, 82 [IS39]	6, 11, 32, 40, 42, 44, 54, 55, 61, 62, 64, 71, 72, 74, 81, 83, 84, 87, 89, 91
(Markowitz et al., 2009)	Seroprevalence 2003–04*	14–59	16, 18	6,11
(Dunne et al., 2011)	Cervicovaginal prevalence 2003–06*	14–59	16, 18	6,11
(Hariri et al., 2011)	Cervicovaginal prevalence 2003–06	14–59	16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 64, 66, 67, 68, 69, 70, 73, 82, 82 [IS39]	6, 11, 40, 42, 54, 55, 61, 62, 71, 72, 81, 83, 84, 89
(Gillison et al., 2012b)	Oral prevalence 2009–10	14–69	16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82	6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 82 [IS39], 83, 84, 89
(Markowitz et al., 2013)	Cervicovaginal prevalence 2003–10*	14–59	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 73, 81, 82, 82 [IS39], 83, 84, 89
(Steinau et al., 2014)	Cervicovaginal–oral prevalence 2009–10	18–59	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 64, 66, 68	6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 67, 69, 70, 71, 72, 73, 81, 82, 83, 84, 82 [IS39], 89
(Chaturvedi et al., 2015)	Oral prevalence 2009–12	14–69	16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82	6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 82 [IS39], 83, 84, 89
(Liu et al., 2016)	Seroprevalence 2005–06*	14–59	16, 18, 31, 33, 45, 52, 58	6, 11
(Brouwer et al., 2015a)	Cervicovaginal, oral, seroprevalence 2003–12	14–59/69	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59	6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 82 [IS39], 83, 84, 89
(Kedarisetty et al., 2016)	Cervicovaginal–oral concordance 2009–12	18–69	16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82	6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 83, 84, 89, 82 [IS39]
(Markowitz et al., 2016)	Cervicovaginal prevalence 2003–12	14–34	16, 18 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 73, 81, 82, 82[IS39], 83, 84, 89
(Han et al., 2017)	Penile prevalence 2013–14	18–59	16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82	6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 82 [IS39], 83, 84, 89
(Gargano et al., 2017)	Penile prevalence 2013–14	14–59	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 73, 81, 82, 82 [IS39], 83, 84, 89
(Patel et al., 2017)	Penile–oral concordance 2013–14	18–59	–	–
(McQuillan et al., 2017)	Genital, oral prevalence 2013–2014	18–59/69	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 73, 81, 82, 82 [IS39] 83, 84, 89
(Sonawane et al., 2017)	Oral prevalence, oral–genital concordance 2011–2014	18–59/69	16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82	6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 82 [IS39], 83, 84, 89
(Lewis et al., 2018)	Cervicovaginal and penile prevalence in the sexually experienced, 2013–14	14–59	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 73, 81, 82, 83, 84, IS39, 89

Table 2
Numbers of tested participants and prevalence. Numbers of people (ages 18 +) conclusively tested (had a positive or negative result) for HPV at genital and oral sites in the 2003–14 National Health and Nutrition Examination Surveys (NHANES) in the U.S. and weighted prevalence and prevalence age-adjusted to the 2010 U.S. population. Here, positive for HPV means that an individual is positive for at least one of the 37 genotypes tested.

	Genital							Oral					
	Women						Men	Women			Men		
	03–04	05–06	07–08	09–10	11–12	13–14	13–14	09–10	11–12	13–14	09–10	11–12	13–14
All	1558	1728	1783	1955	1767	1985	1757	2461	2195	2446	2385	2215	2278
Mexican American	328	409	370	408	190	301	255	504	236	360	508	257	348
All Hispanic	–	–	604	627	378	505	402	799	471	599	762	466	543
Non-Hispanic White	720	726	724	868	573	767	714	1058	694	959	1015	749	906
Non-Hispanic Black	399	439	392	343	505	408	362	451	639	516	480	592	489
18–24	452	479	303	367	351	381	358	392	363	411	400	404	394
25–29	175	228	183	231	193	202	193	255	190	214	209	201	196
30–34	183	206	211	222	206	227	230	227	211	233	209	228	240
35–39	155	158	235	235	204	238	188	236	219	226	225	214	200
40–44	174	196	221	256	206	266	204	266	213	264	229	203	215
45–49	157	178	230	253	202	231	192	256	202	229	226	188	208
50–54	155	162	214	224	236	224	196	227	235	222	247	201	211
55–59	107	121	186	167	169	216	196	173	181	211	208	174	204
60–64	0	0	0	0	0	0	0	262	237	243	236	238	233
65–69	0	0	0	0	0	0	0	167	144	193	186	164	177
Prevalence 18–59	46.8%	41.4%	41.0%	42.8%	39.6%	39.9%	45.2%	3.7%	3.2%	3.2%	10.7%	11.4%	11.2%
Age-adjusted prevalence	46.7%	41.5%	41.3%	43.1%	39.7%	39.9%	45.3%	3.7%	3.2%	3.1%	10.7%	11.4%	11.2%
Prevalence 18–69	–	–	–	–	–	–	–	3.7%	3.1%	3.4%	11.0%	11.9%	11.1%

are possibly oncogenic.

Although many analyses of HPV data in NHANES have focused on a single outcome of interest, there has been increasing interest in multisite concurrence (infection at both sites, possibly of different genotypes) and concordance (infection at both sites by at least one of the same genotype) of HPV infections at genital and oral sites, and previous analyses have begun to explore the epidemiology of HPV as an explicitly multisite infection (Brouwer et al., 2015a; Brouwer et al., 2015b; Kedarisetty et al., 2016; Patel et al., 2017; Sonawane et al., 2017; Steinau et al., 2014). In this analysis, we update our multiyear, multisite overview of HPV data in NHANES (Brouwer et al., 2015b). We contextualize the recently reported penile HPV prevalence and concordance (Gargano et al., 2017; Han et al., 2017; McQuillan et al., 2017; Patel et al., 2017) and recently-summarized cervicovaginal and oral prevalence (McQuillan et al., 2017) by placing them alongside data from the previous surveys. We synthesize and update all oral and genital HPV infection data in NHANES. In particular, we present genital and oral HPV prevalence for both men and women, stratified by age and race, and prevalence of Group 1 HPV genotypes. Concordant infections are identified when both oral and genital data are available. Prevalence by genotype among men and women with genital, oral, and concordant infections are also reported. Finally, we consider the relative risk of an HPV infection at both genital and oral sites given vaccination for both men and women.

2. Methods

2.1. Data

NHANES is a series of cross-sectional surveys conducted by CDC's National Center for Health Statistics (NCHS) over two-year periods that include both physical examinations in a mobile examination center (MEC) and interviews (both in-home and audio-assisted in-MEC) of a representative sample of the non-institutionalized, civilian U.S. population (Centers for Disease Control and Prevention, 2014). The demographic and vaccination data used in this study are self-reported by participants. Study design, weighting, and collection of samples have been previously described (Dunne et al., 2007; Gillison et al., 2012b; Hariri et al., 2011). The NHANES survey 2003–14 was approved by the NCHS Research Ethics Review Board (2003–04: protocol #98–12; 2005–10: protocol #2005–06; 2011–14: protocol #2011–17), and documented consent was obtained from all participants.

Self-collected cervicovaginal swabs were collected and typed for women ages 14–59 in six NHANES surveys (2003–14) for 37 genotypes, namely 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55 (a subtype of 44), 56, 58, 59, 61, 62, 64 (a subtype of 34), 66, 67, 68, 69, 70, 71, 72, 73, 81, 82, 82 subtype IS39, 83, 84, and 89 (formerly CP6108). Self-collected penile swabs were collected and typed for men ages 14–59 in 2013–2014 for the same genotypes. Oral rinses were administered to both men and women ages 14–69 in three surveys (2009–14) and tested for the same genotypes. All samples were genotyped using a polymerase chain reaction (PCR) assay. More detailed laboratory methods are provided by NHANES (Centers for Disease Control and Prevention, 2014). The numbers of individuals sampled by demographic group are reported in Table 2. Data on individuals under 18 is restricted by NCHS and is not included in this analysis.

2.2. Statistical analysis

Statistical analyses were performed in SAS (v. 9.4). Estimates were made using MEC survey weights (Botman et al., 2000). All analyses are restricted to individuals who had valid oral and genital HPV results in survey cycles when both tests were administered. We consider four analyses: i) prevalence of any HPV and Group 1 genotypes at genital and oral sites stratified by sex, age, and race/ethnicity, ii) prevalence of concordant infections, i.e., at least one infection of the same genotype at both genital sites (cervicovaginal or penile) and oral sites, stratified by sex, age and race/ethnicity, iii) genotype prevalence among men and women with genital, oral, and concordant infections, and iv) prevalence of all, Group 1, and vaccine genotypes at genital and oral sites of 18–24-year-old men and women stratified by vaccination status. Individuals reporting at least one dose of an HPV vaccine were considered to be vaccinated. Survey participants self-identified as Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, or Other Race - Including Multiracial (and, in 2011–14, Non-Hispanic Asian). We define All Hispanic participants as those identifying as either Mexican American or Other Hispanic, and, following NCHS recommendations, we censor cycles 2003–06 for this category (National Center for Health Statistics, 2013). Confidence intervals are all at level of significance $\alpha = 0.05$ (i.e., 95% confidence intervals). Statistical details for relative

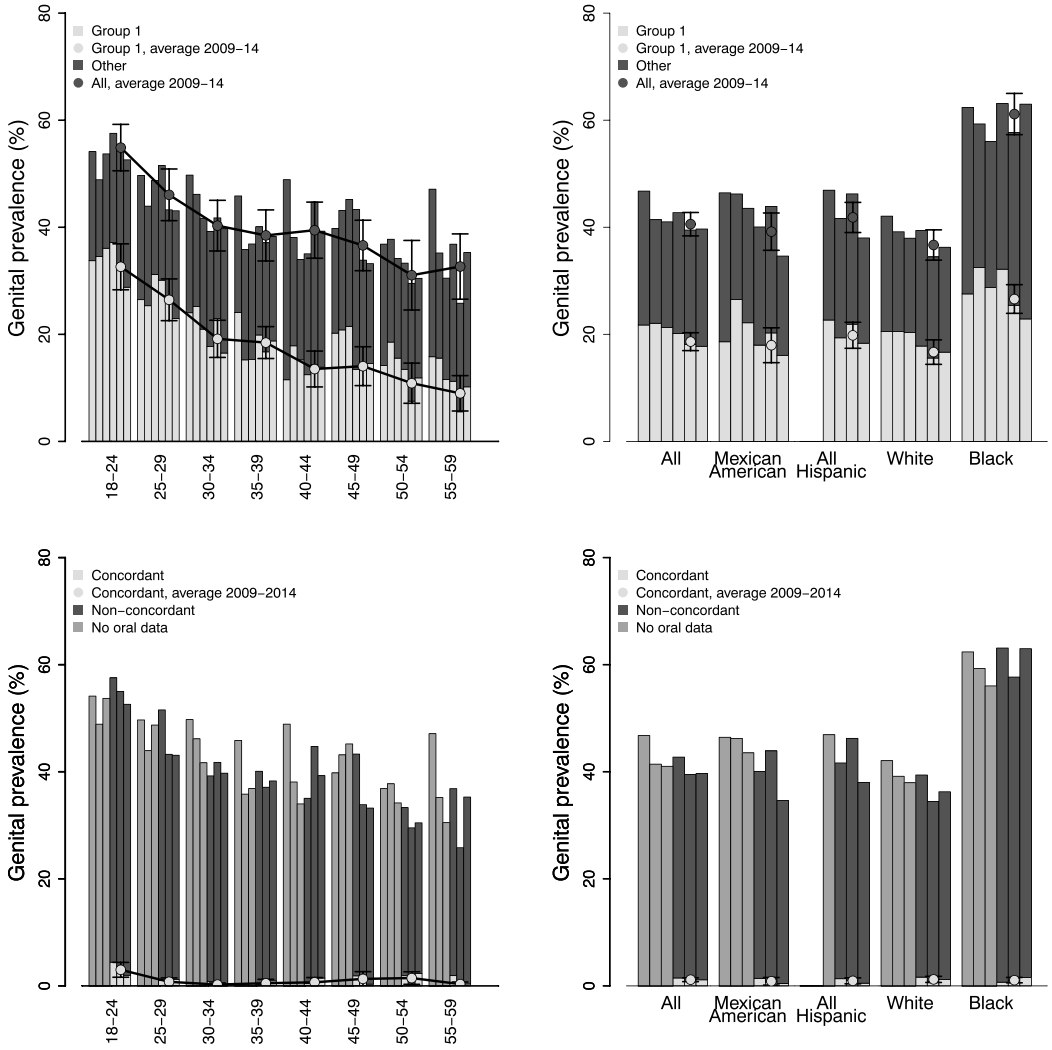

Fig. 1. Cervicovaginal HPV prevalence in women ages 18–59 by genotype group and concordance, stratified by age and race. Stratification of cervicovaginal HPV prevalence in the U.S. by oncogenic potential (Group 1 genotypes are known to cause cancer) in the upper panels is given by age and race, where each bar represents survey cycles 2003–04, 2005–06, 2007–08, 2009–10, 2011–12, and 2013–14, respectively. Stratification by concordance (lower panels) is done similarly (concordant infections are defined as at least one simultaneous oral and genital infection of the same genotype). The points with error bars (95% CIs) give the average of the indicated outcome for the 2009–2014 data. The constraint to this time period allows comparison to oral outcomes.

risk and comparison of population calculations are given in the supplement.

3. Results

3.1. Population prevalence over time

We present the weighted population-level prevalence for genital and oral HPV in Table 2. For oral HPV, we present both the prevalence in the 18–59 year old population (for comparison to the population who were tested for genital HPV) and in the 18–69 year old population. We also age-adjusted the 18–59 year old population for each cycle to the respective female and male populations in the 2010 census; we found very little difference between adjusted and unadjusted prevalences, indicating that changes in the age composition of the U.S. population have not skewed our understanding of prevalence trends.

3.2. Cervicovaginal and penile HPV prevalence

Stacked bar graphs of genital prevalence in women by age and race are given in Fig. 1 for surveys 2003–2014. There is a decrease in HPV cervicogenital prevalence by age. Black women have an almost uniformly higher prevalence than women of other races.

Stacked bar graphs of genital prevalence in men by age and race are given in Fig. 2. Unlike in women, there appears to be a moderate increase in HPV prevalence with age, and black men are more likely than men of other races to have a genital HPV infection.

3.3. Oral HPV prevalence

Stacked bar graphs of oral prevalence in women by age and race are given in Fig. 3. Oral HPV prevalence in women follows a slightly bimodal pattern, peaking around ages 25 and 55, and white women are less likely to have an oral infection than women of other races. The trend in concordant infections in women by age appears to follow the oral prevalence trend more closely than the genital prevalence trend (i.e., is bimodal rather than strictly decreasing).

Stacked bar graphs of oral prevalence in men by age and race are given in Fig. 4. Oral HPV prevalence is no longer clearly bimodal and may instead largely increase with age, peaking around age 60. Black men are more likely to have an oral HPV infection. The concordance trend may also be bimodal, although the second peak around 55–59 might be a data artifact.

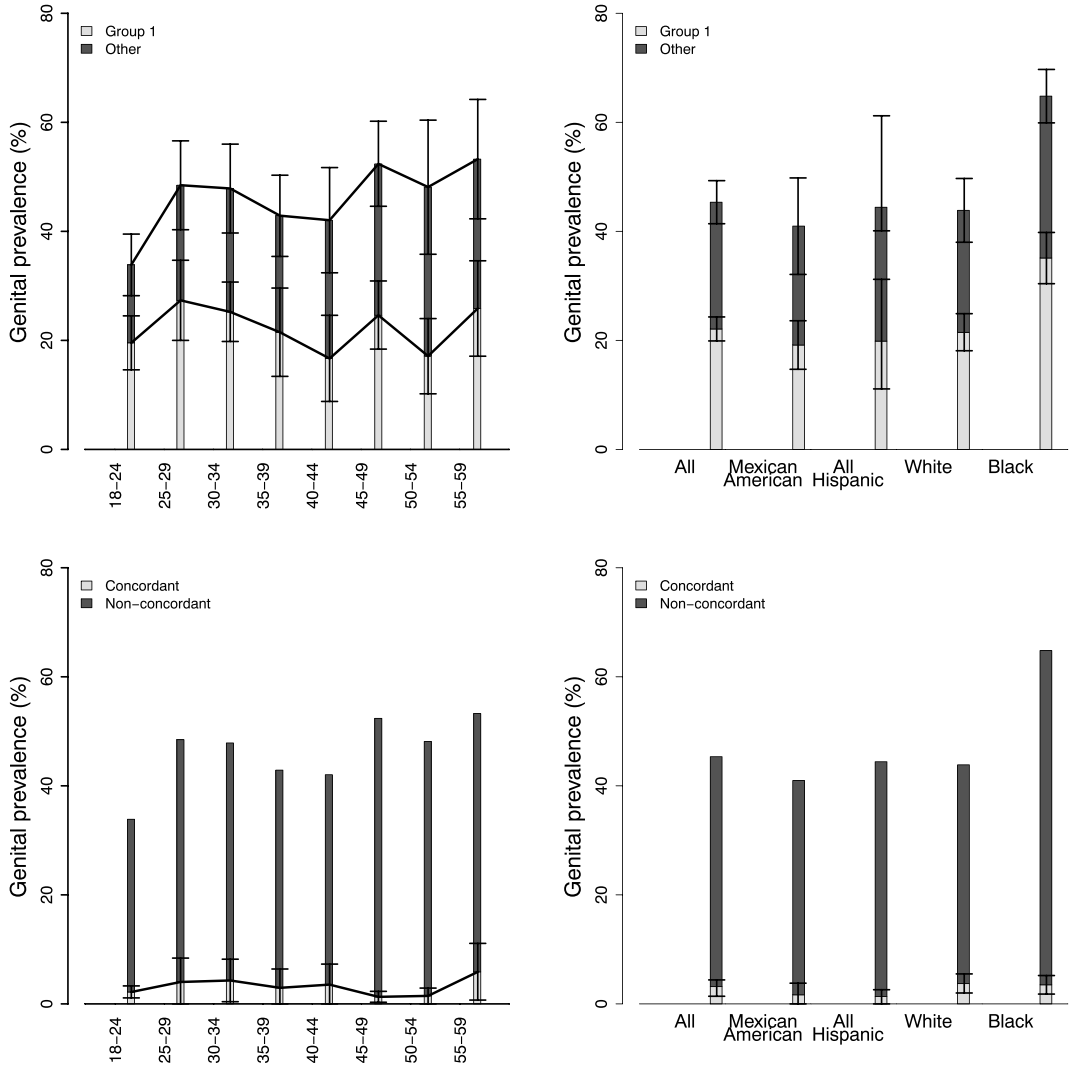

Fig. 2. Penile HPV prevalence in men ages 18–59 by genotype group and concordance, stratified by age and race. Stratification of penile HPV prevalence in the U.S. by oncogenic potential (Group 1 genotypes are known to cause cancer) in the upper panels is given by age and race, where each bar is survey cycle 2013–14. Stratification by concordance (lower panels) is done similarly (concordant infections are defined as at least one simultaneous oral and genital infection of the same genotype). Because there is only one survey with penile outcomes, the error bars (95% CIs) are for this year only.

3.4. Genotypes

In Fig. 5, we present genotype prevalence among men and women who have genital, oral, or concordant infections. E.g., 9.3% of women who had a genital HPV infection tested positive for HPV 16, while 11.2% of women with concordant infections tested positive for HPV 16 (whether or not HPV 16 was the concordant genotype). Data are aggregated 2009–14 for increased power (with the exception of men with genital or concordant infections, where we necessarily constrain to 2013–14). Nevertheless, many results, particularly for those with concordant infections, have a standard error that exceeds 30% and should be treated with additional caution (Parker et al., 2017).

Among women, HPV 16 is the most common oncogenic genotype at all sites; low-risk types 62 and 84 are also common among all sites. Oncogenic genotypes 39, 51, and 52 are also common among genital infections. Genotypes 53, 54, 61 and 89 are more common among women with genital infections than oral infections; while genotype 44 (subtype 55) is more common among oral infections than genital infections. Genotypes 35, 39, 56, and 66 were rare among concordant infections despite moderate prevalence among both genital and oral infections, although this may be an artifact of the small sample size.

Among men, HPV 16 is a common oncogenic strain among penile infections, but so are 39, 51, and 59, as previously seen (Gargano et al., 2017; Han et al., 2017). Indeed, although HPV 16 is by far the most common oncogenic strain among men with oral infections, genotype 59 is the most common concordant oncogenic strain. HPV 62, 84 and 89 are common low-risk genital strains among men in this sample.

3.5. Vaccination

We compare the prevalence of HPV (all, Group 1, and vaccine genotypes) among vaccinated and unvaccinated men and women ages 18–24 at genital and oral sites (Table 3); vaccination status is self-reported. This analysis pools participants in the 2009–10, 2011–12, and 2013–14 cycles, except for male genital infection, which is only available in 2013–14.

There is little evidence of protection by vaccination against all genotypes or all Group 1 genotypes for either sex at either site, with the possible exception of oral infections by Group 1 in women. However, there is strong evidence of protection against the vaccine genotypes 6, 11, 16, and 18 for both men and women at both sites, with the possible exception of penile infections, for which the protective effect was less pronounced. The vaccination effect against oral and genital infections in women appears to be of similar strength. There were no oral

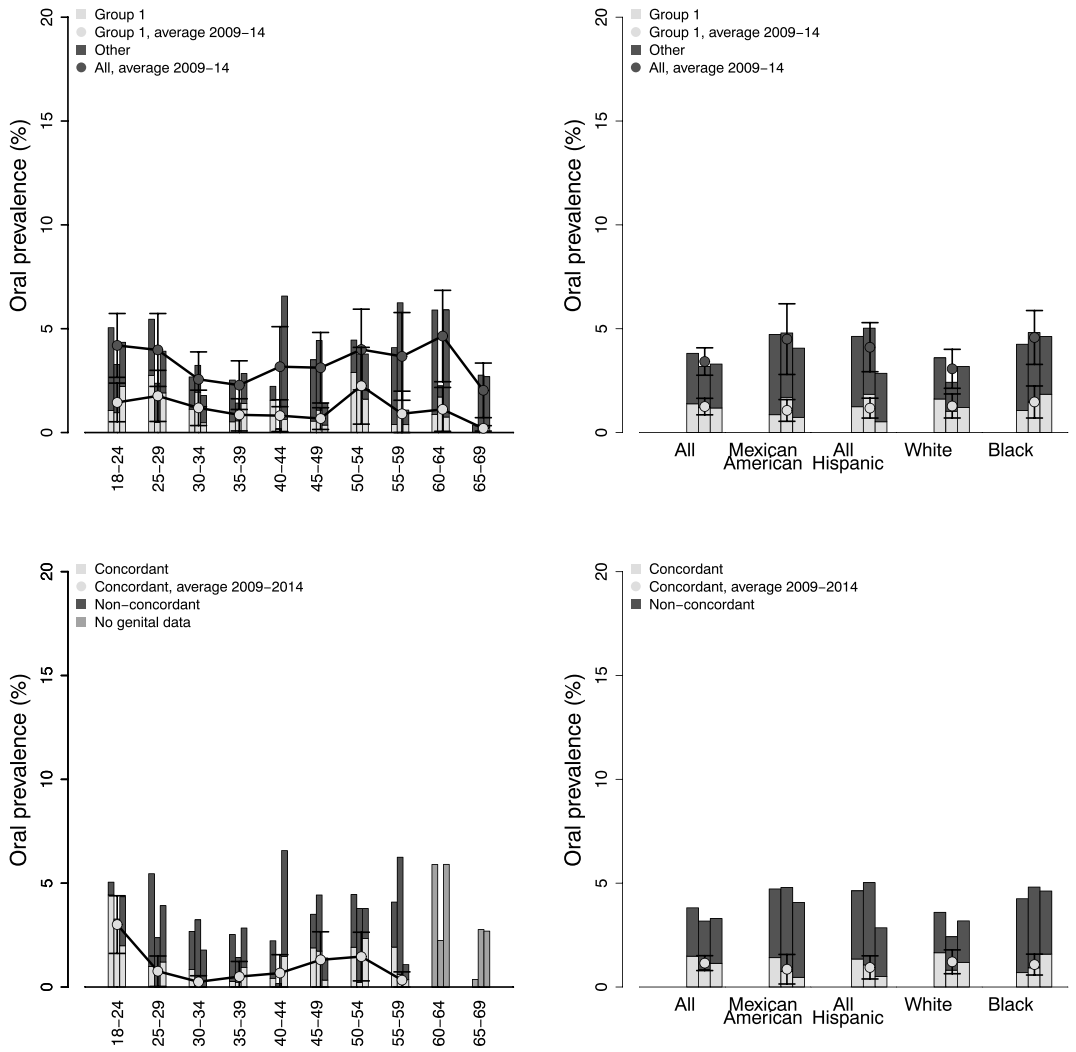

Fig. 3. Oral HPV prevalence in women ages 18–69 by genotype group and concordance, stratified by age and race. Stratification of oral HPV prevalence in women in the U.S. by oncogenic potential (Group 1 genotypes are known to cause cancer) in the upper panels is given by age and race (ages 18–59 only), where each bar represents survey cycles 2009–10, 2011–12, and 2013–14, respectively. Stratification by concordance (lower panels) is done similarly (concordant infections are defined as at least one simultaneous oral and genital infection of the same genotype). The points with error bars (95% CIs) give the 2009–14 average of the indicated outcome.

infections among vaccinated men for any of the vaccine genotypes; as there was 1% prevalence among unvaccinated men, there is evidence of a protective effect, although the number of vaccinated men was relatively small.

4. Discussion

This analysis presents a multiyear, multisite population analysis of genital and oral HPV infection in the U.S., unifying and synthesizing previous results by using the same underlying population and same genotype classification. These consistently analyzed data give us an improved understanding of the demographic patterns of HPV at both sites for both sexes.

The studies profiled in Table 1 display a surprising amount of variation in the list of HPV genotypes considered to be high-risk, and the authors often do not indicate the reasoning behind their classifications. Many studies (Chaturvedi et al., 2015; Gillison et al., 2012a; Han et al., 2017; Kedarisetty et al., 2016; Sonawane et al., 2017) have used the classification given by the International Agency for Research on Cancer (IARC) in 2003 (Muñoz et al., 2003), which classified genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 as carcinogenic and types 26, 53, and 66 as probably carcinogenic. A few early studies (Dunne et al., 2007; Hariri et al., 2011) appear to have extrapolated high-risk status from the α-species genotype groupings. For example, HPV 70 is listed as high-risk in these studies because it is an α7 species, along with 18, 45, 39, and 59. IARC updated its classification in 2012 to designate Group 1 genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59) as having known oncogenic potential, Group 2A genotypes (68) as being probably oncogenic, and Group 2B genotypes (26, 30, 34, 53, 66, 67, 69, 70, 73, 82, 85, 97) as being possibly oncogenic (International Agency for Research on Cancer, 2012). We use this classification in our studies. More recently, FDA-approved clinical HPV tests have come on the market, such as Cobas® HPV test (Roche Molecular Systems, Inc., 2015), which designates genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 as high risk (these are Group 1, Group 2A, and type 66). The confusion over the classification of 66 is likely due to its downgraded status in the latest IARC monograph (International Agency for Research on Cancer, 2012). More recent studies have adopted this classification (Gargano et al., 2017; Lewis et al., 2018; Patel et al., 2017). While the IARC classification is the best-available science, consistency with clinical testing is also important. Ultimately, researchers need to be aware of these conflicting classifications and choose one or more ways of presenting their data to best facilitate the contextualization of their results. Fortunately, despite

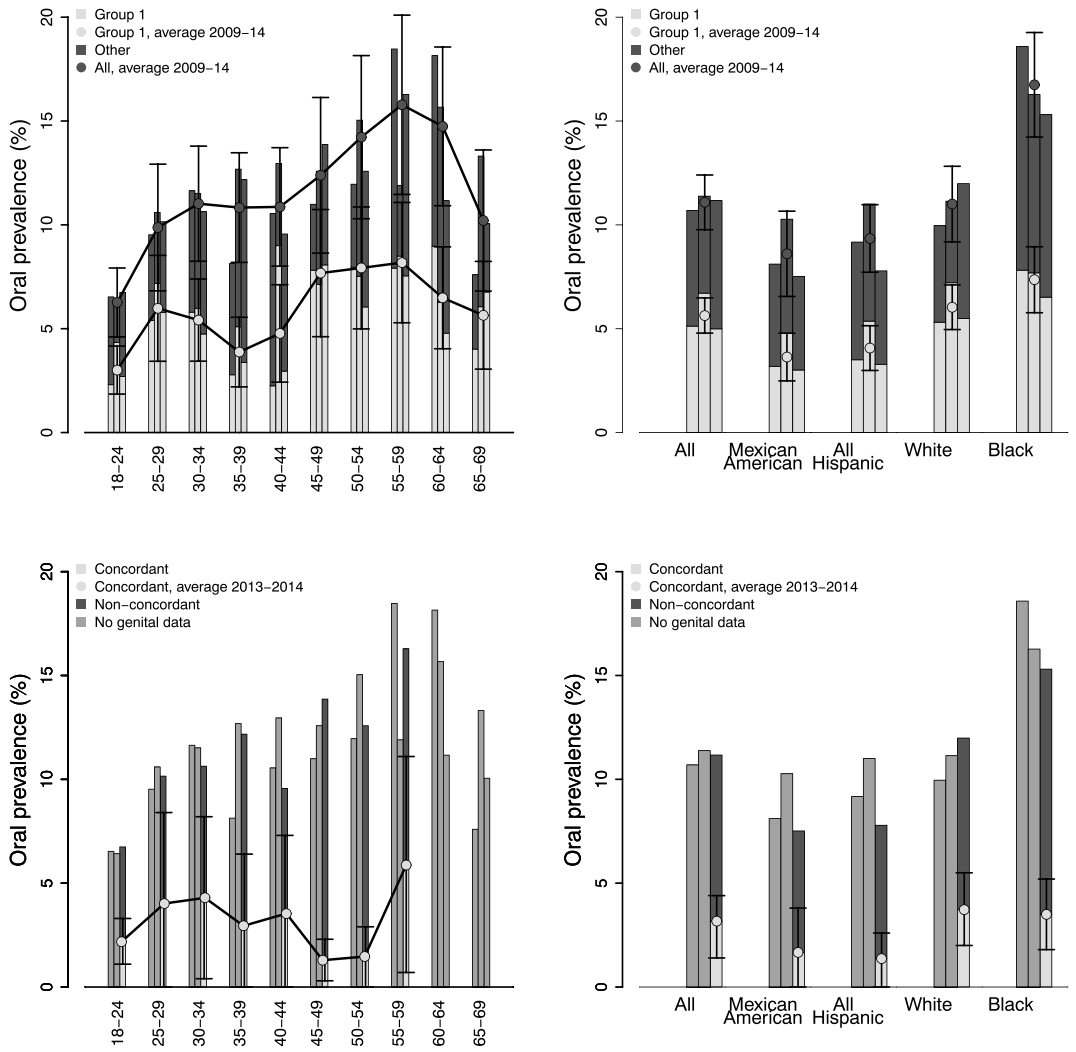

Fig. 4. Oral HPV prevalence in men ages 18–69 by genotype group and concordance, stratified by age and race. Stratification of HPV prevalence in men in the U.S. by oncogenic potential (Group 1 genotypes are known to cause cancer) in the upper panels is given for by age and race (ages 18–59 only), where each bar represents survey cycles 2009–10, 2011–12, and 2013–14, respectively. Stratification by concordance (lower panels) is done similarly (concordant infections are defined as at least one simultaneous oral and genital infection of the same genotype). The points with error bars (95% CIs) give the 2009–14 average of the indicated outcome. Because penile outcomes are only available for 2013–14, the trend and error bars for penile–oral concordance are only for this survey.

the inconsistencies in genotype risk classification across studies, the fundamental conclusions remain largely the same.

In contrast to cervicovaginal HPV prevalence in women, which peaks around age 20, penile HPV prevalence appears to continue to increase with age, which is consistent both with the pattern of oral prevalence and previously reported age-trends for serum antibodies (Brouwer et al., 2015a). However, future surveys will be needed to better understand the variability in the age-specific estimates (i.e., is the increase monotonic, or is there a second peak around age 50?). The bimodal oral prevalence in men noted by Gillison et al. (2012b) in the 2009–10 survey is now significantly less pronounced among the all-genotype data (Fig. 4), although Group 1 genotypes are clearly bimodal. All-genotype oral prevalence now appears to increase with age and peak around age 55 (Fig. 4). The data for women, on the other hand, are still consistent with a bimodal pattern that mimics that of cervicovaginal prevalence in the less-than-40 ages but has a second peak around 55–60 (Fig. 3). A similar bimodal pattern has been observed for cervicovaginal infection in women in Latin America (Herrero et al., 2000; Herrero et al., 2005; Lazcano-Ponce et al., 2001; Molano et al., 2002). It remains to be seen whether this oral bimodal pattern for women is a cohort effect (i.e., the older birth cohorts have a higher oral HPV prevalence (Brouwer et al., 2018)) or is a true age effect (possibly a result of a second sexual debut, loss of immunity, or reactivation of latent infections) (Chaturvedi et al., 2014). To better understand these patterns, future work will need to better understand how age-specific sexual behaviors differ by race and by birth cohort. Since the 1940s, there has been an increase in sexual activity in young people, with lower ages of sexual debut, more sexual partners, and more lenient attitudes toward premarital sex (Liu et al., 2015; Wells and Twenge, 2005). Condom use increased in the 1980s, in response to the HIV/AIDS epidemic and other factors, and reached a plateau in the 2000s (Anderson et al., 2011; Bankole et al., 1999; Catania et al., 1999; Kahn et al., 2012; Sonenstein et al., 1989). Analysis from NHANES has suggested that partner acquisition rates increased up through the 1980s, driving HPV infection (Ryser et al., 2017). There is a complex interplay of factors here that requires continued analysis.

From previous multisite analyses (Brouwer et al., 2015a; Kedarisetty et al., 2016; Patel et al., 2017; Sonawane et al., 2017; Steinau et al., 2014), we know that oral and genital infections are in general poorly correlated and should be tested for separately. Indeed, an individual may have an infection at only one site, infections of different genotypes at genital and oral sites (concurrent infection), or infections of the same genotype (concordant infection). Although testing for anal HPV infection has not been included in NHANES protocols,

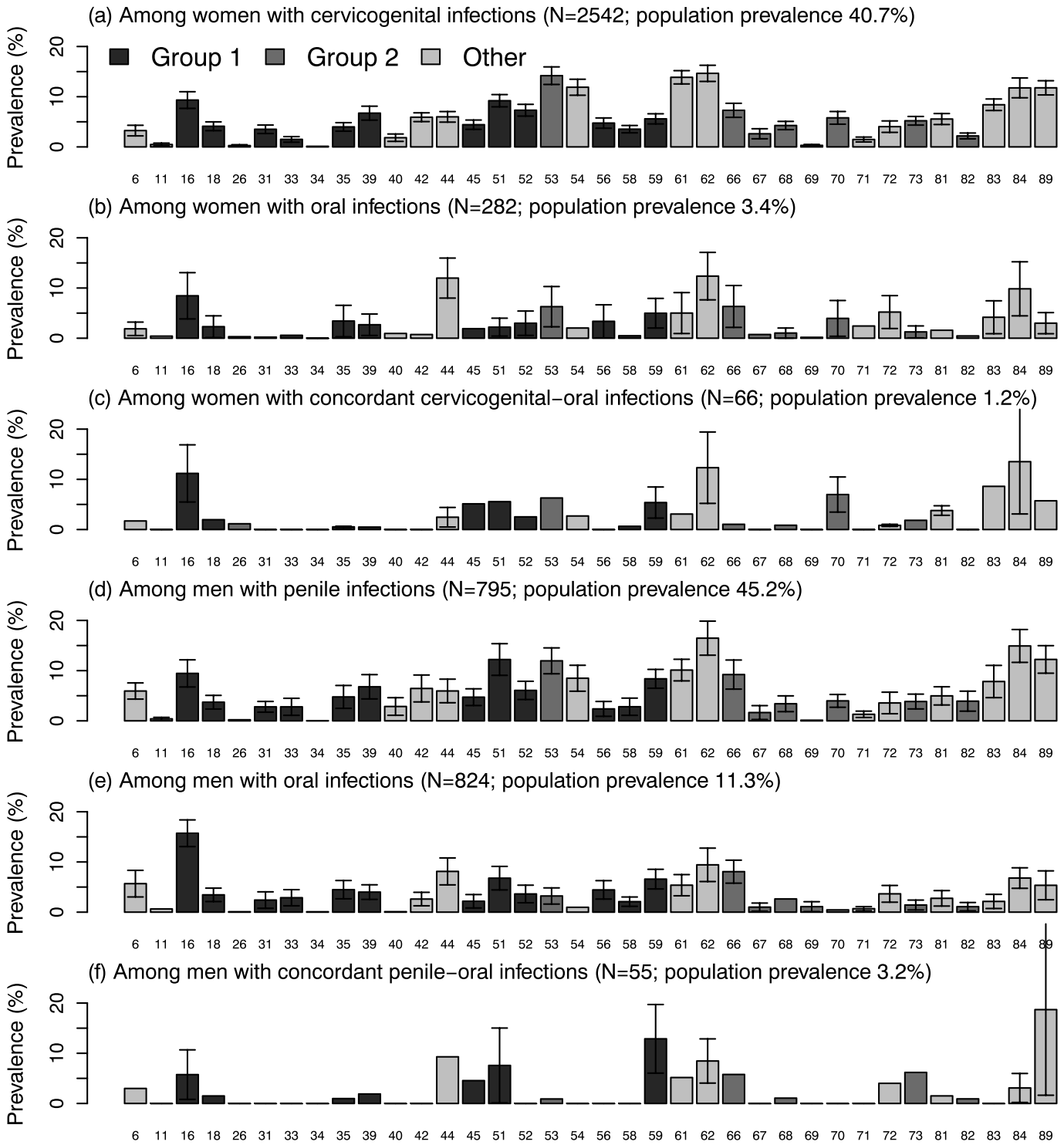

Fig. 5. Genotype prevalence among women and with genital, oral, or concordant HPV infections. Genotype prevalence in U.S. is the 2009–14 average in each case but (f), where it is 2013–14. Each subcaption gives the number of people with the given type of infection and what (weighted) percentage of the population that number represents. Genotypes are color coded by oncogenic potential: Group 1 is oncogenic, Group 2 is possibly oncogenic, and all other are low-risk.

results from smaller studies (e.g., (Goodman et al., 2010; Hernandez et al., 2005; Nunes et al., 2017; Smelov et al., 2018)) similarly suggest important interactions between the anal and cervicovaginal/penile sites. In this synthesis, we see that oral–genital concordance in women is highest in the youngest age group 18–24, possibly suggesting a simultaneous first infection (Fig. 3). It is also higher in the 45–55 age range, which may be consistent with the second-sexual debut hypothesis of the bimodal oral prevalence (Brouwer et al., 2015a; Gillison et al., 2012b). These results are consistent with our previous analysis on the 2009–12 data (Brouwer et al., 2015a). In men, there is no clear age-related pattern of concordance (Fig. 4); in their multivariate analysis, Patel et al. (2017) also found no significant associations by age. As new data becomes available, age-specific patterns of concurrence and concordance should be revisited.

Most genital HPV infections are not concordant with an oral infection (for both men and women), though a larger fraction of oral

Table 3
HPV prevalence by site and genotype group and relative risk by vaccination status. Prevalence of HPV in the U.S. is given for men and women ages 18–24 at genital and oral sites for all, oncogenic (Group 1 genotypes), and vaccine genotypes, stratified by vaccination status. People with at least one dose of vaccine were considered vaccinated. Here, %+ denotes the weighted HPV prevalence of the listed genotypes among the *N* people in the population. Prevalence entries with > 30% relative standard error are marked by * and should be treated with additional caution. *p*-Values for a comparison of proportions test ($\widehat{p}_{vacc} < \widehat{p}_{un}$) are also given; bold *p*-values are significant at the $\alpha = 0.05$ level of significance.

Group	Genotypes	Unvaccinated			Vaccinated			Relative risk		*p*-Value
		N	%+	S.E.	*N*	%+	S.E.	RR	95% CI	
Genital, women 2009–2014	All	635	55.1	2.6	412	57.2	3.3	1.0	0.9–1.2	0.69
	Group 1	635	35.5	2.7	412	30.9	3.3	0.9	0.7–1.1	0.14
	6, 11, 16, 18	635	14.7	2.0	412	2.3	0.6	0.2	0.1–0.3	**< 0.01**
Genital, men 2013–2014	All	252	34.9	3.3	52	32.6	5.6	0.9	0.6–1.4	0.36
	Group 1	252	20.2	2.8	52	15.4	3.1	0.8	0.5–1.2	0.12
	6, 11, 16, 18	252	3.4*	1.3	52	2.3*	2.3	0.7	0.1–5.4	0.34
Oral, women 2009–2014	All	679	4.5	1.1	430	4.0	1.1	1.0	0.4–1.8	0.36
	Group 1	679	1.8*	0.7	430	0.7*	0.3	0.4	0.1–1.2	0.06
	6, 11, 16, 18	679	1.0*	0.5	430	0.1*	0.2	0.1	0.0–1.3	**0.05**
Oral, men 2009–2014	All	603	6.3	1.4	90	8.3	2.6	1.3	0.6–2.8	0.75
	Group 1	603	3.3	1.0	90	5.1*	2.2	1.5	0.6–4.3	0.78
	6, 11, 16, 18	603	1.0*	0.5	90	0.0	0.0	–	–	**0.02**

infections are concordant with genital infections. Interestingly, there are no striking differences in the overall distribution of genotypes among those who have genital, oral, and concordant infections (Fig. 5). Deviations from expected patterns based on overall prevalence could potentially indicate, for instance, differences by genotype in tropism (tissue specificity) or different transmission/autoinoculation pressure from one site versus the other. Given the small numbers of individuals, particularly for concordant infections, it would be premature to interpret the existing slight deviations from expected patterns. Additional data and sophisticated statistical techniques may provide additional insight in the future.

There is a subtle difference in populations when considering multisite vs. single site analyses, namely that, when considering multisite infection, we include only those people who tested conclusively (that is, positively or negatively, not inconclusively) for HPV at both sites, rather than at just one site. Hence, multisite analyses must use slightly restricted populations. This distinction should have little effect on prevalence estimates but can explain what at first glance might appear to be discrepancies between different authors' analyses. E.g. the prevalence of penile HPV in men ages 18–59 in 2013–2014 is given as 45.2% in Han et al. (2017) while it is 45.3% in Patel et al. (2017); Han et al. considered all men who were tested conclusively for penile HPV ($N = 1868$), while Patel considered those tested for both penile and oral HPV ($N = 1683$). While the difference in this example is slight, it should be acknowledged for when comparing study results.

There are currently three prophylactic HPV vaccines with FDA approval: Gardasil (HPV types 6, 11, 16, and 18; approved in 2006 for young women, 2009 for young men), Cervarix (types 16 and 18; approved in 2009 for young women), and Gardasil 9 (types 6, 11,16, 18, 31, 33, 45, 52, 58; approved in 2014 for young women and men) (Food and Drug Administration, 2018). These vaccines target genotypes associated with genital warts (HPV 6 and 11) and those associated with carcinogenesis (HPV 16, 18, 31, 33, 45, 52, and 58). The decision to include HPV 31, 33, 45, 52, and 58 in Gardasil 9 was based on prevalence in cervical cancers (Saraiya et al., 2015) rather than population-level infection prevalence. In both men and women and at both genital and oral sites, Group 1 genotypes 39, 51, and 59, which are not in the nonavalent vaccine, are all as or more prevalent than the majority of Group 1 genotypes in the vaccine (Fig. 5). These genotypes should be closely monitored both in the population and in incident HPV-related cancers as the new vaccine is adopted in the U.S. Because genotype-specific prevalence can vary between populations, future work is needed to continue to address potential health disparities in high-risk populations, such as HIV-infected individuals or men who have sex with men (MSM).

The comparison of HPV prevalence between vaccinated and unvaccinated people presents evidence of vaccine effectiveness against the four vaccine genotypes 6, 11, 16, and 18 (future analyses will have to contend with the impact of added genotypes to the Gardasil 9 vaccine). We see evidence of reduction in prevalence for all of the sites, with the possible exception of genital sites for men (relative risks: 0.2 (cervicovaginal in women), 0.7 (genital in men), 0.1 (oral in women), 0 (no oral positives among vaccinated men)). We should be cautious with the differences in oral prevalence because, although the differences are statistically significant, the absolute prevalence of HPV 6, 11, 16, and 18 (1% in both unvaccinated men and women) is low and the relative standard errors are high. Several studies have found evidence of vaccine impact at the population level (Gargano et al., 2017; Markowitz et al., 2013; Markowitz et al., 2016), and these results complement the work of Markowitz et al. (2016) and Chaturvedi et al. (2018), who found similar results for young people (for cervicovaginal infections and oral infections, respectively). There are a couple of plausible explanations for the less dramatic reduction for genital prevalence in vaccinated men. First, because the male genitals are an external tissue, it is possible that HPV infections of the male genitals do not lead to a strong immune response (i.e., are less immunogenic than infections at other sites) and are less impacted by serum antibodies—whether natural or vaccine derived. However, this explanation belies the reduction in genital warts, which are external lesions, in men in vaccine randomized control trials (Giuliano et al., 2011b). Second, the uptake of the vaccine may be primarily in men who were already sexually active, especially in this older-than-optimal age group of 18–24, who could have received the vaccine no earlier than age 15; these men may have already been infected, reducing the efficacy of the vaccine. The vaccinated population may also have a higher percentage of high-risk men given that vaccination among men overall is low (Han et al., 2017) and reported high levels of willingness to vaccinate among high-risk groups when recommended by a physician (Colón-López et al., 2012; Gerend et al., 2016; Reiter and McRee, 2016). This explanation could also be responsible for the greater than one risk ratios for men at the oral sites for any and Group 1 genotypes.

The strength of this study is the large, well-designed, nationally representative sample that allows for analysis at the U.S. population level. The cross-sectional design with a battery of tests for each individual allows for analysis of multiple outcomes simultaneously, and, in particular, allows for assessment of genotype concordance between oral and genital sites. Because testing for HPV is relatively new and this is the debut of testing for penile HPV, we are limited somewhat in describing patterns and trends. Nevertheless, by synthesizing several cycles of data, we are able to add confidence and context to previous

studies and ensure we use a consistent definition of high-risk infection across all cycles and outcomes.

Competing interests

The authors declare that they have no competing interests.

Author's contributions

AB, RM, ME designed the study. AB performed the data analyses and drafted the manuscript. AB, RM, ME, TC provided clinical and public health insight for analyzing the results and editing the manuscript. All authors read and approved the final manuscript.

Acknowledgements

This work was supported by NIH grant U01CA182915.

References

Anderson, John E., Warner, Lee, MacAluso, Maurizio, 2011. Condom use among us adults at last sexual intercourse, 1996–2008: an update from national survey data. Sex. Transm. Dis. 38 (10), 919–921.

Bankole, A., Darroch, J.E., Singh, S., 1999. Determinants of trends in condom use in the United States, 1988–1995. Fam. Plan. Perspect. 31 (6), 264–271.

Botman, S.L., Moore, T.F., Moriarty, C.L., Parsons, V.L., 2000. Design and estimation for the national health interview, 1995–2004. Vital Health Stat. 2, 130:1–31.

Bouvard, Véronique, Baan, Robert, Straif, Kurt, Grosse, Yann, Secretan, Béatrice, Ghissassi, Fatiha El, Benbrahim-Tallaa, Lamia, Guha, Neela, Freeman, Crystal, Galichet, Laurent, Cogliano, Vincent, 2009. A review of human carcinogens–part B: biological agents. Lancet Oncol. 10 (4), 321–322.

Brouwer, Andrew F., Eisenberg, Marisa C., Carey, Thomas E., Meza, Rafael, 2015a. Trends in HPV cervical and seroprevalence and associations between oral and genital infection and serum antibodies in NHANES 2003–2012. BMC Infect. Dis. 15 (1), 575.

Brouwer, Andrew F., Meza, Rafael, Eisenberg, Marisa C., 2015b. Transmission heterogeneity and autoinoculation in a multisite infection model of HPV. Math. Biosci. 270, 115–125.

Brouwer, Andrew F., Eisenberg, Marisa C., Meza, Rafael, 2018. Case studies of gastric, lung, and oral cancer connect etiologic agent prevalence to cancer incidence. Cancer Res. 78 (12), 3386–3397.

Catania, J.A., Canchola, J., Binson, D., Dolcini, M.M., Paul, J.P., Fisher, L., Choi, K.H., Pollack, L., Chang, J., Yarber, W.L., Heiman, J.R., Coates, T., 1999. National trends in condom use among at-risk heterosexuals in the United States. J. Acquir. Immune Defic. Syndr. 27 (2), 176–82, 2001.

Centers for Disease Control and Prevention, 2014. National Health and Nutrition Examination Survey. http://www.cdc.gov/nchs/nhanes.htm, Accessed date: 20 January 2016.

Chaturvedi, Anil K., Graubard, Barry I., Pickard, Robert K.L., Xiao, Weihong, Gillison, Maura L., 2014. High-risk oral human papillomavirus load in the US population, National Health and Nutrition Examination Survey 2009–2010. J. Infect. Dis. 210, 441–447.

Chaturvedi, Anil K., Graubard, Barry I., Broutian, Tatevik, Pickard, Robert K.L., Tong, Zhen Yue, Xiao, Weihong, Kahle, Lisa, Gillison, Maura L., 2015. NHANES 2009–2012 findings: association of sexual behaviors with higher prevalence of oral oncogenic human papillomavirus infections in U.S. men. Cancer Res. 75 (12), 2468–2477.

Chaturvedi, Anil K., Graubard, Barry I., Broutian, Tatevik, Pickard, Robert K.L., Tong, Zhen Yue, Xiao, Weihong, Kahle, Lisa, Gillison, Maura L., 2018. Effect of prophylactic human papillomavirus (HPV) vaccination on oral HPV infections among young adults in the United States. J. Clin. Oncol. 36 (3), 262–267.

Colón-López, Vivian, Toro-Mejías, Lizbeth M. Del, Ortiz, Ana P., Tortolero-Luna, Guillermo, Palefsky, Joel M., 2012. HPV awareness and willingness to HPV vaccination among high-risk men attending an STI clinic in Puerto Rico. P. R. Health Sci. J. 31 (4), 227–231.

Dunne, Eileen F., Unger, Elizabeth R., Sternberg, Maya, McQuillan, Geraldine, Swan, David C., Patel, Sonya S., Markowitz, Lauri E., 2007. Prevalence of HPV infection among females in the United States. JAMA 297 (8), 813–819.

Dunne, Eileen F., Sternberg, Maya, Markowitz, Lauri E., McQuillan, Geraldine, Swan, David, Patel, Sonya, Unger, Elizabeth R., 2011. Human papillomavirus (HPV) 6, 11, 16, and 18 prevalence among females in the United States–National Health and Nutrition Examination Survey, 2003–2006: opportunity to measure HPV vaccine impact? J. Infect. Dis. 204 (4), 562–565.

Food and Drug Administration, 2018. Human papillomavirus vaccine. https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm172678.htm, Accessed date: 9 January 2019.

Franco, E.L., Villa, L.L., Sobrinho, J.P., Prado, J.M., Rousseau, M.C., Désy, M., Rohan, T.E., 1999. Epidemiology of acquisition and clearance of cervical human papillomavirus infection in women from a high-risk area for cervical cancer. J. Infect. Dis. 180 (5), 1415–1423.

Gargano, Julia W., Unger, Elizabeth R., Liu, Gui, Steinau, Martin, Meites, Elissa, Dunne, Eileen, Markowitz, Lauri E., 2017. Prevalence of genital human papillomavirus in males, United States, 2013–2014. J. Infect. Dis. 215 (Cdc), 2013–2014.

Gerend, Mary A., Madkins, Krystal, Phillips, Gregory I.I., Mustanski, Brian, 2016. Predictors of human papillomavirus vaccination among young men who have sex with men. Sex. Transm. Dis. 43 (3), 185–191.

Gillison, Maura L., Alemany, Laia, Snijders, Peter J.F., Chaturvedi, Anil, Steinberg, Bettie M., Schwartz, Steve, Castellsagué, Xavier, 2012a. Human papillomavirus and diseases of the upper airway: head and neck cancer and respiratory papillomatosis. Vaccine 30 (Suppl. 5), F34–F54.

Gillison, Maura L., Broutian, Tatevik, Pickard, Robert K.L., Tong, Zhen-you, Xiao, Weihong, Kahle, Lisa, Graubard, Barry I., Chaturvedi, Anil K., 2012b. Prevalence of oral HPV infection in the United States, 2009–2010. JAMA 307 (7), 693–703.

Giuliano, Anna R., Lee, Ji-Hyun, Fulp, William, Villa, Luisa L., Lazcano, Eduardo, Papenfuss, Mary R., Abrahamsen, Martha, Salmeron, Jorge, Anic, Gabriella M., Rollison, Dana E., Smith, Danelle, 2011a. Incidence and clearance of genital human papillomavirus infection in men (HIM): a cohort study. Lancet 377 (9769), 932–940.

Giuliano, Anna R., Palefsky, Joel M., Goldstone, Stephen, Moreira, Edson D., Penny, Mary E., Aranda, Carlos, Vardas, Eftyhia, Moi, Harald, Jessen, Heiko, Hillman, Richard, Chang, Yen-Hwa, Ferris, Daron, Rouleau, Danielle, Bryan, Janine, Brooke Marshall, J., Vuocolo, Scott, Barr, Eliav, Radley, David, Haupt, Richard M., Guris, Dalya, 2011b. Efficacy of quadrivalent HPV vaccine against HPV infection and disease in males. N. Engl. J. Med. 364 (5), 401–411.

Goodman, Marc T., Shvetsov, Yurii B., McDuffie, Katharine, Wilkens, Lynne R., Zhu, Xuemei, Thompson, Pamela J., Ning, Lily, Killeen, Jeffrey, Kamemoto, Lori, Hernandez, Brenda Y., 2010. Sequential acquisition of human papillomavirus (HPV) infection of the anus and cervix: the Hawaii HPV Cohort Study. J. Infect. Dis. 201 (9), 1331–1339.

Han, Jasmine J., Beltran, Thomas H., Song, John W., Klaric, John, Choi, Y. Sammy, 2017. Prevalence of genital human papillomavirus infection and human papillomavirus vaccination rates among US adult men. JAMA Oncol. 28307, 1–7.

Hariri, Susan, Unger, Elizabeth R., Sternberg, Maya, Dunne, Eileen F., Swan, David, Patel, Sonya, Markowitz, Lauri E., 2011. Prevalence of genital human papillomavirus among females in the United States, the National Health and Nutrition Examination Survey, 2003–2006. J. Infect. Dis. 204 (4), 566–573.

Hernandez, Brenda Y., McDuffie, Katharine, Zhu, Xuemei, Wilkens, Lynne R., Killeen, Jeffrey, Kessel, Bruce, Wakabayashi, Mark T., Bertram, Cathy C., Easa, David, Ning, Lily, Boyd, Jamie, Sunoo, Christian, Kamemoto, Lori, Goodman, Marc T., 2005. Anal human papillomavirus infection in women and its relationship with cervical infection. Cancer Epidemiol. Biomark. Prev. 14 (11 Pt 1), 2550–2556.

Herrero, R., Hildesheim, A., Bratti, C., Sherman, M.E., Hutchinson, M., Morales, J., Balmaceda, I., Greenberg, M.D., Alfaro, M., Burk, R.D., Wacholder, S., Plummer, M., Schiffman, M., 2000. Population-based study of human papillomavirus infection and cervical neoplasia in rural Costa Rica. J. Natl. Cancer Inst. 92 (6), 464–474.

Herrero, Rolando, Castle, Philip E., Schiffman, Mark, Bratti, M. Concepción, Hildesheim, Allan, Morales, Jorge, Alfaro, Mario, Sherman, Mark E., Wacholder, Sholom, Chen, Sabrina, Rodriguez, Ana C., Burk, Robert D., 2005. Epidemiologic profile of type-specific human papillomavirus infection and cervical neoplasia in Guanacaste, Costa Rica. J. Infect. Dis. 191 (11), 1796.

Ho, G.Y.F., Bierman, R., 1998. Natural history of cervicovaginal papillomavirus infection in young women. N. Engl. J. Med. 338 (7), 423–428.

International Agency for Research on Cancer, 2012. Human papillomaviruses. IARC Monogr. Eval. Carcinog. Risks Hum. 100 (B), 255–296.

Jemal, Ahmedin, Simard, Edgar P., Dorell, Christina, Noone, Anne-Michelle, Markowitz, Lauri E., Kohler, Betsy, Eheman, Christie, Saraiya, Mona, Bandi, Priti, Saslow, Debbie, Cronin, Kathleen A., Watson, Meg, Schiffman, Mark, Henley, S. Jane, Schymura, Maria J., Anderson, Robert N., Yankey, David, Edwards, Brenda K., 2013. Annual report to the nation on the status of cancer, 1975–2009, featuring the burden and trends in human papillomavirus (HPV)-associated cancers and HPV vaccination coverage levels. J. Natl. Cancer Inst. 105 (3), 175–201.

Kahn, Laura, Lowry, Richard, Eaton, Danice, Wechsler, Howell, 2012. Trends in HIV-related risk behaviors among high school students–United States, 1991–2011. Morb. Mortal. Wkly Rep. 61 (29), 556–560.

Kedarisetty, Suraj, Orosco, Ryan K., Hecht, Avram S., Chang, David C., Weissbrod, Philip A., Coffey, Charles S., 2016. Concordant Oral and vaginal human papillomavirus infection in the United States. JAMA Otolaryngol. Head Neck Surg. 8895, 1–9.

Kreimer, Aimée R., 2014. Prospects for prevention of HPV-driven oropharynx cancer. Oral Oncol. 50 (6), 555–559.

Kreimer, Aimée R., Campbell, Christine M. Pierce, Lin, Hui-Yi, Fulp, William, Papenfuss, Mary R., Abrahamsen, Martha, Hildesheim, Allan, Villa, Luisa L., Salmerón, Jorge J., Lazcano-Ponce, Eduardo, Giuliano, Anna R., 2013. Incidence and clearance of oral human papillomavirus infection in men: the HIM cohort study. Lancet 6736 (13), 1–11.

Lazcano-Ponce, E., Herrero, R., Munoz, N., Cruz, A., Shah, K.V., Alonso, P., Hernandez, P., Salmeron, J., Hernandez, M., 2001. Epidemiology of HPV infection among Mexican women with normal cervical cytology. Int. J. Cancer 91 (3), 412–420.

Lewis, Rayleen M., Markowitz, Lauri E., Gargano, Julia W., Steinau, Martin, Unger, Elizabeth R., 2018. Prevalence of genital human papillomavirus among sexually experienced males and females aged 14–59 years, United States, 2013–2014. J. Infect. Dis. 217 (6), 869–877.

Liu, Gui, Hariri, Susan, Bradley, Heather, Gottlieb, Sami L., Leichliter, Jami S., Markowitz, Lauri E., 2015. Trends and patterns of sexual behaviors among adolescents and adults aged 14 to 59 years, United States. Sex. Transm. Dis. 42 (1), 20–26.

Liu, Gui, Markowitz, Lauri E., Hariri, Susan, Panicker, Gitika, Unger, Elizabeth R., 2016. Seroprevalence of 9 human papillomavirus types in the United States, 2005–2006. J. Infect. Dis. 213 (2), 191–198.

Markowitz, Lauri E., Sternberg, Maya, Dunne, Eileen F., McQuillan, Geraldine, Unger, Elizabeth R., 2009. Seroprevalence of human papillomavirus types 6, 11, 16, and 18

in the United States: National Health and Nutrition Examination Survey 2003–2004. J. Infect. Dis. 200 (7), 1059–1067.
Markowitz, L.E., Hariri, S., Lin, C., Dunne, E.F., Steinau, M., McQuillan, G., Unger, E.R., 2013. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003–2010. J. Infect. Dis. 208 (3), 385–393 jun.
Markowitz, Lauri E., Liu, Gui, Hariri, Susan, Steinau, Martin, Dunne, Eileen F., Unger, Elizabeth R., 2016. Prevalence of HPV after introduction of the vaccination program in the United States. Pediatrics 137 (3), 1–9.
McQuillan, Geraldine, Kruszon-moran, Deanna, Markowitz, Lauri E., Unger, Elizabeth R., Paulose-ram, Ryne, 2017. Prevalence of HPV in adults aged 18–69: United States, 2011–2014. NCHS Data Brief 280.
Molano, M., Posso, H., Weiderpass, E., van den Brule, A.J.C., Ronderos, M., Franceschi, S., Meijer, C.J.L.M., Arslan, A., Munoz, N., 2002. Prevalence and determinants of HPV infection among Colombian women with normal cytology. Br. J. Cancer 87 (3), 324–333.
Molano, M., Brule, Adriaan van den, Plummer, Martyn, Weiderpass, Elisabete, Posso, Hector, Arslan, Annie, Meijer, Chris J.L.M., Munoz, Nubia, Franceschi, Silvia, 2003. Determinants of clearance of human papillomavirus infections in Colombian women with normal cytology: a population-based, 5-year follow-up study. Am. J. Epidemiol. 158 (5), 486–494.
Moscicki, Anna-Barbara, Schiffman, Mark, Burchell, Ann, Albero, Ginesa, Giuliano, Anna R., Goodman, Marc T., Kjaer, Susanne K., Palefsky, Joel, 2012. Updating the natural history of human papillomavirus and anogenital cancers. Vaccine 30 (Suppl. 5), F24–F33.
Muñoz, Nubia, Xavier Bosch, F., Sanjosé, Silvia de, Herrero, Rolando, Castellsagué, Xavier, Shah, Keerti V., Snijders, Peter J.F., Meijer, Chris J.L.M., 2003. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N. Engl. J. Med. 348 (6), 518–527.
National Center for Health Statistics, 2013. National Health and Nutrition Examination Survey: analytic guidelines, 1999–2010. Vital Health Statistics 2 (161).
Nunes, Emily M., López, Rossana V.M., Sudenga, Staci L., Gheit, Tarik, Tommasino, Massimo, Baggio, Maria L., Ferreira, Silvaneide, Galan, Lenice, Silva, Roberto C., Lazcano-Ponce, Eduardo, Giuliano, Anna R., Villa, Luisa L., Sichero, Laura, 2017. Concordance of beta-papillomavirus across anogenital and oral anatomic sites of men: the HIM Study. Virology 510 (July), 55–59.
Parker, J.D., Talih, M., Malec, D.J., Beresovsky, V., Carroll, M., Gonzales, J.F., Hamilton, B.E., Ingram, D.D., Kochanek, K., McCarty, F., Moriarty, C., Shimizu, I., Strashny, A., Ward, B., 2017. National Center for Health Statistics Data Presentation Standards for Proportions. Technical Report 175. National Center for Health Statistics.
Patel, Eshan U., Rositch, Anne F., Gravitt, Patti E., Tobian, Aaron A.R., 2017. Concordance of penile and oral human papillomavirus infections among men in the United States. J. Infect. Dis. 215 (8), 1207–1211.
Reiter, Paul L., McRee, Annie-Laurie, 2016. HPV infection among a population-based sample of sexual minority women from USA. Sex. Transm. Infect. 1–7.
Roche Molecular Systems, Inc, 2015. cobas HPV Test. https://www.accessdata.fda.gov/cdrh_docs/pdf10/p100020s017c.pdf, Accessed date: 9 January 2019.
Ryser, Marc D., Rositch, Anne, Gravitt, Patti E., 2017. Modeling of US human papillomavirus (HPV) seroprevalence by age and sexual behavior indicates an increasing trend of HPV infection following the sexual revolution. J. Infect. Dis. 216 (5), 604–611.
Saraiya, Mona, Unger, Elizabeth R., Thompson, Trevor D., Lynch, Charles F., Hernandez, Brenda Y., Lyu, Christopher W., Steinau, Martin, Watson, Meg, Wilkinson, Edward J., Hopenhayn, Claudia, Copeland, Glenn, Cozen, Wendy, Peters, Edward S., Huang, Youjie, Saber, Maria Sibug, Altekruse, Sean, Goodman, Marc T., 2015. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. J. Natl. Cancer Inst. 107 (6).
Satterwhite, Catherine Lindsey, Torrone, Elizabeth, Meites, Elissa, Dunne, Eileen F., Mahajan, Reena, Ocfemia, M. Cheryl Bañez, Su, John, Xu, Fujie, Weinstock, Hillard, 2013. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. Sex. Transm. Dis. 40 (3), 187–193.
Smelov, Vitaly, Muwonge, Richard, Sokolova, Olga, McKay-Chopin, Sandrine, Eklund, Carina, Komyakov, Boris, Gheit, Tarik, 2018. Beta and gamma human papillomaviruses in anal and genital sites among men: prevalence and determinants. Sci. Rep. 8 (1), 1–10.
Sonawane, Kalyani, Suk, Ryan, Chiao, Elizabeth Y., Chhatwal, Jagpreet, Qiu, Peihua, Wilkin, Timothy, Nyitray, Alan G., Sikora, Andrew G., Deshmukh, Ashish A., 2017. Oral human papillomavirus infection: differences in prevalence between sexes and concordance with genital human papillomavirus infection, NHANES 2011 to 2014. Ann. Intern. Med. 167 (10), 714–724.
Sonenstein, Freya L., Pleck, Joseph H., Ku, Leighton C., 1989. Sexual activity, condom use and AIDS awareness among adolescent males. Fam. Plan. Perspect. 21 (4), 152–158.
Steinau, Martin, Hariri, Susan, Gillison, Maura L., Broutian, Tatevic R., Dunne, Eileen F., Tong, Zhen-yue, Markowitz, Lauri E., Unger, Elizabeth R., 2014. Prevalence of cervical and oral human papillomavirus infections among US women. J. Infect. Dis. 209 (11), 1739–1743.
Wells, Brooke E., Twenge, Jean M., 2005. Changes in young people's sexual behavior and attitudes, 1943–1999: a cross-temporal meta-analysis. Rev. Gen. Psychol. 9 (3), 249–261.