Human Papillomavirus Infections in the Southern and Other United States Regions

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Dudith Pierre-Victor , *Florida International University, Department of Epidemiology*, dpier014@fiu.edu

Mary Jo Trepka , *Department of Epidemiology and Center for Substance Use and HIV/AIDS Research on Latinos in the United States (C–SALUD), Florida International University*, trepkam@fiu.edu

Dionne Stephens , *African & African Diaspora Studies Program, Florida International University*, stephens@fiu.edu

See next page for additional authors

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Abstract

Human papillomavirus (HPV) infection is the most common sexually transmitted infection worldwide and has been linked to several cancers, including cervical cancer. In the United States, the Southern region has a disproportionate burden of cervical cancer, and research about the epidemiology of HPV in the region is scarce. This study estimates the prevalence and correlates of HPV infection among 14–59 year-old females.

Data from 4,250 females aged 14–59 years collected during the 2007–2010 National Health and Nutrition Examination Survey (NHANES) were used. We estimated the prevalence of HPV infection for the South and the rest of the country. We performed weighted chi-square test and logistic regression to examine the association between HPV infection and various demographics.

Among 14–26 year-old females, the prevalence of high-risk oncogenic HPV types was 25.6% (95% confidence (CI): 22.4– 33.3) in the South and 29.1% (95% CI: 24.8– 33.8) in the rest of the country (p= 0.15). Among 27–59 year-old women, infection from high-risk oncogenic types was 20.9% (95% CI: 17.4– 24.9) in the South compared to 14.5% (95% CI: 12.9– 16.3) in the rest of the country (p=0.0001).

This study found a higher prevalence of infection from high-risk oncogenic types among 27– 59 year-old females in the South compared to the rest of the country, but not among the 14– 26 year-olds. These findings highlight the importance of promoting HPV vaccination as well as cervical cancer screening, particularly in the Southern region.

Keywords

HPV infection; Prevalence; Southern region; Geographic disparities

Cover Page Footnote

Address correspondence to: Dudith Pierre-Victor, Florida International University- Department of Epidemiology, 11200 SW 8th Street AHC5-477, Miami, Florida, 33199 dpier014@fiu.edu phone: 1-305-348-0497 Fax: 305-348-7782

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Authors

Dudith Pierre-Victor, Mary Jo Trepka, Dionne Stephens, Tan Li, Timothy Page, and Purnima Madhivanan

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School of Community Health Sciences
University of Nevada, Las Vegas

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Dudith Pierre-Victor, Florida International University
Mary Jo Trepka, Florida International University
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Corresponding Author: Dudith Pierre-Victor, Florida International University-Department of Epidemiology, 11200 SW 8th Street AHC5-477, Miami, Florida, 33199 dpier014@fiu.edu phone: 1-305-348-0497 Fax: 305-348-7782

ABSTRACT

Human papillomavirus (HPV) infection is the most common sexually transmitted infection worldwide and has been linked to several cancers, including cervical cancer. In the United States, the Southern region has a disproportionate burden of cervical cancer, and research about the epidemiology of HPV in the region is scarce. This study estimates the prevalence and correlates of HPV infection among 14–59 year-old females.

Data from 4,250 females aged 14–59 years collected during the 2007–2010 National Health and Nutrition Examination Survey (NHANES) were used. We estimated the prevalence of HPV infection for the South and the rest of the country. We performed weighted chi-square test and logistic regression to examine the association between HPV infection and various demographics.

Among 14–26 year-old females, the prevalence of high-risk oncogenic HPV types was 25.6% (95% confidence (CI): 22.4−33.3) in the South and 29.1% (95% CI: 24.8−33.8) in the rest of the country (p= 0.15). Among 27–59 year-old women, infection from high-risk oncogenic types was 20.9% (95% CI: 17.4−24.9) in the South compared to 14.5% (95% CI: 12.9−16.3) in the rest of the country (p=0.0001).

This study found a higher prevalence of infection from high-risk oncogenic types among 27−59 year-old females in the South compared to the rest of the country, but not among the 14−26 year-olds. These findings highlight the importance of promoting HPV vaccination as well as cervical cancer screening, particularly in the Southern region.

Keywords: HPV infection; Prevalence; Southern region; Geographic disparities

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide (World Health Organization, 2016) and has been consistently linked to head, neck, pharyngeal, and anogenital cancers (Forman et al., 2012). Over 100 HPV types infect humans, and 40 of these HPV types infect mainly the anogenital tract (Franco, Duarte-Franco, & Ferenczy, 2001). Most HPV-related cancers result from infections from HPV types 16 and 18 (Muñoz et al., 2003). According to their association with pre-malignancy and invasive cancer, HPV types are classified as high or low risk oncogenic, and non-oncogenic (Bosch, Lorincz, Muñoz, Meijer, & Shah, 2002; Franco et al., 2001; Wright, Denny, & Kuhn, 2000).

Among HPV-related cancers, cervical cancer is the most prevalent. Cervical cancer disproportionately affects women in developing and underdeveloped countries. In developed countries, cervical cancer affects poor and disadvantaged women (International Agency for Research on Cancer, 2014). In the United States, cervical cancer mainly affects disadvantaged, poor women with limited access to healthcare such as those living in the Appalachia and the Southern region (Horner et al., 2011). The United States is divided into four census regions: The West, the Midwest, the Northeast, and the South. The South is comprised of 17 states: Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia, Alabama, Kentucky, Mississippi, Tennessee, Arkansas, Louisiana, Oklahoma, and Texas (U.S. Census Bureau, 2013b). In 2013, the national cervical cancer incidence was 7.2 per 100,000. The five states with the highest cervical cancer incidence rates were all located in the South: Arkansas (10.6 per 100,000), Oklahoma (9.5), Alabama (9.1), Tennessee (8.9), and Texas (8.7) (U.S. Statistics Working Group, 2016).

Women residing in the Southern region are disproportionately affected by cervical cancer. However, research studies estimating the prevalence of HPV infection and associated socio-demographic and behavioral characteristics in the region are lacking. Such information is crucial to increase HPV vaccination and cervical cancer screening in order to reduce disparities. We estimated the prevalence of HPV infection from oncogenic and non-oncogenic types and examined the correlates of HPV infections in the American South using the National Health and Nutrition Examination Survey (NHANES) data.

METHODS

Study design and population

NHANES data are collected through a multifaceted probability sampling strategy (Curtin, Lester et al., 2013). The detailed methodologies have been published elsewhere (Curtin, Lester et al., 2013; Zipf et al., 2013). Dwelling units were randomly selected, and individuals of any age were randomly selected to participate in the survey. Any individual who was selected was considered eligible for the survey. NHANES data collection occurred in two stages: a home interview and a health examination. After the home interview survey, participants were invited to the Mobile Examination Center (MEC) for computer-assisted personal interview (CAPI) questionnaires, Audio computer-assisted personal self-interview (ACASI) health examination, and biological specimen collection (Zipf et al., 2013). The NHANES survey process was explained to each sample individual. Subsequently, informed consent was obtained from each selected adults. Parents and guardians gave permission for minors to participate, and minors provided assent prior to participation. Consent was obtained from the home interview and then for the health examination (Zipf et al., 2013).

From 2003 to 2010, females 14−59 years were asked to self-collect vaginal samples. A systematic review comparing self-collected and physician-collected samples for low- and high-risk types HPV DNA detection from 18 studies estimated the average detection rate at 27.4% for self-sampling and 28.0% for physician-sampling (Petignat et al., 2007).

Two NHANES survey cycles, 2007−2008 and 2009−2010, were combined for the analysis. For the 2007−2008 NHANES survey cycle, 78.4% of individuals screened for eligibility consented for the home interview. Participation rates were 79.4% for the home interview for the 2009−2010 cycle (National Centers for Health Statistics, 2013). Among selected females, the response rate for health examination was 75.5% in the 2007−2008 cycle and 77.4% for the 2009−2010 cycle (National Centers for Health Statistics, 2013). NHANES reports HPV test results as positive, negative, inadequate or missing for 40 HPV types. A total of 4,250 females aged 14−59 years provided adequate self-collected vaginal samples for HPV DNA detection from 2007 to 2010. Based on HPV vaccine eligibility, the sample was divided into those still eligible for HPV vaccine (14−26 years) and those no longer eligible (27−59 years).

Variables

HPV infection status was the outcome of interest. Following the classification scheme developed by several researchers (Bosch et al., 2002; Bouvard et al., 2009; Franco et al., 2001), HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59 were classified as high risk oncogenic types. HPV types 6, 11, 16, 18, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 55, 56, 58, and 59 were classified as oncogenic types. The remaining HPV types were classified as non-oncogenic. Females who tested positive for at least one of the high-risk oncogenic types were classified as being infected with high-risk oncogenic HPV types. The same criterion was used for any oncogenic types. HPV infection status, race/ethnicity, country of birth, country of citizenship, federal poverty level, health insurance status, healthcare utilization variables, HPV infection status, use of contraception, duration of contraception use, age at first sexual intercourse, and number of lifetime partners were included in the analysis. Smoking, although an important covariate, could not be included in the analysis due to missing data, especially in the 14−26 years age-group.

Participants' state of residence were not publicly available. As a result, publicly available variables−socio-demographics, sexual behavior, reproductive health, and HPV infection status−along with the restricted variables were merged by a staff at the Restricted Data Center. The dataset was not released to the investigators but was accessed and analyzed at the Restricted Data Center in Atlanta, Georgia. For several variables, the levels were combined to prevent the reporting of small cell sizes that could potentially lead to the identification of participants. First, the respondents' region of residence rather than the state was specified in the dataset used for the analysis. Additionally, not every state was sampled in any given survey cycle. As a result, the four U.S. Census regions were used in the analysis rather than the nine U.S. Census divisions. Moreover, the race/ethnicity categories were non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic, and other (including multiracial individuals). Individuals in the "other" category comprised about 6% of the sample. Mexican Americans, other Hispanics, and individuals of other racial and ethnic groups were combined. The study was granted exempt status by the investigators' Institutional Review Board.

Statistical Analysis

STATA svy (StataCorp, 2013) commands were used to conduct the analyses to account for the complex multistage study design and sample weight. Since two survey cycles were combined, we followed NHANES guidelines to compute the new MEC sample weight for the analysis.

Women 14−59 years of age from all racial/ethnic groups were included in the analysis. The proportion of respondents who tested positive for high-risk oncogenic, any oncogenic, and non-oncogenic types HPV for 2007−2010 were computed for the South separately and the three other regions combined (Northeast, Midwest, and West).

A 95% confidence interval was computed for each proportion. Weighted chi-square analyses were performed to examine the association between HPV infection and important demographic, healthcare utilization, and sexual behavior variables. Variables that were significantly associated with HPV infection were included in a stepwise multivariable logistic regression to identify factors independently associated with HPV infection among sexually active women. Interactions were not examined due to the modest sample size. We performed analysis with all females for whom the variables and outcome of interest were present. A 5% significance level was used for all analyses.

RESULTS

Unadjusted HPV Prevalence

14–26 year-old females. Among 14–26 year-old females, the prevalence of infection from high-risk oncogenic types was 25.6% (95% CI: 22.4−33.3) in the South and 29.1% (95% CI: 24.8−33.8) in the rest of the country (p=0.15). The prevalence of infection from any oncogenic types was 31.7% (95% CI: 26.4−37.6) in the South and 32.3% (95% CI: 27.9−36.9) in other regions (p=0.84). Non-oncogenic types HPV prevalence was 36.5% (95% CI: 30.0−43.4) in the South and 31.9% (95% CI: 26.9−37.4) in the other regions (p=0.08) (Table 1).

27−59 year-old women. Among 27–59 year-old women, infection from high-risk oncogenic types was 20.9% (95% CI: 17.4−24.9) in the South compared to 14.5% (95% CI: 12.9−16.3) in other regions (p=0.0001). For infection from any oncogenic types, infection rates were 24.0% (95% CI: 19.9−28.7) and 17.9% (95% CI: 16.3−19.5) for the South and other regions respectively (p=0.0001). Non-oncogenic types HPV prevalence was 32.4% (95% CI: 29.6−35.4) in the South and 28.1% (95% CI: 26.3−30.1) in the other regions (p=0.014) (Table 1).

Demographics Associated with HPV Infection

14–26 year-old females. Infection from high-risk oncogenic types varied significantly by history of contraceptive use, sexual activity status, and number of lifetime sex partners in both the South and the rest of the country (Table 2) whereas infection from any oncogenic types varied by race/ethnicity, history of contraceptive use, sexual activity status, and number of lifetime sex partners (Table 2).

27–59 year-old women. Among 27–59 year-old women residing in the South as well as those residing in the rest of the country, infection from high-risk oncogenic types varied significantly by race/ethnicity, marital status, poverty index, insurance status, and number of lifetime sex partners (Table 3). Infection from any oncogenic types varied by race/ethnicity, marital status, poverty index, insurance status, and number of lifetime sex partners in both the Southern region and the rest of the country (Table 3).

Table 1. Prevalence of high-risk oncogenic, oncogenic, and non-oncogenic types HPV

14-26 year-old females	Region[a]		p-value
	South (n=532)	**Other[b] (n=811)**	
High-risk oncogenic[c] types infection			0.15
Yes	25.6 (22.4-33.3)	29.1 (24.8-33.8)	
No	74.4 (66.7-77.5)	70.9 (66.2-75.2)	
Any oncogenic[d] types infection			0.84
Yes	31.7 (26.4-37.6)	32.3 (27.9-36.9)	
No	68.3 (62.4-73.6)	67.7 (63.0-72.1)	
Non-oncogenic[e] types infection			0.08
Yes	36.5 (30.0-43.4)	31.9 (26.9-37.4)	
No	63.4 (56.6-69.9)	68.1 (62.6-73.1)	
27-59 year-old females	**South (n=1,066)**	**Other [b] (n=1841)**	
High-risk oncogenic[c] types infection			**0.0001**
Yes	20.9 (17.4-24.9)	14.5 (12.9-16.3)	
No	79.1 (75.1-82.6)	85.5 (83.7-87.1)	
Any oncogenic[d] types infection			**0.0001**
Yes	24.0 (19.9-28.7)	17.9 (16.3-19.5)	
No	76.0 (71.3-80.1)	82.1 (80.5-83.7)	
Non-oncogenic[e] types infection			**0.014**
Yes	32.4 (29.6-35.4)	28.1 (26.3-30.1)	
No	67.6 (64.6-70.4)	71.9 (69.9-73.7)	

[a]To prevent potential disclosure, the region rather than the state of residence was included in the dataset
[b]Northeast, West, and Midwest combined
[c]HPV types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59
[d]HPV types: 6, 11, 16, 18, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 55, 56, 58, and 59
[e]All other HPV types

Table 2. Socio-demographic and behavioral characteristics associated with infection from high-risk types among 14-26 year-old females

Characteristics	HR Oncogenic[a] types						Any oncogenic[b] types HPV					
	South (n= 532)			Other[b] (n=811)			South (n= 532)			Other[b] (n=811)		
	Infection		p-value	Infection		p-value	Infection		p-value	Infection		p-value
	Yes	No		Yes	No		Yes	No		Yes	No	
Race/Ethnicity	%	%	***0.04***	%	%	0.2	%	%	***0.015***	%	%	*0.14*
Non-Hispanic White	44.2	55.7		65.6	63.0		43.6	56.7		65.6	62.8	
Non-Hispanic Black	34.2	19.0		11.4	8.9		34.4	18.0		11.7	8.7	
Hispanic and Other	21.6	25.3		23.0	28.1		22.0	25.3		22.7	28.5	
Country of birth			0.28			0.7			0.15			0.8
US	89.9	88.0		86.5	88.4		90.8	87.4		87.4	88.0	
Other	10.1	12.0		13.5	11.6		9.2	12.8		12.6	12.0	
Country of citizenship			0.58			0.9						0.6
US	93.8	92.0		91.7	91.6		94.4	92.2	0.35	92.3	91.3	
Other	6.2	7.4		8.3	8.4		5.6	7.8		7.7	8.7	
Marital status			*0.5*			***0.00001***			0.5			***0.00001***
Married	22.5	31.3		4.8	25.2		23.4	31.6		5.1	26.7	
Never married	65.3	65.3		69.3	53.2		64.2	55.3		69.4	51.7	
Divorced/separated/widowed	12.2	13.1		25.9	21.6		12.4	13.1		25.5	21.6	
Poverty index			*0.45*			***0.03***			0.3			*0.3*
<100%	35.6	25.2		26.1	24.4		36.2	24.3		26.6	24.0	
100-299%	22.8	25.5		23.6	20.1		21.9	26.1		23.8	19.8	
300-499%	27.4	30.8		29.1	24.4		29.6	29.9		27.5	25.0	
≥ 500%	14.2	18.5		21.2	31.1		12.3	19.7		22.1	31.2	

Health insurance			*0.55*			***0.036***			0.6			***0.02***
Yes	69.1	74.3		68.3	79.3		70.3			67.6	80.2	
No	30.9	25.7		31.7	20.7		29.7	74.0		32.4	19.8	
Type of place most often go for healthcare			*0.39*			0.7		26.0	0.13			*0.8*
Doctor's office	60.3	66.9		74.0	71.8		56.6	69.0		71.6	72.8	
Other	39.7	33.1		26.0	28.2		43.4	31.0		28.4	27.2	
No. of healthcare visits last year			*0.69*			0.8			0.92			0.5
None	10.4	13.2		12.2	10.8		11.9	12.7		12.9	10.3	
≤3	57.2	52.2		50.1	52.2		54.7	53.1		48.8	53.0	
≥4	32.4	34.6		37.7	37.0		33.4	34.2		38.3	36.7	
Ever taken birth control pills			***0.005***			***0.0001***			***0.0005***			***0.0001***
Yes	70.2	45.6		62.2	42.5		69.8	44.4		63.3	41.2	
No	29.8	54.4		37.8	57.5		30.2	55.6		36.7	58.8	
No. of years of birth control pills			*0.51*			0.5			0.11			0.8
<2	43.2	47.6		44.4	50.8		41.8	48.9		44.2	51.4	
≥2	56.8	52.4		55.6	49.2		58.2	51.1		55.8	48.6	
Ever had sex			***0.00001***			***0.00001***			***0.00001***			***0.00001***
Yes	95.5	67.1		95.0	62.7		95.2	65.7		95.4	61.2	
No	4.5	32.9		5.0	37.3		4.8	34.3		4.6	38.8	
Age at first sexual intercourse			*0.96*			0.6			0.8			*0.5*
9-14 years	23.8	23.9		25.5	22.4		23.1	24.3		25.4	22.2	
>= 15 years	76.2	76.1		74.5	77.6		76.9	75.7		74.6	77.8	
No. of lifetime sex partners			***0.00001***			***0.00001***			***0.00001***			***0.00001***
≤3	20.5	66.3		27.3	64.7		22.0	68.9		27.0	67.0	
≥4	79.5	33.7		72.7	35.3		78.0	31.1		73.0	33.0	

No. of sex partners 5+ years older			*0.52*			***0.002***			0.08			***0.001***
None	71.1	75.8		59.0	75.9		68.3	78.1		59.2	76.9	
≥1	28.9	24.2		41.0	24.1		31.7	21.9		40.8	23.1	

[a]HPV types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59
[b]HPV types: 6, 11, 16, 18, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 55, 56, 58, and 59
[c]Northeast, West, and Midwest combined

Table 3. Socio-demographic and behavioral characteristics associated with infection from high-risk oncogenic types among 27-59 year-old females

Characteristics	HR Oncogenic[a] types South (n= 1,066) Infection Status		p-value	Other[c] (n=1841) Infection Status		p-value	Any oncogenic[b] types HPV South (n=1,066) Infection Status		p-value	Other[c] (n= 1,841) Infection Status		p-value
	Yes	No		Yes	No		Yes	No		Yes	No	
Race/Ethnicity	%	%	***0.017***	%	%	***0.004***	%	%	***0.02***	%	%	***0.015***
Non-Hispanic White	57.9	59.0		64.8	73.1		56.9	59.4		66.4	73.1	
Non-Hispanic Black	26.1	18.9		13.8	7.3		25.9	18.6		12.5	7.3	
Hispanic and Other	16.0	22.1		21.5	19.6		17.2	22.0		21.2	19.6	
Country of birth			***0.04***			0.9			0.02			*0.7*
US	91.0	83.2		82.4	82.1		90.8	82.9		83.7	81.9	
Other	9.0	16.8		17.6	17.9		9.2	17.1		16.3	18.1	
Country of citizenship			0.06			0.6			0.15			0.32
US	93.5	90.6		91.3	90.2		93.3	90.5		92.0	90.0	
Other	6.5	9.4		8.7	9.2		6.7	9.5		8.0	10.0	
Marital status			***0.00001***			***0.00001***			***0.00001***			***0.00001***
Married	38.1	66.6		36.1	65.9		39.6	67.4		40.1	66.2	
Never married	18.4	8.9		20.3	11.4		18.1	8.6		17.4	11.7	

Divorced/separated/widowed	43.5	24.5		43.6	22.7		42.3	24.0		42.4	22.1	
Poverty index			***0.008***			***0.0002***			***0.006***			***0.001***
<100%	27.9	16.8		21.9	10.9		27.2	16.5		20.0	10.9	
100-299%	22.3	21.5		22.1	16.6		23.3	21.2		21.3	16.5	
300-499%	27.7	26.8		19.9	28.9		28.1	26.6		21.3	29.0	
≥ 500%	22.1	34.9		36.1	43.6		21.4	35.6		37.4	43.6	
Health insurance			***0.006***			***0.02***			***0.004***			*0.05*
Yes	64.2	76.9		79.2	85.6		64.0	77.5		80.8	85.5	
No	35.8	23.1		20.8	14.4		36.0	22.5		19.2	14.5	
Type of place most often go for healthcare			0.7			***0.01***			*0.4*			***0.01***
Doctor's office	76.1	77.5		71.0	77.3		74.8	77.9		71.6	77.5	
Other	23.9	22.5		29.0	22.7		25.2	22.1		28.4	22.5	
No. of healthcare visits last			0.5			***0.041***			0.8			0.4
None	14.9	12.0		13.3	12.0		13.6	12.3		12.4	12.2	
≤3	47.8	48.8		55.5	48.5		48.5	48.6		52.9	48.7	
≥4	37.3	39.2		31.2	39.5		37.9	39.1		34.8	39.1	
Ever taken birth control pills			0.97			0.43			0.9			0.9
Yes	83.7	83.6		84.8	82.8		83.2	83.7		83.3	83.1	
No	16.3	16.4		15.2	17.2		16.8	16.3		16.7	16.9	
No. of years of birth control pills			0.15			***0.04***			0.2			0.08
<2	30.6	25.0		34.1	25.2		30.4	24.9		32.6	25.2	
≥2	69.4	75.0		65.9	74.8		69.6	75.1		67.4	74.8	
Ever had sex			0.15			0.14			0.5			0.2
Yes	98.2	98.3		98.8	97.7		97.9	97.4		98.6	97.7	
No	1.8	1.8		1.2	2.3		2.1	2.6		1.4	2.3	

Age at first sexual intercourse			0.47			***0.016***			*0.3*		***0.0003***
9-14 years	17.3	13.9		14.1	9.9		18.0	13.5		15.5	90.6	
>= 15 years	82.7	86.1		85.9	90.1		82.0	86.5		84.5	9.2	
No. of lifetime sex partners			***0.0004***			***0.00001***			***0.004***			***0.00001***
≤3	21.8	38.7		20.3	41.4		21.7	39.4		21.6	42.0	
≥4	78.2	61.3		79.7	58.6		78.3	60.6		78.4	58.0	
No. of sex partners 5+ years older			0.17			***0.0002***			*0.3*			***0.003***
None	58.1	72.7		58.4	75.2		62.0	71.9		60.2	75.6	
≥1	41.9	27.3		41.6	24.8		38.0	28.1		39.8	24.4	

[a]HPV types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59
[b]HPV types: 6, 11, 16, 18, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 55, 56, 58, and 59
[c]Northeast, West, and Midwest combined

Predictors of HPV Infection among Sexually Active Women

14–26 year-old females. Among 14–26 year-old females in the South, those whose income was 300–499% above the federal poverty level had lower odds of infection from high-risk oncogenic types compared to those whose income was below the federal poverty level (adjusted odds ratio (aOR)= 0.36; p< 0.01). Additionally, females who had four or more lifetime sex partners had greater odds of infection with high-risk oncogenic types compared to those who had three or fewer sex partners (aOR= 8.27; p<0.001) (Table 4). Among 14–26 year-old females living in other regions, those who have never been married had greater odds to be infected with high-risk oncogenic types compared to those who were married (aOR= 12.79; p<0.001), and those who were divorced or separated had higher odds of infection (aOR= 6.09; p<0.001). Those who had four or more sex partners had higher odds of infection compared to those who had three partners or fewer (aOR=4.03; p<0.001) (Table 4).

For infection from any oncogenic types in the South, females whose income was 300–499% above the poverty index had lower odds of infection compared to those whose income was below the poverty index (aOR= 0.45; p<0.05) (Table 4). Southern females who had insurance coverage had higher odds of infection compared to those who had no coverage (aOR=2.48; p<0.01). Those who had four or more sex partners had higher odds of infection compared to those who had three partners or fewer (aOR=8.51; p<0.001). For females in other regions, females who have never been married had greater odds to be infected with high-risk oncogenic types compared to those who were married (aOR= 14.1; p<0.001), and those who were divorced or separated had higher odds of infection (aOR= 6.13; p<0.001). Additionally, females who had four or more sex partners had higher odds of infection compared to those who had three partners or fewer (aOR=4.40; p<0.001) (Table 4).

27–59 year-old females. Among 27–59 year-old women in the South, those who have never been married had increased odds to be infected with high-risk oncogenic types (aOR= 5.14; p<0.01) compared to married women. Those who had four or more sex partners had higher odds of infection compared to those who had three partners or fewer (aOR=1.32; p<0.05) (Table 4). In the other regions, women who have never been married (aOR= 2.38; p<0.01) and those who were previously married (aOR= 4.26; p<0.05) had higher odds of infection from high-risk oncogenic types. Women with household income 300–499% above the poverty index had lower odds to be infected (aOR= 0.26; p<0.01). Additionally, women who had one or more sex partners at least five years older (aOR= 1.84; p<0.01) and who had four or more sex partners (aOR= 3.78; p<0.01) had greater odds to be infected (Table 4).

Table 4. Odds of HPV infections among sexually active 14−59 year-old females by socio-demographic and sexual behavioral characteristics

Characteristics	14-26 year-old females				27-59 year-old females			
	HR onocogenic[a] types HPV		Any oncogenic[b] types HPV		HR oncogenic[a] types HPV		Any oncogenic[b] types HPV	
	South	Other[c]	South	Other[c]	South	Other[c]	South	Other[c]
	aOR[d]	aOR[d]	aOR[d]	aOR[d]	aOR[d]	aOR[d]	aOR[d]	aOR[d]
Race/Ethnicity								
Non-Hispanic White	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Non-Hispanic Black	1.79 (0.62-5.2)	0.85 (0.35-2.1)	1.73 (0.74-4.0)	1.09 (0.47-2.6)	0.72 (0.32-1.7)	0.63 (0.25-1.6)	0.88 (0.36-2.1)	0.52 (0.22-1.2)
Hispanic and Other	1.21 (0.56-2.6)	0.73 (0.39-1.4)	1.32 (0.60-2.94)	0.69 (0.40-1.19)	0.57 (0.24-1.3)	0.76 (0.31-1.8)	0.71 (0.39-1.29)	0.78 (0.36-1.7)
Marital status								
Married	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Never married	1.56 (0.44-5.5)	12.79(4.8-34.1)***	1.33 (0.18-1.4)	14.1 (6.3-31.4)***	5.14 (1.7-15.2)**	2.38 (1.23-4.6)**	4.27 (1.44-12.6)**	2.20 (1.34-3.61)**
Divorced/separated / widowed	1.62 (0.47-5.5)	6.09 (2.2=16.6)**	1.41 (0.36-5.5)	6.13 (2.4-15.8)***	2.98 (0.98-9.1)	4.26 (1.37-13.3)*	2.09 (0.69-7.5)	4.16 (1.76-9.8)**
Poverty index								
<100%	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
100-299%	0.59 (0.25-1.4)	1.79 (0.51-6.2)	0.50 (0.17-1.4)	2.18 (0.59-8.0)	0.57 (0.15-2.2)	0.51 (0.19-1.4)	0.56 (0.15-2.2)	0.58 (0.26-1.3)
300-499%	0.36 (0.17-0.75)**	1.59 (0.65-3.9)	0.41 (0.17-0.99)*	1.32 (0.57-3.1)	1.12 (0.52-2.4)	0.26 (0.10-0.66)**	1.32 (0.50-3.5)	0.34 (0.15-0.78)*

≥ 500%	0.52	(0.13-2.2)	1.01	(0.31-3.2)	0.36	(0.07-1.9)	1.16	(0.41-3.3)	0.79	(0.33-1.9)	0.57	(0.25-1.28)	0.80	(0.38-1.7)	0.69	(0.31-1.5)
Health insurance																
No	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Yes	2.17	(0.79-5.9)	0.66	(0.27-1.6)	2.48	(1.23-5.02)**	0.60	(0.24-1.51)	0.58	(0.27-1.2)	0.92	(0.30-2.78)	0.45	(0.20-1.02)	0.97	(0.32-2.9)
No. of sex partners 5+ years older																
None	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
≥1	0.65	(0.24-1.8)	1.32	(0.66-2.7)	0.94	(0.44-1.97)	1.43	(0.68-3.0)	1.92	(0.45-8.3)	1.84	(1.13-3.0)**	1.64	(0.40-7.1)	1.57	(0.92-2.6)
No. of lifetime sex partners																
≤3	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
≥4	8.27	(2.8-24.4)***	4.03	(2.2-7.4)***	8.51	(3.7-19.6)***	4.40	(2.4-8.2)***	1.32	(1.02-2.23)*	3.78	(1.6-9.0)**	1.43	(0.8-2.53)	3.9	(1.9-8.0)***
Age at first sexual intercourse																
9-14 years									Ref.		Ref.		Ref.		Ref.	
≥ 15 years									1.26	(0.5-3.2)	0.87	(0.59-1.3)	.07	(0.42-2.74)	0.47	(0.24-0.93)*

[a]HPV types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59
[b]HPV types: 6, 11, 16, 18, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 55, 56, 58, and 59
[c]Northeast, West, and Midwest combined
[d]adjusted odds ratio
*p<0.05; ** p<0.01; *** p<0.001

For any oncogenic types, in the South, women who have never been married had higher odds of infection (aOR= 4.27; p<0.01). In the rest of the country, women who have never been married had greater odds to be infected (aOR= 2.20; p<0.01) and those who were divorced, separated, or widowed also had increased odds to be infected (aOR= 4.16; p<0.01). Women whose income was 300–499% above the poverty index had lower odds of infection from any oncogenic types (aOR= 0.34; p<0.01). Those who had four or more sex partners had higher odds of infection (aOR= 3.90; p<0.001), and those who had their sexual debut at 15 years or older had lower odds to be infected with any oncogenic types compared those who had their sexual debut at 14 years or younger (aOR= 0.47; p<0.01) (Table 4).

DISCUSSION

Cervical cancer is more prevalent in the South compared to the rest of the United States, and this study found the prevalence of HPV infections from high-risk oncogenic types to be higher in the South than the rest of the United States among women aged 27−59 years, but not among those 14−26 year-old. A study estimated HPV prevalence among women in the Appalachia, a region with high rates of cervical cancer and predominantly non-Hispanic White population, and found higher prevalence of high-risk infection among Appalachian women (Reiter et al., 2013) when compared to the national estimates for non-Hispanic White females (Hariri et al., 2011; Reiter et al., 2013). The difference in the prevalence of infection from high-risk and any oncogenic types among 27−59 year-old females in the South compared to the rest of the country appears to be smaller than the difference in cervical cancer incidence and mortality. Therefore, this difference in the prevalence of HPV infection from high-risk oncogenic types is not large enough to account for the higher prevalence of cervical cancer in the South.

Among 14−26 year-olds, the prevalence of infection from high-risk oncogenic or any oncogenic HPV types was not higher in the South compared to the rest of the country. Using the 2003−2006 and the 2007−2010 NHANES survey periods, a study investigated the change in the prevalence of infection from HPV types 6, 11, 16, or 18 (Markowitz et al., 2013) and found that among females aged 14−19 years, HPV infection prevalence declined from 11.5% in 2003−2006 to 5.1% in 2007−2010. A similar decline was not observed in the older age-groups (Markowitz et al., 2013). Comparable rates of infection from high-risk or any oncogenic types among 14−26 year-olds between the South and the rest of the country are probably due to the national decline in HPV infection in the vaccine-eligible age-group.

Among 14−26 year-old females residing in the South, those living at 300−499% federal poverty level had lower odds of infection from high-risk and any oncogenic HPV types compared to those living below 100% federal poverty level. Among 27−59 year-old females residing in other regions, the odds of infection from high-risk and any oncogenic HPV types were lower among those living at 300−499% federal poverty level compared to those living below 100% federal poverty level. Previous studies have reported that higher income and higher education levels are associated with lower rates of HPV infection (Hariri et al., 2011; Shi, Devarakonda, Liu, Taylor, & Mills, 2014). The present study also found sexually active, unmarried women to have greater odds of infection from any oncogenic and high-risk oncogenic types. Several studies have reported a higher prevalence of HPV infection among unmarried women (Bui et al., 2017; Dunne et al., 2007; Kahn, Lan, & Kahn, 2007; Reiter et al., 2013). The absence of a long-term and committed sex partner facilitates multiple or short-term sexual partnerships. This may help explain the higher

prevalence of infection from high-risk and any oncogenic types observed among unmarried sexually active women.

Among 14−26 year-old females, this study found that having four or more lifetime sex partners was positively associated with infection from high-risk and any oncogenic types in the South and the rest of the country. However, among 27−59 year-old females, having four or more lifetime sex partners was positively associated with infection from high-risk and any oncogenic types in the rest of the country but not in the South. Previous research has reported that increasing number of lifetime sex partners was associated with HPV infection (Dunne et al., 2007; Markowitz, Sternberg, Dunne, McQuillan, & Unger, 2009; Reiter et al., 2013; Thorsteinsson et al., 2016). It is not clear as to why the increasing number of sex partners was not associated with infection from high-risk or any oncogenic types in the South.

There were several limitations to this study. First, sexual behaviors were self-reported, which can be biased by poor recall and social desirability. Most individuals are not enthusiastic about revealing their sexual practices due to social stigma, embarrassment, or fear of disclosure (Brener, Billy, & Grady, 2003; Kelly, Soler-Hampejsek, Mensch, & Hewett, 2013; O'Sullivan, 2008). Consequently, such behaviors may be underrepresented. In the same vein, previous research has reported that responses to sexual behavior questionnaire through ACASI are generally more accurate compared to face-to-face interviews (Ghanem, Hutton, Zenilman, Zimba, & Erbelding, 2005; Phillips, Gomez, Boily, & Garnett, 2010). NHANES collects sexual behavior data using ACASI thereby reducing social desirability bias in this study; the survey also accounts for participant non-response and collects health information from a nationally representative sample which is robust against selection bias. These aspects lend to more reliable and valid findings. Additionally, missing data were a limitation to this study as it hindered the analysis of HPV infection risk factors by different racial and ethnic groups, smaller age-groups, and smaller geographic divisions. Moreover, due to the risk of potential disclosure, several levels of variables had to be combined, and some important variables, such as smoking, had to be excluded from the analysis altogether. Further, religious affiliation influences attitudes toward HPV vaccine uptake (Thomas, Blumling, & Delaney, 2015), but its association with HPV infection could not be analyzed as such data were not collected in the survey. Despite the limitations, this study contributes to the literature addressing geographic disparities in HPV infection. In the future, racial and ethnic groups, such as American Indians (Centers for Disease Control and Prevention, 2016; Watson et al., 2014) and Vietnamese (Ma et al., 2012), who experience disparities in HPV-related diseases should be oversampled in national surveys collecting HPV samples to facilitate investigations of disparities in HPV infections.

CONCLUSION

This study estimated the prevalence of infection among females for the South and the rest of the country and found a higher prevalence of infection from high-risk oncogenic and any oncogenic HPV types among 27−59 year-old females residing in the South compared to the rest of the country, but not among the 14−26 year-olds. Women in the Southern region remain at higher risk of developing and dying from cervical cancer, and the higher prevalence of infection from high-risk and any oncogenic HPV types among 27−59 year-olds in the South partially explains the higher prevalence of cervical cancer in the South. However, this difference in HPV prevalence seems to be smaller than the difference in cancer incidence between the South and other regions. This suggests that the disparities in cervical cancer incidence and mortality are not only being

driven by the differences in the epidemiology of HPV alone, but also by disparities in cervical cancer screening. Efforts to make cervical cancer screening accessible to disadvantaged women and those at higher risk of infection must continue in order to reduce disparities in cervical cancer incidence and mortality.

Among 14−26 year-olds, the prevalence of infection from high-risk oncogenic and any oncogenic HPV types is relatively high in the South and the rest of the country. These findings reiterate the need for HPV vaccination to be administered to pre-teens, prior to their sexual debut. Additionally, females aged 14− 26 years are still eligible for HPV vaccination catch-up. Consequently, healthcare providers should recommend the vaccine to 14−26 year-old females even if they are already infected with one HPV type as they can be protected from other HPV types covered by the vaccine.

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Conflict of Interests

The authors do not have any conflict of interests to disclose.

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