UNIVERSITY OF CALIFORNIA SAN DIEGO

SAN DIEGO STATE UNIVERSITY

Human Papillomavirus-Related Oropharyngeal Cancer: Understanding Knowledge, Prevention, and Provider Perceptions

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy

in

Public Health (Health Behavior Sciences)

by

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2022

The dissertation of Erin L. Dougherty is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

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Chair

University of California San Diego

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2022

DEDICATION

To my wonderful and supportive husband, Dustin.
I could not have done this without you.

EPIGRAPH

To laugh often and much; to win the
respect of intelligent people and
the affection of children; to earn the
appreciation of honest critics and
endure the betrayal of false friends;
to appreciate beauty; to find the
best in others; to leave the world a
bit better whether by a healthy child,
a garden patch, or a redeemed social
condition; to know that one life has
breathed easier because you lived.
This is to have succeeded.

Ralph Waldo Emerson

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Chapter 2 is currently being prepared for submission for publication. Co-authors include Dr. Tracy Finlayson, Dr. Heather Corliss, Dr. Noe Crespo, Dr. Donna Kritz-Silverstein, Dr. David Strong, and Dr. Sudha Nagalingam. The dissertation author was the primary investigator and author of this material.

Chapter 3 is currently being prepared for submission for publication. Co-authors include Dr. Tracy Finlayson, Dr. Heather Corliss, Dr. Noe Crespo, Dr. Donna Kritz-Silverstein, and Dr. David Strong. The dissertation author was the primary investigator and author of this material.

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2022 Doctor of Philosophy in Public Health
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2014 Master of Public Health, Health Behavior Health Promotion
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RESEARCH EXPERIENCE

2017-2019 Institute for Behavioral and Community Health
San Diego State University Research Foundation
Research Assistant III/Graduate Student

- Conducted quality assurance checks on data collected in the field
- Assisted in grant writing & reporting- focus on NIH Mechanisms
- Conducted in-depth interviews with research participants in San Diego County
- Led a systematic literature review assessing the relationship caregiver social support and child oral health status
- Partnered with local Federally Qualified Health Centers to analyze electronic health record data from research participants

2009 Carlson Child Development Lab
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Dougherty, E.L., Corliss, H.L., Kritz-Silverstein, D., Strong, D.R., Crespo, N.C., Finlayson, T.L. (2022) Relationship between sexual orientation and human papillomavirus-related oral cancer knowledge and awareness. *LGBT Health* doi: https://doi.org/10.1089/lgbt.2021.0146

Manuscripts in Progress:

Dougherty, E.L., Corliss, H.L., Kritz-Silverstein, D., Strong, D.R., Crespo, N.C., Nagalingam, S., Finlayson, T.L. (In Preparation) Factors associated with young adults' human papillomavirus vaccine initiation in a Federally Qualified Health Center.

Dougherty, E.L., Kritz-Silverstein, D., Corliss, H.L., Strong, D.R., Crespo, N.C., Finlayson, T.L. (In Preparation) HPV-related oropharyngeal cancer: Attitudes and perceptions regarding patient engagement among FQHC dental and medical providers.

RESEARCH PRESENTATIONS

Dougherty, E. & Finlayson, T.L. (2017). Literature Review: Does caregiver social support affect children's oral health? San Diego State University- Student Research Symposium

Summary: Social support has not been measured in a systematic way in dental public health research and mixed study findings indicate the need for continued research in the field.

Dougherty, E., Reinschmidt, K. and Roe, D. (2014). Impact of preventive dentistry on oral health outcomes for youth in Tucson, AZ. University of Arizona- MPH Internship Conference

Summary: Mixed methods retrospective analysis examining the influence of nutritional counseling, fluoride varnish treatment, and oral hygiene instruction on caries experience, primarily for Latino youth.

Dougherty, E., Asgari, P., Stamm, N., Finlayson, T.L. (2018) Factors Associated with Flossing Behavior among Mexican Migrants in California (Accepted: APHA- Oral Health Section; poster presentation 11/2018)

*****Finlayson, T.L. & **Dougherty, E.L**. (2022) Role of Dental Providers in HPV and Oropharyngeal Cancer Prevention. American Association for Dental, Oral, and Craniofacial Research.

*Finlayson, T.L. & **Dougherty, E.L**. (2022) Role of Dental Providers in HPV Vaccination and Oropharyngeal Cancer Prevention. National Oral Health Conference.

*Data collected and prepared by Erin Dougherty, presented by Dr. Tracy Finlayson

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ABSTRACT OF THE DISSERTATION

Human Papillomavirus-Related Oropharyngeal Cancer: Understanding Knowledge, Vaccine Initiation and Provider Perceptions

by

Erin L. Dougherty

Doctor of Philosophy in Public Health (Health Behavior Sciences)

University of California San Diego, 2022
San Diego State University, 2022

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Background: Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States, with nearly 80% of the population infected at some point in their lifetime. HPV is the cause of approximately 70% of oropharyngeal cancers (OPC). **Methods**: Chapter 1 utilized data from the Health Information National Trends Survey 5, cycles 1-3; logistic regression analyses examined differences in HPV-related oral cancer knowledge between sexual minorities and their heterosexual counterparts. Chapter 2 utilized electronic health record data of patients without prior history of HPV vaccination. Logistic regression modeling, guided by the Andersen Behavioral Model, examined associations

between predisposing, enabling, and need factors with HPV vaccine initiation. Chapter 3 utilized survey data from medical and dental providers that assessed attitudes regarding HPV-related OPC patient engagement. Guided by the Theory of Planned Behavior, HPV-related OPC responses were compared between medical and dental providers using chi-square tests and linear regression analyses.

Results: In Chapter 1, HPV-related oral cancer knowledge overall was low and there were no significant differences in knowledge for sexual minority men or women compared to heterosexual counterparts. In Chapter 2, HPV vaccine initiation rates overall, were relatively low (20%). For males, minority sexual orientation (OR:1.75; 95% CI:1.20-2.55) and HIV+ status (OR:2.63; 95% CI:1.16-5.97) were associated with greater odds of HPV vaccine initiation; as age increased, odds of HPV vaccine initiation decreased (OR:0.74; 95% CI:0.66-0.84). For females, non-White race (OR:1.26; 95% CI:1.04-1.53), having a nurse practitioner/physician assistant as a provider (OR:1.33; 95% CI:1.08-1.65), and more frequent utilization (OR:1.54; 95% CI:1.31-1.80) were associated with greater odds of HPV vaccine initiation. In Chapter 3, regression analysis indicated dental providers had higher levels of agreement related to perceived behavioral control (greater confidence/feeling adequately trained to engage patients) compared to medical providers ($p<0.001$).

Conclusion: Findings showed HPV-related OPC knowledge and HPV vaccine initiation were low and providers reported lack of adequate training/confidence in HPV-related OPC patient engagement. Action should be taken to increase HPV-related OPC knowledge for vulnerable populations, promote HPV vaccination while considering behavioral risk profiles, and provide continuing education opportunities for providers to improve confidence regarding HPV-related OPC patient engagement.

INTRODUCTION

Human Papillomavirus

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) in the United States (US), with nearly 80% of the population infected at some point in their lifetime.[1,2] HPV infections do not usually present with any symptoms and are easily passed between sexual partners.[3] There are more than 200 strains of HPV, of which, 14 are classified as high risk, with the remainder, categorized as low risk.[3] While the immune system typically clears HPV infections, lingering high risk strains can cause anal, cervical, oropharyngeal, penile, vaginal, and vulvar cancers.[3]

Oropharyngeal Cancer

Oropharyngeal cancer is a type of head and neck cancer. Specifically, oropharyngeal cancer occurs on the back one third of the tongue, soft palate, tonsils, and throat (see Figure I.1).[4] Early symptoms are often mild and the location makes it difficult to diagnose.[4,5]

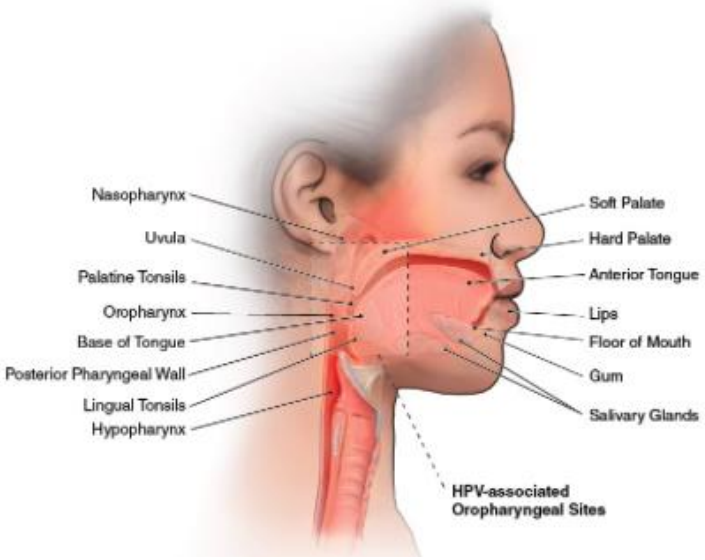

Figure I.1. Head and Neck Cancer Diagram. Note: Image copied directly from Centers for Disease Control and Prevention[4]

According to the National Cancer Institute, there will be an estimated 54,000 new cases of oropharyngeal cancer resulting in 11,230 deaths in the US during 2022.[6] Between 2001-2017, oropharyngeal cancer incidence increased 2.7% among men and 0.5% among women in the US.[7] The five-year survival of oropharyngeal cancer from 2012-2018 was 68 percent.[6]

HPV & Oropharyngeal Cancer Connection

HPV-related oropharyngeal cancer is the most common HPV-related cancer[4,5,8] and approximately 70% of oropharyngeal cancers are caused by HPV.[3] HPV-16 is an oncogenic strain of HPV and is the leading cause of oropharyngeal cancer.[9,10] Historically, oral and oropharyngeal cancers were attributed to tobacco and alcohol use among older individuals; currently, those at highest risk are White, non-smoking, males between the ages of 35-55 years.[9] Risk factors for HPV-related oropharyngeal cancer center primarily around number of sexual partners; risk increases with greater number of sexual partners for both genital and oral HPV infection.[9] Additionally, individuals with a suppressed immune system are at greater risk for developing HPV-related cancers.[9] The presence of oral HPV infection is also associated with alcohol use and cigarette use; with heavy cigarette use related to worse survival outcomes for individuals with HPV-related oropharyngeal cancer.[11–15]

HPV-related oropharyngeal cancer is rapidly on the rise, with a 225% increase in incidence between 1988-2004.[16] However, the U.S. Preventive Services Task Force does not currently recommend population-based screenings and there are no approved screening guidelines or tools to detect HPV-related oropharyngeal cancer.[17–19] Furthermore, there is a lack of understanding regarding population-level knowledge, prevention, and patient/provider engagement of HPV-related oropharyngeal cancer.

Understanding HPV-Related Oropharyngeal Cancer Knowledge

The field of HPV-related oropharyngeal cancer research is growing, however, there remains a need to understand HPV-related oropharyngeal cancer knowledge among health-disparate populations. This is especially important for sexual minority populations who may face an increased risk of HPV-related oropharyngeal cancer but have been historically underrepresented or excluded from research. Additionally, sexual minority populations face social stigma, discrimination and encounter many healthcare barriers, including lower utilization and fewer cancer screenings compared to their heterosexual counterparts.[20–23]

Previous studies have reported that sexual minority women perceived their risk of contracting HPV as relatively low and only six percent knew that HPV could be passed between women.[24,25] However, research has found that sexual minority women had a higher prevalence of oral HPV[26,27] and were more likely to receive an oropharyngeal cancer diagnosis compared to their heterosexual counterparts.[28] Specific to men, studies have showed that sexual minority men in the US were more aware and had a higher prevalence of HPV and related diseases compared to their heterosexual counterparts.[29,30] One study found that most men who have sex with men (MSM) had HPV present in their anal cavity and MSM who have human immunodeficiency virus (HIV) had higher rates of HPV associated cancer compared to their HIV negative counterparts.[31] The long-term use of immunosuppressive medications for individuals with HIV is a risk factor for developing HPV-related cancers; the incidence in HPV-related head and neck cancers among those with HIV is three times higher compared to the general population in the US.[32,33]

Research shows that sexual minority women and men present different risk profiles and levels of awareness of HPV. As the rates of HPV-related oropharyngeal cancer increase rapidly there is a need to explore awareness among sexual minority groups; given the distinct

experiences among men and women, awareness must be examined separately based on sex. Improved understanding can help inform future educational campaigns focused on increasing HPV-related oropharyngeal cancer knowledge.

Role of HPV Vaccine

The HPV vaccine prevents HPV-related cancers and recent estimates suggest that 80% of males and females would need to be vaccinated to eliminate certain cancer-causing types of HPV.[34,35] While the HPV vaccine is approved by the U.S. Food & Drug Administration and has been in use for over a decade,[36] it was not until 2020 that the vaccine was indicated in the prevention of oropharyngeal and other head and neck cancers.[37,38]

HPV vaccination is approved for individuals aged 9-45 years, with the greatest effectiveness in prevention observed if administered prior to any HPV exposure.[38–41] The HPV vaccine is routinely recommended during adolescence, however, vaccination rates in the US in 2020 were only 54.5% for those 13-15 years old.[42] With relatively low vaccination rates among adolescents, there is a need for catch up vaccination for those 18-26 years old.

Among adults in the US, HPV vaccination rates are lower among Hispanics and the HPV-related cancer burden is highest in low-income communities.[43,44] Existing literature predominantly focuses on adolescent HPV vaccine uptake and there is a need to explore HPV vaccination among ethnic minority adults, especially within lower income communities. Additionally, it is important that studies reach beyond fixed individual factors associated with HPV vaccination (i.e., sex at birth, race, ethnicity, etc.) and examine factors/health behaviors that may increase an individual's susceptibility to HPV infection and potential development of cancer. Improved understanding of factors associated with HPV vaccination can help inform targeted vaccine campaigns, with a special focus on those at highest risk for HPV and related diseases.

Role of Medical and Dental Providers in HPV-Related Oropharyngeal Cancer Patient Engagement

Given the rising rate of HPV-related oropharyngeal cancer, professional medical and dental associations support patient engagement around HPV and related diseases.[45-47] However, research findings suggest that medical and dental providers report hesitancy and knowledge gaps regarding HPV-related oropharyngeal cancer. Specifically, dental providers have reported they are hesitant to engage patients in discussions related to HPV and lack comfort and knowledge regarding HPV-related oropharyngeal cancer patient engagement.[48,49] Among medical providers, findings suggest gaps in knowledge and screening abilities regarding HPV and related oropharyngeal cancer.[50–52]

The lack of comfort, confidence, and ability to engage patients in these important discussions is alarming because primary care medical and dental providers are likely the first providers consulted if a patient notices subtle, but concerning changes in the head and neck region, which may be early signs of HPV progressing into oropharyngeal cancer.[53] Early detection is linked to less invasive treatment and improved outcomes and survival of HPV-related oropharyngeal cancer.[18]

Recent systematic reviews on the topic have noted the need for theory-driven research to examine provider perceptions of HPV-related oropharyngeal cancer patient engagement and the importance of confident and knowledgeable general practice providers to recognize early signs and symptoms.[48,53] Furthermore, the Oral Cancer Foundation has called for more inclusive provider studies. Studies should include physicians and dentists but also dental hygienists and advance practice medical providers.[54]

It is important to understand how medical and dental providers view their role in HPV-related oropharyngeal cancer patient engagement because each plays a unique role in

patient care. There is a lack of understanding patient comfort levels and preferences regarding which type of provider patients prefer to discuss HPV and related oropharyngeal cancer. Therefore, it is crucial to understand how different general practice providers perceive their role, so they are poised to address patient questions and concerns while promoting the prevention of HPV. Using a theory-driven research design, public health professionals can begin to understand what shapes provider intentions and subsequent HPV-related oropharyngeal cancer patient engagement.

Aim of Dissertation

The overall aim of this dissertation was to explore HPV-related oropharyngeal cancer knowledge among vulnerable populations, investigate factors associated with HPV vaccine initiation, and understand how medical and dental providers perceive their role in HPV-related oropharyngeal patient engagement.

Chapter 1 of this dissertation utilized data from the publicly available dataset, Health Information National Trends Survey (HINTS) 5, Cycles 1-3. Since 2003, HINTS has been administered by the National Cancer Institute to collect information about 'knowledge of, attitudes toward, and use of cancer- and health-related information' from a nationally representative sample.[55] As described by the National Cancer Institute, HINTS sampling relies on a two-stage design; the first of which uses a sample of residential addresses and the second a single adult (per household) selected to participate.[56–58] The HINTS 5, Cycles 1-3 data were collected between January 2017-April 2019.[56–58] Cycles 1 and 2 were collected via paper survey and Cycle 3 offered options for either paper survey or web survey completion.[56–58] A total of 12,227 participants completed a survey in HINTS 5, Cycle 1-3 and 10,859 respondents were included in the dissertation analysis.[56–58] These robust and nationally representative datasets provided an opportunity to explore HPV-related

oropharyngeal cancer knowledge. Chapter 1 contributed to the literature by focusing on sexual minority populations, often excluded and/or underrepresented in research. Specifically, this analysis examined the relation between sexual orientation and awareness of HPV-related oropharyngeal cancer, general HPV awareness, and HPV knowledge in a sex-stratified analysis using three merged HINTS datasets. Findings from Chapter 1 will help inform educational campaigns aimed at increasing HPV-related oropharyngeal cancer knowledge.

Chapter 2 of this dissertation utilized HPV vaccination data from El Rio Health, a large Federally Qualified Health Center located in Tucson, Arizona. El Rio Health serves a predominantly Hispanic/Latinx community in Southern Arizona and delivered healthcare to over 113,000 patients in 2020.[59] The analysis focused on HPV vaccine initiation for individuals 18-26 years old who were not previously vaccinated during adolescence. The analytic sample consisted of 1,645 individuals aged 18-26 years old who have an established health home and received care at El Rio Health between January 2018-December 2019. Chapter 2 was guided by the Andersen Behavioral Model and aimed to examine factors associated with HPV vaccine initiation. Findings from Chapter 2 will help clinicians and public health professionals identify groups of individuals who may be missed for HPV vaccine initiation and vulnerable to contracting HPV.

Chapter 3 of this dissertation relied on primary data collection at two large Federally Qualified Health Centers, El Rio Health (located in Tucson, AZ) and a large health center located in San Diego, CA. Guided by the Theory of Planned Behavior, the dissertation author developed the survey based on prior published surveys and medical and dental provider input. The purpose of the study was to understand how medical and dental providers

viewed their role in HPV-related oropharyngeal cancer patient engagement. Medical providers included physicians, nurses, nurse practitioners, and physician assistants; dental providers included dentists and registered dental hygienists. A total of 575 providers were invited via email to complete a one-time survey and 156 providers completed the survey. Findings from Chapter 3 will help health centers determine how medical and dental care teams perceive their role in HPV-related oropharyngeal cancer patient engagement and identify opportunities for collaboration between medical and dental teams.

In conclusion, this dissertation contributes to the literature focused on HPV and related oropharyngeal cancer in three distinct ways. Chapter 1 quantifies the overall awareness of HPV-related oropharyngeal and examines differences in knowledge and awareness between sexual minorities and heterosexuals; chapter 2 highlights factors associated with HPV vaccine initiation among vulnerable populations, which is crucial in the prevention of HPV and potential oropharyngeal cancers; chapter 3 demonstrates the differences between medical and dental providers regarding adequate training and confidence to engage patients in HPV-related oropharyngeal cancer discussions.

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CHAPTER 1:
RELATIONSHIP BETWEEN SEXUAL ORIENTATION AND HUMAN PAPILLOMAVIRUS-RELATED ORAL CANCER KNOWLEDGE AND AWARENESS

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Abstract

***Purpose*:** Human Papillomavirus (HPV)-related oral cancers are increasing, and lesbian, gay, bisexual, and other people with a minority sexual orientation may be disproportionately impacted. This study examined the relationship between sexual orientation and HPV-related oral cancer knowledge.

***Methods*:** Data from 10,859 adult participants in the 2017-2019 Health Information National Trends Survey 5, cycles 1-3, were obtained. The three datasets were merged, and weighted multiple imputation (n=15) was applied to address missingness. Weighted logistic regression analyses examined differences in HPV-related oral cancer knowledge between sexual minority versus heterosexual participants by sex, after adjustment for race, ethnicity, age, education, income, insurance, regular medical provider, and smoking status.

***Results*:** In this weighted sample, age ranged from 18-101 years (mean=56.3 years); 42% were males, 5.2% sexual minority men/women, and 94.8% heterosexual/straight. Overall, only 19% of respondents were aware HPV can cause oral cancer. After controlling for sociodemographic factors, there were no significant differences in HPV-related oral cancer knowledge for sexual minority men (adjusted odds ratio (AOR): 1.10; 95% confidence interval (CI): 0.86-1.42) or women (AOR: 0.98; 95% CI: 0.76-1.26) compared to those who were heterosexual/straight.

***Conclusion*:** Overall, knowledge of HPV-related oral cancer was low, regardless of sexual orientation. There were no differences in HPV-related oral cancer knowledge between sexual minority men or women compared to their heterosexual counterparts. Educational programs are needed to increase awareness of the HPV/oral cancer link. Further research on differences in HPV-related oral cancer knowledge and attitudes by sexual orientation and the intersection of other demographic factors is warranted.

Introduction

Oropharyngeal cancer has surpassed cervical cancer as the most common human papillomavirus (HPV)-related cancer in the United States (U.S.).[1–3] There were 18,917 cases of oropharyngeal cancer in 2015, an increase of 2.7% per year in men and 0.8% per year in women from 1999-2015.[1] Historically, oral and oropharyngeal cancers were attributed to tobacco and alcohol use, with higher prevalence in older populations.[4,5] Currently, approximately 70% of oropharyngeal cancers are caused by HPV.[6] HPV is the most common sexually transmitted infection in the U.S., with 80% expected to be infected with HPV in their lifetime.[5,7]

Human papillomavirus is a group of 200+ viruses, of which, approximately 11 are classified as oncogenic.[5,7–10] Specifically, oncogenic HPV-16 is the leading cause of oropharyngeal cancer.[5,11] Risk factors for HPV-related oropharyngeal cancer include having numerous sexual partners, engaging in oral sex, and having a sexual encounter with a partner with numerous partners.[5] Research also suggests tobacco use is an additional risk factor for developing oropharyngeal cancer when HPV is present in the oral cavity.[12] Analyses from the National Health and Nutritional Examination Survey (2011-2014) reported that oral HPV infection was associated with increased[13] and current[14] cigarette use, and number of lifetime sexual partners.[13,14] Additionally, a recent systematic review found heavy cigarette smoking was related to worse survival outcomes for individuals with HPV-related oropharyngeal cancer.[15]

Although oropharyngeal cancer is the most common HPV-related cancer, the U.S. Preventive Services Task Force has no recommendations for HPV-related oropharyngeal cancer screening.[16] A recent review concluded screening is ‘not currently justified’ because methods that currently exist are not sufficiently robust.[17,18] Without guidelines or sufficiently

sensitive/specific screening tests for early detection, identification of HPV-related oral cancers can often rely on providers/patients noticing changes in the oral cavity.[5,17] The lack of screening guidelines and diagnostic tools highlight the importance of understanding population-level knowledge/awareness regarding HPV-related oral cancers.

Despite a 225% increase in incidence between 1988 and 2004,[19] comprehensive understanding of HPV-related oropharyngeal cancer is lacking, especially within health disparate-populations, such as those with a minority sexual orientation. Sexual minority populations are historically underrepresented in research, due in part to the lack of sexual orientation data collection.[20] In 2011, the National Academy of Medicine called for research to capture sexual orientation data and demographics in an effort to improve the health of sexual minority populations.[21] Now, national surveys, including the Health Information National Trends Survey (HINTS), collect information on sexual orientation, supporting the study of health-related experiences of sexual minority persons.

Sexual minority persons face social stigma and discrimination that may negatively impact their health.[22] Research suggests they have lower health care utilization, encounter more barriers and discrimination when accessing health care, get fewer cancer screenings, and lack social support compared to heterosexual persons.[21,23,24] Additionally, sexual minority individuals are more likely than heterosexual individuals to use tobacco,[25–29] a known risk factor for oral HPV.

Previous studies have examined the sexual minority population's knowledge and perceptions about HPV. In one U.S. study, 30% of lesbian, bisexual, or transgender women did not know/believe HPV could be sexually transmitted between women, and 30% were unaware of the HPV/cancer association.[30] Similarly, an Australian study found non-

heterosexual women perceived their risk of acquiring HPV as relatively low; only 6% believed HPV could be sexually transmitted between women.[31] Qualitative follow-up found a low perceived risk of HPV acquisition, which the authors attributed to dominant heterosexual scripts, which do not always include behaviors of non-heterosexual women.[31]

Furthermore, a study conducted in England found lesbian and bisexual women were more likely to have received an oropharyngeal cancer diagnosis than their heterosexual counterparts.[32] Additionally, a small study in Mexico found that women who have sex with women (WSW) had a higher prevalence of oral HPV compared to women who reported having sex exclusively with men.[33,34] Finally, a U.S. study found performing cunnilingus was associated with the presence of oral HPV.[35] This underscores the need to explore how individuals who engage in cunnilingus understand the HPV-oral cancer relation and ensure they are aware of oral-genital HPV acquisition and associated cancer risks, especially given a higher risk of HPV transmission between oral/vaginal contact compared to oral/penile.[34]

HPV also has negative health consequences for men, including oral, penile, and anal cancers.[36,37] Compared to heterosexual men, gay and bisexual men have a higher prevalence of HPV and related disease.[38] A systematic review found most men who have sex with men (MSM) had HPV in the anal canal, and MSM who were positive for human immunodeficiency virus (HIV) had higher rates of anal HPV infection and cancer than their HIV-negative counterparts.[39] Research shows long-term immunosuppression, often experienced by individuals with HIV, is a risk factor for HPV-related cancers.[40]

In an analysis examining data from 17 studies in the North American AIDS Cohort Collaboration on Research and Design, incidence of HPV-related head and neck cancers were more than 3 times higher in people living with HIV compared to the U.S. general

population.[41] In a U.S. based study, gay and bisexual men had higher levels of HPV awareness compared to heterosexual men and regardless of sexual orientation only 23% knew HPV could cause oral cancer.[38] In a probability-based U.S. sample of men, Gilbert et al. (2011) found that gay and bisexual men were more aware of HPV compared to heterosexual men (79% vs. 62%), and more willing to receive the HPV vaccine (73% vs. 37%), respectively, and also reporting a higher level of perceived worry about HPV-related disease.[42]

Due to low perceived risk, research suggests women with minority sexual orientation may be less aware of HPV,[31] whereas men with minority sexual orientation may be more aware of HPV than their respective heterosexual counterparts.[38,42] This supports the need to examine disparities and experiences among men and women separately. Given the disproportionate use of tobacco among those with minority sexual orientation, the established connection between tobacco use and oral HPV infection, the differences in HPV knowledge and perceptions among sexual minority persons compared to heterosexual persons, and the sharp increased incidence of HPV-related oropharyngeal cancer, there is a need to understand the association between sexual orientation and HPV-related oral cancer knowledge.

The purpose of this analysis is to fill the knowledge gap regarding the relationship between sexual orientation and awareness of the association between HPV and oral cancer. Using data from a nationally representative sample, it was hypothesized there would be a significant difference in HPV-related oral cancer knowledge and HPV awareness/knowledge based on sexual orientation, such that sexual minority men would be significantly more knowledgeable and aware, whereas sexual minority women would be significantly less knowledgeable and aware compared to their same-sex heterosexual counterparts.

Methods

Study Design and Setting

This study was an analysis of Health Information National Trends Survey (HINTS) 5, Cycles 1-3 data; each cycle was self-administered, cross-sectional survey with a two-stage sampling strategy design informed by a database of addresses.[43–46] Data were collected for Cycle 1 between January 25-May 5, 2017,[44] Cycle 2 between January 26-May 2, 2018,[45] and Cycle 3 between January 22-April 30, 2019.[46] Paper surveys were used in all three cycles and Cycle 3 also offered two web-based options for survey completion. HINTS received IRB approval from the Westat IRB. As determined by San Diego State University, this analysis was exempt from IRB review because the data used were publicly available and de-identified with no way of linking responses to respondents.

Study Population

A total of 12,227 unique participants were randomly selected and completed one of the HINTS 5 surveys in 2017-2019.[43–46] The analytic sample included participants who responded to the 'self-gender' and 'sexual orientation' items, for an analytic sample of 10,859. This method allowed for multiple imputation across variables, with the exception of the independent (sexual orientation) and stratification (sex) variables.

Measures

HPV-related oral cancer knowledge was assessed with the question: *"Do you think HPV can cause oral cancer?"* ('yes', 'no', 'not sure'). Data were analyzed as 'yes' vs. 'no'/'not sure,' with 'yes' indicating greater knowledge. HPV awareness was assessed through a single item: "*Have you ever heard of HPV? HPV stands for Human Papillomavirus. It is not HIV, HSV, or herpes"* ('yes' vs. 'no'). Responding 'yes' indicated awareness. HPV knowledge was assessed in HINTS 5; Cycle 1 only, by two items. Item 1:

"*Do you think that HPV is a sexually transmitted disease (STD)?"* ('yes', 'no', 'not sure'). Data were analyzed as 'yes' vs. 'no'/'not sure', with 'yes' indicating greater knowledge. Item 2: *"Do you think HPV requires medical treatment or will it usually go away on its own without treatment?"* Data were analyzed as collected with 'will usually go away on its own' indicative of greater HPV knowledge.

Sexual orientation was assessed as: 'heterosexual, or straight'; 'homosexual, or gay or lesbian'; 'bisexual'; 'something else'. Due to the sample size, sexual orientation data was collapsed and analyzed as a dichotomous variable, heterosexual vs. Lesbian, Gay, Bisexual (LGB) and 'something else' [Sexual Minority]. The additional demographic characteristics assessed included: sex (defined as 'self-gender', men vs. women), age (18-34 years; 35-49 years; 50-69 years; 70+ years), insurance (insured vs. uninsured), regular medical provider (yes vs. no), education ('high school or less' vs. 'greater than high school'), ethnicity ('Not Hispanic' vs. 'Hispanic/Latino), race (White, Black, Asian/Native Hawaiian/Pacific Islander, and American Indian/Alaskan Native), income (<$20,000; $20,000-$34,999; $35,000-$49,999; $50,000-$74,999; ≥$75,000), and cigarette smoking status (never smoker vs. ever smoker defined as 100+ cigarettes/lifetime).

Statistical Analysis

Sexual orientation, HPV-related oral cancer knowledge, and HPV awareness were examined using HINTS 5, Cycles 1-3 data and general HPV knowledge was examined in a sub-analysis using HINTS 5, Cycle 1 data. Analyses were adjusted for survey wave and used the appropriate weighting for the HINTS design, which corrected for differences in selection probabilities.[44] This allowed for U.S. population estimation, although the sample consisted of 10,859 participants. As described in HINTS methodology reports, 'replicate weights were calculated using the delete one, jackknife replication method'.[44–46] The analytic process

began by generating descriptive statistics to characterize the sample and summarize frequencies. Multiple imputation (15 datasets) was used to address missingness. Percent missing data was determined for each covariate by sex.

All analyses were stratified by sex. The HINTS cycles were merged, and appropriate weights were applied, following HINTS best practices for merging and weighting data.[47,48] The data from all three cycles were merged to create the analytic sample with one final sample weight and 150 replicate weights (50 weights per cycle included in this analysis).[47,48] Weighted chi-square tests were used to examine the differences in categorical variables (race, ethnicity, education, smoking status, income, insurance, regular medical provider, and age) by sexual orientation.

After applying appropriate weights, a missing data pattern analysis was conducted to assess the Missing at Random assumption and multiple imputation (through fully conditional specification) was determined to be an appropriate method to handle missing data.[49–51] Following multiple imputation (stratified by sex and informed by all covariates in the model) a weighted bivariate analysis using logistic regression examined unadjusted associations of HPV knowledge and awareness between sexual minority persons and heterosexual persons.

The final model used weighted logistic regression, adjusting for demographic characteristics and survey cycle, to examine associations of HPV knowledge and awareness between sexual minority persons and heterosexual persons. In the bivariate analysis and final model, weighted percentages, standard errors, odds ratios, and 95% confidence intervals were computed. The same analytic process was followed for the sub-analysis, with the exception of merging HINTS cycles because only HINTS 5, Cycle 1 was used in the sub-analysis (N=2,941). All analyses were conducted using SAS 9.4.[52]

Results

Sample Characteristics

Overall, 5.2% of respondents reported their sexual orientation as LGB or something else; 4.8% of women and 7.6% of men identified as sexual minorities. Men were more likely to identify as sexual minorities compared to women ($p<0.01$). Among women, age (range: 18-101 years) was significantly different; comparisons showed that sexual minority women were younger ($p<0.01$), more likely to smoke ($p=0.01$), had lower income ($p=0.02$), and were less likely to have a regular medical provider ($p<0.01$) than heterosexual women (Table 1.1). Among men, age (range: 18-99 years) was significantly different; sexual minority men were younger ($p = 0.02$) than their heterosexual counterparts (Table 1.1).

HPV as a Cause of Oral Cancer and Awareness

Overall, 19% of respondents were aware HPV can cause oral cancer. There was no significant difference in HPV-related oral cancer knowledge based on sexual orientation for men or women in unadjusted (Table 1.2) and adjusted models (Table 1.3). Most respondents were aware of HPV (66%). There was no significant difference in HPV awareness based on sexual orientation for men or women in unadjusted (Table 1.2) and adjusted models (Table 1.3).

Cycle 1 Sub-Analysis

Only 44% of respondents were aware that HPV is a STD. There was no significant difference in knowledge of HPV as a STD based on sexual orientation for men or women in unadjusted (Table 1.2) and adjusted models (Table 1.4). Approximately 95% of participants responded that HPV requires medical treatment, indicating it would not resolve without medical intervention. There was no significant difference in knowledge of HPV not typically

Table 1.1. Demographic Characteristics of Health Information National Trends Survey 5, Cycles 1-3; Respondents by Sex and Sexual Orientation

Sexual Orientation	Women (N=6,294)					Men (N=4,565)				
	Heterosexual		*Sexual Minority*		p-value [a]	*Heterosexual*		*Sexual Minority*		p-value [a]
	n (%[b])	**SE**	**n (%[b])**	**SE**		**n (%[b])**	**SE**	**n (%[b])**	**SE**	
Race					0.06					0.14
White	4,214 (77.5)	0.6	175 (64.9)	4.7		3,200 (78.4)	0.8	188 (63.7)	5.9	
Black	1,099 (14.4)	0.5	51 (14.4)	2.8		524 (11.8)	0.8	33 (18.1)	5.3	
Asian/Pacific Islander	314 (6.1)	0.5	24 (14.8)	4.1		274 (7.5)	0.6	31 (16.3)	4.9	
Native American	187 (2.1)	0.2	18 (5.9)	2.4		105 (2.3)	0.4	14 (1.9)	0.8	
Ethnicity					0.22					0.98
Not Hispanic	4,878 (84.9)	0.6	220 (80.2)	3.7		3,481 (84.4)	0.7	220 (84.5)	4.9	
Hispanic/Latinx	784 (15.1)	0.6	46 (19.8)	3.7		594 (15.6)	0.7	38 (15.5)	4.9	
Education					0.95					0.87
High School or Less	1,487 (29.1)	0.7	65 (29.4)	4.2		976 (30.6)	0.9	52 (29.5)	6.9	
Greater than High School	4,481 (70.9)	0.7	217 (70.6)	4.2		3,283 (69.4)	0.9	225 (70.5)	6.9	
Smoking Status					0.01					0.73
Never Smoker	3,925 (67.1)	0.9	160 (55.2)	4.7		2,378 (59.1)	1.4	152 (57.2)	5.5	
Ever Smoker	2,064 (32.9)	0.9	122 (44.8)	4.7		1,885 (40.9)	1.4	125 (42.8)	5.5	
Income					0.02					0.50
<$20,000	1,092 (17.8)	0.9	74 (22.7)	3.9		548 (15.1)	1.1	57 (20.5)	4.4	
$20,000-$34,999	810 (12.7)	0.8	40 (15.3)	4.1		459 (10.4)	0.9	41 (9.5)	4.3	
$35,000-$49,999	737 (13.7)	0.8	44 (18.6)	3.8		510 (13.8)	0.9	24 (13.0)	5.2	
$50,000-$74,999	1,008 (18.3)	0.8	31 (9.7)	2.5		756 (18.9)	1.1	43 (12.9)	3.5	
≥$75,000	1,896 (37.5)	0.9	78 (33.7)	5.9		1,769 (41.8)	1.3	104 (44.1)	5.8	
Insurance					0.06					0.19
Uninsured	700 (16.1)	0.9	59 (24.1)	4.1		390 (16.6)	1.1	38 (25.1)	5.9	
Insured	5,201 (83.9)	0.9	215 (75.9)	4.1		3,816 (83.4)	1.1	235 (74.9)	5.9	
Primary Care Provider					<0.01					0.29
No Regular Provider	1,602 (30.1)	1.1	113 (46.8)	5.3		1,230 (37.8)	1.4	77 (32.1)	5.4	
Regular Provider	4,321 (69.9)	1.1	168 (53.2)	5.3		3,022 (62.2)	1.4	194 (67.9)	5.4	

Table 1.1. Demographic Characteristics of Health Information, Continued

Sexual Orientation	Women (N=6,294)					Men (N=4,565)				
	Heterosexual		*Sexual Minority*		p-value [a]	*Heterosexual*		*Sexual Minority*		p-value [a]
	n (%[b])	**SE**	**n (%[b])**	**SE**		**n (%[b])**	**SE**	**n (%[b])**	**SE**	
Age					<0.01					0.02
18-34 years	791 (22.3)	0.8	79 (45.0)	4.5		442 (22.1)	1.4	54 (40.4)	5.5	
35-49 years	1,202 (26.5)	0.8	72 (26.7)	4.3		803 (28.2)	1.4	43 (18.0)	4.7	
50-69 years	2,621 (37.2)	0.7	99 (21.2)	3.2		1,971 (38.0)	1.0	137 (35.2)	4.7	
70+ years	1,319 (14.0)	0.3	33 (7.1)	1.9		1,029 (11.6)	0.3	39 (6.4)	1.8	

Sexual Minority (Women) = Lesbian/Bisexual/Something Else; Sexual Minority (Men) = Gay/Bisexual/Something Else; SE = Standard Error of Row Percent; [a] p-value comparing heterosexual women vs. sexual minority women and heterosexual men vs. sexual minority men; [b] Weighted Percent. Note: Percent Missingness was calculated for each covariate, by sex: Race (Women (W):3.8; Men (M):4.6); Ethnicity (W:5.8 M:5.1); Age (W:1.2; M:1.0); Education (W:0.7; M:0.6); Smoking Status (W:0.4; M:0.5); Income (W:7.7; M:5.6); Insurance (W:1.9; M:1.9); Regular Medical Provider (W:1.4; M:0.9)

Table 1.2. Unadjusted and Adjusted Logistic Regression Models of Human Papillomavirus-Related Awareness and Knowledge by Sex, based on Sexual Orientation[a]; Health Information National Trends Survey 5, Cycles 1-3

	Women		Men	
HPV Variables	*OR (95% CI)*	*AOR (95% CI)*	*OR (95% CI)*	*AOR (95% CI)*
Cycles 1-3				
Heard of HPV	1.04 (0.86-1.27)	1.00 (0.81-1.25)	1.14 (0.86-1.51)	1.14 (0.87-1.51)
HPV Can Cause Oral Cancer	0.96 (0.76-1.22)	0.98 (0.76-1.26)	1.16 (0.89-1.52)	1.10 (0.86-1.42)
Cycle 1[b]				
HPV is an STD	0.97 (0.69-1.38)	1.05 (0.72-1.54)	1.15 (0.78-1.68)	1.25 (0.89-1.77)
HPV will usually go away on its own	0.72 (0.43-1.23)	1.39 (0.87-2.21)	0.60 (0.29-1.25)	0.51 (0.23-1.14)

[a] Comparison of sexual minority women who identify as Lesbian, Bisexual or something else to their heterosexual counterparts (referent group) and comparison of sexual minority men who identify as Gay, Bisexual, or something else to their heterosexual counterparts (referent group)

[b]Cycle 1, subanalysis only

OR= Unadjusted Odds Ratio;

95% CI = 95% Confidence Interval;

AOR = Adjusted Odds Ratio, adjusted for: race, ethnicity, education, smoking status, income, insurance, primary care provider, age, and survey cycle (survey cycle only for Heard HPV and HPV Cause Oral Cancer)

HPV = Human Papillomavirus

STD = Sexually Transmitted Disease

Note: Percent missingness was calculated for each HPV variables: Heard of HPV: 0.69%; HPV Can Cause Oral Cancer: 4.1%; HPV is an STD: 1.3%; HPV will usually go away on its own: 2.2%

Table 1.3. Adjusted Logistic Regression Model of Human Papillomavirus Awareness and Human Papillomavirus-Oral Cancer Knowledge by Sex (Health Information National Trends Survey, Cycles 1-3)

	Heard of HPV (Awareness)						HPV Can Cause Oral Cancer					
	Women			Men			Women			Men		
	AOR	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*
Sexual Orientation												
Sexual Minority	1.00	0.81-1.25	0.97	1.14	0.87-1.51	0.33	0.98	0.76-1.26	0.87	1.10	0.86-1.42	0.44
Heterosexual	*Ref*			*Ref*			*Ref*			*Ref*		
Race												
Black	1.24	0.98-1.57	0.07	0.97	0.70-1.36	0.88	0.77	0.56-1.08	0.13	1.06	0.70-1.62	0.78
Asian/Pacific Islander	0.41	0.30-0.56	<0.01	0.57	0.40-0.82	<0.01	0.85	0.59-1.21	0.37	1.15	0.73-1.81	0.56
Native American	1.33	0.85-2.07	0.22	1.46	0.85-2.49	0.17	1.10	0.70-1.74	0.67	0.75	0.35-1.64	0.48
White	*Ref*			*Ref*			*Ref*			*Ref*		
Ethnicity												
Hispanic/Latinx	0.90	0.77-1.05	0.20	0.94	0.80-1.10	0.41	0.98	0.82-1.17	0.82	1.05	0.85-1.30	0.65
Not Hispanic	Ref			Ref			Ref			Ref		
Education												
High School or Less	0.63	0.56-0.72	<0.01	0.65	0.56-0.74	<0.01	0.70	0.60-0.82	<0.01	0.68	0.57-0.81	<0.01
Greater than High School	*Ref*			*Ref*			*Ref*			*Ref*		
Smoking Status												
Ever Smoker	1.10	0.99-1.22	0.09	1.24	1.09-1.41	<0.01	0.99	0.89-1.12	0.99	1.04	0.91-1.18	0.58
Never Smoker	*Ref*			*Ref*			*Ref*			*Ref*		
Income												
<$20,000	0.66	0.53-0.82	<0.01	0.83	0.60-1.16	0.28	0.93	0.63-1.36	0.70	1.14	0.77-1.67	0.51
$20,000-$34,999	0.87	0.71-1.08	0.20	0.67	0.49-0.90	0.01	1.07	0.81-1.40	0.65	0.99	0.66-1.49	0.96
$35,000-$49,999	1.17	0.94-1.45	0.15	1.05	0.76-1.44	0.78	1.02	0.76-1.36	0.89	0.69	0.49-0.98	0.04
$50,000-$74,999	1.08	0.87-1.33	0.48	1.23	0.90-1.68	0.20	0.94	0.76-1.17	0.59	0.92	0.71-1.21	0.57
≥$75,000	*Ref*			*Ref*			*Ref*			*Ref*		
Insurance												
Uninsured	0.98	0.81-1.18	0.80	0.93	0.72-1.19	0.55	0.94	0.77-1.15	0.57	0.95	0.74-1.21	0.67
Insured	*Ref*			*Ref*			*Ref*			*Ref*		
Primary Care Provider												
No Regular Provider	0.83	0.73-0.93	<0.01	0.83	0.70-0.98	0.03	0.92	0.80-1.05	0.22	0.81	0.68-0.97	0.02
Regular Provider	*Ref*			*Ref*			*Ref*			*Ref*		

Table 1.3. Adjusted Logistic Regression Model, Continued

	Heard of HPV (Awareness)						HPV Can Cause Oral Cancer					
	Women			Men			Women			Men		
	AOR	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*
Age												
18-34 years	*Ref*			*Ref*			*Ref*			*Ref*		
35-49 years	1.57	1.28-1.92	<0.01	1.55	1.26-1.91	<0.01	1.29	1.06-1.56	0.01	1.10	0.88-1.38	0.39
50-69 years	0.90	0.75-1.07	0.22	0.87	0.73-1.03	0.11	1.07	0.93-1.24	0.34	0.98	0.80-1.20	0.82
≥70 years	0.32	0.26-0.39	<0.01	0.39	0.31-0.49	<0.01	0.66	0.52-0.84	<0.01	0.69	0.54-0.88	<0.01
Survey												
Cycle 1	1.01	0.86-1.19	0.89	0.90	0.77-1.06	0.22	1.03	0.88-1.22	0.67	1.07	0.86-1.32	0.54
Cycle 2	0.85	0.73-0.98	0.03	0.74	0.63-0.87	<0.01	0.91	0.76-1.09	0.30	0.75	0.60-0.93	0.01
Cycle 3	*Ref*			*Ref*			*Ref*			*Ref*		

Sexual Minority = Individuals who identify as Lesbian, Gay, Bisexual, and Something Else; AOR = Adjusted Odds Ratio; 95% CI = 95% Confidence Interval

Table 1.4. Adjusted Logistic Regression Model of Human Papillomavirus-Related Knowledge, by Sex (Health Information National Trends Survey 5, Cycle 1)

	HPV is a STD						HPV will usually go away on its own					
	Women			Men			Women			Men		
	AOR	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*
Sexual Orientation												
Sexual Minority	1.05	0.72-1.54	0.79	1.25	0.89-1.77	0.20	1.39	0.87-2.21	0.17	0.51	0.23-1.14	0.10
Heterosexual	*Ref*			*Ref*			*Ref*			*Ref*		
Race												
Black	1.28	0.84-1.95	0.24	0.71	0.35-1.43	0.34	1.23	0.66-2.32	0.51	1.22	0.32-4.61	0.76
Asian/Pacific Islander	0.82	0.47-1.44	0.49	0.80	0.41-1.55	0.50	0.57	0.22-1.46	0.24	0.84	0.22-3.12	0.79
Native American	0.55	0.29-1.06	0.07	1.05	0.38-2.96	0.92	2.11	0.95-4.72	0.07	0.84	0.10-7.23	0.87
White	*Ref*			*Ref*			*Ref*			*Ref*		
Ethnicity												
Hispanic/Latinx	0.97	0.75-1.24	0.79	1.02	0.74-1.42	0.89	0.82	0.54-1.23	0.33	1.05	0.55-2.02	0.88
Not Hispanic	*Ref*			*Ref*			*Ref*			*Ref*		
Education												
High School or Less	0.61	0.49-0.75	<0.01	0.75	0.58-0.97	0.03	0.76	0.50-1.14	0.19	0.69	0.36-1.30	0.25
Greater than High School	*Ref*			*Ref*			*Ref*			*Ref*		
Smoking Status												
Ever Smoker	1.08	0.92-1.27	0.35	1.20	0.97-1.48	0.09	1.13	0.85-1.51	0.38	1.11	0.74-1.69	0.61
Never Smoker	*Ref*			*Ref*			*Ref*			*Ref*		
Income												
<$20,000	0.53	0.36-0.77	<0.01	0.95	0.49-1.84	0.88	0.66	0.34-1.29	0.22	1.90	0.54-6.70	0.32
$20,000-$34,999	0.83	0.56-1.22	0.35	0.44	0.21-0.95	0.04	0.55	0.24-1.25	0.15	1.31	0.42-4.08	0.64
$35,000-$49,999	1.36	0.92-2.01	0.13	1.46	0.81-2.62	0.21	1.68	0.91-3.11	0.10	0.51	0.11-2.30	0.38
$50,000-$74,999	1.08	0.78-1.48	0.66	1.21	0.76-1.95	0.42	0.96	0.47-1.98	0.92	0.86	0.35-2.11	0.75
≥$75,000	*Ref*			*Ref*			*Ref*			*Ref*		
Insurance												
Uninsured	1.23	0.95-1.58	0.11	0.96	0.63-1.47	0.84	0.96	0.63-1.45	0.85	0.93	0.54-1.62	0.81
Insured	*Ref*			*Ref*			*Ref*			*Ref*		
Primary Care Provider												
No Regular Provider	0.91	0.75-1.10	0.31	0.86	0.69-1.08	0.21	0.80	0.57-1.14	0.22	1.30	0.83-2.05	0.25
Regular Provider	*Ref*			*Ref*			*Ref*			*Ref*		

Table 1.4. Adjusted Logistic Regression Model, Continued

	HPV is a STD						HPV will usually go away on its own					
	Women			Men			Women			Men		
	AOR	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*	*AOR*	*95% CI*	*p-value*
Age												
18-34 years	*Ref*			*Ref*			*Ref*			*Ref*		
35-49 years	1.14	0.87-1.48	0.35	2.14	1.51-3.04	<0.01	1.33	0.83-2.13	0.23	1.17	0.59-2.33	0.65
50-69 years	0.99	0.79-1.26	0.98	0.57	0.43-0.76	<0.01	0.88	0.54-1.48	0.62	0.91	0.42-1.96	0.81
≥70 years	0.47	0.34-0.65	<0.01	0.36	0.24-0.55	<0.01	0.40	0.18-0.89	0.03	0.27	0.10-0.69	<0.01

STD=Sexually Transmitted Disease; Sexual Minority = Individuals who identify as Lesbian, Gay, Bisexual, and Something Else; AOR = Adjusted Odds Ratio; 95% CI = 95% Confidence Interval

requiring medical treatment based on sexual orientation for men or women in unadjusted (Table 1.2) and adjusted models (Table 1.4).

Discussion

This analysis showed that regardless of sexual orientation, a majority of people (66%) were aware of HPV, but not that HPV can cause oral cancer (19%). As the most common HPV-related cancer[1–3], it is imperative that public awareness is increased and that individuals understand the risk factors and early signs/symptoms. Currently, there is no recommended screening protocol for HPV-related oral cancer and diagnosis relies on individuals noticing subtle changes in their health and consulting a healthcare provider.[53] Although HPV-related oral cancers are more responsive to treatment than non-HPV oral cancers,[11] early diagnosis and treatment are still vital for recovery and survival.

The results of this analysis did not support the *a priori* hypotheses that sexual minority men are more knowledgeable, whereas sexual minority women are less knowledgeable, of HPV-related oral cancer than their heterosexual counterparts. As previously described, lesbian and bisexual women have lower rates of medical utilization and experience discrimination in the medical setting than heterosexual women.[21] They may experience similar risks as their heterosexual counterparts, but may not be provided the same level of care and information from medical providers.[21]

A recent HINTS analysis found LGB respondents were less likely to consult medical professionals than heterosexual respondents.[54] In this study, sexual minority women were significantly less likely than heterosexual women to have a regular medical provider, and HPV awareness was associated with having a regular medical provider for both men and women. Without a regular provider, people may not be receiving crucial HPV information, highlighting the importance of increasing HPV awareness through alternative means (i.e., not

solely relying on providers), especially for sexual minority women who may face healthcare barriers.

Furthermore, consistent with previous research, this analysis found that sexual minority women were more likely than heterosexual women to report they smoked cigarettes, which can contribute to the development of HPV-related oral cancer.[12,26] Interestingly, research has found that smoking is significantly associated with oral HPV infection for women, but not for men.[55] HPV-related oral cancer educational campaigns must consider behavioral factors such as smoking, that may be more common in sexual minority persons, which can contribute to HPV-related oral cancer.

This analysis highlighted demographic differences in HPV knowledge and awareness for both men and women. Results are in accord with the patterns in HPV knowledge described by McBride and Singh (2018).[56] Noticeably, HPV awareness was associated with younger age (less than 50 years), higher education, and having a regular medical provider for both men and women. Among men higher education and having a regular medical provider were significantly associated with HPV-related oral cancer knowledge. While for women, higher education and age (less than 50 years old) were significantly associated with HPV-related oral cancer knowledge.

The demographic characteristics associated with HPV awareness in this analysis align with results from previous HINTS cycles[37,56,57] and suggest multiple factors must be considered when creating interventions to increase awareness. Therefore, the statuses of subpopulations of sexual minority persons with intersectional multiple minority/disadvantaged statuses must be considered to appropriately intervene on health disparities.[58–61] Due to a limited sample size, this study was unable to examine the joint

influences of multiple minority statuses. Additional research is needed to understand how the intersections of sexual orientation with other demographic factors impact HPV-related oral cancer awareness and knowledge.

Researchers and clinicians are making remarkable advancements in the field of prevention and diagnostics of HPV-related oral cancer.[62–64] Wang et al., (2020) found that using an acoustofluidic platform for saliva may be an effective way to identify the presence of HPV-16 in the mouth.[62] Another promising advancement in early identification of oral cancers uses a computer-based algorithm to identify cancerous lesions.[63] As of June 2020, the U.S. Food and Drug Administration listed Gardasil 9 (HPV-vaccine) as preventing oropharyngeal and other head and neck cancers for men and women.[65] Previously, it was listed for the prevention of cervical and anal cancers.[66]

As clinical scientific discoveries advance the field of HPV-related head and neck cancers, the behavioral science field must examine population-level knowledge, awareness, and risk perceptions of HPV and related cancers, especially oral cancers, due to its rapidly increasing incidence. Improved understanding will allow public health professionals to tailor campaigns to populations at greater risk for developing HPV-related oral cancers or those less likely to receive appropriate and timely oral cancer treatment. Improved understanding can be achieved through qualitative methods to provide context to perceptions and inform quantitative studies designed to evaluate population-level knowledge, awareness, risk perceptions and behaviors.

Limitations

Although the sample was large, the number of sexual minority respondents was relatively small, especially when stratified by sex. This resulted in relatively low power to detect differences based on sexual orientation. Additionally, the sample sizes for the sexual

minority group were too small to examine sexual minority subgroups. This small sample size limited the ability to accurately depict the knowledge and awareness of subgroups within this diverse population.

Furthermore, alcohol use is an important factor to consider when studying oral HPV acquisition. However, alcohol use was not collected in all three HINTS iterations, and was therefore not included in the analysis. Another important factor to consider is number of sexual partners, specifically oral sexual partners (a risk factor for oral HPV), but this information was not collected as part of HINTS. The sub-analysis had a very limited sample size and results should be interpreted with caution. Due to the cross-sectional nature of the data, causal inferences cannot be established.

Strengths

This study was strengthened by multiple merged waves of weighted data which yielded a large sample size. The analysis used a population-based sample, generating generalizable U.S. estimates. Additionally, HINTS participants were sampled without respect to their sexual orientation, therefore the comparison between sexual minority and heterosexual participants is strengthened.

Future Research

As the rates of HPV-related oral cancer increase, individuals must understand their risk for HPV and oral cancer. Public health researchers must prioritize recruiting sexual minority populations to properly power analyses that do not conflate sexual minority subgroups. This approach will allow for a more accurate characterization of their HPV-knowledge/attitudes, and awareness.

Conclusion

Sexual minority and heterosexual adults had comparable, HPV-related oral cancer knowledge. Although HPV awareness was high, knowledge of HPV-related oral cancer was low. This demonstrates a significant gap in prevention efforts. Novel behavioral campaigns must be developed to target the overall population as well as marginalized populations, including sexual minority men and women.

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CHAPTER 2:
FACTORS ASSOCIATED WITH YOUNG ADULTS' HUMAN PAPILLOMAVIRUS (HPV) VACCINE INITIATION IN A FEDERALLY QUALIFIED HEALTH CENTER

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Abstract:

Purpose: This study examined factors associated with Human Papillomavirus (HPV) vaccine initiation in a Federally Qualified Health Center (FQHC).

Methods: Electronic health record data included 1,645 FQHC patients aged 18-26 years who received medical care from January 2018-December 2019, with no prior documented history of HPV vaccination. Descriptive statistics characterized the sample, and multiple imputation was used to address missingness, followed by logistic regression to examine multivariable associations. Regression modeling was guided by Andersen Behavioral Model's factors: 'predisposing' (race, ethnicity, age, gender identity, and sexual orientation), 'enabling' (insurance, provider type, and utilization frequency), and 'need' (tobacco use, human immunodeficiency virus (HIV) diagnosis, sexually transmitted disease (STI) testing, and history of STIs). The outcome, HPV vaccine initiation, was defined as receiving at least one dose of the HPV vaccine series during the study period.

Results: Young adults had relatively low HPV vaccine initiation rates (males=19%; females=21%). For males, minority sexual orientation (OR:1.75; 95% CI:1.20-2.55) and HIV+ status (OR:2.63; 95% CI:1.16-5.97) were associated with greater odds of HPV vaccine initiation; as age increased, odds of HPV vaccine initiation decreased (OR:0.74; 95% CI:0.66-0.84). For females, non-White race (OR:1.26; 95% CI:1.04-1.53), having a nurse practitioner/physician assistant as a provider (OR:1.33; 95% CI:1.08-1.65), and more

frequent utilization (OR:1.54; 95% CI:1.31-1.80) were associated with greater odds of HPV vaccine initiation.

Conclusion: Only one in five young adults initiated HPV vaccination during the study period. Findings may help FQHCs attend to the differences between individuals through tailored efforts to increase HPV vaccine initiation.

Background

According to the Centers for Disease Control and Prevention (CDC), over 45,000 people in the United States (US) are diagnosed with cancer caused by Human Papillomavirus (HPV), annually.[1] HPV is the most common sexually transmitted infection (STI) in the US[2] and there are over 200 strains of the virus with varying classifications of risk.[3] The high-risk strains of HPV can develop into cervical, penile, anal, and oropharyngeal cancers;[1] however, it is estimated that over 90% of cases of HPV-related cancer cases could be prevented through timely vaccination.[4,5]

The HPV vaccine was approved by the US Food and Drug Administration (FDA) and has been recommended as a routine vaccination for men and women since 2011. The vaccine can be administered from ages 9 to 45 years, as a two dose series for those 9-14 years old and three dose series for those 15+ years old.[6–8] While the vaccine is routinely recommended in primary care settings, in 2020, only 54.5% of US adolescents aged 13-15 years were vaccinated.[9] Given that HPV vaccination rates are low during adolescence, it is necessary for catch-up vaccination. However, catch-up vaccination rates are even lower than among adolescents with 40% of 18-26 year old individuals receiving at least one dose and only 22% completing the three dose series.[10]

HPV vaccination prevents HPV-related cancers and reduces the burden on patients and the healthcare system. It is estimated that approximately 80% of males and females would need to be vaccinated in order to eliminate certain oncogenic HPV strains.[11,12] A recent analysis found that 'routine adolescent HPV vaccination' could save $5.1 billion annually in HPV-related cancer costs; and including catch up vaccination (up to 26 years) could save an additional $3.8 billion annually.[13]

In the US, HPV vaccine initiation in adulthood is higher among non-Hispanic Whites (42%) compared to Hispanics (36%)[10] and the HPV-related cancer burden is highest among low-income counties in the US.[14] Given the effectiveness of the HPV vaccine in preventing HPV-related cancers, it is important to understand factors that contribute to vaccine uptake, especially among Hispanics with lower vaccination rates and among lower income communities that carry a higher HPV-related cancer burden. Due to the increasing proportion of Hispanics receiving health care at Federally Qualified Health Centers and the considerable number of low income patients served, an FQHC setting was selected for the study.[15]

This study was guided by the Andersen Behavioral Model which posits that predisposing, enabling, and need factors contribute to health care service utilization (i.e., HPV vaccine initiation).[16] Predisposing factors include demographic and other fixed characteristics (e.g. race, ethnicity, age, gender, sexual orientation) while enabling factors refer to factors that allow an individual to access health care services (e.g. healthcare utilization, health insurance, provider type).[16] Need factors contribute to an individual's actual need or perception of need for particular health care services based on their health/risk behaviors (e.g. tobacco use, HIV status, STI history).[16] This model was used to classify multilevel factors (at individual, interpersonal, and organizational levels) potentially associated with HPV vaccine initiation (see Figure 2.1).[16]

This study fills gaps in the HPV vaccination literature by focusing on a predominantly low-income, Hispanic population, aged 18-26 years old. Additionally, this study included variables not often included in HPV vaccination research, specifically history of, and testing for STIs. STI history and testing have the potential to be critical decision points for the initiation of HPV vaccination for patients and providers and should be

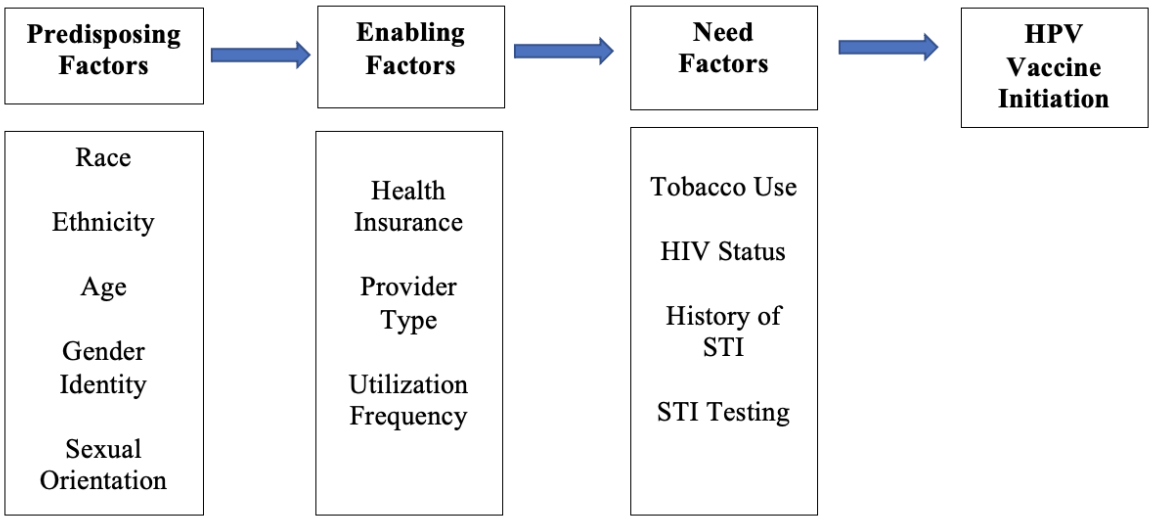

Figure 2.1. Andersen Behavioral Model for Human Papillomavirus Vaccine Initiation in a Federally Qualified Health Center. Note: The analysis was stratified by sex at birth (male/female) and the gender identity variable was created by comparing sex at birth to gender identity listed in the electronic health record. The gender identities included in the analysis were: cisgender, transgender/other gender minority, and unknown/missing.

considered when examining factors associated with HPV vaccine initiation.[17] The purpose of this study was to identify multilevel factors associated with HPV vaccine initiation among individuals 18-26 years old who are patients at a large FQHC.

Methods

Study Design & Setting

This study analyzed Electronic Health Record (EHR) data collected at El Rio Health (El Rio) in Tucson, AZ. El Rio is a large FQHC serving over 113,000 patients annually.[18] This study was deemed exempt by the San Diego State University Institutional Review Board (IRB). Following IRB review and determination, the study was reviewed and approved by three oversight committees at El Rio prior to data extraction.

Study Population

The EHR dataset for this study included 1,645 patients aged 18-26 years who received care at El Rio from January 1, 2018, to December 31, 2019, and who met all the

following inclusion criteria. Patients had to have an assigned primary care provider and a minimum of two visits during the two-year study period, with at least one medical visit in each calendar year, and at least six months between each visit. These two conditions for medical visits were applied to ensure only patients who regularly accessed medical care at El Rio were included in the analysis. Additionally, patients had to have no history of HPV vaccination prior to 2018. Vaccines could have been administered outside of El Rio, and the EHR system at El Rio extracts data from the Arizona State Immunization Information System (ASIIS), which captures vaccination data from across the state, therefore improving the accuracy of vaccine status for the analysis.[19] These strict criteria were selected so the final analytic sample would focus only on young adult patients with an established medical home at El Rio (who were eligible for HPV vaccination), as it relied on the accuracy and completion of medical charts.

Measures

All data were extracted directly from the EHR, and de-identified prior to the research team receiving the encrypted file. The health behavior of interest in the analysis was **HPV vaccine initiation** defined as receiving at least one dose of the HPV vaccination in 2018-2019 ('yes' vs. 'no'). **Sex at Birth** was used as a stratification variable for the analysis and extracted from the EHR as 'Male' or 'Female'.

Predisposing factors in this analysis included: race, ethnicity, age, gender identity, and sexual orientation. **Race** was collected as 'White', 'Asian', 'Black', 'Native Hawaiian/Pacific Islander', 'Native American/American Indian', and 'Other'. Due to sample size constraints after sex (at birth) stratification, **race** was analyzed as 'White' vs. 'Non-White'. **Ethnicity** was collected as 'Hispanic' vs. 'Non-Hispanic'. **Age** was collected as a continuous variable, ranging 18-26 years. **Gender Identity** was collected as 'Female',

'Male', 'Male to Female', 'Female to Male', 'Other', and 'Choose not to Disclose'. **Gender Identity** was compared to **Sex at Birth** and a new variable was created and analyzed as 'Cisgender' (i.e., 'sex at birth' and 'gender identity' matched) vs. 'Transgender/Other Gender Minority'. Those who selected 'Choose not to Disclose' were classified as 'Unknown/Missing'. **Sexual Orientation** was collected as 'Heterosexual/straight', 'Bisexual', 'Lesbian/Gay', 'Choose not to Disclose', 'Don't Know', 'Something Else' and analyzed as 'Lesbian/Gay/Bisexual/Something Else' vs. 'Straight/Heterosexual'. Those who selected 'Choose not to Disclose' or 'Don't Know' were classified as 'Unknown/Missing'.

Enabling factors in this analysis included: health insurance status, provider type (physician vs. advanced practice provider such as nurse practitioner/physician's assistant vs. certified nurse midwife), and medical utilization frequency. **Health Insurance** type was collected as 'Commercial' (employer based), 'Medicaid', 'Medicare', 'Medicare Advantage', and 'Uninsured' and analyzed as 'Commercial', 'Medicaid, Medicare/Medicare Advantage' and 'Uninsured'. While health insurance type could have changed during the study period, only health insurance type at last visit was available for data extraction and was therefore used for the analysis. **Provider Type** was collected as 'Certified Nurse Midwife' (CNM) (for women only), 'Nurse Practitioner'(NP), 'Physician', and 'Physician's Assistant'(PA) and analyzed as 'CNM', 'NP/PA', and 'Physician'. Patients may seek care from more than one medical provider at El Rio, however the analysis relied on the provider that was assigned as their 'primary care provider'. **Utilization Frequency** was collected continuously and analyzed as 'two-four visits' vs. 'five or more visits.'

Need factors in this analysis included: tobacco use (due to being a health risk behavior for HPV and related cancer acquisition), HIV status, and testing/diagnostic history

of sexually transmitted infections (STI).[10,14,17,20,21] **Tobacco Use** was analyzed as collected, 'Ever Use' vs. 'Never Use'. **HIV Status** was analyzed based on diagnostic codes as 'Ever Diagnosed' vs. 'Never Diagnosed'. **History of STI** was analyzed as 'Ever Diagnosed' vs. 'Never Diagnosed'. **STI Testing** was analyzed as 'Ever Tested' vs. 'Never Tested'. For both STI variables, the following infections were included in the data extraction: gonorrhea, chlamydia, syphilis, human papillomavirus, hepatitis B and C, and trichomoniasis. Diagnostic criteria for any STI were based on either a positive test result or ICD-10 code in the electronic health record (to capture labs performed outside of El Rio).

Statistical Analysis

Descriptive statistics were generated to characterize the sample, understand the distribution of variables, extent of missingness (which ranged from 5% to 18%), and inform data manipulation, such as categorizing variables into analytic categories (see Table 2.1). During this process, a significant interaction was identified between sex at birth and sexual orientation, therefore the analyses were stratified by sex at birth to appropriately examine how HPV vaccine initiation differed between males and females (sex at birth). There were missing data for several predisposing factors (race, gender identity, sexual orientation, and ethnicity), but there were no missing data for enabling and need factors. To test the assumption of data 'missing at random', a missing data pattern analysis was conducted. To address missing data, multiple imputation, through fully conditional specification, (n=15) was used, given the inclusion of both continuous and categorical variables.[22] Following multiple imputation (stratified by sex at birth and informed by all covariates in the model), logistic regression was used. Model building followed the Andersen Behavioral Model, introducing predisposing, enabling, and need factors to determine what factors were

significantly associated with HPV vaccine initiation.[16] Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated for the HPV vaccine initiation models.

Results

Sample Characteristics

Overall, 30% of the participants were assigned male sex at birth and 70% were assigned female sex at birth. Those assigned male sex at birth and female sex at birth had similar HPV vaccine initiation rates, 19% and 21%, respectively. See Table 2.1 for the distribution of sample characteristics. In the bivariate analysis for individuals assigned male sex at birth (Table 2.1, left columns), those who initiated HPV vaccination were younger ($p<0.01$), identified as transgender/other gender identity ($p<0.01$), and had a minority sexual orientation ($p<0.01$) compared to those who did not initiate vaccination. Additionally, those with five or more medical visits (utilization frequency) had more HPV vaccine initiations compared to those with two to four visits ($p<0.01$). Finally, there was a statistically significant difference in HPV vaccination initiation based on HIV status ($p<0.01$), history of STI testing ($p<0.01$), and history of STI diagnosis ($p<0.01$). Specifically, those with an HIV diagnosis reported higher HPV vaccine initiation compared to those without an HIV diagnosis. Those with a history of STI testing and/or diagnosis had more frequent HPV vaccine initiation compared to those who were not tested and/or diagnosed with an STI.

In the bivariate analysis, among individuals assigned female sex at birth, HPV vaccine initiation was more likely among those who identified as non-White ($p=0.02$) compared to those who identified as White. Furthermore, those with five or more medical visits (utilization frequency) had more HPV vaccine initiations compared to those with two

Table 2.1. Demographic Characteristics of Patients by Sex at Birth and Human Papillomavirus Vaccine (HPV) Status; Results of Bivariate Analysis

	Individuals Assigned Male Sex at Birth (n=486)					Individuals Assigned Female Sex at Birth (n=1,159)				
	HPV Vaccine Initiated (n=94)		**No HPV Vaccine (n=392)**			**HPV Vaccine Initiated (n=242)**		**No HPV Vaccine (n=917)**		
Predisposing Factors					**p-value**					**p-value**
Age	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**		**Mean (SD)**	**Range**	**Mean (SD)**	**Range**	
18-26 Years	22.9 (2.2)	19-26	24.0 (2.0)	18-26	<0.01	23.3 (2.3)	18-26	23.4 (2.3)	18-26	0.48
	n (%)		**n (%)**			**n (%)**		**n (%)**		
Race					0.12					0.02
White	50 (18.1)		227 (81.9)			148 (19.5)		612 (80.5)		
Non-White	29 (25.0)		87 (75.0)			54 (27.1)		145 (72.9)		
Gender Identity					<0.01					0.52
Cisgender	73 (17.4)		346 (82.6)			226 (21.2)		841 (78.8)		
Transgender/Other	18 (43.9)		23 (56.1)			9 (25.7)		26 (74.3)		
Sexual Orientation					<0.01					0.29
Straight/Heterosexual	50 (15.1)		281 (84.9)			184 (21.0)		691 (79.0)		
LGB/Something Else	32 (44.4)		40 (55.6)			31 (25.2)		92 (74.8)		
Ethnicity					0.11					0.64
Non-Hispanic	25 (21.4)		92 (78.6)			65 (22.3)		227 (77.7)		
Hispanic	40 (14.8)		230 (85.2)			147 (20.9)		555 (79.1)		
Enabling Factors										
Health Insurance					0.08					0.27
Commercial/Private	36 (19.2)		152 (80.8)			88 (21.8)		315 (78.2)		
Medicare/Medicaid	53 (22.0)		188 (78.0)			137 (21.3)		506 (78.7)		
Uninsured	5 (8.8)		52 (91.2)			17 (15.0)		96 (85.0)		
Provider Type					0.75					<0.01
Certified Nurse Midwife	0		0			31 (14.0)		191 (86.0)		
NP/PA	42 (20.0)		168 (80.0)			109 (24.9)		328 (75.1)		
Physician	52 (18.8)		224 (81.2)			102 (20.4)		398 (79.6)		
Utilization Frequency					<0.01					<0.01
2-4 Visits	39 (14.8)		224 (85.2)			76 (13.6)		481 (86.4)		
5+ Visits	55 (24.7)		168 (75.3)			166 (27.6)		436 (72.4)		
Need Factors										
Tobacco Use					0.36					0.29
Ever Use	18 (23.1)		60 (76.9)			25 (25.0)		75 (75.0)		
Never Use	76 (18.6)		332 (81.4)			217 (20.5)		842 (79.5)		

Table 2.1. Demographic Characteristics of Patients, Continued

	Individuals Assigned Male Sex at Birth (n=486)			Individuals Assigned Female Sex at Birth (n=1,159)		
	HPV Vaccine Initiated (n=94)	**No HPV Vaccine (n=392)**		**HPV Vaccine Initiated (n=242)**	**No HPV Vaccine (n=917)**	
Predisposing Factors			**p-value**			**p-value**
HIV Status			<0.01			N/A
Ever Diagnosed	10 (76.9)	3 (23.1)		0	0	
Never Diagnosed	84 (17.1)	389 (82.2)		0	0	
History of STI			<0.01			0.46
Ever Diagnosed	24 (36.4)	42 (63.6)		48 (22.8)	163 (77.3)	
Never Diagnosed	70 (16.7)	350 (83.3)		194 (20.5)	754 (79.5)	
STI Testing			<0.01			0.79
Ever Tested	55 (28.8)	136 (71.2)		149 (21.2)	556 (78.9)	
Never Tested	39 (13.2)	256 (86.8)		93 (20.5)	361 (79.5)	

Note. LGB/Something Else = Individuals who identify as lesbian, gay, bisexual, or something else/other sexual minority; NP/PA = Nurse Practitioner/Physician Assistant; STI= Sexually Transmitted Infection; SD= Standard Deviation; Missing Data: Race n=293 (18%), Gender Identity n=83 (5%), Sexual Orientation n=244 (15%), Ethnicity n=264 (16%)

to four visits ($p<0.01$). Finally, those with a NP/PA as a primary care provider had more frequent HPV vaccine initiation ($p<0.01$) compared to those with another type of primary care provider.

Modeling of Predisposing +Enabling+ Need Factors

Male Sex at Birth (Table 2.2): In the final, fully adjusted multivariable model, two predisposing factors were associated with HPV vaccine initiation for individuals assigned male sex at birth. As age increased, odds of HPV vaccination decreased (OR: 0.74; 95% CI: 0.66-0.84) and individuals identifying as lesbian, gay, bisexual, or something else had higher odds than their heterosexual counterparts of initiating the HPV vaccine (OR:1.75; 95% CI: 1.20-2.55). One need factor (HIV status) was associated with HPV vaccine initiation. Those with a diagnosis of HIV had higher odds of HPV vaccine initiation compared to those who did not have an HIV diagnosis (OR:2.63; 95% CI: 1.16-5.97).

Female Sex at Birth (Table 2.3): In the final, fully adjusted model, one predisposing factor was associated with HPV vaccine initiation for individuals assigned female sex at birth. Non-white females (sex at birth) had higher odds than their white counterparts of HPV vaccine initiation (OR:1.26; 95% CI:1.04-1.53). Two enabling factors were associated with HPV vaccine initiation. Specifically, individuals with a CNM as a primary care provider had lower odds of initiating HPV vaccination compared to those who had a physician assigned as a primary care provider (OR:0.71; 95% CI:0.53-0.95). Those who had a NP/PA assigned as primary care provider had higher odds of initiating HPV vaccination compared to those who had a physician assigned as a primary care provider (OR:1.33; 95% CI:1.08-1.65). Finally, those with five or more visits in the study period had higher odds than those with two to four visits of initiating HPV vaccination (OR: 1.54; 95% CI: 1.31-1.80).

Table 2.2. Predisposing, Enabling, and Need Factors Associated with Human Papillomavirus Vaccine Initiation among Individuals Assigned Male Sex at Birth^

	Individuals Assigned Male Sex at Birth					
	Predisposing Factors		Predisposing +Enabling Factors		Predisposing+ Enabling+ Need Factors	
Predisposing Factors	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Age						
18-26 Years	0.77*	0.69-0.87	0.76*	0.68-0.86	0.74*	0.66-0.84
Race						
White	*Ref*		*Ref*		*Ref*	
Non-White	1.33	0.98-1.79	1.30	0.98-1.72	1.28	0.92-1.76
Gender Identity						
Cisgender	*Ref*		*Ref*		*Ref*	
Transgender/Other	1.23	0.77-1.95	1.16	0.73-1.84	1.18	0.74-1.86
Sexual Orientation						
Straight/Heterosexual	*Ref*		*Ref*		*Ref*	
LGB/Something Else	2.11*	1.48-3.01	2.02*	1.42-2.87	1.75*	1.20-2.55
Ethnicity						
Non-Hispanic	*Ref*		*Ref*		*Ref*	
Hispanic	1.1	0.79-1.53	1.16	0.84-1.60	1.26	0.89-1.77
Enabling Factors						
Health Insurance						
Commercial/Private			*Ref*		*Ref*	
Medicare/Medicaid			1.42	0.90-3.23	1.44	0.89-2.31
Uninsured			0.55	0.26-1.16	0.52	0.24-1.14
Provider Type						
Certified Nurse Midwife			N/A	N/A	N/A	N/A
NP/PA			1.03	0.80-1.32	0.97	0.75-1.26
Physician			*Ref*		*Ref*	
Utilization Frequency						
2-4 Visits			*Ref*		*Ref*	
5+ Visits			1.27	0.98-1.64	1.13	0.87-1.49
Need Factors						
Tobacco Use						
Ever Use					1.14	0.81-1.60
Never Use					*Ref*	

Table 2.2. Predisposing, Enabling, and Need Factors, Continued

	Individuals Assigned Male Sex at Birth					
	Predisposing Factors		Predisposing +Enabling Factors		Predisposing+ Enabling+ Need Factors	
Predisposing Factors	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
HIV Status						
Ever Diagnosed					2.63*	1.16-5.97
Never Diagnosed					*Ref*	
History of STI						
Ever Diagnosed					1.11	0.75-1.65
Never Diagnosed					*Ref*	
STI Testing						
Ever Tested					1.32	0.98-1.78
Never Tested					*Ref*	

Note. ^= Results of Logistic Regression; LGB/Something Else = Individuals who identify as lesbian, gay, bisexual, or something else/other sexual minority; NP/PA = Nurse Practitioner/Physician Assistant; STI= Sexually Transmitted Infection; *Significance at $\alpha = 0.05$

Table 2.3. Predisposing, Enabling, and Need Factors Associated with Human Papillomavirus Vaccine Initiation among Individuals Assigned Female Sex at Birth^

	Individuals Assigned Female Sex at Birth					
	Predisposing Factors		Predisposing +Enabling Factors		Predisposing+ Enabling+ Need Factors	
Predisposing Factors	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Age						
18-26 Years	0.98	0.92-1.05	0.96	0.90-1.03	0.96	0.90-1.03
Race						
White	*Ref*		*Ref*		*Ref*	
Non-White	1.22*	1.02-1.45	1.26*	1.03-1.52	1.26*	1.04-1.53
Gender Identity						
Cisgender	*Ref*		*Ref*		*Ref*	
Transgender/Other	1.02	0.66-1.56	0.98	0.63-1.53	0.97	0.62-1.53
Sexual Orientation						
Straight/Heterosexual	*Ref*		*Ref*		*Ref*	
LGB/Something Else	1.12	0.88-1.42	1.05	0.82-1.34	1.05	0.81-1.35
Ethnicity						
Non-Hispanic	*Ref*		*Ref*		*Ref*	
Hispanic	1.01	0.85-1.20	1.04	0.87-1.24	1.06	0.87-1.25
Enabling Factors						
Health Insurance						
Commercial/Private			*Ref*		*Ref*	
Medicare/Medicaid			1.12	0.89-1.42	1.12	0.88-1.41
Uninsured			0.72	0.50-1.04	0.72	0.50-1.04
Provider Type						
Certified Nurse Midwife			0.71*	0.54-0.94	0.71*	0.53-0.95
NP/PA			1.33*	1.08-1.65	1.33*	1.08-1.65
Physician			*Ref*		*Ref*	
Utilization Frequency						
2-4 Visits			*Ref*		*Ref*	
5+ Visits			1.54*	1.32-1.80	1.54*	1.31-1.80
Need Factors						
Tobacco Use						
Ever Use					1.06	0.82-1.36
Never Use					*Ref*	

Table 2.3. Predisposing, Enabling, and Need Factors, Continued

	Individuals Assigned Female Sex at Birth					
	Predisposing Factors		Predisposing +Enabling Factors		Predisposing+ Enabling+ Need Factors	
Predisposing Factors	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
HIV Status						
Ever Diagnosed					N/A	N/A
Never Diagnosed						
History of STI						
Ever Diagnosed					1.04	0.85-1.26
Never Diagnosed					*Ref*	
STI Testing						
Ever Tested					0.99	0.84-1.17
Never Tested					*Ref*	

Note. ^= Results of Logistic Regression; LGB/Something Else = Individuals who identify as lesbian, gay, bisexual, or something else/other sexual minority; NP/PA = Nurse Practitioner/Physician Assistant; STI= Sexually Transmitted Infection; *Significance at $\alpha = 0.05$

Discussion

This study found that HPV vaccine initiation from 2018-2019 was approximately 20% for individuals who were not previously vaccinated and utilized a FQHC for regular health care. It is important that HPV vaccination is a focus of primary health care visits due to the effectiveness of the vaccine in preventing HPV-related cancers. When examining factors associated with HPV vaccine series initiation, distinct factors emerged for those assigned male versus female sex at birth. Among those assigned male sex at birth, those who were younger, identified as gay, bisexual, or something else, and were diagnosed with HIV had higher odds of beginning the HPV vaccine series. Among those assigned female sex at birth, those with non-White race, an NP/PA as a primary care provider and more frequent healthcare utilization had higher odds of HPV vaccine initiation.

For those assigned male sex at birth, these findings align with the 2011 CDC HPV vaccine recommendation from the Advisory Committee on Immunization Practices (ACIP), which reported that men who have sex with men are at higher risk for HPV-related disease compared to their heterosexual counterparts, and that those living with HIV/AIDS experience a higher burden of HPV-related cancers.[23] As a result, the ACIP recommends male HPV vaccination, especially for these populations at higher risk for HPV-related diseases.[23]

Specific to those assigned female sex at birth, higher health care utilization was associated with an increased likelihood of HPV vaccine series initiation, which has been noted in other studies.[21,24] Race emerged as a significant factor, contrary to previous findings,[25] this analysis found that women who reported their race as non-White were more likely than their White counterparts to initiate the HPV vaccine series. However, this study had a smaller sample size and was not nationally representative. Furthermore, race was collapsed to a dichotomous variable because of the small sample sizes of each race (other

than white). Analyses by provider type showed that compared to physicians, female (sex at birth) patients with a CNM assigned provider were less likely to initiate the HPV vaccine whereas those with an assigned provider as a NP/PA were more likely to initiate the HPV vaccine. Previous studies have demonstrated that provider recommendation is associated with HPV vaccination initiation among women.[26,27] Given the importance of provider recommendation, this finding is particularly important for health centers that employ a variety of providers – it is key that other providers are reminded of the importance of HPV vaccination.

Although STI related findings were not significant at alpha level<0.05 in this analysis, it should be noted that STI testing was nearly significant for those assigned male sex at birth. This signaled potential null bias error (OR: 1.32; 94% CI:0.98-1.78). This association was weaker among those assigned female sex at birth, underscoring the importance of sex-stratified analyses regarding HPV vaccine initiation.

Strengths/Limitations

Due to the significant interaction term identified during the analytic process, sex at birth-stratified analyses were conducted, which created relatively smaller sample sizes, which led to reduced statistical power and may have caused potential null bias error, especially among men (n=486) for various factors, including race, ethnicity, health insurance, and history of STI testing. This study relied entirely on EHR data. While informative, the data were restricted to pre-determined fields, without patient perspectives. Though EHR data are restricted to information entered in the patient chart, the use of these systems offers the opportunity to combine data sources.

Specific to vaccination data, the Arizona Department of Health Services "Arizona State Immunization Information System (ASIIS)", allowed the EHR system at El Rio (and

other health care organizations) to import vaccination data for patients (given the vaccine was administered in Arizona). This strengthened the study by capturing vaccination status, regardless of administration location; however, it is possible that the analysis erroneously allocated patients to an 'unvaccinated' status if they received the vaccine outside of Arizona and did not report it to El Rio.

Given the data available, this analysis was not able to determine whether patients requested the vaccine or providers suggested the vaccine and patients agreed to vaccination. Finally, this analysis focused only on HPV vaccine initiation. Ideally, the analysis would examine HPV vaccination series completion, however, given the already small sample size, restricting to series completion would have reduced the sample further, making it too small to conduct a meaningful analysis. In an analysis of Planned Parenthood Centers, researchers found that only 29% of HPV vaccine initiators completed the series within 12 months.[28] While understanding HPV vaccine initiation is important, ideally analyses should examine vaccine series completion.

This study was strengthened by using the Andersen Behavioral Model as a guiding model.[16] Following the model, the analysis included multiple risk factors that put individuals at higher risk for HPV acquisition, such as tobacco use, STI history and/or testing, and HIV status. Finally, the study was strengthened by performing a sex-stratified analysis, which allowed for the examination of distinct factors for males and females, separately.

Implications for Practice, Policy, and Research

From a practice perspective, FQHCs should consider focused vaccine efforts, targeting those less likely to initiate the vaccine series. Additionally, especially for FQHCs serving women, it may be beneficial to work with all provider types to ensure consistent messaging about the importance of HPV vaccination. HPV vaccine promotion from health

care providers is critical for those 18-26 years old who were not vaccinated as adolescents, because the vaccine is most effective prior to any exposure to HPV.[20] Finally, providers should consider the many healthcare transitions for individuals 18-26 years old. For example, individuals may be transitioning from pediatric medicine to adult/family medicine providers. If individuals are changing providers, it's important that newly assigned providers are discussing and offering HPV vaccination to patients. Additionally, as patients age out of pediatrics, they are likely making more independent health care decisions (apart from parents/guardians), which can influence choices around HPV vaccine initiation. Furthermore, patients may be concurrently experiencing a change in healthcare coverage, such as aging out of Medicaid coverage, or private (employer based) insurance provided by their parents/guardians (at 26 years old), which may influence vaccination decisions.

Results of this study have the potential to inform policy within health centers and among health care providers. For example, by understanding which patients are more or less likely to initiate the vaccine series, specific groups can be targeted for HPV vaccination. One potential broader policy consideration is mandating the HPV vaccine on a national level with stricter opt-out language.[29,30]

Future research should focus on FQHCs and utilize mixed methods approaches to explore HPV vaccine initiation and series completion; qualitative research offers the opportunity to explore patient and provider perspectives to understand engagement around HPV vaccination. Importantly, future work must include HPV behavioral risk profiles. Analyses should include behaviors/need factors that put an individual at higher risk for HPV and related cancers, including, but not limited to: current tobacco use, immunocompromising diseases, STI testing, and STI diagnosis.[14,17,20] Lastly, studies should include participants not

actively seeking healthcare to understand HPV vaccination patterns of those without a medical home.

Conclusion

Overall, HPV vaccine initiation rates among those aged 18-26 years who access primary health care through a FQHC from 2018-2019 were relatively low (20%). By conducting the analysis stratified by sex at birth, unique predisposing, enabling, and need factors for HPV vaccine initiation emerged. Among individuals assigned male sex at birth, those who were younger, had minority sexual orientation (predisposing factors) and had a positive HIV status (need factor) had higher odds of HPV vaccine initiation. For individuals assigned female sex at birth, those who were non-white race (predisposing factor), had a NP/PA as a primary care provider, and more frequent healthcare utilization (enabling factors) had higher odds of HPV vaccine initiation. Findings may be used to promote HPV vaccination during critical vaccination windows to reduce the HPV-related cancer burden in future years.

**Chapter 2 is being prepared for submission for publication of the material. The co-authors include: Heather L. Corliss, MPH, PhD, Donna Kritz-Silverstein, PhD, David R. Strong, PhD, Noe C. Crespo, MS, MPH, PhD, Sudha Nagalingam, MD Tracy L. Finlayson, PhD. The dissertation author was the primary investigator and author of this material.*

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CHAPTER 3:
DENTAL AND MEDICAL PROVIDERS' ATTITUDES ABOUT DISCUSSING HUMAN PAPILLOMAVIRUS-RELATED OROPHARYNGEAL CANCER WITH PATIENTS

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Abstract

Objectives: To assess how medical and dental providers at two Federally Qualified Health Centers (FQHCs) perceive their role in patient engagement regarding Human Papillomavirus (HPV) and related oropharyngeal cancer (OPC).

Methods: Online surveys were collected during July-October 2021 from FQHC medical and dental providers to assess attitudes via 24 closed-ended questions, guided by the Theory of Planned Behavior, rated on a 5-point Likert scale. Descriptive statistics were generated to characterize the sample. Medical and dental providers were compared on HPV-related OPC responses with chi-square tests; linear regression analyses were used to perform comparisons controlling for age, gender identity, age of patients, and clinic location.

Results: Of 156 participants, 103 were medical and 53 were dental providers. When asked if HPV-related OPC discussions were the responsibility of the dental team, 55% of medical providers compared to 74% of dental providers agreed (X^2=4.9, p=0.03). Furthermore, 44% of medical providers compared to 60% of dental providers agreed they were adequately trained to discuss HPV-related OPC with patients (X^2=3.9, p=0.04); 26% of medical providers compared to 85% of dental providers indicated they were adequately trained to screen for signs of oral cancer (X^2=48.5, p<0.01). Regression analysis indicated dental providers had higher levels of agreement related to perceived behavioral control (greater confidence/adequate training to engage patients) compared to medical providers (p<0.001).

Conclusion: Medical and dental providers share a sense of responsibility regarding HPV-related OPC patient engagement; dental providers reported higher levels of confidence and training in addressing HPV-related OPC.

Introduction

Human Papillomavirus (HPV) is the most common sexually transmitted infection (STI), with an estimated 42.5 million people living with HPV in the United States (US).[1] High risk strains of HPV have the potential to develop into cancer, including oropharyngeal cancer (OPC), which is the most common HPV-related cancer.[2] OPCs occur on the back third of the tongue, roof of the mouth, and the tonsils/throat, making it difficult to diagnose.[3,4]

According to the National Cancer Institute, the five-year relative survival of OPC is 68%; an estimated 11,230 deaths are expected to occur in 2022.[5] Although approximately 54,000 new cases of OPC will occur in the US in 2022, the United States Preventive Services Task Force (USPSTF) does not recommend population-based screenings.[5,6] Given the increasing prevalence of HPV-related OPC, limited detection tools, and lack of screening recommendations, it is important to understand how different health care providers view their role around HPV-related OPC patient engagement.

Currently, health care providers do not have clearly defined roles for raising HPV-related OPC awareness and discussing risk and prevention with patients. Despite the lack of formal guidelines, the American Dental Association, American Academy of Pediatric Dentistry, and American Medical Association (pending review) all support patient engagement regarding HPV-related OPC awareness and prevention.[7-9] While professional associations support HPV-related OPC patient engagement, providers may not be prepared to engage in these conversations. Research shows gaps in knowledge and screening abilities for OPCs and related patient engagement for medical providers[10–12] and dentists and dental hygienists have reported hesitancy and a lack comfort and knowledge in discussing HPV-related OPC with patients.[13,14] As primary care medical and dental providers are often the

first professionals consulted when symptoms of HPV-related OPC present, low levels of awareness and understanding may be a potential barrier to early detection and survival.[15]

Given the increasing number of HPV-related OPC cases, limited research, and importance of the provider role, the Oral Cancer Foundation has highlighted areas for continued research. Specifically, they call for an improved understanding of medical and dental provider perceptions around HPV-related OPC and including dental hygienists, physician's assistants and nurses in prevention and care.[16] Additionally, Walker, et al. (2019) called for more theory-driven research to evaluate HPV-related OPC perceptions among providers.[14] To inform study design, health care leaders at two Federally Qualified Health Centers (FQHCs) were consulted to assess feasibility and gauge interest in the topic. FQHCs were selected as study sites because they employ a variety of medical and dental providers. Discussions with the leaders indicated an interest in exploring the topic due to the rise in cases of HPV-related OPC and they shared their medical and dental providers are not regularly engaging patients in discussions around HPV-related OPC given the lack of screening guidelines.

The present study filled gaps in the literature by including many medical and dental providers, not just physicians and dentists, and used the Theory of Planned Behavior (TPB) to guide survey development and analyses. As the focus of this study was to assess provider intentions, the TPB was selected, which has been widely used in examining healthcare provider intentions regarding clinical practice.[18] The TPB posits that ones' attitudes, subjective norms, and perceived behavioral control shape intention and subsequent behavior (i.e. HPV-related OPC patient engagement).[18] For this study, attitudes refer to how providers view their role regarding patient engagement around HPV and OPC. Subjective norms refer

to provider beliefs about approval/disapproval of engaging with patients in HPV and OPC-related conversations by others of influence (i.e., professional organizations and colleagues). Perceived behavioral control refers to provider ability, confidence, and perceptions of the difficulty (or ease) of engaging patients in HPV and OPC discussions. Overall, the purpose of this study was to examine and compare how medical and dental care providers in FQHC settings perceived their role in discussing HPV and HPV-related OPC with their patients by exploring their attitudes, subjective norms, and perceived behavioral control.

Methods

Setting & Participants

A convenience sample included medical and dental providers employed at one of two FQHCs. One located in Tucson, Arizona and the other in San Diego, California. Only medical and dental providers engaged in providing direct patient care (i.e., not in a solely administrative role) at either FQHC at the time of survey administration were eligible and invited to participate. Eligible medical providers included physicians (MD/DO), Registered Nurses (RN), Nurse Practitioners (NP), and Physician Assistants (PA). Eligible dental providers included dentists (DMD/DDS) and registered dental hygienists (RDH). Students training in any of the previously mentioned provider roles were excluded. A total of 575 providers were eligible and invited to participate, 156 completed and submitted the survey (103 medical providers and 53 dental providers for a response rate of 27%).

Data Collection

A cross-sectional survey was administered through the Qualtrics online platform between July-October 2021. Eligible participants were identified by each FQHC, and professional email addresses were shared with the study team. An email invitation from the study team with a link to the survey was sent three separate times throughout July and

August 2021. Due to an initial low response rate (13%) and reports that providers believed the email could have been malicious, brief presentations to describe the study were conducted at each FQHC via electronic video platforms. After the presentations, two additional emails were sent out inviting providers to participate, yielding a final response rate of 27% (N=156) at the end of data collection in October 2021. All study materials were approved by the San Diego State University Institutional Review Board (IRB), then were submitted to each FQHC. Both FQHC research committees reviewed the IRB-approved research materials and approved the study prior to survey administration.

Measures

The survey included 24 TPB-informed statements with responses on a 5-point Likert scale: strongly disagree, disagree, neither agree/disagree, agree, strongly agree. The initial survey development was informed by previous surveys[19–28] and the TPB.[18] The previous surveys did not report reliability or validity statistics, but several used adapted scales and reported their surveys had face validity.[20,21,24,26] While existing surveys provided initial structure, the survey was reviewed and modified based on feedback from three medical leaders, two dental leaders, and two FQHC leaders. The final survey included eight questions (listed below), specific to HPV-related OPC, to capture distinct TPB constructs of attitudes, subjective norms, and perceived behavioral control. Given the ordinal nature of the data, a polychoric correlation was conducted to assess the correlation between items within each construct.[29] Correlations were found to be acceptable within each construct with attitude items having a correlation of 0.82, subjective norm items ranging from 0.52-0.64, and perceived behavioral control items ranging from 0.48-0.75.

Attitudes

1. It is my responsibility to discuss HPV-related oropharyngeal cancer with my patients.
2. I am comfortable discussing HPV-related oropharyngeal cancer with my patients.

Subjective Norms

1. Expert recommendations encourage me to discuss HPV-related oropharyngeal cancer with my patients.
2. It is the responsibility of the dental team to discuss HPV-related oropharyngeal cancer with patients.
3. It is the responsibility of the medical team to discuss HPV-related oropharyngeal cancer with patients.

Perceived Behavioral Control

1. I am adequately trained to discuss HPV-related oropharyngeal cancer with patients.
2. I am adequately trained to screen my patients for signs of oral cancer.
3. I am confident in my ability to discuss HPV-related oropharyngeal cancer with my patients.

To conduct chi-square tests, response categories were collapsed as follows: 'strongly agree' and 'agree' were combined to indicate that a provider agreed with the statement; 'neither agree/disagree', 'disagree' and 'strongly disagree' were combined to indicate that a provider did not agree with the statement.

For the linear regression, distinct scales were created for each TPB construct (attitudes, subjective norms, and perceived behavioral control). Point values were assigned for each response option as follows: 1-strongly disagree; 2-disagree; 3-neither agree/disagree;

4-agree; 5-strongly agree. The scale for 'attitudes' included two items and ranged from 2-10 points. 'Subjective norms' and 'perceived behavioral control' each included three items and ranged from 3-15 points (included items are previously listed under 'Measures'). Higher scores indicated greater level of agreement.

Demographic data were obtained with questions on age (collected and analyzed in years, as a continuous variable), gender identity (collected as male, female, other, or prefer not to answer; analyzed as male vs. female/other/prefer not to answer), clinic (collected and analyzed as Health Center 1 vs. Health Center 2), provider type (Physician, Dentist, RN, NP, PA, RDH; analyzed as medical (physician, RN, NP, PA) vs. dental (dentist, RDH)), length of time in practice (collected as a continuous variable; analyzed as 'less than one year', '1-5 years', '6-10 years', and '10+ years'), and description of regular clinical practice (collected as 'I typically see pediatric patients 0-17 years'; 'I typically see adult patients 18-64 years'; or 'I typically see older adults/geriatric patients 65+ years'; analyzed as 'Pediatric Patients' vs. 'Adult Patients').

Statistical Analysis

All analyses were conducted in SAS 9.4. Descriptive statistics were generated to characterize the sample and understand the distribution of variables. There were no missing data given that only complete surveys were allowed to be submitted; however, two survey respondents entered incorrect values for their age (zero years old and two years old) and based on the distribution of age, median imputation was used for these two values. HPV and OPC variables of interest were examined to determine any differences between medical and dental providers. Initially, chi-square tests compared responses of medical and dental providers on HPV-related OPC statements.

Linear regression analyses were conducted to examine the associations between provider type with HPV-related OPC attitudes and perceptions after adjustment for age, gender identity, age of patients seen in practice and clinic. Covariates were introduced into the model in a hierarchal manner to determine how each set of variables influenced the dependent variable(s) as follows: age and gender identity first, followed by age of patients served in practice and clinic and finally provider type (medical vs. dental). Length of time in practice and age were highly correlated, and age was selected as the covariate to include in the analysis.

Results

Demographic characteristics of participants are presented in Table 3.1.

Bivariate Associations Between Provider Type & Theoretical Constructs (Table 3.2)

There were three TPB items that showed statistically significant differences between medical and dental provider agreement. Specifically, dental providers were more likely than medical providers to agree on the subjective norm item that the dental team is responsible for discussing HPV-related OPC with patients (74% vs. 55%, respectively, $p=0.03$). Two perceived behavioral control items showed statistical significance. Regarding training to discuss HPV-related OPC with patients, over 60% of dental providers agreed they were adequately trained compared to 44% of medical providers ($p=0.04$). Finally, when asked if adequately trained to screen for signs of oral cancer, 85% of dental providers agreed compared to only 26% of medical providers ($p<0.01$). Neither of the attitude items were significantly different between medical and dental providers.

Table 3.1. Demographic Characteristics of Participants by Provider Type

Demographic Characteristics	Medical Providers (n=103)		Dental Providers (n=53)	
	Mean (SD)	**Range**	**Mean (SD)**	**Range**
Age (in years)	46.2 (11.1)	26-71	45.6 (9.8)	31-67
	n (%)		**n (%)**	
Length of Time in Practice				
Less than one year	4 (4)		0 (0)	
1-5 years	23 (22)		10 (19)	
6-10 years	21 (20)		13 (24)	
More than 10 years	55 (54)		30 (57)	
Gender Identity				
Male	18 (17)		21 (40)	
Female	81 (79)		31 (58)	
Other	2 (2)		0 (0)	
Prefer Not to Say	2 (2)		1 (2)	
Federally Qualified Health Center				
Health Center 1	71 (69)		24 (45)	
Health Center 2	32 (31)		29 (55)	
Provider Type				
Physician (MD/DO)	54 (53)		N/A	
Physician Assistant (PA)	3 (3)		N/A	
Nurse Practitioner (NP)	25 (24)		N/A	
Registered Nurse (RN)	21 (20		N/A	
Dentist (DMD/DDS)	N/A		37 (70)	
Registered Dental Hygienist (RDH)	N/A		16 (30)	
Age of Patients Seen in Practice				
Pediatric (0-17 years)	20 (19)		17 (32)	
Adults (18-64 years)	68 (66)		35 (66)	
Older Adults (65+ years)	15 (15)		1 (2)	

Notes: Medical Providers include physicians, physician assistants, nurse practitioners, and registered nurses; Dental Providers include dentists and registered dental hygienists. SD = Standard Deviation; n = sample size; % = percent. Age of Patients Seen in Practice defined as who the provider typically sees in their regular practice.

Table 3.2. Bivariate Associations Between Medical and Dental Providers within each Theoretical Construct

Survey Statement by Theoretical Construct	Providers in Agreement with Statement		
Attitudes	**Medical n (%)**	**Dental n (%)**	**p-value**
It is my responsibility to discuss HPV-related OPC with my patients	79 (77)	41 (77)	0.93
I am comfortable discussing HPV-related OPC with my patients	68 (66)	39 (74)	0.33
Subjective Norms			
Expert recommendations encourage me to discuss HPV-related OPC with my patients	65 (63)	36 (68)	0.55
It is the responsibility of the dental team to discuss HPV-related OPC with patients	57 (55)	39 (74)	0.03*
It is the responsibility of the medical team to discuss HPV-related OPC with patients	83 (81)	43 (81)	0.93
Perceived Behavioral Control			
I am adequately trained to discuss HPV-related OPC with my patients	45 (44)	32 (60)	0.04*
I am adequately trained to screen my patients for signs of oral cancer	27 (26)	45 (85)	<0.01*
I am confident in my ability to discuss HPV-related OPC with my patients	59 (57)	33 (62)	0.55

Notes: HPV= Human Papillomavirus; OPC = oropharyngeal cancer; All listed theoretical constructs are part of the Theory of Planned Behavior; * significance at alpha level 0.05

Linear Regression Results within Theoretical Constructs (Table 3.3)

After adjusting for demographic covariates, dental providers had perceived behavioral control agreement scores that were on average about 1.8 points higher than medical providers ($p<0.001$). There were no significant associations of provider type with attitude and subjective norm constructs after adjusting for covariates.

Table 3.3. Hierarchal Linear Regression Model within each Theoretical Construct

Models	Independent Variables	Dependent Variables (Theoretical Constructs)		
		Attitudes	**Subjective Norms**	**Perceived Behavioral Control**
1	Age	-0.003	-0.020	-0.011
	Gender Identity	0.178	-0.085	0.136
	Adjusted R^2	-0.011	-0.003	-0.011
2	Age	-0.001	-0.020	-0.007
	Gender Identity	0.231	-0.003	0.100
	Age of Patients	0.834	0.532	1.103
	Clinic	-0.389	-0.436	-0.091
	Adjusted R^2	0.008	-0.002	-0.009
3	Age	-0.001	-0.020	-0.003
	Gender Identity	0.160	-0.086	-0.314
	Age of Patients	0.744	0.427	0.584
	Clinic	-0.445	-0.0503	-0.418
	Provider Type	0.317	0.374	1.835*
	Adjusted R^2	0.008	-0.004	0.080

Notes: All listed theoretical constructs are part of the Theory of Planned Behavior; * significance at alpha level 0.05

Discussion

Results of this study suggest there is a similar high sense of responsibility among medical and dental care providers to engage their patients in discussions around HPV-related OPC even though there are no USPSTF guidelines for screening.[6] While over three-fourths of both medical and dental providers indicated a responsibility for HPV-related OPC patient engagement, fewer medical than dental providers felt adequately trained (44% vs. 60%, respectively) or confident in their ability to discuss HPV-related OPC with patients (57% vs. 62%, respectively). These results point to the importance of increased training to build provider confidence in discussions of HPV-related OPC.

Interestingly, within the construct of subjective norms, medical and dental providers agreed that it is the responsibility of the medical team to discuss HPV-related OPC with patients (81% for both), but they disagreed that it is the responsibility of the dental team (medical:55%; dental:74%; p-value<0.03). Medical providers reported it is their responsibility, however, many were not adequately trained or confident in their ability to have this discussion. When analyzing the theoretical constructs through linear regression, findings were only significant within perceived behavioral control, indicating higher levels of confidence and adequate training among dental providers.

While medical and dental providers reported varying levels of adequate training and confidence, most providers (medical: 85%; dental: 83%) are interested in continuing education opportunities regarding HPV. Given their interest in learning more about HPV and the increasing prevalence of HPV-related OPC it is important that continuing education is offered to all health care providers. This high level of interest in continuing education provides an opportunity for intervention to increase HPV-related OPC confidence and training.

Study findings agree with previous studies in that both medical and dental providers believe they have a role in HPV-related OPC and patient engagement/care.[14,15] However, there remains a need to understand the distinct roles of each provider type and develop targeted opportunities for continuing education.[30] In accord with previous studies, more dental providers than medical providers agreed they were adequately trained to screen for oral cancer.[11] According to Patton (2006) dental providers would benefit from continuing education focused on OPC prevention, while medical providers would benefit from more training around oral examination skills.[11] Recent literature describes that providers continue

to report a need for continuing education and low levels of HPV-related OPC knowledge.[11–13] While this study did not focus on HPV-related OPC knowledge, results suggest a need for continuing education to improve confidence and ability regarding patient engagement.

Findings should be interpreted while considering the study limitations. The TPB was used to guide survey development and subsequent analyses, but it was not used to explain the behavioral outcome. Rather, the constructs of 'attitude', 'subjective norm', and 'perceived behavioral control' were analyzed to understand how different provider types may intend to engage in HPV-related OPC discussions with patients. The sample size was relatively small, which may have resulted in low power and a type 2 error. Two recent systematic reviews, one focused on knowledge gaps of HPV-related OPC among health care providers and patients and the other focused on dental providers' perceptions around HPV and HPV-related OPC patient engagement both noted the paucity of literature devoted to HPV-related OPC.[14,15] Thus, this study's findings contribute to the limited literature and provide direction and a foundation for future research. Although the two FQHCs engaged in this study are among the largest in the US, findings have limited generalizability because all participants were FQHC employees and located in a similar geographic area.

This study included medical and dental providers outside of physicians and dentists, however, providers were collapsed into medical or dental groups. The sample size did not allow for an analysis with the rigor and specificity intended at the onset of the study. All analyses were conducted with only physicians and dentists and then compared to analyses with all respondents divided between medical and dental groups. Given the results did not change when including all providers, the final analysis included all those who completed the survey.

Unfortunately, there is not a validated scale to assess HPV-related OPC provider perceptions. As discovered when reviewing the existing literature, many studies, including this one, relied on adapting existing scales and utilizing medical and dental providers to review and provide feedback to establish face validity. While important, surveys must not rely too heavily on face validity. Future work in this area should include rigorous scale development with a focus on intentions and direct behavior assessment among diverse provider groups.

This study was originally conceptualized and designed for in-person data collection. Due to the COVID-19 pandemic, it was necessary to shift data collection to an online platform. Furthermore, the survey was originally circulated around the same time as a malware attack at one FQHC. The information technology team at the affected FQHC shared the concerns from providers. The research team responded immediately with an email to participants confirming the link was not malicious; however, the concern over the malware attack may have discouraged providers from participating in the survey. Follow-up emails regarding the study were sent from internal email accounts within each health center to avoid further security concerns.

Overall, providers have a high sense of responsibility regarding HPV-related OPC patient engagement, however there are varying levels of confidence and feelings of adequate training between medical and dental providers. There is a need and interest in continuing education opportunities focused on HPV and related OPC among medical and dental providers. In a setting such as a FQHC, collaboration between medical and dental teams should be encouraged to promote HPV-related OPC patient engagement.

**Chapter 3 is being prepared for submission for publication of the material. The co-authors include: Heather L. Corliss, MPH, PhD, Donna Kritz-Silverstein, PhD, David R. Strong, PhD, Noe C. Crespo, MS, MPH, PhD, and Tracy L. Finlayson, PhD. The dissertation author was the primary investigator and author of this material.*

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DISCUSSION

Oropharyngeal cancer is the most common HPV-related cancer and it has been estimated that 54,000 cases will occur in the US in 2022.[1] Although scientific advancements have improved diagnostic capabilities, gaps remain in understanding awareness, prevention efforts, and healthcare provider/patient engagement.[2–5] This dissertation focused on addressing these gaps. First, HPV-related oropharyngeal cancer knowledge and awareness were examined among sexual minority populations using a national dataset. Second, factors associated with HPV vaccine initiation rates were studied among 18–26-year-olds who utilized a Federally Qualified Health Center (FQHC) as their medical home. Finally, medical and dental provider attitudes and perceptions regarding HPV-related oropharyngeal cancer patient engagement were compared at two large FQHCs. While each was a distinct study, all contributed to the advancement of the HPV-related oropharyngeal cancer research field with a unique call to action.

HPV-Related Oropharyngeal Cancer Awareness

Chapter 1 findings showed that HPV-related oropharyngeal cancer awareness and knowledge were relatively low, regardless of sexual orientation. Overall, only 19% of respondents knew of the connection between HPV and oropharyngeal cancer. There was no significant difference in HPV-related oropharyngeal cancer knowledge based on sexual orientation for men or women.

In general, Chapter 1 findings, specific to HPV were consistent with what has been reported in previous literature.[6–8] Previous HINTS analyses showed that sexual minority respondents were less likely than their heterosexual counterparts to seek health information from a medical provider.[9] In this study, HPV awareness was associated with having a regular medical provider and sexual minority women were significantly less likely to report having a

regular medical provider, compared to their heterosexual counterparts. Therefore, it is possible that sexual minority women, who can face comparable (or higher) HPV risk compared to heterosexual women[10–13], are not receiving important information about HPV.

Understanding risk is an important part of health care decision making.[14] Overall, over half of HINTS respondents were aware of HPV, but far fewer knew about the connection between HPV and oropharyngeal cancer. Knowing that HPV can develop into oral cancers could influence prevention and health behaviors, therefore it is essential that the public health field prioritize tailored campaigns targeting populations at high risk for HPV acquisition and related disease.

HPV Prevention

HPV vaccination is critical to prevent the acquisition and spread of HPV. Chapter 2 findings highlighted opportunities for targeted HPV vaccine campaigns for patients who utilize a FQHC for regular medical care. HPV vaccine initiation rates were low for both those with male and female sex at birth (approximately 20%), however, different factors were associated with HPV vaccine initiation based on sex at birth. For individuals assigned male sex at birth, those who were younger, identified as a sexual minority (gay, bisexual, or something else) and had a diagnosis of Human Immunodeficiency Virus (HIV) had higher odds of HPV vaccine series initiation. In comparison, for individuals assigned female sex at birth, those with non-White race, having a nurse practitioner/physician assistant (as a primary care provider, PCP) and more frequent health care utilization had higher odds of HPV vaccine initiation.

Among those assigned male sex at birth, findings were in line with Advisory Committee of Immunization Practices HPV vaccine recommendations for men who have sex with men and those living with HIV and experience a higher burden of HPV-related

disease.[15] Of note, a novel contribution in Chapter 2 was the inclusion of sexually transmitted infection (STI) testing and history (need factors). Although STI findings overall, were not statistically significant (at alpha level<0.05), it was of borderline significance for those assigned male sex at birth (OR: 1.32; 94% CI:0.98-1.78) and there was likely null bias error. For those assigned female sex at birth, the association was much weaker. This difference between males and females underscored the importance of conducting a sex stratified analysis. Further analyses should include larger sample sizes to explore the association more adequately between STI testing and history and HPV vaccine series initiation and completion.

Among those assigned female sex at birth, more frequent healthcare utilization (enabling factor) was associated with higher odds of vaccination, as noted in other studies.[16,17] In contradiction to previous research,[18] this study found that those with non-White race (predisposing factor) had higher odds of HPV vaccine initiation compared to those with White race. However, this study had a smaller sample size which required that the race was collapsed into a dichotomous variable of non-White compared to White. Study findings regarding race may be a result of combining several races into a 'non-White' category.

Provider type (enabling factor) was also significant for individuals assigned female sex at birth. Those with a Certified Nurse Midwife assigned as a PCP had lower odds of HPV vaccine initiation (compared to physician PCP) while those with a Nurse Practitioner/Physician Assistant assigned as PCP had higher odds of HPV vaccine initiation (compared to physician PCP). As provider recommendation is associated with HPV

vaccination,[19,20] this was an important finding for a FQHC that employs a variety of healthcare providers.

It is imperative that providers deliver consistent messaging to patients regarding HPV vaccination. Future work must focus on ensuring that providers are adequately trained to discuss the HPV vaccine with patients, and that opportunities for continuing education are provided when necessary. Furthermore, FQHCs may consider targeted campaigns to increase HPV vaccination with special focus on those at a heightened risk for HPV acquisition based on behavioral risk profiles and/or those less likely to initiate the vaccine series.

HPV-related Oropharyngeal Cancer Patient/Provider Engagement

Chapter 3 findings suggested that medical and dental providers share a high sense of responsibility regarding HPV-related oropharyngeal cancer patient engagement. Although there are no recommendations or screening guidelines for HPV-related oropharyngeal cancer,[21] over 75% of medical and dental providers indicated feeling they have a responsibility to discuss HPV-related oropharyngeal cancer with their patients. However, only 44% of medical and 60% of dental providers felt adequately trained and only 57% of medical and 62% of dental providers felt confident in their ability to engage patients in HPV-related oropharyngeal cancer discussions. When analyzed within the constructs of the Theory of Planned Behavior, only perceived behavioral control was significant. Hierarchal linear regression findings indicated that dental providers had higher levels of confidence and adequate training regarding HPV-related oropharyngeal cancer compared to medical providers.

While adequate training and confidence were somewhat low, over 80% of providers were interested in HPV related continuing education opportunities. It is encouraging to find

that both medical and dental providers believe they have a role in patient engagement. However, the lack of training and confidence necessary to address HPV related oropharyngeal cancer with their patients may impede engagement. The high level of interest in continuing education is an opportunity for intervention by providing continuing education focused on improving provider training and confidence.

Chapter 3 findings were in accord with previous literature which found that medical and dental providers believe they have a role in HPV-related oropharyngeal cancer and patient engagement/care.[22,23] Literature also describes the reported need for continuing education.[24–26] While future research is needed to better understand how different types of providers perceive their role in HPV-related oropharyngeal cancer patient engagement, there is overwhelming evidence that continuing education opportunities are necessary and desired by providers in the immediate future.

Strengths/Limitations

This dissertation utilized three distinct data sources to better understand HPV-related oropharyngeal cancer knowledge, prevention, and provider/patient engagement. Chapter 1 analyzed data from a national health survey, Chapter 2 utilized electronic health record data, and Chapter 3 relied on primary data collection with medical and dental providers. Each data source and analysis presented a unique set of strengths and limitations that should be considered while examining the findings from this dissertation.

Chapter 1 utilized the Health Information National Trends (HINTS) 5, Cycles 1-3 data collected between 2017-2019. All analyses conducted with HINTS were cross sectional and therefore causal inferences cannot be established. While HINTS 5 (cycles 1-3) was large and nationally representative, the sample size of sexual minority individuals was small and further minimized when stratified by sex. Given that only 5% of respondents included in the

analysis identified as sexual minorities, there was low power to detect differences in HPV-related oral cancer knowledge based on sexual orientation. Another limitation, specific to the sexual minority populations in the analyses, was the combination of all sexual minorities into one analytic group; sample size constraints did not allow for the subpopulations of sexual minorities to be examined. While necessary, given the sample sizes, these combinations limited the ability of the analyses to accurately describe the knowledge and awareness of HPV-related oral cancers within diverse subgroups. Finally, Chapter 1 analyses only included the variables collected during each HINTS cycle 1-3. As previously described in the Introduction, number of sexual partners is an important risk factor to consider for oral HPV and subsequent cancer, however this information was not collected in HINTS 5, Cycles 1-3 and was not included in the analysis. The study was strengthened by the combination of three waves of data and findings are generalizable in the United States, given the national sample.

Chapter 2 utilized electronic health record (EHR) data from El Rio Health, a large Federally Qualified Health Center in Tucson, Arizona. Data were limited to pre-determined fields in the EHR, therefore extracted data relied entirely on the information entered by healthcare professionals and did not reflect patient perspectives. However, the accuracy of the EHR vaccination data was likely improved through the use of the Arizona State Immunization Information System (ASIIS).[27] Although not possible to prove without an in depth chart reviews, EHR data are likely more accurately reporting vaccination status with the imported ASIIS data.

Ideally, vaccine series completion would have been explored, as series completion is necessary for the highest level of protection and remains low;[28] however, the sample size was

too small to conduct meaningful analysis examining series completion. Given the sample size of this sex-stratified analysis there was potential null bias error especially among men for race, ethnicity, health insurance, and history of sexually transmitted infection (STI) testing. Although power was reduced, the sex-stratified analysis allowed for the identification of distinct factors associated with vaccine initiation for men and women, separately.

Chapter 2 was strengthened by utilizing the Andersen Behavioral Model. Following this model allowed for covariates to be classified as predisposing, enabling, and need factors.[29] Specifically, this allowed for the classification of multiple risk factors (tobacco use, STI history/testing, HIV status) that increase risk for HPV acquisition and should be included in HPV vaccination analyses.[30]

Chapter 3 relied on primary data collection via convenience sampling at two Federally Qualified Health Centers located in the southwestern United States. The fact that all providers who participated were employed at one of the participating Federally Qualified Health Centers located in a similar geographic area, limited the generalizability of the results. The Theory of Planned Behavior was used to guide survey development and analysis but was not used to explain the outcome of interest (HPV-related oropharyngeal cancer patient engagement); rather, the constructs within the theory were examined to understand how medical and dental providers intend to engage with patients regarding HPV-related oropharyngeal cancer. Additionally, the sample size was small leading to low power when running a comparison analysis between medical and dental providers and may have resulted in type II error.

The survey used was developed by the dissertation author as a validated scale does not exist to examine medical and dental provider perceptions around HPV-related

oropharyngeal cancer. The lack of a validated scale is a limitation, however, survey findings and lessons learned during development provide a foundation and direction for future research. This study included medical and dental providers beyond physicians and dentists. Nurses, physician assistants, and registered dental hygienists were also surveyed. The intention was to examine how distinct providers viewed their role in HPV-related oropharyngeal cancer patient engagement, however, the sample size did not support these analyses.

Chapter 3 was strengthened by including medical and dental provider input during survey development and by using theory to guide survey development and subsequent analyses. Additionally, Chapter 3 examined comparisons between medical and dental providers, while most existing literature focuses on either medical providers or dental providers independent of one another.

It is important to note that this dissertation was extensively overhauled due to the COVID-19 pandemic. Chapter 2 was originally an IRB approved qualitative study focused on understanding how individuals living with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome perceive their risk of HPV-related oropharyngeal cancer and with which types of providers they would feel comfortable discussing the disease and risk factors. Ideally, this would have provided patient perspectives before surveying medical and dental providers. Due to the COVID-19 pandemic, the study was suspended, and a new study was developed to meet doctoral requirements. Chapter 3 was originally designed for in person data collection but was transitioned to an electronic platform due to the COVID-19 pandemic and restrictions around group gatherings.

Future Directions

It is imperative that public health professionals address the rising rate of HPV-related oropharyngeal cancer through multi-level approaches. Based on behavioral risk profiles, there may be an increased risk of HPV-related oropharyngeal cancer for sexual minority men and women. Future analyses must be adequately powered to detect differences in HPV-related oropharyngeal cancer awareness between sexual minority populations and their heterosexual counterparts. Additionally, future work should aim to examine sexual minority sub-populations independently because the risk profiles and experiences differ (e.g., bisexual women have different experiences and risks for HPV compared to lesbian women). Furthermore, it would be beneficial to include more behavioral risk factors in future analyses, specifically number of oral sex partners and alcohol use, both of which are associated with the development of oropharyngeal cancer. While future research is necessary and important to advance our understanding, taking action to raise awareness of HPV-related oropharyngeal cancer is critical. Regardless of sexual orientation, knowledge on a national level hovers below 20% and as the most common HPV-related cancer, it is imperative the public is made more aware of this cancer and its etiology through novel educational campaigns.

Regarding the study of HPV vaccination, future work should build upon dissertation findings, but expanded to include all eligible age groups and vaccine series completion. Given that adequate levels of vaccination have the potential to eliminate HPV-related cancers, it is important to understand vaccination patterns and gaps in vaccine coverage for all eligible populations. Furthermore, patient attitudes and perceptions around vaccination should be explored in concert with health record data to explain vaccination patterns and acceptability more fully. Tailored HPV vaccine campaigns should be developed, targeting men and women separately, to increase HPV vaccination.

The pilot work around provider attitudes and perceptions lays the groundwork for future investigations and highlights health care providers' desire for continuing education opportunities around HPV-related oropharyngeal cancer. Continuing education opportunities should be prioritized and provided to medical and dental providers. Further research should focus on creating a validated scale to assess provider attitudes around HPV-related oropharyngeal cancer. Additionally, building upon findings, research should be expanded to include providers in more diverse geographic areas throughout the United States.

Conclusions

With most of the population unaware of the connection between HPV and oropharyngeal cancer, lack of screening guidelines, low HPV vaccination rates, and increasing number of cases, the health care field must work to improve knowledge, prevention, and early detection. While further research is warranted, it is equally important that action is taken to increase HPV-related oropharyngeal cancer knowledge through targeted, tailored campaigns, promote HPV vaccination among men and women while considering behavioral risk profiles, and provide continuing education opportunities to medical and dental providers to increase confidence regarding HPV-related oropharyngeal cancer patient engagement.

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