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# Risk Factors of Human Papillomavirus Positive Oropharyngeal Cancer in Men

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Abstract

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Doctoral Study Submitted in Partial Fulfillment

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## Abstract

The human papillomavirus (HPV) is a leading domestic and global sexually transmitted disease. The purpose of this secondary quantitative, cross-sectional study is to investigate if there is an relationship between the rate of oral HPV-oropharyngeal squamous cell carcinoma (OPSCC) and race, exposure to smoking cigarettes (tobacco), risky sexual behavior, and participation in oral sex of male-to-male contact vs. male-to-female contact. The social cognitive theory grounded this study. The University of Alabama at Birmingham cancer database population supplied the study's sample size of 337 males greater than 18 years of age with a diagnosis of OPSCC. I conducted descriptive analyses using Pearson chi-square and multivariable logistic regression to investigate the relationship between the dependent and independent variables. The results of the descriptive analysis indicate that white males had a higher prevalence of OPSCC compared to African Americans and Hispanics; smoking history had a higher prevalence than never smoked or unknown status; heterosexuals had a higher prevalence than homosexual or bisexual status. Multivariate logistic regression indicated no significant relationships were found between smoking and OPSCC or sexual orientation and OPSCC. The study has considerable social change potential since outreach efforts can target population groups to lower transmittal of HPV to reduce the secondary conditions of HPV-related genital warts and cancer.

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# Dedication

This dissertation is dedicated to those with human papillomavirus oropharyngeal squamous cell carcinoma looking for better treatment to sustain a better quality of life and my family that gave me the motivation to bring this topic to forefront of research.

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## Introduction

The human papillomavirus (HPV) is a leading domestic and global sexually transmitted disease. It also has the highest relationship to cancer in several areas of the body and is the cause of anogenital warts (Serrano et al., 2018). Genital warts are highly contagious and are caused by HPV Types 6 and 11; however, evidence shows that many individuals exposed to both genital warts and coinfection of oncogenic types of HPV such as 16, 18, 31, 33, 45, 52, and 58 (Giuliano et al., 2010). Another condition caused by HPV is recurrent respiratory papillomatosis. This rare condition causes lesions in the respiratory tract that may obstruct the airway (Giuliano et al., 2010). The HPV DNA protein associated with this condition is also Type 6 and 11. This condition is seen equally among males and females but more commonly in children than adults, as its rate is 4.3 per 100,000 in children and 1.8 per 100,000 in adults (Giuliano et al., 2010). Its transmission is more familiar from mother to child during childbirth. Its current form of treatment is surgery of the lungs in the thoracic cavity.

Although there are many preventative strategies for HPV related to cervical cancer, HPV-related cancers in other parts of the body are consistent with causing the increased rate of morbidities and mortalities in many parts of the world, significantly in the less developed countries (Serrano et al., 2018). Domestically, there are nearly 80 million Americans with HPV, with an estimation of 14 million new cases annually reported to the Centers for Disease Control and Prevention (National Institute of Health, 2020). Of all sexually active individuals, about 80% will contract HPV at some point in

their lifetime (CDC, 2018a). The United States statistics suggest that approximately 10% of its male and 3.6% of its female population have oral HPV and that HPV is responsible for about 70% of all oropharyngeal squamous cell carcinoma OPSCC (CDC, 2021). The predominant demographic with HPV-positive OPSC is middle-aged White males between the ages of 45 and 59 (Hay & Nixon, 2018). There is a direct link between public health issues related to the increased HPV-positive OPSCC and the elevated rate of HPV transmission.

The HPV relation with head and neck cancer has surpassed tobacco-related (CDC, 2019). The rate of HPV has elevated over the past 3 decades, as has the rate of HPV-OPSCC (Yakin et al., 2018). The CDC used population estimates that of the 44,000 new cases of cancer found in parts of the body such as the vagina, vulva, penis, anus, rectum, and oropharynx, nearly 34,800 of these cases are positive for HPV (CDC, 2019). It also demonstrates severe functional morbidities and a healthcare cost burden for treatment. The dependent variable for this research is the rate of HPV-OPSCC, and the independent variables are race, use of tobacco, and oral sexual contact with male-to-male and male-to-female. I researched the rate of adult males with HPV. Then I investigated to what extent there is an association between the rate of HPV-OPSCC race and smoking tobacco cigarettes, as well as oral sex contact with male-to-female vs. male-to-male.

## Problem Statement

Data from clinical research investigated by doctoral researchers and physicians show the relationship between smoking and cancer, specifically OPSCC (Yakin et al., 2018). Tobacco was the leading cause of OPSCC; however, a sexually transmitted

disease called HPV has taken its place (Yakin et al., 2018). Yakin et al. (2018) noted a rise in the global incidence of OPSCC in males. In the United States alone, the HPV-positive OPSCC population showed a 225% increase in prevalence, with similar suggestions in Australia and New Zealand. Clinical data show more accurately that OPSCC incidence has significantly increased globally over the past 3 decades, and the United States contributes critically to that prevalence (Yakin et al., 2018). OPSCC is no longer plaguing the older population of men and women 60 and over due to the HPV-positive component. The primary population diagnosed with HPV-positive OPSCC consist of those between 45 and 59 years of age (Hay & Nixon, 2018). This range is 33.93-19.93 years below life expectancy in the United States, as the United States' life expectancy is 78.93 years of age (Macrotrends LLC, 2020). Therefore, physicians and researchers seek to improve the treatments for OPSCC because specific treatments tremendously affect the patient's quality of life (Hay & Nixon, 2018). This research can aid in their compilation of information.

When tobacco was the primary cause of OPSCC, treatment consisted of mandibulotomy to access the oropharynx, resulting in long-term airway support due to tracheostomy and gastrostomy for feeding (Hay & Nixon, 2018). Morbidities from past techniques, such as cutting large incisions exposing tissue and organs from open surgery for OPSCC, caused a decrease in functions such as speech and swallowing (Golusiński & Golusińska-Kardach, 2019). Seeking to conduct minimally invasive surgery helps limit the requirement of large incisions to decrease recovery time, reduce infections, and help reduce decreased morbidities functions. Also, open surgery, in many cases, is followed-

up with concurrent toxic chemotherapy and reconstruction surgery due to the location of the disease (Golusiński & Golusińska-Kardach, 2019). Otolaryngologists seek to reduce these many morbidities of head and neck cancer and are researching vigorously for better treatment options that minimize introduction to unnecessary procedures and medication. It is imperative to perform less invasive procedures while delivering effective treatment (Golusiński & Golusińska-Kardach, 2019). Golusiński and Golusińska-Kardach (2019) indicated that surgery allows for accurate assessment of disease versus chemoradiotherapy; however, the question arises do we comprise proper diagnosis for de-intensification in some of the population?

The 80 million Americans with HPV, with an annual incidence of 14 million new cases reported to the Centers for Disease Control and Prevention, need more options (National Institute of Health, 2020). The United States public health officials need to understand why males are disproportionally affected at a rate of 10% of the U.S. population compared to 3.6% of the U.S. female population with oral HPV. HPV accounts for about 70% of all OPSCC (CDC, 2021). From this data, an investigator can conclude that tobacco and alcohol products or environmental toxins cause the remaining 30% of HPV-negative OPSCC.

Oropharyngeal squamous cell carcinoma appears in the throat, mouth, base of the tongue, and salivary glands (CDC, 2019). Recent articles in medical journals for head and neck diseases covering HPV show that males, mainly White males 4559 years old, have an increased rate of HPV-positive OPSCC (Hay & Nixon, 2018). There are many theories regarding this population's higher incidence. The goal of this study is to

precisely investigate why this occurs in efforts to reduce HPV transmission and cancer development. Therefore, looking at factors such as HPV and smoking, HPV and risky sexual behavior, and HPV, where males engage in oral sex, is essential and can help fill the literature gap regarding this specific population. The literature gap on de-escalating treatment also keeps physicians and patients in a hesitant state of mind concerning increasing the quality of life from surgery while possibly increasing recurrence (Mirghani & Blanchard, 2017). The increased incidence of OPSCC within this population raises the question if this population has an increased rate of exposure to smoking, risky sexual behavior, and the frequency of engaging in oral sex.

## Purpose of the Study

The purpose of this study was to investigate if there is an association between the rate of oral HPV-OPSCC and race, exposure to smoking cigarettes (tobacco), risky sexual behavior, and participation in oral sex of male-to-male contact vs. male-to-female contact. The United States population's quantitative data indicate an increase in the prevalence of HPV-positive OPSCC over the past 3 decades (Yakin et al., 2018). Physicians and researchers could benefit from the secondary quantitative analysis to better understand HPV-OPSCC and risk factors in this population. This knowledge could serve as a framework for improving the medical standard of care practices and patients' preventative education model.

## Research Questions and Hypotheses

RQ 1: What is the rate of oral HPV-positive OPSCC in adult men $\geq$18 years old?

RQ 2: To what extent is there an association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old?

$H_o2$: There is no statistically significant association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old.

$H_1 2$: There is a statistically significant association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old.

RQ 3: Is there a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level?

$H_o3$: There is no statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level.

$H_1 3$: There is a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level.

## Theoretical Foundation

The theoretical framework of social cognitive theory assesses the relationship among person, behavior, and environment when explaining how health behavior occurs. For this study, I attempted to show the makeup of the person's biology and hormones

(person), the basis of social influence (environment), and smoking and risky sexual contact without the use of protection (behavior) on how it relates to developing HPV-OPSCC. SCT, previously social learning theory, was started in the 1960s by Albert Bandura and changed to SCT in 1986 (LaMorte, 2018). The nature vs. nurture premise might explain the argument; however, the biological imprints may still influence decision-making.

The six primary constructs of SCT consist of reciprocal determination, behavior capacity, observation learning, reinforcement, expectation, and self-efficacy (LaMorte, 2018). Reciprocal determination refers to learned experience and the environment that influences behavior: behavioral capacity and behavioral performance through knowledge and skills. Observational learning accounts for individuals following the tone of what surrounds them. The reinforcement construct relates to the interaction of internal and external responses that encourage or discourage continued behavior. Expectation refers to an expected outcome or anticipated consequence of a person's behavior. Lastly, self-efficacy refers to the confidence level of a person's ability to complete a response. Observational learning and reinforcements may better explain sexual behavior.

Because sexual contact is the center of HPV transmission; how individuals think about perceived susceptibility influences their sexual behavior. A social environment such as high school peer pressure, a college campus, a house party, or a bachelor pad may lead one to employ the lack of sound judgment and communication associated with safer sex, the reduction of sexual partners, and the delay of sexual interaction. Nguyen et al. (2016) reviewed a study comparing college students from the 1990s to those of 2007. The

group from the 90s showed 59% reported oral-genital contact as not having sex. With another group of 477 college students reported in 2007, the percentage of those believing oral sex is not sex was 80% (Nguyen et al., 2016). The SCT surrounding the societal perception of oral sex accounts for those limiting protection and engaging in multiple partners. Greifender et al. (2017) argued that SCT helps navigate these questions. This theory plays an essential role in social psychology, focusing on the cognitive processes that comprise how individuals think and perceive their social environment (Greifender et al., 2017). Males and females need to understand what they see as a risk when initiating sexual encounters, deciding on how many and whom to engage in sexual intercourse with, and whether to engage in oral sex.

One can also use SCT to see how the medical society treats their patients with HPV-positive OPSCC vs. HPV-negative OPSCC and why they have not taken a sooner approach to change the treatment methods. This theory suggests that the interaction of behavior, environment, and the individual promotes learning (LaMorte, 2018). SCT stands to observe and understand the interaction and experiences related to developing HPV and diagnosing and treating HPV-OPSCC (LaMorte, 2018). SCT usage helped explain whether there is an association between smoking tobacco and the increased rate of oral HPV-OPSCC in adult men. The research explored their exposure and use of tobacco. I used this theory to investigate the environment (exposure) and behavior (usage) of smoking tobacco products and oral sex between male-to-female vs. male-to-male. I helped fill the literature gap to help other investigators understand if there is a significant difference in the rate of HPV-OPSCC in White compared to other races.

Although the social cognitive theory was the theoretical framework that guided the present study, this study did not test constructs related to SCT. Instead, this study focused on how an individual's engagement in sexual behaviors might lead to an increased prevalence of HPV. SCT guided the study since health behaviors attributed to the health problem can be explained by SCT. There is no cure for HPV; however, in some cases, it resolves on its own. When it does not, the disease stands to develop into genital warts or cancer (CDC, 2021). Risk factors such as experience with multiple partners, engaging in oral-anal sex or engaging in oral-genital sex play a significant role in HPV development (Yakin et al., 2018). Because of the increasing prevalence of HPV and HPV-OPSCC, SCT can help understand how a person's environment influences risky sexual behavior.

## Nature of the Study

Using quantitative secondary analysis, I investigated behavior using statistical models through measurement and research (Kenton, 2019). Secondary data analysis allowed the use of data previously gathered by another researcher to offer a different perspective from its original usage. This process also helped to save on time and cost that primary data analysis incurs. I used this approach to display the investigation of the variables using the correlational design and logistic regression using a data source from the University of Alabama at Birmingham (UAB) Health Services i2b2. The methodology consisted of reputable peered-reviewed medical literature as well as database searches.

The nature of the study consisted of secondary data collection. The population under study is adult men $\geq$ 18 years old. The dependent variable is the HPV-OPSCC rate. The independent variables are race, smoking, and participation in oral sex, with control education and income as mediating variables. The study evaluated their association with the rate of HPV-OPSCC in adult men. Each research question has binary dependent variable; therefore, a quantitative statistical approach was logistic regression.

## Literature Search Strategy

HPV is a sexually transmitted infection with approximately 40 strains that affect the genital and anal regions of the body. Sexual partners can transfer the virus to the oropharyngeal space through oral sex (CDC, 2019). In most cases, search engines populating information from within the last 5 years provided the attest description of the disease. Examples of these search engines are Surveillance Epidemiology, and End Results (SEER) or Cancer Center-based hospitals such as the UAB as it relates to the rate of HPV and OPSCC are more helpful. Behavioral Risk Factor Surveillance System and PubMed were used to review the rate of sexual behavior comparing oral sex with male-to-male compared male-to-female partners in search engines such as.

Keywords consisted of *the rate of HPV controlling for income and education, OPSCC controlling for income and education, risky sexual behavior and HPV,* and *tobacco and HPV*. Many medical databases store information on head and neck diseases relative to HPV-positive OPSCC; finding the database with variables to answer the desired research questions were critical. Some reliable sources are the American Academy of Otolaryngology-Head and Neck Surgery, SEER Program, Behavioral Risk

Factor Surveillance System, National Cancer Database, MEDLINE, and Cancer Centers such as the UAB, which I searched using keywords: *HPV-positive OPSCC, tobacco usage*, and *same-gender sex.*

## Literature Review

### Human Papillomavirus Leading United States Sexually Transmitted Disease

Human papillomavirus is responsible for 4.5% of all new cancer cases worldwide (Serrano et al., 2018). Histological testing has shown positive HPV in the cervical, vulva, vagina, penis, anus, and head and neck cancer (Serrano et al., 2018). Morbidities and mortalities dramatically affect an individual's quality of life (Serrano et al., 2018). Fifteen HPV strains with HPV-16-protein (16p) are highly detected in the vulva, vagina, penis, anus, and specific head and neck cancers (Berman & Schiller, 2017; Candotto et al., 2017). Approximately 95% of HPV-positive OPSCC have HPV 16p (Berman & Schiller, 2017). The International Agency for Research on Cancerexternal icon discovered thirteen HPV types that can cause cervical cancer; however, the most common strains are 16p and 18p (CDC, 2018). It was not until Merck, one of the leading pharmaceutical companies, created an approved vaccine for women in 2006 that the public started to become aware of its significance.

Merck continued to market the vaccine to females 9-26 until they developed a vaccine for both men and women in 2017, Gardasil-9 (Makiyama, Hirai, & Matsuzaki, 2017). The researchers aimed to investigate the efficacy of Gardasil injection against the recurrence of HPV. Makiyama, Hirai, and Matsuzaki (2017) describe the antibody titers before and after vaccination using a case series study approach in 12 men from the ages

of 32-74 with positive laryngeal papillomatosis. Their serum antibody titer of HPV-18, -16, -11, and -6 was measured by a competitive Luminex-based immunoassay before vaccination and seven months after. The conclusion of that titers increased with Gardasil injection in post-adolescent males, while results showed that serum titers were low before dosage (Makiyama, Hirai, & Matsuzaki, 2017). One weakness of the study is the small population, but it provides promise for the positive footprints regarding vaccination.

The vaccine has been studied in various populations, such as males and females with HPV-positive or HPV-negative histology, testing the efficacy of preventing initial and recurrence conditions such as abnormal pap smear results and laryngeal papillomatosis and cervical cancer (Makiyama et al., 2017). The vaccine has been a medical breakthrough. The vaccine, along with HPV screening during pelvic exams, has significantly reduced the incidence of cervical cancer; however, there is no screening tool for men.

Peirson, Fitzpatrick-Lewis, Ciliska, and Warren (2013) conducted a systemic review of MEDLINE, Embase, and Cochrane Central studies from 1995-2012. They extracted data from randomized controlled trials and observational studies with females aged 15-70 who had been screened using HPV testing, liquid-based cytology, or conventional cytology. The investigation of over 15,000 screened citations noted that even the minimum of one test throughout a lifetime significantly minimized mortality risk. Whether from the incidence of advanced cervical cancer, as it either established a baseline, discovered abnormal pre-cancerous cells, or detected the disease compared to no screening, it contributed to decreasing mortality. Results show mortality: risk ratio

0.65, 95% confidence interval 0.47, 0.90; incidence: relative risk 0.56, 95% confidence interval 0.42, 0.75 (Peirson et al., 2013). Although their review helped to identify evidence that supports screening during annual pelvic exams, Peirson et al. (2013) understood the need for new technology for screening. After cytology, acknowledging this literature gap questions the effectiveness of other HPV screening techniques

**The Risks for Developing HPV**

Candotto et al. (2017) aimed to describe the epidemiology and incidence of HPV oral infection. Their method was a review of the literature to uncover the modes of transmission of HPV. Although physicians and researchers had become familiar with the effects of oral HPV, dentists were unaware of the prevalence of oral HPV and its effects on the lingual base of the tongue and tonsils.

Mature viruses such as HPV inhabit the surface layers of the cell by desquamation, allowing them to transmit directly from horizontal contact, for example, sexual intercourse with genitalia or the oral cavity (Candotto et al., 2017). Unfortunately, indirect contact from contaminated medical instruments with a mucous membrane can also lead to transmission (Candotto et al., 2017). The contraction of HPV is related to the dramatic change in sexual behavior over the recent decades. The epidemiology of HPV is a response to the earlier onset of sexual contact (Candotto et al., 2017). It is also associated with the increased number of sexual partners, and oral sex contact has increased the prevalence of HPV in both the genital and oropharynx (Candotto et al., 2017). Researchers aimed to study the transmission of oral HPV, for instance, whether the incidence may be self-inoculated or direct contact with an infected partner (Candotto

et al., 2017). Although research has indicated a positive outcome for those that are vaccinated, Candotto et al. (2017) understand that vaccines for developing countries are still expensive.

Self-inoculation means the person has a genital infection of HPV; then, he somehow transfers that infection to the oral cavity. Perhaps bodily fluids from masturbation are carried to the oral cavity. The other form of transmission to the oral cavity is by performing sex with a person with an infected genital or oral cavity through oral sex. Those that have both oral and genital infections are a direct result of their sexual behavior, e.g., cunnilingual, fellatio, and intense kissing (Candotto et al., 2017). This knowledge helps guide the medical consideration of oral and genital screening tools.

The lack of an FDA-approved screening tool for males during urology exams or the ability to test saliva for the presence of HPV DNA or mRNA increases the spread of the disease (Gipson, Robbins, Fakhry, & D'Souza, 2018). Screening tools such as the Papanicolaou (Pap) smear were implemented in the 1950s, arming physicians with the ability to diagnose cervical squamous cell carcinoma. Despite the clinical hypothesis, early detection did not initially decrease mortality (Berman & Schiller, 2017). It was not until histologic classification identifying and understanding the presence of HPV were medical professionals able to combat cervical cancer (Berman & Schiller, 2017). This ability allowed physicians to remove abnormal cells from the cervix before they developed into cancer.

Not only can HPV increase the risk of genital warts and cancer, but it may also cause individuals to become more susceptible to contracting the human

immunodeficiency virus (HIV). Many sexually transmitted infections increase inflammation within the mucosal membrane to prevent pathogens (Shannon et al., 2017). Shannon et al. noted that HPV does not implement the body's immune system cervical T-cell inflammatory response to create pathogen clearance but activates an alteration in the structure and makeup of the vaginal microbiota with Langerhans cells (Shannon et al., 2017). Therefore, HPV also has the potential to increase susceptibility to HIV. During this study's recruitment, participants answered a flyer in the primary care clinic called Women's Health in Women's Hands Community Health Centre in Toronto, Canada. The primary patient population was African/Caribbean women. The study consisted of a clinical and sexual behavior questionnaire, testing for common genital infections for pre-menopausal women, and self-collection of cells from cytobrush-collected t-cells (Shannon et al., 2017). There was no significant difference between HPV-negative and HPV-positive women concerning age and number reporting sexual intercourse in the past week.

**The Relationship Between HPV and Oropharyngeal Squamous Cell Cancer**

There are approximately 16,000 new cases of HPV-Positive of OPSCC in the United States (Lewis et al., 2018). Other parts of the world, such as Northern European countries, have similar statistics as the United States; however, other parts of Europe show that approximately 15-30% of OPSCC is related to HPV. In Central and South America, HPV contributes to 36% of OPSCC and an estimated 17% in Asia (Lewis et al., 2018). Lewis et al. (2018) convened a panel of clinicians and research experts to conduct a systematic literature review in the MEDLINE database focusing on areas of surgery,

medical, radiation, molecular pathology, and oncology to develop a better standard of practices for diagnosing and setting prognosis for HPV-OPSCC.

Today's patients diagnosed with head and neck cancers would typically receive a high-risk (HR)-HPV test. The testing results allow clinicians' feedback on how to provide a prognosis for the patient's outcome. When an individual has HPV-positive pathology and metastatic SCC to a cervical lymph node, the oropharynx is the region of initial disease more often. Physicians must know when to test for HPV, where to test for HPV and the specific purpose of a fine-needle aspiration (FNA) sample. The authors assess study quality to monitor the validity of their investigation and ensure the studies met their inclusion criteria (Lewis et al., 2018). The panel's weakness initially addressed any conflict of interest by revealing financial interest with the College of American Pathologists (CAP). Nine of the 11 members on the expert panel (EP) were free of any conflict of interest and keeping the other two members did not prevent CAP from funding the project. The study confirms that it is medically necessary for the standard of practice to include HR-HPV testing when there is an expectation of OPSCC. Their guidelines improve medical practices and help reduce treatment errors.

Data from clinical research investigated by doctoral researchers and physicians show the relationship between alcohol, smoking, and cancer, specifically oropharyngeal squamous cell carcinoma (OPSCC) (Mirghani & Blanchard, 2017; Yakin et al., 2018). HPV-positive oropharyngeal cancer has a substantially better outcome than OPSCC caused by tobacco or alcohol, as there is an approximately 50% reduction in disease recurrence and a 28 % reduction in mortality rate. However, the increased national and

international rate of HPV-positive OPSCC has become alarming due to prevalence, unnecessary treatment exposure, HPV status causing recurrence, and trying to understand why adult males significantly increased the rate of occurrence (Berman & Schiller, 2017). HPV has surpassed tobacco as the leading cause of the increased annual incidence of OPSCC (Yakin et al., 2018). Further investigation has explored the possibility of transmission outside of skin-to-skin contact from one host to the other. Nevertheless, it is vital to show that genital HPV infection is transferred from the genital area to the oral cavity from direct contact to possible simultaneous infection in multiple anatomic sites of the body through oral sex (Candotto et al., 2017). Vaccines, sex education, and prevention campaigns aid in increased public awareness.

OPSCC appears in the throat, mouth, base of the tongue, and salivary glands (CDC, 2019). Recent articles in medical journals for head and neck diseases covering HPV showed that males, specifically white males 45-59 years old, have an increased rate of HPV-positive OPSCC (Hay & Nixon, 2018). There are many theories regarding this population's higher incidence, such as the lifetime number of sexual partners and males' inability to rid of HPV as sufficiently as women (CDC, 2018a). However, the researchers aim to investigate precisely why this occurs in efforts to reduce transmission. Therefore, looking at factors such as the relationship between HPV and smoking and risky sexual behavior, along with education and socioeconomic status, may shed some light on the topic. The Gardisil-9 vaccine coverage for males has only been out for approximately three years. The literature gap leaves one to understand there is a need for clinical research to show the relationship between the administration of the HPV vaccine and the

occurrence of HPV and HPV-OPSCC in men. The data observed from such trials reviewed by physicians and researchers can help determine whether creating a screening tool for men is feasible.

Also, when focusing on the risk factors for developing HPV, much of the literature focuses on the risk of female acquirement. This analysis is due to the overwhelming advantage the Pap smear provides as a screening tool. The statistics from a CDC (2019) report indicate that otolaryngologists diagnose more men than women with OPSCC. The prevalence of OPSCC disproportionally accounts for 15,540 cases for men compared to 3,460 cases for women (CDC, 2019). The report further indicated that HPV is present in approximately 72% of men with OPSCC and 63% of women with OPSCC (CDC, 2019). Although patients with HPV-positive OPSCC have a higher survival rate than those with OPSCC-HPV-negative, treatment may critically diminish their quality of life (Hay & Nixon, 2018). I want to explore if medical standards can do more for the preventative spectrum to help guide primary care physicians, dentists, oral surgeons, oncologists, and otolaryngologists into a collaborative patient-centered treatment model.

**Tobacco Relation to HPV**

Although the sensitivity and detectability of HPV through pathology testing has tremendously affected OPSCC, considering the independent factor of tobacco exposure leads to questioning its effect on activating HPV into cancerous cells. A study researching the current tobacco exposure and high-risk genital HPV prevalence in adult females in the United States gives some rationale for testing current tobacco use in males (Han, Tarney, Klaric, & Beltra, 2017). Tobacco is a taxable product in the United States,

and the proceeds from the sale of tobacco go to the funding of specific federal programs. The commercial sale of tobacco is the fermentation product from its leaves that house nicotine, an addictive property. Clinical trial results show that smoking and chewing tobacco cause exposure to harmful carcinogenic chemicals (South et al., 2019). When a person's OPSCC is related to tobacco, physicians have a more challenging time providing a prognosis due to variations in brands of tobacco products, years of smoking, and the number of products used in a day, along with other variations. Overall, tobacco causes mutation of cells that develop into tumor growth because the mutation changes the sequence of the nucleotides (South et al., 2019). It is the detection of this mutation that helps clinicians understand tobacco as a contributing factor to SCC.

With a cross-section of the United States population, the National Health and Nutrition Examination Survey (NHANES) reviewed 2838 females with an HPV diagnosis. Using the method of collecting vaginal DNA from the self-collection swab, Han et al. (2017) found nicotine to predict HR-genital HPV in females. Therefore, current tobacco use is associated with the diagnosis, treatment method, 5-year survival rate, and recurrence (South et al., 2019). Consequently, they also observed that the current smokers' population also showed markers for at least one HPV vaccine quadrivalent. The researchers did, however, adjust their analysis for sexual behavior.

**Sexual Behavior**

Sexual behavior contributes to the contraction of any sexually transmitted disease. Approximately 26% of the United States youth population contributes to new HIV cases and other sexually transmitted infections (STIs) (Addoh, Sng, and Loprinzi 2017).

Because the Southern Region of the United States has the highest incidence of sexually transmitted diseases (STD), Addoh, Sng, and Loprinzi (2017) deemed it necessary to focus on the sexually active population of five colleges in the southern region. A multivariable logistic regression model examines the association between safe sex and self-efficacy as it relates to mechanics, partner disapproval, assertiveness, and intoxicants when it comes to the use of latex condom barriers (Addoh, Sng, and Loprinzi 2017). The group classified safe sex practices as sexual activity with emphasis on sexual intercourse concerning condom usage and monogamy, practicing minimizing exposure to STIs.

A random sample of undergraduates and graduate students receive a Qualtrics online survey from the Office of Institutional Research, Effectiveness, and Planning. The study's limitations were limited information related to the association between the four variables. However, the authors believe that there is a plausibility between safe self-efficacy and safe-sex practices. Their results show a consistent association with increase odds of safe-sex practice and self-efficacy.

**HPV as It Relates to Oral Sex**

In the beginning, the discussion surrounding HPV relates to vaginal intercourse and cervical cancer (Stock, Peterson, Houlihan, & Walsh, 2013). The premise that HPV was somehow related to OPSCC in abundance was not until approximately two decades ago. With the prevalence of oral sex, so has an increase in HPV risk. So, the question remains, how does male-to-female oral sex engagement compare to male-on-male oral sex as a risk factor for HPV and HPV-OPSCC? Stock et al. (2013) conducted a study using 238 college students, grouping them into two categories. One category read the

information on oral sex, HPV, and cancer compared to the other group that did not. The group that read information demonstrated higher perceived risk and concern, lower willingness to engage in oral sex, and knowledge of the topic (Stock et al., 2013). This study's surveying aspect allows for open discussion of sexual behavior among male and female college students.

The young adult population can most benefit from vaccination and preventative measures related to the number of partners and oral sexual risk, as the vaccine is proven efficacy against HPV-induced genital warts (Nguyen et al., 2016). However, statistics from one's study of 2775 females aged 9-59 years showed that only 15.2% between the ages of 11 and 26 had received HPV vaccination (Nguyen et al., 2016). Although it is ideal for both sexes to become vaccinated, there is an assumed benefit of more females getting the vaccine. Understanding the prevalence of oral sex in the OPSCC population is essential to target education from primary care physicians. Nguyen et al. (2016) aimed to study the prevalence of oral sex and the relationship between HPV p16 infection and OPSCC in the United States. Therefore, their team of investigators learned by conducting a systematic review of the prevalence of oral sex among Americans in different age groups and the prevalence of HPV-Positive OPSCC.

The workforce of individuals between the ages of 20 and 44 primarily results in the sustainment of the United States economy. Therefore, if the population is affected by a communicable or chronic disease, it burdens the health system and the economy (Nguyen et al., 2016). The investigators concluded from the study that oral sex is prevalent among adolescents and sexually active adults due to a lack of risk education

and protection during fellatio. The limitation of this study was data related to the male frequency of vaccination. If research now shows that OPSCC is more prevalent in males, a comparable vaccination statistic between the relationship of males and females is needed; however, the researchers' limitation relates to the current literature of that time.

Another group of investigators targeted males to exclude females due to the likelihood of the HPV vaccination. D'Souza, Agrawal, Halpern, Bodison, and Gillison (2009) investigate whether sexual behaviors increase the risk of OPC by using a cross-sectional study. The control group consists of 332 outpatient participants ≥18 with no history of cancer, and the other group houses 210 college-age males aged 18-23 (D'Souza et al., 2009). The results show HPV in 4.8% of the control group and 2.9% of the college group (D'Souza et al., 2009).

Both groups received a survey asking if they perform oral sex, defined as placing their mouth on a vagina or penis, or open-mouth kissing by placing their tongue in the mouth of another female or male (D'Souza et al., 2009). In the control group, 24% had never performed oral sex, 2.6% had never had vaginal sex, and the median lifetime number of partners was 2–5. In the college group, 9% had never engaged in open-mouthed kissing, 28% had never performed oral sex, and 30% had never had vaginal sex (D'Souza et al., 2009). A study such as this helps provide some rationale to research question 3: *Is there a statistically significant association between the rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlling for income and education level?* The authors report limitation of the study is that it was not population-based; however, the strength is that their method

was comparable to age groups shown in the NHANES. (D'Souza et al., 2009). D'Souza later worked with another group on the project entitled *Differences in oral sexual behaviors by gender, age, and race explain observed differences in prevalence of oral human papillomavirus infection.* D'Souza, Cullen, Bowie, Thorpe, and Fakhry (2014) sought to answer whether gender, age- cohorts (20–29, 30–44, 45–59, 60–69), and race differences in oral sexual behavior account for the demographic distribution of oral-HPV and HPV-positive OPSCC (D'Souza et al., 2014). They analyze to include 2116 males and 2140 females that provide an oral rinse sample for HPV detection and a 2009-2010 NHANES behavioral questionnaire. Their results showed that most men and women had performed oral sex at least once; however, men had more encounters in their lifetime with oral sex and vaginal sexual partners.

The investigators explained the difference in HPV distribution as there is a noticeable difference in oral-HPV prevalence in men. There are significant limitations and strengths in their study. The limitation is seemingly related to the lack of some sexual data for one of the age-cohort (age 60). It also showed a significantly small number of those diagnosed with HPV16p. Another limitation is that the NHANES and SEER data are not linked; therefore, the results come from two different populations. This study's strength is its sample size representation of the population, including blacks and other minorities, which is an issue across many investigations. Another strength is the research interpretation ability to provide meaningful context regarding the effects of changes in sexual behavior.

The sexual behavior pre-diagnosis of HPV is one issue, but how do those after diagnosis respond? Taberna et al. (2017) attempted to answer this question as they aimed to investigate the effects of OSCC diagnosis and treatment on subsequent relationship stress and sexual behavior as there is a gap in the literature as it relates to these topics. Cases of HPV-positive and HPV-negative OPSCC in patients with a partnered relationship and those with partners of OPSCC were eligible. The study participants received surveys at their diagnosis and 6-month follow-up to assess relationship distress, HPV transmission, and any concerns about sexual behavior (Taberna et al.,2017). There were 262 patients with OPSCC and 81 partners that enrolled. Of those, HPV-positive represents 54.2% and HPV-negative 45.8%; there was a dramatic decline in the frequency of vaginal and oral sexual behavior at follow-up regardless of tumor HPV status (Taberna et al., 2017). The researchers did note that the study population may not have been the best representation of those diagnosed with OPSCC.

Also, there was a significant level of participation from eligible partners of OPSCC and even a lower number of HPV-negative partners. The study's time only includes a 6-months follow-up, which could result from funds for the study. It would have probably been a great design to follow the patients every six months for five years since the recurrence of cancer calculates the survival rate within the first five years of diagnosis. Further studies could help identify if the behavior changes over time. Undergoing the disease burden for patients and their partners may significantly affect their outlook.

**Breaking down the Research on Oropharyngeal Squamous Cell Carcinoma.**

The medical world was taken by storm when researchers learned that an infectious disease could lead to OPSCC. Chaturvedi et al. (2011) saw that although oropharyngeal cancers increased, the survival rate improved. However, there was no medical explanation for these findings. The team sought to review three- population-based from 271 individuals from Hawaii, Iowa, and Los Angeles, California [LA] cancer registries in the Surveillance, Epidemiology, and End Result Residual Tissue Repositories by using HPV16mRNA expression, HPV16 viral load, and polymerase chain reaction and genotyping (Chaturvedi et al., 2011). The logistic regression helped the researchers to map trends in HPV prevalence across four calendar periods.

The status of HPV was then investigated in all the oropharyngeal cancer registries to prepare for the nonrandom selection and calculate incidence trends. The researchers used the multivariable Cox regression analyses to estimate the survival of both HPV-positive and HPV-negative. This method is because of the investigation of several variables over the given time from diagnosis and Kaplan-Meier, a medical statistic estimator used to estimate the survival probability from lifetime data based on treatment received. Their findings showed that HPV-positive patients had a longer survival rate than HPV-negative.

For this reason, medical advances must consider the treatment standard of the two or even preventative measures. The strengths of this study were the use of comparative analysis for HPV-positive and HPV-negative survival rate instead of merely showing the trend of the increased rate of HPV-positive OPSCC. This evidence supports a vital consideration that the treatment burden of large incisions from open-invasive surgery

impedes the quality of life for those that can carry out a long life. The population size attributes to the weakness of this study. The study did not specify that the population of 271 was in three equal groups, approximately 90 from each state. The patients were not randomly selected, although they tried to use the inverse of sampling probability to account for weight and reweight for the HPV prevalence of OPSCC. Nonrandom selection may help to reduce cost, but the investigator needs to be well versed on the hypotheses about their population on interest and ensure that there is not a selection of equal men and women to prevent confounding variables of gender influence.

HPV is a global issue. Other researchers sought to investigate HPV's overall impact on cancer once there was a rise in awareness of HPV association with OPSCC. There is confirmation that HPV is associated with cervical cancer (Berman & Schiller, 2017). The investigators reviewed the GLOBOCAN 2012 version for the number of cases in 2012. (de Martel, Plummer, Vignat, & Franceschi, 2017). The formula used in this study was AF=pc, as attributable fractions (AF) is equal to the prevalence (p) in cancer tissue (c) of transforming HPV infection. Researchers divided the sites into categories housing focused on cervical, penile, and laryngeal in one area, while other sites concentrated on the anus, vulva, and vagina data.

Subsites that researched the oral cavity, oropharynx, and pharynx came to evidence from cancer registries in the Cancer in Five Continent database (de Martel et al., 2017). The researchers calculated the number of HPV-positive cases per country. Then they divided those into eight geographical regions from the guidance of the United Nations classification used in the GLOBOCAN (de Martel et al., 2017). In many cases, it

was essential to show the characteristic of less developed and more developed regions as attributes to the population's education, income, and access to health care. The global impact on HPV-related cancer cases is 570,000 per year in women and 60,000 in men, respectively, 8.6% and 0.8% (de Martel et al., 2017). The researchers indicated that high universal coverage of vaccination could achieve prevention. Statistics also show that the target audience of females between the ages of 10-20 has reached approximately 118 million individuals. Nevertheless, only 1% are in less developed countries (de Martel et al., 2017). Understanding the burden of HPV infection among adult men is very intriguing.

Although they have a low incidence of overall HPV-related cancer, they hold the most prevalent HPV in the oral cavity and pharyngeal space (Golusiński & Golusińska-Kardach, 2019). An investigator can read the final report of de Martel et al. (2017) and gather the burden of cancer associated with HPV. Together there are approximately 630,000 new cases of cervical cancer, other anogenital cancers, and head and neck cancers per year worldwide HPV-relate (de Martel et al., 2017). This study's method demonstrates a reliable comparison of disease burden in different geographical areas.

This geographical distribution allowed public health servants to assess the target area for sex education, the use of condoms, and more critical advanced medicine such as vaccines. The study investigators suggest that 70-90% of all HPV-attributed patients would have achieved prevention amidst a universal high-coverage HPV vaccination (de Martel et al., 2017). Disproportionately women account for 570,000 cases of HPV cancer, while men only account for 60,000. Nevertheless, men are more likely to have

OPSCC than women (de Martel et al., 2017; Hay & Nixon, 2018). North America and North Europe are seeing an influx of OPSCC. The limitation of the study showing the worldwide burden of HPV per site is attributable to fractions (AF) instead of age-standardized incidence rates (ASR). AF, such as total cancer occurrence, significantly influences the variation of the denominator. There is no way to avoid the confounding variable of the incidence of noninfectious-related cancers across less developed countries than in more developed countries. These findings cause further investigation into the epidemiology and pathology of HPV disease in males.

The definitive diagnosis of genital warts in males caused by HPV is highly transferrable, showing that 65.2% of males with HPV are asymptomatic (Giuliano et al., 2010). With a systematic review of the literature on the natural history of HPV infection in men, Giuliano et al. (2010) noted that the variation in men's detectable HPV is likely due to the differences in population within the study samples and the difference in HPV DNA detection. Today there is more information on the direct benefit for males and the indirect benefit for women of male vaccination. Still, the data was limited in 2010 when Giuliano et al. (2010) conducted their study—leaving questions to understand better HPV infection, men's prognosis of a benign cell to a cancerous cell when to implement vaccination series, and the efficacy of that series.

What their study did reveal is that a lifetime number of sexual partners was the most critical risk component for acquiring HPV, which leads this study's investigation of whether a male vs. female partner plays a significant role in the acquisition of HPV-OPSCC (Giuliano et al., 2010). This contagious property causes the problem of

unknowingly transmitting the disease to a partner. Because of the significant burden of HPV in cervical cancer, researchers study how men had to carry the virus to women. Because of the lack of sensitivity and specificity, modern medicine has abandoned histology in electronic or optical microscopy, immunocytochemistry, and serology (Candotto et al., 2017). As more and more men engage in sexual intercourse, their role in transmitting the disease to their male partners was needed to help minimize the public issue.

As a result of research over the years, clinical evidence has shown HPV is not only detrimental to women but also seen in 85% of anal cancer and a significant rate of age-adjusted rate of penile cancer in males. This study's method was a systematic review of the literature to extract the progression of the HPV burden on males. Giuliano et al. (2010) study showed 49% of men with short-lasting infections with proven regression of HPV and only 31% of women from data in a 2004 report. Women with a definite HPV diagnosis in their cervix also had a positive male partner in 75% of the cases; however, a random selection of men with positive HPV in their semen only experienced a positive partner in 30% of cases (Giuliano et al., 2010). These statistics suggest that men are more likely to transmit the disease to their female partners.

Are these circumstances actual when comparing male-to-male sexual contact with male-to-female oral sex? The purpose of Giuliano et al. (2010) study is to provide the medical details of HPV epidemiology and pathology in men. The social change this study has is understanding the risk factor for transmission through sexual contact from male to female versus female to male. The limitation of the study by Giuliano et al. (2010) is that

it does not provide a specific population number from several small studies. The population's affected percentage is not validated without that defined population, for example, N-100, N-500, or N-5000. The sample size is crucial in understanding if the sample is a good representation of the target population. The goal is that the knowledge probably gained from this study might prompt the use of condoms during sexual contact. It may also encourage the validity of the sensitivity and specificity of testing to detect HPV in OPSCC.

There is currently no standard preventative testing for oral HPV. Only when a patient presents to a specialty service office with systems of lesions or possible carcinoma will a physician conduct testing such as a CT scan of the head and neck and an endoscope review of the oropharyngeal space. From experience in otolaryngology, confirmed pathology of HPV comes from cells scraped off during an endoscope procedure or not until surgery. Gipson et al. (2018) noted that oral samples are easy to obtain; however, there is a literature gap in the diagnostic accuracy of oral HPV detection for classing HPV-positive head and neck tumors.

In 1990, HPV only accounted for 20% of OPSCC, as its leading cause was tobacco and alcohol (Gipson et al., 2018). Twenty years later, 70% of HPV showed a 225% jump. Although body immunity usually clears oral HPV infection, in most cases, persistent oral HPV will develop into OPSCC (Gipson et al., 2018). A systematic review allowed Gipson et al. (2018) to identify eight studies of head and neck squamous cell carcinoma (HNSCC) patients meeting their inclusion-exclusion requirements. They reviewed publications within the past ten years, which was great for showing the trend of

HPV-positive OPSCC. The reviewed studies had to have at least 15 HNSCC cases, and each patient needed a positive HPV detection from an oral rinse or swab sample. The researchers performed a meta-analysis to calculate the sensitivity and specificity of the disease. The results showed specificity at 92% and moderate sensitivity of 72% using a 95% confidence interval. The results showed fewer false-positive in those with previous HNSCC diagnoses but may miss 25%-50 % of HPV-related cases.

Oral rinse and oral swabs that only look for HPV-16p are not a good indicator of collecting HPV-related cancer as other oncogenic strains contribute to the disease and only moderately detect the p16 strain. The strength of this study is that it helps eliminate detection devices for oral HPV that are only sensitive to p16. The rationale is that oral HPV commonly exhibits p16 because there are other oncogenic strains; the best tool detects all stains associated with oral HPV. Also, the efficacy of the sensitivity needs improvement 28% of positive HPV patients can go undetected. This unfortunate result would burden calculating prevalence in specific demographics and make diagnosing in less developed areas even harder. The sensitivity aspect of this research poses the question are external factors change the DNA of HPV, such as smoking tobacco.

Smoking tobacco has been a controversial issue across the world. It is a known cancer-causing agent, yet it is available in almost any gas station, supermarket, and corner store. The federal and state government imposes a tobacco tax on the consumer. Healthcare programs use financial resources from that tax to fund cancer research and programs to help citizens stop smoking (Kagan, 2018). Surgery and chemoradiation are two of the most common OPSCC treatments (Vawda, Banerjee, & Debenham, 2019).

Medical experience notes that those diagnosed with cancer do not magically quit smoking. Vawda et al. (2019) pointed out that tobacco exposure alters the biological behavior of HPV-OPSCC compared to HPV-positive non-smoking and smoking non-HPV tumors.

Conducting a chart review of 352 patients with known p16-positive HPV-OPSCC tumors, these researchers could observe the survival outcome and recurrence incidence using the Kaplan-Meier method. The patients placed in groups of those that underwent primary chemoradiation therapy (CRT) were 67.6% (n-238) and 32.4% (n-114) with primary surgery plus or minus adjuvant treatment. The median smoking accounted for a pack-year of 15, which means packs of cigarettes smoked per day times years of patient smoke. There were three categories for smoking: current smokers (27%), former smokers (40.3%), and (32.7%) who never smoked (Vawda et al., 2019). Those who smoked had a more inferior overall survival rate and worse relapse-free survival compared to those who had never smoked and former smokers.

Comparison of the 5-year survival among those with pack-year of 10, 20, and 30 showed an overall survival of 73.2%, 64.7%, and 59.1%, respectively (Vawda et al., 2019). The more years a person smoked, the decrease in their survival rate. A strength of this study is that it also showed no clinically significant difference in CRT treatment compared to surgery concerning the HPV-positive nature of the patient's tumor (Vawda et al., 2019). The limitation of this study is the variability of those former smokers, and there can be upwards of a 30-year gap compared to 30 days as former smokers. The strength of the method used in this study is that it studies the effects on tobacco on HPV-

OPSCC survival and may show that CRT is equivalent to surgery, which may prompt more testing in this area. One of the biggest concerns of HPV-positive OPSCC is the invasive treatment associated with it.

**Burdens of Treatment**

Through research, investigators found that an HPV-positive diagnosis of OPSCC has a better prognosis than an HPV-negative diagnosis. Four eras emerged from OPSCC: the tobacco era, the organ preservation era, the improvement in the radiation era, and the HPV era (Hay & Nixon, 2018). Each period was studied to understand how the variable affected OPSCC, whether it was a cause or a treatment option; however, differences in opinions still plague the standard of treatment for HPV testing and tumor extraction for OPSCC patients (Hay & Nixon, 2018). Wagner et al. (2017) felt that regardless of treatment, it was the HPV status of tumors that predicted survival.

Therefore, surgeons soon evaluated their treatment options and practices. Physicians and researchers seek to improve the treatments for OPSCC because specific treatments tremendously affect the patients' quality of life (Hay & Nixon, 2018). These treatments are invasive, such as open surgical procedures followed by concurrent chemoradiotherapy. Tumors associated with HPV-positive OPSCC are responsive to CRT. However, CRT can cause morbidities such as trismus (lockjaw), xerostomia (dry mouth), osteoradionecrosis (bone death), fibrosis (scarring), and dysphagia (difficulty swallowing) (Golusiński & Golusińska-Kardach, 2019). The inability to speak, difficulty chewing, and the need for reconstructive surgery are nearly a result of all head and neck invasive open surgery (Golusiński & Golusińska-Kardach, 2019). These adverse findings

appeared to note that unnecessary procedures or options such as chemotherapy and radiation were too vigorous of treatment for HPV-positive diagnosis.

Surgeons investigated whether HPV-positive OPSCC patients should undergo the same treatment plan as HPV-negative OPSCC, given their better prognosis. The scientific and medical practices must perform less invasive procedures while delivering effective oncological favorable treatment that better outcomes (Mirghani & Blanchard, 2017). Investigators using the clinical trial aim to research four primary techniques, radiation with cetuximab with cisplatin as the comparative. Treatments included an introduction to chemotherapy followed up with reduced exposure to radiation dosages. The third option is radiation alone instead of the combination of chemoradiation.

And lastly, transoral surgery with or without postoperative radiotherapy (Mirghani & Blanchard, 2017). Even though HPV-positive OPSCC has a better prognosis than HPV-negative OPSCC, the death outcome occurs in about 20% of the HPV-positive OPSCC population. Therefore, the dilemma of treating physicians face is their ability only to de-escalate treatment in low-risk patients as one cannot compromise tolerability with existence. The other issue is the physical burden displayed upon those who smoke vs. those who do not (Mirghani & Blanchard, 2017). Many treatment plans involve surveillance of the human immune system's ability to rid the body of infection. Diagnosed HPV-OPSCC at advanced-stage disease causes multimodality treatment, such as simultaneous cisplatin-based chemotherapy with surgery or radiation. Physicians believe that less invasive measures can yield the same results without significantly burdening the quality of life. HPV-positive OPSCC is a precursor to recurrence (Gipson

et al., 2018). Understanding disease risk and treatment can positively improve the social impact of OPSCC.

## Definitions

*Cigarettes:* a cylinder tobacco product used for smoking; it was once the primary cause of HPV-OPSCC (Vawda et al., 2019).

*Education:* covariate datapoint that can influence the outcome of the results as it measures the level of retained knowledge or instruction from an institution or a person (Merriam-Webster, 2020b).

*Human papillomavirus oropharyngeal squamous cell carcinoma (HPV-OPSCC*): derived from the most common sexually transmitted disease is a type of squamous cell carcinoma in the oropharyngeal region such as base of the tongue, tonsillar, mouth, saliva glands, and throat (CDC, 2019).

*Income:* covariate datapoint that is measured by the total wages or capital a person collects in a year (Merriam-Webster, (2020c). Income represented by national poverty line is 12,490 for an individual and an addition 4420 for every other person in the household (Assistant Secretary for Planning and Evaluation, 2019)

*National Health and Nutrition Examination Survey (NHANES):* is a program of studies whose focuses on the assessment of health and nutritional status of adults and children in the United States (CDC, 2017).

*Oral sex:* oral stimulation of the genital cavity (Candotto et al., 2017).

*Race:* described by white-Caucasian, black-African American, Hispanic within their grouping of humans characterized based due to their physical or social qualities into distinct categories generally by society (Merriam-Webster, 2020a).

*Surveillance Epidemiology and End Results (SEER):* a database that stores data on cancer statistics for the United States (National Institute of Health, 2020b).

*University of Alabama at Birmingham Hospital:* University of Alabama at Birmingham (UAB) Health System is an academic health center located in Birmingham, Alabama. It was established in 1945 as the teaching hospital for the University of Alabama School of Medicine and, today is one of the four largest academic medical centers in the United States.

## Assumptions

One fundamental assumption is that the lack of usage of the female condom barrier can account for the increased rate of OPSCC in men compared to women, but this study does not investigate this concept. This assumption is significant because sexual behavior is a known risk of contracting HPV related to the number of partners, use of condoms, and participation in oral sex. Because the third research question relates to male-to-male oral sex compared to female-to-male oral sex, knowing whether the use of condoms or an immune response contributes to the incidence of OPSCC is essential. Physicians need to know whether the female vagina clears up HPV faster and more effectively than the male genitalia to reduce the spread of the disease. Another assumption is that the report of oral sex is accurate as some individuals, both male and

female, may shy away from answering the question, and the response in a survey could be left blank.

These assumptions are necessary within the study because they are associated with research question 3. If there is no accurate account for those engaging in oral sex, the target population can be left unknown. This deletion of information may cause a failure in the educational campaign for the prevention and can result in an increased rate of HPV-OPSCC in men and cause the female statistic to become clinically significant. For example, in the earlier 2000s, there was a public campaign for using female condoms (French et al., 2003). The sexually transmitted disease that prompted this campaign was the rapid spread of HIV among the African and Asian communities. Although the FDA ruled the female condom a medical device III in 1993, they were not widely used (French et al., 2003). Women have the highest rate overall of genital HPV but do not hold that rank compared to men as it relates to oral HPV. The primary cause of cervical cancer and OPSCC is HPV in women; however, cervical cancer is more prevalent among women than in OPSCC.

## Scope and Delimitation

The specific aspect of risk factors associated with men's rate of HPV is race, smoking tobacco cigarettes, and the act of oral sex. The independent variables of race, specifically among minority groups such as African Americans and Hispanics, are associated with compound variables such as low income, access to healthcare or health insurance, and less education (Moreno et al., 2018). However, HPV-positive OPSCC is seen more often in white, middle-aged males. This finding asks whether white males are

genetically predisposed to OPSCC or are external factors such as smoking tobacco are more of a contributing factor. This study does not investigate other theories most related to whether men are more susceptible to OPSCC and have more experience with oral sex than vaginal sex. Another theory is that tobacco activates abnormal DNA in HPV cells, causing the secondary condition of cancer.

## Significance, Summary, and Conclusions

The human immune system design clears up HPV in most individuals within two years, but for others, it may develop into a secondary condition (CDC, 2018a). There are over 150 strains of HPV clinically categorized into two classifications, low-risk and high-risk (CDC, 2018a). The strains that are considered low-risk HPV cause infections such as anogenital warts and respiratory papillomatosis (Makiyama et al., 2017). The strains found as high-risk HPV cause various squamous cell carcinomas in both men and women (Makiyama et al., 2017). In the past, the population of OPSCC consisted of older individuals above 60 and had a significant association with the routine use of tobacco and alcohol (Golusiński & Golusińska-Kardach, 2019). A substantial incidence of OPSCC diagnoses of the tonsillar or base of the tongue is HPV-positive (Golusiński & Golusińska-Kardach, 2019). Golusiński and Golusińska-Kardach (2019) also observe that the overall population received an earlier stage diagnosis, were younger than the previous dominant population, were more likely non-smokers, and had a better prognosis.

The HPV-positive OPSCC population's younger age and increased rate of long-term survival due to the stage at diagnosis prompted the need to minimize the health burden of this disease caused by treatment. Concurrent chemoradiotherapy (CRT) also

cause morbidities such as trismus, xerostomia, osteoradionecrosis, fibrosis, and dysphagia (Golusiński & Golusińska-Kardach, 2019). In contrast, Han et al. (2017) showed an association between tobacco use and high-risk (carcinogenic) genital HPV infection among United States females. This comparison makes investigating further the tobacco association more significant.

The statistics from a CDC (2019) report indicated that otolaryngologists diagnose more men than women with OPSCC. The prevalence of OPSCC disproportionally accounts for 15,540 cases for men compared to 3,460 cases for women (CDC, 2019). The report further indicates HPV is present in approximately 72% of the men with OPSCC and 63% of women with OPSCC (CDC, 2019). Although patients with HPV-positive OPSCC have a higher survival rate than those with OPSCC-HPV-negative, treatment may critically diminish their quality of life (Hay & Nixon, 2018). I want to explore if medical standards can do more for the preventative spectrum to help guide primary care physicians, dentists, oral surgeons, oncologists, and otolaryngologists into a collaborative patient-centered treatment model.

The possible social change from understanding the risk factors associated with adult men $\geq$ 18 increasing rates of oral HPV is the promotion of preventative measures during oral sexual intercourse. The insight learned from this data may help encourage public health officers and healthcare providers to conduct education sessions through public outreach or standard examination. It is plausible to suspect that a decrease in oral HPV will cause a reduction in OPSCC. Researchers can use campaigns to educate society on the pros and cons of HPV vaccination to contemplate whether to get the injection to

help minimize the transition of HPV as a sexual infection to squamous cell carcinoma (Jean, Elshafei, & Buttenheim, 2018). The feedback from educational campaigns may indicate the social implications of HPV incidence as more and more individuals get familiar with the association between cancer and HPV and the morbidities associated with them. Research shows that preventative sexual education can help minimize the transmission of disease.

United Kingdom Census of 2011 showed that those with higher incomes had a higher rate of vaccines than those with lower incomes. Although this study's overall method controlled for education and income, there is a correlation between higher income and higher education (Jean, Elshafei, & Buttenheim, 2018). Individuals suffering from HPV-OPSCC undergo significant morbidities such as the inability to speak, chew, and swallow food, hair loss from chemotherapy, and potential death (Ward, Mehta, & Moore, 2016). The price per new diagnosis of HPV-related head and neck cancer costs $43,200, with an approximate annual cost in the United States of $306 million, based on 2004–2007 numbers (Ward, Mehta, & Moore, 2016). Inference suggests that cost increased along with the rate of HPV-OPSCC increase from 2004-2007 (CDC, 2018). I aim to help reduce the rate of OPSCC. A secondary outcome may be encouraging the researcher to explore the importance of HPV screening in males as a preventative method. It is so essential to prevent HPV through screening programs to decrease the risk of developing cancer.

HPV can be present in multiple areas of the body. It increases the risk of HPV-positive cancer throughout the body and increases the probability of transmission to the

partner affecting the public's health. (CDC, 2019). This disease transmission cycle can potentially cause more than one type of cancer, such as cervical, penile, or anal, within the same male or female or cause cancer in the person receiving the infection from the sexual partner (CDC, 2019). The investigation did not show a significant association with the independent variables; however, preventative measures such as public health campaigns can target adult males $\geq$ 18.

Section 2: Research Design and Data Collection

## Introduction

This study's purpose is to investigate if there is an association between the rate of oral HPV-OPSCC and race, exposure to smoking cigarettes (tobacco), risky sexual behavior, and participation in oral sex of male-to-male contact vs. male-to-female contact. The United States population's quantitative data indicate an increase in the prevalence of HPV-positive OPSCC over the past 3 decades (Yakin et al., 2018). Physicians and researchers could benefit from the secondary quantitative analysis to better understand HPV-OPSCC and this population's risk factors. This knowledge could serve as a framework for improving the medical standard of care practices and patients' preventative education models.

The human immune system design clears up HPV in most individuals within 2 years, but for others, it may develop into a secondary condition (CDC, 2018a). There are over 150 strains of HPV clinically categorized into two classifications, low-risk and high-risk (CDC, 2018a). High-risk HPV is of great concern, as it causes various squamous cell carcinomas in both men and women; however, it is more predominant in men (Makiyama et al., 2017). Because of HPV, the OPSCC population's demographics have changed from older individuals above 60 with a significant association with tobacco and alcohol use to younger individuals between 45 and 59 (Golusiński & Golusińska-Kardach, 2019). One pro is that the new population receives an earlier stage diagnosis, is younger than the previous dominant population, is more likely non-smokers, and has a better prognosis (Golusiński & Golusińska-Kardach, 2019). Through research and clinical practice,

investigation of the four eras of OPSCC disease: the tobacco era, organ preservation era, improvement in the radiation era, and the HPV era, the HPV era has a better prognosis (Hay & Nixon, 2018). However, the treatment burden is still the same, causing many morbidities that diminish life quality.

Each period was studied to understand how race, smoking, and gender-based oral sex affects OPSCC, whether they cause OPSCC, and how it could affect the treatment rendered. However, differences in medical treatment still plague the standard of practices for HPV testing and tumor extraction for OPSCC patients. No routine testing device is created for oral HPV or men genitalia during annual wellness exams (Hay & Nixon, 2018). Wagner et al. (2017) felt that regardless of treatment, it was the HPV status of tumors that predicted survival. This section discusses the research design and rationale, methodology, threats to validity, and summary of the research design and data collection.

## **Research Design and Rationale**.

The study's secondary quantitative cross-sectional design is a practical methodology. It allowed rate analysis of established information for HPV-positive OPSCC patients across an existing data set in adult males. The synthesizing information from peer-reviewed journals helps to validate the public health issue HPV has on cancer patients. The secondary quantitative analysis also investigates trends between race, smoking tobacco, and oral sex between male-to-male and male-to-female. The cross-sectional design choice was consistent with the secondary quantitative research design because it is formatted to serve a population-based study. It is cost-effective when analyzing an extensive dataset vs. running a primary data analysis of primary data. A

systematic approach to secondary quantitative analysis still warrants an empirically based data collection, statistical analysis, and repeatable research design. The data of HPV-positive OPSCC are well known; however, what triggers the HPV transformation from abnormal cells to carcinoma is unclear. Observing trends helped analyze if the independent variables directly affect this disease's rate. The rationale supports understanding the impact of the HPV sexually transmitted disease that has 15 strains that are responsible for approximately 5% of all global cancer cases in the vulva, vagina, penis, anus, and specific head and neck cancers (Berman & Schiller, 2017; Candotto et al., 2017). Of those 15 strains, protein H16 accounts for an estimated 95% detection in OPSCC (Berman & Schiller, 2017). The increased morbidities and mortalities are devastatingly affecting individuals' quality of life.

This circumstance warrants the research of the rate of oral HPV-OPSCC in adult men $\geq$18 years old and to what extent there is an association between the rate of oral HPV-OPSCC and race and smoking tobacco in the form of cigarettes, controlling for income and education level. It also promotes further research on whether there is an association between the rate of oral HPV-OPSCC and male-to-male oral sex than male-to-female oral sex in controlled for income and education level (Serrano et al., 2018). The dependent variable for the study is the rate of HPV-OPSCC. In contrast, the independent variables are race, exposure to smoking cigarettes (tobacco), and risky sexual behavior such as oral sex of male-to-male contact vs. male-to-female contact. Male patients could benefit from the secondary quantitative analysis to better understand HPV-OPSCC and their risk factors, as descriptive analysis shows the prevalence among men. This

information contributes to the growing knowledge of HPV's effects on OPSCC; it is essential to investigate whether the numbers are still increasing. Therefore, understanding if there is an association between the second and third independent variables, race and smoking tobacco in the form of cigarettes controlling for income and education level affects the rate of oral HPV-OPSCC in adult men ≥18 years old.

This knowledge could serve as a framework for improving the health literacy of male patients and well as their risk for contracting HPV as well as its development into OPSCC. One challenge faced with secondary data research is finding information related to the investigator's topic. The UAB Health Services i2b2 database is an excellent tool for incidence and prevalence information related to cancer epidemiology in the United States. However, it does not capture the behavioral aspect of individuals' perspectives on risky sexual acts associated with contracting HPV. Another burden of secondary research is time management. Time management is imperative when conducting secondary research; however, it may be more involved than primary research.

## Research Questions and Hypotheses

RQ 1: What is the rate of oral HPV-positive OPSCC in adult men ≥18 years old?

RQ 2: To what extent is there an association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old?

$H_o2$: There is no statistically significant association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old.

$H_1$2: There is a statistically significant association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old.

RQ 3: Is there a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level?

$H_o$3: There is no statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level.

$H_1$3: There is a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level.

## Selected Variables and Their Purpose

The study investigated several independent variables regarding whether they play a role in transforming abnormal cells of HPV into OPSCC. The dependent variable was HPV-positive OPSCC/HPV-negative OPSCC. The first independent variable is race, a discrete variable that a person cannot control. White, Black, and Hispanic will characterize it. Research results show that race correlated to genetic makeup and socioeconomic conditions (Drope et al., 2018). This variable is vital to see if race is a predictor of diagnosis. The second independent variable is smoking tobacco cigarettes: a cylinder of tobacco products used for smoking. It was measured with yes or no as it relates to whether the person was an active smoker at the time of diagnosis. Because it

was once the primary cause of HPV-OPSCC, it is reasonable to investigate if there is an association, perhaps a possible definitive answer on whether it activates abnormal cells and catalyzes the process of developing into cancer (Vawda et al., 2019). These variable yields two covariates of education and income, as there is an association between low-income and low education and tobacco use (Drope et al., 2018). Therefore, controlling for these covariates helps to reduce bias in the outcomes.

The third independent variable is the act of oral sex. It perceived measurement derived from the marital status of whether a person engages in oral sex. This variable is reasonable to explore because females had less incidence of anal HPV when comparing men with sex with women (MSW) to men with sex with men (MSM). If an association shows a higher incidence of oral sex of MSM vs. MSW, more education can guide this group for prevention.

## Methodology

### Study Population

In the United States, HPV is the leading sexually transmitted disease. Recurrent visits for speech pathology (including learning how to swallow), tube feeding placement, and, in some cases, follow-up surgeries, chemotherapy, and radiation are contributors to the social impact that burdens life quality and the financial aspect of the healthcare system. I used the secondary quantitative research method to reach male target audiences $\geq$18 with OPSCC. The systematic review is flexible yet provides empirical data (Johnson, 2017). Because there are nearly 15,500 males diagnosed with HPV-positive OPSCC compared to less than 4,000 females annually, the range of 155-200 would represent at

least 10% of the annual diagnosed population (CDC, 2019). The descriptive analysis provided trends in the OPSCC population regarding the presence of HPV. Retrieving that sample size was made possible using the UAB Health Services i2b2 data set of those with OPSCC while exploring the categorical aspects of race, smoking status, and risky sexual behavior. That pattern further analyzed whether an association between race, smoking, and sexual behavior existed. The statistical process delivers results that the investigator may prove valuable for prevention.

This study explores the sample size of males 18 and over with OPSCC. The cause of OPSCC will be reduced based on reducing the HPV status. The following indicate operational variables: adult males: person assigned male gender at birth at least 18 years of age with a clinical diagnosis OPSCC. I further investigated the HPV virus-positive pathology in tissue samples completed during biopsy or surgery against other operational variables such as race, categorized as White, Black, and Hispanic. I treated "Smoking tobacco" as a current smoker and included those with a former history in the second analysis. The sample was used to measure the association between HPV-OPSCC and operational variables. The current history of smoking tobacco was used, and oral MSM and oral MSW will be analyzed to look at behavior.

## Sampling Procedures for Data Collection

The sampling strategy that best fits this analysis is simple random sampling. The UAB Health Services i2b2 population assessed the categorical aspects of race, smoking status, and marital status. The justification of simple random sampling ensures that everyone has an equal chance of selection. This method is transparent, allows the

calculation of sampling error, and reduces bias. There are six crucial steps for simple random sampling: establishing the population, selecting the sample size, stating the population in a statistical analysis tool, assigning numbers to the unit, finding random numbers, and formulating the sample (Lund Research Ltd, 2012). Inclusion and exclusion criteria must be developed to determine precise sample size.

The inclusion criteria allowed for the male gender greater than 18 with OPSCC. Everyone must have a history of OPSCC (cancer at the base of the tongue, tonsillar, soft palate, or back or sidewalls of the throat). The exclusion was those diagnosed with any other form of head and neck cancer. Because this is a secondary analysis, there was no primary relationship with the patient. The data collection was from a dataset provided by UAB Health Services i2b2 for OPSCC male patients.

The UAB Health Services i2b2, the University's Institutional Review Board (IRB), and the Office of Sponsor Procedures were contacted by email regarding my interest in the male population with OPSCC, providing graduate students' status. The UAB has agreed to such information and has continuously provided recent articles on HPV and OPSCC. In addition to UAB cooperation, I obtained permission to complete a data analysis through Walden University's ethical committee in the IRB. The codebook is the data dictionary that helps lay out the descriptions of collected data. It allows one to decide on a coding system to represent the variables analyzed (The Graduate Institute of Geneva, 2020). For example, the independent variable race is decoded as 1 White, 2 Black, and 3 Hispanic. Smokers were decoded as 1, former smoker 2, never smoked as 3, and unknown status as 4. Lastly, Research Question 3's independent variables were

denoted bisexual as 1, heterosexual as 2, homosexual as 3, and unknown as 4—all procedures for recruitment, participation, and data collection associated with the secondary data set.

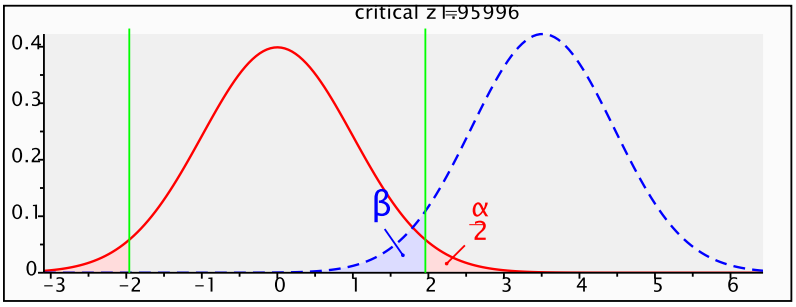
## Power Analysis

Power analysis combines statistical analysis, the literature review topic, and the specification for the most beneficial sample size. The statistical power is the probability that I determined the sample's statistical significance from the total population as the researcher. Power analysis is crucial for human participants' studies because a great sample depends on power, type 1 error, and outcome variability (Bagiella & Chang, 2019). The effect size between the dependent and independent variables is a quantitative measure of the magnitude of how to experiment. When the effect is higher in magnitude the vigorous the association between two the variables. The alpha level is the probability of rejecting the null hypothesis and is set for 0.05 with a confidence level of 95%. Because there is no immediate threat if the statistical analysis is off, the common use of 0.05 is appropriate for this analysis. I used the Statistical Package for the Social Sciences (SPSS) software to calculate the analyses.

A logistic regression is more appropriate when studying a bivariate analysis for diagnostic accuracy (Gipson et al., 2018). The GPower software helps calculate a logistic regression model helped to interpret whether there was a relationship between the multivariate response of DV HPV-OPSCC with IVs (predictors), race, smoking, and oral sex. Figure 1 demonstrates this calculation.

**Figure 1.**

*GPower*




*Note.* Distribution plot of the a priori power analysis.

When conducting the a priori power analysis, I used the family test of z-test, the statistical test of logistic regression, and the type of power as A priori. I selected a two-tail, alpha err prob 0.05, power (1-β err prob.) = 0.95, and the actual power for this analysis was 0.950077. The odds ratio for the study is 1.5, which is consistent with other similar studies (Jamieson et al., 2020). The total sample size needed for this study is 337 participants.

## Data Analysis Plan

With the SPSS, the correlational and logistic regression design allows collecting data for a male sample population more significant than 18 years old diagnosed with OPSCC. The software can provide descriptive and inferential statistical analyses, and descriptive statistics help yield specific populations' descriptions through mathematical calculations such as mean, standard deviations, and sample error. Inferential statistics

make educated guesses or predictions about a population based on the sample of data selected to answer research questions.

## Data Analysis Plan for Research Questions

Data analysis for each research question is outlined in this section, along with the hypothesis below.

RQ 1: What is the rate of oral HPV-positive OPSCC in adult men ≥18 years old?

**Data analysis plan for RQ1**: A descriptive analysis was run on a sample size of 337 males ≥18 to find the rate of those with HPV-OPSCC. Then another descriptive analysis ran on the sample size of those positive with HPV.

RQ 2: To what extent is there an association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old?

$H_o2$: There is no statistically significant association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old.

$H_12$: There is a statistically significant association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old.

**Data analysis plan for RQ2:** The bivariate analysis used Pearson chi-square and a multivariate logistic regression because the DV and the IV are categorical variables. This analysis assessed the smoking status of those with HPV-OPSCC and its relationship with

HPV-OPSCC. The choices were current smokers former-smoker, and non-smoker, controlling for education and income.

RQ 3: Is there a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level?

$H_o3$: There is no statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level.

$H_1 3$: There is a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level.

**Data analysis plan for RQ3:** The bivariate Pearson chi-square analysis assessed those that engage in male-to-male vs. male-to-female relationship sex. The multivariate logistic regression model assessed whether there is an association with HPV-OPSCC because the because the DV and the IV are categorical variables.

**Table 1**

*Statistical Procedures per Research Question and Hypothesis*

| **Research Question** | **Hypothesis ($H_a$)** | **Variables**[1] | **Statistical procedures/analysis** |
|---|---|---|---|
| RQ1: Quantitative: What is the rate of oral HPV-OPSCC in adult men ≥18 years old? | $H_a$: The rate of HPV-positive OPSCC in adult males is higher than in adult with HPV-negative OPSCC. | IV: Positive OPSCC<br>DV: adult men ≥ 18 | Descriptive statistics: mean, standard deviation, median and interquartile range for continuous variables; frequencies for categorical variables. |
| RQ2: Quantitative: To what extent is there an association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old? | $H_a$: There is a statistically significant association between rate of oral HPV-OPSCC and race, and smoking tobacco in the form of cigarettes, controlled for income and education level in adult men ≥18 years old | IV: Race and Smoking tobacco.<br>DV: HPV status of OPSCC | Bivariate analysis: Chi-square<br>Multivariable analysis: logistic regression: DV and IV are categorical. |
| RQ3: Quantitative: Is there a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level? | $H_a$: There is a statistically significant association between rate of oral HPV-OPSCC and male-to-male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlled for income and education level. | IV: engaging in oral sex.<br>DV: HPV status of OPSCC | Bivariate analysis: Chi-square<br>Multivariable analysis: logistic regression: DV and IV are categorical.<br>. |

[1]*variables with binary (e.g., Positive or Negative) outcome will be managed as categorical variables.*

## Threats to Validity

### Constraints With Research Design

When research professionals conduct research, the assumption is that they perform all ethical processes to ensure the results are repeatable and accurate. However, external and internal factors frequently play a role in obscuring the data. Sometimes it is done purposely because individuals have allowed ego to overshadow science, and sometimes inexperience is the factor that leads to misleading results. So, what lies in the balance is information that cannot transition bench research into implementable standards that improve the human race's public health issues. A specific threat to this study is finding empirical data that found behavior factors such as social tobacco usage and sexual behavior important enough to gather when diagnosing HPV-positive OPSCC.

Because the act of sexual contact causes HPV-positive OPSCC, the sexual behavior of both the individual and their partner influences their possibility of contracting the disease. Valuable information for understanding whether HPV will transition into cancer is the number of sexual partners, the type of sexual partners, and the rate of how oral sex engagement would increase the probability of contracting high-risk strains. Also, it may help predict the age at which it is more likely to transition into cancer; this information may not always be available. These are the correct angles to explore. What improves the validity of a randomization and sample size? Unbiased choosing of individual data reduces bias to promote accurate conclusions. One challenge faced with secondary data research is finding information related to the investigator's topic.

The internal threat to validity is that the UAB Health Services i2b2 database is an excellent tool for the incidence and prevalence of cancer epidemiology in the United States. However, it does not capture the behavioral aspect of individuals' perspectives on risky sexual acts associated with contracting HPV. I used logistic regression because it measures the probability that the independent variables affect the dependent variable (Meurer & Tolles, 2017). The rationale behind multivariate logistic regression relates to its predictive properties associated with a dichotomous dependent variable (HPV-positive or HPV-negative) and at least one nominal, ratio-level, ordinal, or interval-independent variable.

The research design is needed to advance knowledge in preventative medicine, treatment options, and health literacy. By understanding the disease's gravity, researchers and physicians can work closer to help transition bench and secondary research into standard medical practice. Develop better strategies to introduce vaccines early and reduce exposure (Makiyama et al., 2017). Physicians and patients were previously hesitant to de-escalating treatment to improve the quality of life from surgery (Mirghani & Blanchard, 2017). This research may provide an additional investigation into the safety of treatment measures. Through behavior capacity and self-efficacy, critical components of the social cognitive theory framework, patients can better understand the social influences that contribute to their biological and hormonal response to sexual encounters.

## Ethical Procedures

### Walden University Institutional Review Board Procedures

I performed the Walden IRB submission after receiving approval for the proposal process from the Office of the study Research Administration. Subsequently, before recruiting research participants, accessing, collecting data, or performing analysis of the UAB Health Services i2b2 dataset, I also acquired the University of Alabama at Birmingham IRB approval. The database listed generic numbers for the patients to deidentify them for confidentiality purposes. UAB Health Services' i2b2 database supplied information on their HPV-positive OPSCC status and the independent variables.

## Data Storage

The University of Alabama at Birmingham Health Services i2b2 dataset is treated confidentially. I stored the data in a secure hard drive password-protected, that only I am going to have access to it. Data will be destroyed 5 years after the completion of the study.

## Data Sources and Data Collection

The cancer burden among United States citizens is the second leading cause of death. UAB Hospital’s Health Services i2B2 data warehouse was created to store cancer statistics information to decrease the population’s burden. In secondary quantitative analysis, UAB Hospital Health Services i2B2 data warehouse search engine provides a dataset used for a statistical model that provides an alternate perspective of the association among the variables and HPV mutation into cancerous cells. It can also evoke more research to investigate the cause of HPV mutation in cancerous cells. Previously gathered data may offer a different perspective from its original usage. This process also helped to save on the time and cost that primary data analysis incurs. Other faculty

investigators, doctoral students, and outside researchers and entities faculty use the UAB Hospital Health Services i2B2 data warehouse as it has a respectable reputation among peer-reviewed medical literature and database searches. The goal is to seek a dataset populating information from the last five years that describes the disease.

## Summary

This section's purpose is to outline the investigation statistical analysis process to investigate if there is an association between the rate of oral HPV-OPSCC and race, exposure to smoking cigarettes (tobacco), risky sexual behavior, and participation in oral sex of male-to-male contact vs. male-to-female contact. Over the past 30 years, the United States population's quantitative data indicates an increase in the prevalence of HPV-positive OPSCC, affecting the quality of life of those diagnosed (Yakin et al., 2018). The study's secondary quantitative research cross-sectional design is a useful methodology. It allows rate analysis of established information for HPV-positive OPSCC patients across an existing dataset in adult males. The synthesized information from peer-reviewed journals helped to validate the public health issue HPV has on cancer patients. I aim to understand which variable is associated with the males' target audiences $\geq$ 18 with OPSCC. The systematic review is flexible yet provides empirical data (Johnson, 2017). Retrieving that sample size was made possible using the UAB Health Services i2b2 dataset of those with OPSCC while exploring the categorical aspects of race, smoking status, and risky sexual behavior.

This method is transparent, allows sampling error calculation, and reduces bias. The challenge with secondary data research is coming across valid primary data that help

to assist in any new research questions. Before accessing, collecting, or analyzing any, I gained all necessary IRB approval for data analysis. The following steps ensured Preliminary Ethic Feedback for IRB approval: submission of Form A (Description of Data Sources and Partner Sites). I emailed the Research Ethics Support Specialist for the necessary documents for the Doctor of Public Health program, secondary data analysis requirement, data sources, and affiliated organizations. The UAB Hospital Health Services i2b2 database is an excellent tool for the incidence and prevalence of cancer epidemiology in Alabama and oncology referrals from surrounding states. However, it does not capture the behavioral aspect of individuals' perspectives on risky sexual acts associated with contracting HPV.

I used multivariate logistic regression analyses because it measures the probability that the independent variables affect the dependent variable (Meurer & Tolles, 2017). The cancer burden among United States citizens is the second leading cause of death. The cancer center committee for The University of Alabama at Birmingham Health System created a database warehouse to store cancer statistics information to decrease the population’s burden. In secondary quantitative analysis, UAB Health Services i2b2 search engine provided a dataset used for a statistical model that provides an alternate perspective of the association among the variables and HPV mutation into cancerous cells. With the SPSS, the correlational and logistic regression design allows collecting data for a male sample population $\geq$ 18 years old diagnosed with OPSCC. The software can provide descriptive and inferential statistical analyses.

Section 3: Presentation of the Results and Findings

## Introduction

I aimed to determine which independent variable, i.e., race, smoking tobacco, or the choice of male vs. female sexual engagement, increases the chances of contracting HPV-Positive OPSCC. Understanding these independent variables' impact on activating cancer from HPV can help develop preventative education taught through in-office visits, college-based-sex health courses, and pharmaceutical vaccination campaigns, as HPV is the determining predictor of survival rate from OPSCC (Wagner, 2017). In addition, this information may help solve the medical dilemma. Physicians need to resolve how the current invasive treatment of OPSCC causes patients to cope with lockjaw, dry mouth, bone death, scarring, and difficulty swallowing (Golusiński & Golusińska-Kardach, 2019). The current treatment has medical teams deciding on the best combination of treatments to reduce the recurrent rate and increase the quality of life for those diagnosed with OPSCC.

The risk assessment of those diagnosed with HPV-OPSCC needs a treatment de-escalation (Wagner, 2017). Three critical questions to help resolve the de-escalation public health issue are: RQ1: What is the rate of oral HPV-positive OPSCC in adult men $\geq$18 years old among races? RQ 2: To what extent is there an association between the rate of oral HPV-OPSCC among race and smoking tobacco in the form of cigarettes, controlling for income and education level in adult men $\geq$18 years old? RQ 3: Is there a statistically significant association between the rate of oral HPV-OPSCC and male-to-

male oral sex, compared to male-to-female oral sex in adult men ≥18 years old, controlling for income and education level?

## Accessing the Data Set for Secondary Analysis

This section entails the secondary analysis of the data collection for the Risk Factors of Human Papillomavirus Positive Oropharyngeal Cancer in Men for males > 18. Data collection for this project took approximately 6 months due to the processes of initial Walden University IRB approval and a request for a change of procedure in July 2021. Using a second academic institution, I obtained an information data agreement approval on October 8, 2021, and IRB approval on October 31, 2021, from UAB, which allowed secondary submission to Walden University. The IRB granted a Change in Procedure IRB approval on December 3, 2021, and the appropriate data set was made available on January 9, 2022. It is essential to ensure that the search engine one was able to provide all dependent and independent variables.

The initial thinking was that retrieving a dataset from the SEER database could provide the cancer-dependent variable as it is a powerhouse of cancer statistics (National Institute of Health, 2020b). This search engine is used countless times for secondary analysis to research causes, correlations, the prediction of prognosis, and several other variables of scientists' and physicians' interest. However, it does not capture behavioral variables such as tobacco status and sexual orientation. Therefore, as the primary investigator, seeking another source of information was necessary.

The UAB Health System is academic healthcare and Comprehensive Cancer Center located in Birmingham, Alabama. Established in 1945 as the teaching hospital for

the University of Alabama School of Medicine, it is one of the four largest academic medical centers in the United States. Its Comprehensive Cancer Center conducts secondary quantitative research, such as retrospective analysis, on patients with Stage IV NSCLC who received systemic treatment from UAB Cancer Center between 2002 and 2012 (Badawy et al., 2018). Other examples are qualitative studies such as the collection and review of perspectives of patients and medical and nonmedical cancer center staff on the cost of care (CoC) conversations (Pisu et al., 2019). UAB's i2b2 group received a list of corresponding ICD-10 codes and needed variables because OPSCC represents cancer in the throat, mouth, base of the tongue, and salivary glands. This process should have been described more thoroughly in Section 2.

As the investigator, I desired a clearly defined sexual orientation response for all 337 participants; however, marital status of married, divorced, or widowed to the opposite sex equals male-to-female sexual contact in incidences where the dataset does not provide the patient's response. Unless otherwise denoted, also single equals males-to-female. A response such as life partner, homosexual, and bisexual equals male-to-male contact. The use of smoking status at the first clinic encounter was used rather than the last visit status to capture exposure to smoking tobacco. Unknown statuses do not represent an exclusion. There were missing data in some research cases, but the direct response of e-cigarettes, smokeless tobacco, or chewing tobacco is inclusionary in the sample size. Deceased patients were also excluded from the sample size because their age was not captured in the dataset to confirm greater than 18. Also, here, one can find an

outline of any baseline descriptive and demographic characteristics of the sample of 337 males with OPSCC.

## Baseline Descriptive and Demographic Characteristics of the Sample

The UAB i2b2 team retro-analyzed the UAB patient population from 2011 to 2021 with OPSCC. The data arrived in three different subgroups. Group 1, entitled Person, included deidentified patients with OPSCC, including race, ethnicity, age (at last clinic encounter), and marital status. Group 2 HPV_Clinical_Events included deidentified patients with positive HPV. Group 3 Social History included the social status for smoking status and some patients' direct response to sexual orientation and sexual activity. The sample includes 337 males (White, Black, or Hispanic), smoking status, HPV status, and perceived sexual orientation. Many individuals within the sample are White males with a current or former smoking history. Hay and Nixon (2018) indicated that the predominant demographic with HPV-positive OPSCC are middle-aged White males between 45 and 59. UAB’s population demonstrates a public health issue for Alabama; however, bordering states such as Mississippi, Tennessee, Georgia, and Florida have residents that become patients of UAB for cancer treatment. Further investigation can move into avenues of genetically predisposed White males for OPSCC.

## Results

Completing the descriptive analysis performed on a sample size of 337 men (confidence interval .95) who visited the UAB with OPSCC yielded the following statistical results:

**Table 2**

*OPSCC HPV Status*

| Status | Frequency | Percent | Std. error | 95% confidence interval | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| Negative | 301 | 89.3 | 1.6 | 85.8 | 92.3 |
| Positive | 36 | 10.7 | 1.6 | 7.7 | 14.2 |
| Total | 337 | 100 | .0 | 100 | 100 |

The extracted data show that the individual male status with HPV negative is 89.3%, and those positive with HPV yield 10.7%. The rate of oral HPV-positive OPSCC in adult men ≥18 years old within this sample size is 10.7%; Bias-1.0 for negative and 1.0 positive; Std Error for both positive and negative is 1.6. The sample represents those diagnosed with OPSCC in Alabama, as there were only 520 oral and pharyngeal cancer cases in Alabama in 2018 (CDC, 2021b). The prevalence of OPSCC disproportionally accounts for 15,540 cases for men, and Alabama contributes 0.03% (520/15540; CDC, 2021b). The average person in the United States with HPV-OPSCC statistics suggest that approximately 10% of its male population combined with 3.6% of its female have oral HPV. Nevertheless, these percentages are responsible for about 70% of all oropharyngeal squamous cell carcinoma OPSCC (CDC, 2021). From this data, an investigator can conclude that tobacco and alcohol products or environmental toxins cause the remaining 30% of HPV-negative OPSCC.

**Table 3**

*Race Distribution*

| Race | Frequency | Percentage | Bias | Std. error | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| White | 287 | 85.2 | -.1 | 1.9 | 81.1 | 88.7 |
| Black/African American | 49 | 14.5 | .1 | 1.9 | 11 | 18.4 |
| Hispanic Latino | 1 | .3 | .0 | .3 | .0 | 1.2 |

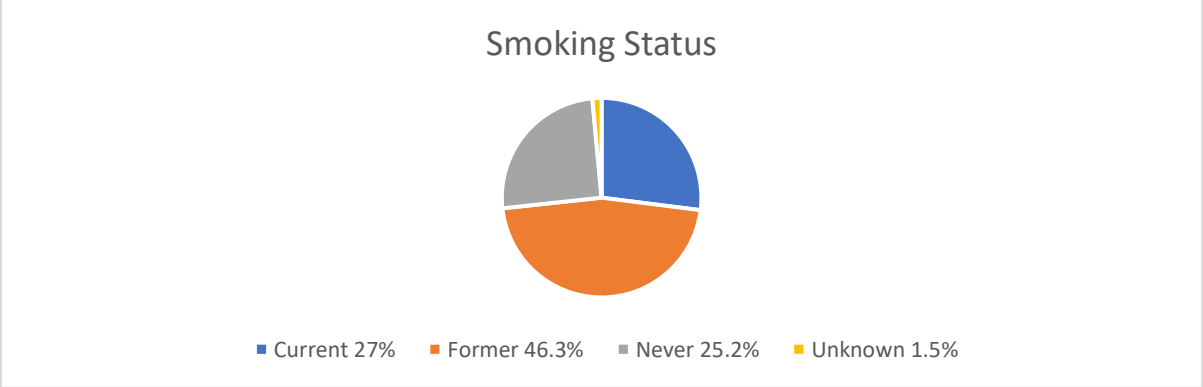
**Table 4**

*Smoking Status OPSCC 337 Sample Size*

| Smoking status | Frequency | Percentage | Bias | Std. error | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| Current | 91 | 27% | .1 | 2.5 | 22.3 | 32.0 |
| Former | 156 | 46.3% | .1 | 2.9 | 40.4 | 52.4 |
| Never | 85 | 25.2% | -.1 | 2.5 | 20.3 | 30.3 |
| Unknown | 5 | 1.5% | .0 | .6 | .4 | 3.0 |

**Figure 2**

*Smoking Status Sample Size*



After running a descriptive analysis on the smoking status, the categorial criteria contribute the following: Unknown 1.5%; Never 25.2%; Former 46.3%; Current 27%. The investigation showed a conducted descriptive analysis on only HPV-Positive OPSCC as a comparison.

**Table 5**

*Smoking Status OPSCC- HPV Positive (36)*

| Smoking status | Frequency | Percentage | Bias | Std. error | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| Current | 5 | 13.9% | -1.0 | 6.9 | 2.4 | 25.0 |
| Former | 16 | 44.4% | .8 | 8.3 | 27.8 | 58.7 |
| Never | 14 | 38.9% | .2 | 9.9 | 18.8 | 52.8 |
| Unknown | 1 | 2.8% | .1 | 2.6 | .0 | 8.3 |

The smoking status categorical criteria contributes to the following statuses Unknown 2.8%; Never 38.9%; Former 44.4%; Current 13.9%. By reviewing the descriptive analysis and combining the percentages of Current and Former smoking status criteria, a history of smoking tobacco exposure for both the sample size of 337 (73.3%) and HPV-OPSCC (58.3%) suggests that smoking still has an impact on OPSCC. Tobacco was the leading cause of OPSCC (Yakin et al., 2018). However, it is worth investigating if tobacco shares a relationship with HPV. Research Question 2 explored this portion of the investigation.

Oral sex contributes to sexual behavior. Although both heterosexuals and homosexuals engage in oral sex, I wanted to investigate the association between sexual orientation and oral HPV. Societal perception is that homosexual males engage in oral

sexual activity more than heterosexual males. Because oral HPV is the type of HPV that contributes to HPV-OPSCC, Research Question 3 demonstrated an investigation of the sexual orientation relationship with HPV-OPSCC. After analyzing the sample size using a 0.95 confidence interval, the categorical criteria for perceived sexual orientation and their respective percentages are Bisexual (.3, Bias .0, Std. Error .3), Heterosexual (73, Bias -.3, Std. Error 2.4), Homosexual (.9, Bias 0.0, Std. Error .5), Unknown (25.8, Bias .3, Std. Error 2.3). This variable's association with perceived sexual orientation is because of the use of marital status where the data did not clearly define sexual orientation. Married-Widowed-Divorce equals heterosexual; Life Partner-Homosexual; Single when not specified equals Unknown.

**Table 6**

*Descriptive Perceived Sexual Orientation*

| Sexual orientation | Frequency | Percent | Bias | Std. error | 95% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| Bisexual | 1 | .3 | 0 | .3 | 0 | .9 |
| Heterosexual | 246 | 73.0 | -.3 | 2.4 | 67.7 | 77.4 |
| Homosexual | 3 | .9 | 0 | .5 | .0 | 2.1 |
| Unknown | 87 | 25.8 | .3 | 2.3 | 21.5 | 30.9 |

After descriptive analysis of HPV-Positive Sample, the categorical criteria for perceived sexual orientation and their respective percentages are Heterosexual (97.2, Bias -.4, Std Error 3.0) and Homosexual (2.8; Bias .4; Std. Error 3.0). Bisexual and unknown were not associated with this sample. The LGBTQ represented 3.1% of Alabama's population in 2019 (Movement Advancement Project, 2022)

**Table 7**

*Descriptive Perceived Sexual Orientation HPV-Positive OPSCC (36)*

| Orientation | Frequency | Percentage | Bias | Std. error | 90% confidence interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| Heterosexual | 35 | 97.2 | -.4 | 3.0 | 91.3 | 100.00 |
| Homosexual | 1 | 2.8 | .4 | 3.0 | 0 | 8.7 |

**Results Question 2**

The confidence interval of 95% provides a p-value of 0.05. The bivariate chi-square analysis results for smoking status and race have a value of 21.94, and an associated Sig with the chi-squared is 0.055. The chi-square analysis in Table 8 shows whether there was an association between smoking and race. Because the Sig value of .055 is slightly greater than .05, there is no association between smoking status and race, but it suggests that some confounding data may impact the value.

**Table 8**

*Correlation of Smoking and Race With HPV-OPSCC Omnibus Tests of Model Coefficients*

| | | | | |
|---|---|---|---|---|
| **Step 1** | Step | Chi-Squared | df. | Sig. |
| | | 21.994 | 13 | .055 |
| | Block | 21.994 | 13 | .055 |
| | Model | 21.994 | 13 | .055 |

Table 9 demonstrates the findings of the multivariate logistic regression showing three categorical races and corresponding Sig values .000 White (.850), Black (.569), and

Hispanic (1.000). All values are more significant than 0.05; therefore, I fail to reject the null hypothesis and cannot accept the alternative hypothesis. Smoking Sig values show categories as Never (.411), Smoking History (.216), and Unknown (.27). The analysis attempted to control for education and employment status, as there is a direct connection between income and employment status. The significance data suggests no statistically significant association between smoking history and positive HPV compared to never smoking status; however, the odds ratio suggest the sample size is insufficient. This information suggests there is no statistically significant association between the rate of oral HPV-OPSCC and race and smoking tobacco in the form of cigarettes, controlled for employment status and education level in adult men $\geq$18 years old. Therefore, the likelihood that these two variables are associated with HPV-Positive status is insignificant in this sample size, and the two variables are independent.

Table 9

*HPV-Smoking Status and Race- Variables in the Equation.*

| | B | Std. Error | Wald | df | Sig. | Odds ratio | 95% Confidence Interval for Odds ratio | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| **Race** ref: White | | | .325 | 2 | .850 | | | |
| Black/African American | -.367 | .645 | .325 | 1 | .569 | .693 | .196 | 2.450 |
| Hispanic | -18.435 | 40192.970 | .000 | 1 | 1.00 | .000 | .000 | |
| **Smoking Status** ref: Unknown | | | 2.613 | 2 | .271 | | | |
| Never | -.983 | 1.195 | .676 | 1 | .411 | .374 | .036 | 3.894 |
| Smoking History | -1.449 | 1.170 | 1.534 | 1 | .216 | .235 | .024 | 2.325 |
| **Employment Status** ref: Unknown | | | 13.200 | 5 | .022 | | | |
| Disabled | .037 | 1.082 | .001 | 1 | .972 | 1.038 | .125 | 8.647 |
| Employed | 1.579 | .445 | 12.592 | 1 | .000 | 4.852 | 2.028 | 11.608 |
| Part-time | -18.435 | 40192.970 | .000 | 1 | 1.000 | .000 | .000 | |
| Retired | .714 | .512 | 1.944 | 1 | .163 | 2.041 | .749 | 5.568 |
| Unemployed | .230 | 1.086 | .045 | 1 | .833 | 1.259 | .149 | 10.634 |
| **Education** ref: Unknown | | | .000 | 4 | 1.000 | | | |
| College Degree | -19.149 | 28420.722 | .000 | 1 | .999 | .000 | .000 | |
| High School Graduate | -19.474 | 15946.483 | .000 | 1 | .999 | .000 | .000 | |
| Postgraduate | -19.746 | 22519.753 | .000 | 1 | .999 | .000 | .000 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Some College | -20.217 | 23137.266 | .000 | 1 | .999 | .000 | .000 | |
| Constant | -1.319 | 1.125 | 1.376 | 1 | .241 | .2674 | | |

a. Variable(s) entered on step 1: Race, Smoking Status, Employment Status, Education.

Table 9. shows a multivariate regression analysis for race and smoking tobacco controlling for education and employment. Education references are high school graduates, some college, college degrees, and postgraduates. The data showed employment status categorical information for disabled, employed, part-time, retired, and unemployed. Research questions 2 and 3 use the education and employment categories.

**Inferential Statistics for Research Question 3**

The bivariate chi-square analysis assessed the association between the perceived sexual orientation of heterosexuals and homosexuals using marital status, as orientation is not clearly defined. The chi-squared correlation analysis tests the likelihood perceived sexual orientations had on HPV-OPSCC status. The distribution of observation shows a chi-square value of 38.982 and an associated Sig value of .000. The larger chi-square and the Sig value of less than the p-value of .05 demonstrate that the two categories of sexual orientation are not independent of each and pose a statistically significant value. In comparison, the multivariate logistic regression shows perceived heterosexuality and homosexuality with a Sig value of .996 and the reference point of Unknown with a significance value of .775. The confidence interval is 95%, with a p-value of .05. These values indicate that the Sig is more than the .05 significance level; thus, there is no statistically significant association between sexual orientation and HPV-OPSCC.

Therefore, I failed to reject the null hypothesis and cannot accept the alternate hypothesis. There is no statistically significant association between the rate of oral HPV-OPSCC and male-to-male oral sex compared to male-to-female oral sex in adult. The elevated odds ratio of research question three suggest that the sample size was insufficient to run the multivariate analysis for the independent variables.

**Table 10**

*Correlation of Perceived Sexual Orientation and HPV-OPSCC Omnibus Tests of Model Coefficients.*

| **Step 1** | | Chi-Squared | df. | Sig. |
|---|---|---|---|---|
| | Step | 38.982 | 11 | .000 |
| | Block | 38.982 | 11 | .000 |
| | Model | 38.982 | 11 | .000 |

**Table 11**

*HPV-Status and Perceived Sexual Orientation.*

| | **B** | **Std. Error** | **Wald** | **df** | **Sig.** | **Odds ratio** | **95% Confidence Interval for Odds ratio** | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower Bound | Upper Bound |
| **Perceived Sexual Orientation** ref : Unknown | | | .509 | 2 | .775 | | | |
| Heterosexual | 19.195 | 4201.832 | .000 | 1 | .996 | 216930938.9 | .000 | |
| Homosexual | 20.156 | 4201.832 | .000 | 1 | .996 | 566962265.3 | .000 | |
| **Employment Status** Ref: Unknown | | | 12.269 | 5 | .031 | | | |
| Disabled | .065 | 1.097 | .004 | 1 | .953 | 1.067 | .124 | 9.166 |
| Employed | 1.482 | .437 | 11.512 | 1 | .001 | 4.402 | 1.870 | 10.361 |
| Part-time | -18.941 | 40192.970 | .000 | 1 | 1.000 | .000 | .000 | |
| Retired | .495 | .510 | .942 | 1 | .332 | 1.640 | .604 | 4.454 |
| Unemployed | .155 | 1.152 | .018 | 1. | .893 | 1.168 | .122 | 11.160 |
| **Education** ref: Unknown | | | .000 | 4 | 1.000 | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| College Degree | -19.435 | 28420.722 | .000 | 1 | .999 | .000 | .000 | |
| High School Graduate | -19.001 | 13959.122 | .000 | 1 | .999 | .000 | .000 | |
| Postgraduate | -19.848 | 22832.316 | .000 | 1 | .999 | .000 | .000 | |
| Some College | -20.821 | 22837.048 | .000 | 1 | .999 | .000 | .000 | |
| Constant | -21.457 | 4201.832 | .000 | 1 | .996 | .000 | | |

a. Variable(s) entered on step 1: Perceived Sexual Orientation, Employment Status, Education.

## Summary

The analysis assessed a sample size of 337 patients from the University of Alabama at Birmingham Hospital of OPSCC from 2011 to 2021. Of the 337 with OPSCC, 36 tested positive for the Human Papillomavirus, or approximately 11%. This percentage is significantly less than the US population, showing that approximately 70% of those newly diagnosed with OPSCC have HPV. This difference raises the question: Are all individuals with OPSCC tested for HPV at the cancer site and within the oral cavity? Both multivariate logistic regression analyses for smoking status and race (research question 2) and perceived sexual orientation (research question 3) do not show a statistically significant association with HPV-OPSCC. There is no statistically significant association between the rate of oral HPV-OPSCC and race and smoking tobacco in the form of cigarettes, controlling for income and education level in adult men $\geq$18 years old. The chi-square did show that the categories of sexual orientation are significantly independent of one another. There is no statistically significant association between the rate of oral HPV-OPSCC and male-to-male oral sex compared to male-to-female oral sex in adult men $\geq$18 years old, controlling for income and education level. Because HPV is a sexually transmitted disease, there is no surprise that an association exists. However, there is evidence suggesting heterosexuality has an increased

association. Standard-of-care implementation can use the two findings of smoking cessation for preventative measures and, hopefully, the creation of HPV testing for men during urology visits.

Section 4: Application to Professional Practice and Implications for Social Change

## Introduction

This study investigated the risk factors associated with HPV-OPSCC in males over 18. Identifying and reducing the risk factors aim to improve preventative education for the most accessible males and improve the standard practice during annual urology exams, including HPV testing. HPV is the cause of nearly 35,000 of 44,000 new cases of cancer found in human anatomy areas of the cervix, vagina, vulva, penis, anus, rectum, and oropharynx; nearly 34,800 of these cases are positive for HPV (CDC, 2019). Research shows that understanding and identifying the presence of HPV testing during pelvic exams have reduced the causes of cervical cancer and improved survival rates (Berman & Schiller, 2017). Women with a definite HPV diagnosis in their cervix also had a positive male partner in 75% of the cases; however, a random selection of men with positive HPV in their semen only experienced a positive partner in 30% of the patients (Giuliano et al., 2010). This information means that the male has the potential to transfer genital HPV orally, causing OPSCC.

Treatment for tobacco-induced OPSCC consists of a mandibulotomy to access the oropharynx, causing the usage of the trachea for long-term airway and, in many cases, a feeding tube for nutrition (Hay & Nixon, 2018). These conditions can have a negative emotional, physical, and mental impact on the persons diagnosed and their caregivers. Further morbidities from past surgical techniques, such as making large incisions exposing neck tissue and organs from open surgery for OPSCC, caused a decrease in other daily functions, such as speech and swallowing society may take for granted

(Golusiński & Golusińska-Kardach, 2019). HPV-positive oropharyngeal cancer has a substantially better outcome than OPSCC caused by tobacco or alcohol. There is an approximately 50% reduction in disease recurrence and a 28 % reduction in mortality rate. However, the increased national and international rate of HPV-positive OPSCC has become alarming due to its prevalence, recurrence caused by HPV, and debilitating treatment exposure (Berman & Schiller, 2017). Understanding why males are affected more, specifically White males ages 45-59, have a significantly increased rate of occurrence, which will help reduce the severe functional morbidities and a healthcare cost burden for treatment.

Imagine how society can improve the quality of life by reducing HPV-OPSCC as a contributing factor to head and neck cancer. From 2004 to 2007, the price per new diagnosis of HPV-related head and neck cancer cost $43,200, with an approximate annual cost in the United States of $306 million (Ward, Mehta, & Moore, 2016). There will be a global impact on the healthcare burden from HPV as it increases the number of OPSCC and head and neck cancers. From 2018-to 2030, when conducting a statistical analysis of findings from the World Development Indicators and the 2016 Global Burden of Disease, the United States is projected to spend an estimated $535 billion US dollars (USD) on the impact of diseases related to HPV (Patterson et al., 2020). Other areas of the globe, such as Oceania, East Asia, and Southeast Asia, will suffer the most incredible gross domestic product (GDP) losses at USD 180 billion. South Asia will lose USD 133 billion. Also, Patterson et al. (2020) noted that individuals in low- and middle-income countries and regions would have limited access to surgical interventions due to the lack of surgeons

and physicians to help treat the diagnosis. This research shows that this virus affects the borders of the United States and causes a global burden

## Interpretation of Findings

The prevalence of OPSCC disproportionally accounts for 15,540 cases for men in the United States. A literary report in 2019 further indicates HPV is present in approximately 72% of men with OPSCC and 63% of women with OPSCC (CDC, 2019). The CDC's most recent report (2021) in the United States noted approximately 20,236 males with OPSCC, of which HPV caused 70% (14,400 cases). The increase in oral HPV prevalence has increased the indication of more OPSCC global cases than tobacco products. However, for Research Question 1, the descriptive analysis of the sample size of 337 males, there were 36 males positive for HPV-OPSCC, which is approximately 11%. The literature reveals that the most common demographic is middle-aged White males between the ages of 45 and 59.

In conjunction with the literature, this study investigation suggests that White males are more prevalent, showing 33 of the 36 Caucasian/White and three African American/Black individuals. When interpreting the age portion of the demographics, for those positive for HPV, 15 males range from 42-59, while 21 range from 60-84. A confounding factor could be the inability to confirm diagnosis age and only having the age of the first encounter with the UAB, where the patient received either the confirmation of diagnosis or completion of treatment/follow-up. Seeing how Alabama only contributes to about 3% of those diagnosed with HPV-OPSCC in the United States, this number is not surprising. The sample size of 337 represents those in the United States

with HPV-OPSCC when collecting data from multiple states. SEER would have provided more of a diverse population; however, its data does not capture smoking status, specific pathology related to HPV, and sexual behavior. It only specifies cancer and various demographics such as race, age, and gender. Therefore, limiting the researcher from conducting a better quantitative analysis.

During the literature review, I discovered a trial researching a female population, considering whether the independent factor of tobacco exposure activates HPV in females. Using the cross-section for the United States female population, an analysis of 2,838 females with HPV vaginal DNA found nicotine to be a predictor of HR-genital HPV. The trial results showed that smoking and chewing tobacco caused harm to normal tissues as the tobacco-caused mutation of the cells developed into tumors (South et al., 2019). South et al.'s (2019) research gave some pause to testing his theory in males.

When analyzing Research Question 2, results showed that 73% of the sample had a smoking history (current or former). When analyzing smoking status with the chi-squared and multivariate logistic regression, both Sig values were more than the p=.05. The results failed to reject the null hypothesis. The former smoker may have initially caused a limiting issue; one must define when establishing a former smoker whether 1 month, 3 months, 6 months, or 1 year may impact the results. Of the positive HPV-OPSCC, 22 of the 36 displayed status of current or former smokers; however, the overall analysis of the 337-sample size did not show a statistically significant relationship between tobacco and HPV-OPSCC. These results disconfirm an association within the male sample size with HPV-OPSCC compared to females with HPV-positive cervical

cancer. These findings spark more investigation into whether tobacco activates the HPV cells to cause cancerous tissue. There was not much literature on sexual behavior to explore sexual orientations of heterosexuality and homosexuality risk of contracting HPV-OPSCC. However, when defining sexually risky behavior, there is a connection between multiple partners and early-age engagement in sexual intercourse. Approximately 26% of the United States youth population contributes to new cases of HIV and other forms of STIs (Addoh et al., 2017). Scientists and physicians discovered HPV to contribute to OPSCC in the early 1990s (Stock et al., 2013). Because of oral HPV oral sex transmission, the rationale is to investigate whether there was a statistical difference between heterosexual and homosexual sexual interactions.

Early studies tested primarily male populations because this population was not approved to receive the HPV vaccine. Both groups received a survey asking if they perform oral sex, defined as placing their mouth on a vagina or penis, or open-mouth kissing by placing their tongue in the mouth of another female or male (D'Souza et al., 2009). In the control group, 24% had never performed oral sex, 2.6% had never had vaginal sex, and the median lifetime number of partners was 2–5. In the college group, 9% had never engaged in open-mouthed kissing, 28% had never performed oral sex, and 30% had never had vaginal sex (D'Souza et al., 2009). This study population is consistent with the low percentage of males that have perceived homosexual orientation 30% had never engaged in vaginal sex in the college group and 2.6% in the control group. Never engaging in oral sex in both groups, 24% (controlled) and 28% (college) engaged in oral sex, and 30% of the experimental group never engaged in vaginal sex. These findings

mean 72-76% participate in oral sex, but there is no clinical significance of whether the mouth is being placed on a vagina or a penis. Compared to the analysis presented in the dissertation, this study shows a perception of the control as possibly heterosexual and the experimental group as possibly homosexual, showing independence from one another. There was no evidence of an increased risk of male-to-male sexual relationships vs. male-to-female relationships.

The theoretical framework of social cognitive theory assesses the relationship among person, behavior, and environment when explaining how health behavior occurs. For this study, I attempted to show the makeup of the person's biology and hormones (person), the basis of social influence (environment), and smoking and risky sexual contact without the use of protection (behavior) on how it relates to developing HPV-OPSCC. SCT, previously social learning theory, was started in the 1960s by Albert Bandura and changed to SCT in 1986 (LaMorte, 2018). The nature vs. nurture premise might explain the argument; however, the biological imprints may still influence decision-making. The six primary constructs of SCT consist of reciprocal determination, behavior capacity, observation learning, reinforcement, expectation, and self-efficacy (LaMorte, 2018). Although the social cognitive theory was the theoretical framework that guided the present study, this study did not test constructs related to SCT. Instead, this study focused on how an individual's engagement in sexual behaviors might lead to an increased prevalence of HPV. SCT guided the study since health behaviors attributed to the health problem can be explained by SCT. There is no cure for HPV; however, in some cases, it resolves on its own. When it does not, the disease stands to develop into

genital warts or cancer (CDC, 2021). Risk factors such as experience with multiple partners, engaging in oral-anal sex or engaging in oral-genital sex play a significant role in HPV development (Yakin et al., 2018). Because of the increasing prevalence of HPV and HPV-OPSCC, SCT can help understand how a person's environment influences risky sexual behavior. The race variable is nominal and cannot be changed; however, the fifth construct of SCT, expectation, can relate to this variable. An expected outcome demonstrated that the category of White/Caucasian would have the highest prevalence of OPSCC. Research on the male gender tends to show an association between their emotional intelligence and the likelihood to smoke and an association with considering sex and age as factors (Sharma et al., 2017). Observational learning and reinforcement principles account for individuals following the tone of what surrounds them and interacting with internal and external responses that encourage or discourage continued behavior.

## Limitation

The sample size was derived from only one research/medical center in Alabama compared to a better sample of 337 if collected from multiple treatment centers in Alabama. The sample size of 337 represents those in the United States with HPV-OPSCC when collecting data from various states. SEER would have provided more of a diverse population; however, its data do not capture smoking status, specific pathology as it relates to HPV, and sexual behavior. It only specifies cancer and various demographics such as race, age, and gender, limiting the research from conducting a better quantitative analysis. Research Question 2 showed that 73% of the sample had a smoking history

(current or former smoker). One would like to believe this elevated prevalence of smoking history has a relationship with HPV-OPSCC.

After analyzing smoking status in Research Question 2, the Sig values in the chi-squared and multivariate logistic regression were greater than p=.05. The results failed to reject the null hypothesis. The former smoker's status may have initially caused a limiting issue; one has to define the establishment of a former smoker as 1 month, 3 months, 6 months, or 1 year. Former and current categories were grouped as a smoking history because the male had some exposure to tobacco at some point. The limitation of this study is the variability of those former smokers. Because participants had exposure to smoking tobacco at some point, combining the former and current categories as a smoking history seemed more appropriate.

The limitation of this study is the variability of those former smokers. Perceived sexual orientation based on marital status when status was not identified caused a notable limitation. A person can be married to the opposite gender but have a history of homosexual relationships. Also, when a person's status was single and unspecified heterosexual or homosexual, the ethical thing to do was to place that individual into the unknown category. Because risky behavior can be explored and engaged within either orientation, the increase of sexual partners and the early introduction of sexual interaction increases the chance of contracting HPV. A better way to serve this research regarding sexual behavior is by comparing homosexual males with OPSCC only and the rate with HPV. The elevated odds ratio of research question three suggest that the sample size was insufficient to run the multivariate analysis for the independent variables.

Research shows that income and education are socioeconomic determinants that impact health outcomes. McBride and Singh (2017) conducted a multivariable regression to identify predictors for four HPV knowledge categories as follows: (1) general knowledge, (2) cervical cancer knowledge, (3) "other" cancer knowledge (i.e., anal, oral, penile), and (4) vaccine knowledge. Their findings show women were more likely to report receiving a vaccine recommendation than men, demonstrating a bias or lack of education providers have regarding preventative medicine for male patients. Even though more than 70% of the researched population knew HPV caused cervical cancer, only 14.9-31.5% knew HPV caused other cancers such as OPSCC (McBride & Singh, 2017). The predictors for the knowledge of HPV and HPV vaccine were a parent having a child under the age of 18, as well as education, income, gender, and race. Although income was not collected for this population by the University of Alabama at Birmingham Database, employment is a relatable variable, as there is a direct relationship between income and the type of career a person has. Employment statuses were employed, retired, disabled, part-time, and unemployed. Also, the analysis perhaps was confounded by the unknown status of both employment status and a large percentage of unknown education status. This research could provide more validity if not for possible confoundment of the unknown status of all variables for a more significant percentage of the sample size.

## Recommendation

The results appear inconsistent with previous research when variables are individually studied. When tobacco was the causality of OPSCC, treatment consisted of a mandibulotomy to access the oropharynx, resulting in long-term airway support due to

tracheostomy and gastrostomy for feeding (Hay & Nixon, 2018). The current literature has denoted middle-aged White males between the ages of 45-59 predominant demographic with HPV-positive OPSCC (Hay & Nixon, 2018). Because there is no association between race and smoking history in multivariable analysis, that does not mean these two variables studied independently in a different sample size do not show statistical significance.

I recommend primary research on a population with OPSCC to gather the participants' risk factors for contracting HPV and OPSCC and study the association between the two risk factors. Of course, there is an exclusion of those with HPV-Negative OPSCC from the trial. If the sample size is consistent with only HPV-Positive individuals, the study of risk factors would be more profound in efforts to create preventative education to minimize the contraction and spread of HPV. This population would address the continuation of this study and help reduce the current limitation of less diverse populations and the inclusion of both HPV-Positive and HPV-Negative. The survival rate of HPV-Positive OPSCC is greater than HPV-Negative; therefore, exploring less invasive treatment methods can help improve quality of life (Bigelow et al., 2020). Because of the greater survival rate, investigators have pondered whether a population of patients can safely undergo a study to receive de-escalation of treatment to minimize the severe morbidities associated with the current treatment of open-invasive surgery and chemotherapies (Bigelow et al., 2020). The goal is to reduce morbidities yet control for recurrence.

## Implications for Professional Practice and Social Change

The implications for a professional practice derived from the study results would be providing preventative education to males, more importantly, white males, with the highest incidence of HPV-OPSCC. During pediatric visits, Pediatricians can discuss with parents the preventative intervention of the HPV vaccine. The HPV vaccine has been approved for males ages 09-47 since 2014 (McSeveney, 2018). Gardasil-9 protects against p-16, the HPV protein primarily found in HPV-OPSCC (Berman & Schiller, 2017). Makiyama, Hirai, and Matsuzaki (2017) investigated 12 men from ages 32-74, drawing HPV titer before and after Gardasil-9 injections, and discovered an increased titer post-dose compared to pre-dose. It is essential to not only improve the parents' perspective of the HPV vaccine, but it is also essential for the HPV vaccine to be included in Alabama's Medical School curriculum to include more information and training on HPV, HPV vaccination, and counseling (Daniel et al., 2021). The earlier these lessons are introduced and continued within the educational programs, the more familiar the medical student may become. Although OPSCC among this population did not show a statistically significant association with smoking tobacco, the descriptive analysis shows that most white males with HPV-OPSCC had a history of smoking tobacco. Also, other research trials have connected race and smoking with risk factors for developing OPSCC and HPV-OPSCC. This sample size's limitations can explain why the findings were descriptively similar but not statistically significantly similar.

The results of the sexual behaviors of heterosexuals significantly impacted HPV-OPSCC, which disconfirms the hypothesized homosexual behavior. The young population needs more information on the risk of oral sex, as its perceived association

with STI and STD is not as high as the perceived association with genital or anal intercourse or contact. Sexual education courses taught in high school seem to have become less frequent. The educational, preventative measure can contribute to social change in conjunction with pediatric preventative medical intervention. Examples of education consist of the use of condoms by both males and females, abstinence, knowing and understanding one's partner's STI and STD status, and the importance of annual check-ups; all play a role in the social change factors that can lead to the reduction of the spread of HPV.

Lastly, another professional practice is to assess the HPV status of all individuals with OPSCC, as it is crucial to understand the full pathological makeup of oropharyngeal cancer. Surgeons currently assess during surgical procedures and, depending upon the location of cancer, a tissue biopsy. The HPV status may soon prompt a different treatment regimen as the literature has suggested that the quality of life for HPV-Positive OPSCC is more significant than those with HPV-Negative OPSCC (Mirghani & Blanchard, 2017). These steps can help move towards a more positive social change.

## Positive Social Change

The potential social change from understanding the risk associated with the male population with HPV-OPSCC is the lower transmittal of HPV. HPV is the most common sexually transmitted disease both domestically and globally, and HPV causes both genital warts and cancer. However, evidence shows that individuals with genital warts show exposure to coinfection of oncogenic types of HPV, such as 16, 18, 31, 33, 45, 52, and 58 (Giuliano, Anic, & Nyitray, 2010). While reducing the rate of oral HPV, one hopes it also

reduces the prevalence of OPSCC. The goal is to show a clinical need for an oral or urological screening test for males during standard-of-care treatment. Also, a clear explanation of the risk factors can help healthcare providers use the social cognitive theory to understand how their patients perceive the susceptibility to HPV and then HPV-OPSCC. Introduction to the vaccine earlier helps reduce the chances of developing HPV (McSeveney, 2018). Some school systems have adopted HPV as a requirement for school registration.

## Conclusion

The purpose of this study was to research whether there was an association between the rate of oral HPV-OPSCC and race, exposure to smoking cigarettes (tobacco), risky sexual behavior, and participation in oral sex of male-to-male contact vs. male-to-female contact. Although the descriptive analysis proved consistent with the literature, the multivariate logistic regression analysis used for research questions two and three did not show statistical significance. These findings only further validate the need to understand why males, considerably white males are more likely to contract HPV-OPCSS and what risk factors increase their risk of developing this debilitating disease. Race and heterosexuality are still risk factors that have some barrens on HPV-OPSCC. In this population, smoking status and homosexually perceived orientation did not. These findings suggest that more work is needed to understand the risk associated with the male population developing OPSCC. Although patients with HPV-positive OPSCC have a higher survival rate than those with OPSCC-HPV-negative, treatment may diminish their

quality of life (Hay & Nixon, 2018). Diminished quality of life leads to a burden on the patient as well as caregivers.

The theoretical framework of social cognitive theory, using four of its six principles, reciprocal determination, observation, learning, reinforcement, and expectation, helps to understand one social environment and the perceived susceptibility influence of risky behavior. Professional practices are responsible for informing their patients of the risk of developing HPV and the preventative measures of the HPV vaccine, as well as preventive education on reducing the risk of sexual behaviors, such as the use of protection and annual testing for HPV. Because routine HPV testing is unavailable to males, I hope research such as this prompts medical companies to develop testing for males during urological exams.

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