



## REVIEW ARTICLE

## Reducing HPV-Associated Oropharyngeal Cancer Risk and Exploring the Role of Safe Sexual Activity and Behavioral Modifications

Chinonyelum Emmanuel Agbo, B.Pharm<sup>1\*</sup>, Uzochukwu Emmanuel Chima, B.Pharm<sup>1</sup>, Olanrewaju Faith Omotayo, B.Pharm<sup>1,2</sup>, Jideofor Collins Amoke, B.Pharm<sup>1</sup>, Mmesomachi Sylvia Mbaji, B.Pharm<sup>1</sup>, Onyebuchi Oliver Offor, B.Pharm<sup>1</sup>, Sunday Chibueze Ogbobe, B.Pharm<sup>1</sup> and Abdulmuminu Isah, PhD<sup>1</sup>

<sup>1</sup>Faculty of Pharmaceutical Sciences, University of Nigeria Nsukka, Enugu State, Nigeria

<sup>2</sup>University of the People, California



\*Corresponding author: Chinonyelum Emmanuel Agbo, B.Pharm, Faculty of Pharmaceutical Sciences, University of Nigeria Nsukka, Enugu State, Nigeria, Tel: +234-7062223437

### Abstract

Human Papillomavirus (HPV) is the most prevalent sexually transmitted infection, posing a significant public health concern with HPV-associated oropharyngeal cancer emerging as the most common HPV-associated cancer (HPV-aOC). Risky sexual behaviours, notably, oral sex emerge as a critical risk factor for HPV-aOC. Despite its profound impact, there exists a poor awareness of the connection between HPV and oropharyngeal cancer, coupled with suboptimal vaccine uptake. By elucidating the nexus between sexual behaviour and HPV-aOC, this paper aims to foster a paradigm shift towards modified sexual activity, ultimately leading to a reduced risk of HPV-aOC. This study also advocates for multi-faceted approaches such as the use of protective barriers, reducing the number of oral sex partners, increasing awareness through public health education, and augmenting vaccine uptake to limit the prevalent risks of HPV-aOC. Through these concerted efforts, it is envisaged that the incidence and prevalence of HPV-aOC can be mitigated.

### Keywords

HPV, Oropharyngeal cancer, Risky sexual behaviours, Oral sex, Recommendations

### Introduction

Head and neck cancers are malignancies located in the oral cavity, hypopharynx, and oropharynx [1]. The oropharynx is located at the back of the mouth,

extending from the soft palate to the base of the tongue. With an estimated yearly burden of 563,826 incident cases (including 274,850 oral cavity cancers, 159,363 larynx cancers, and 52,100 oropharynx cancers) and 301,408 deaths, head and neck cancer is the sixth most frequent cancer in the world [2]. In general, head and neck cancer incidence has declined in recent years in the United States, which is consistent with the country's declining cigarette use [3,4]. In contrast, it appears that the prevalence of HPV-associated oropharyngeal cancer (HPV-aOC) is rising [5-7]. Human Papillomavirus (HPV) is the most prevalent sexually transmitted infection [8]. Almost anyone who engages in sexual activity will contract HPV incidentally at some point in their lifetime due to its widespread distribution [9]. One of the cancers whose incidences are rising the fastest in high-income nations is oropharyngeal squamous cell carcinoma (OPSCC), which is HPV-associated [10]. Studies have identified HPV as the cause of 71% and 51.8% of all oropharyngeal cancers in the UK and the USA, respectively [6,11-13]. Several studies have shown a significant relationship between sexual activity and HPV-aOC [14-17]. These studies show a link between HPV-aOC and some risky sexual behaviours like oral sex, multiple sexual partners, same-sex partners and even passionate kissing. Given that these sexual behaviours persist among individuals, it is imperative to bolster



**Citation:** Agbo CE, Chima UE, Omotayo OF, Amoke JC, Mbaji MS, et al. (2024) Reducing HPV-Associated Oropharyngeal Cancer Risk and Exploring the Role of Safe Sexual Activity and Behavioral Modifications. Int J Oral Dent Health 10:164. doi.org/10.23937/2469-5734/1510164

**Accepted:** June 12, 2024; **Published:** June 14, 2024

**Copyright:** © 2024 Agbo CE, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

awareness and foster a shift towards healthier, more respectful expressions of intimacy.

This paper endeavours to investigate the correlation between HPV-aOC and risky sexual behaviours and to further propose effective strategies for mitigating high-risk sexual behaviours, and ultimately preventing its prevalence.

## HPV Types and Strains

HPV encompasses a wide array of types and strains, each with distinct characteristics that influence its transmission dynamics and association with various diseases, including oropharyngeal cancer. HPV strains are characterized according to their oncogenic potentials into; high-risk (HPV 16, 18); intermediate (HPV 29, 31, 33, 45, 51, 56, 58, and 59) and low-risk strains (6 and 11) [18-20]. The low-risk HPV strains are primarily responsible for genital warts, representing 15% of all cases [21], and benign lesions in the genital and oropharyngeal regions [22]. While they can be transmitted through sexual activity, they are less likely to lead to severe health complications. HPV 16 and 18 are the most concerning in terms of their association with oropharyngeal cancer, with HPV 16 responsible for at least 85% of all HPV-positive oropharyngeal cancers [10], 50% of all cervical cancers [23]. They are transmitted primarily through sexual activity, particularly through oral-genital contact. These high-risk types categorized thus, can persist in mucosal tissues and have a greater propensity to cause malignant transformations, making them significant contributors to oropharyngeal and cervical cancers [24]. HPV types and strains play a crucial role in the context of sexual transmission, and understanding these strains is crucial for managing associated health risks.

## HPV High-Risk Groups and the Associated Factors

### Socio-demographic and economic factors

While oropharyngeal cancer has historically been linked to tobacco and alcohol use [25-28], the landscape has shifted due to the rising incidence of HPV-related cases, necessitating a reevaluation of at-risk populations. HPV is a prevalent infection that can affect individuals across various demographics, with certain groups at a higher risk of contracting the cancer. Young adults typically aged 15-24, are particularly susceptible to HPV due to their increased engagement in sexual activity [29]. Oropharyngeal cancer affects both males and females alike, although a disproportionate high prevalence (3.5-4.8 times higher) have been attributed to males [30], particularly due to an associated likelihood of males to initiate both oral sex and vaginal sexual intercourse earlier than women. More so, there is a noticeable rise in the incidence of HPV-aOC in White men aged  $\geq 65$  years with 10% of cases reported in men aged  $\geq 70$  years [31,32]. Nevertheless, HPV-aOC prevalence persists in both younger and older persons, and while the burden

is shifting in favour of older persons, higher prevalence is still recorded in those under 65 years [33-35]. Race or ethnic affiliations also presents as a risk factor for HPV-aOC. Although, an increasing prevalence has been observed among Blacks and Hispanic Americans [32,36], a significant lower prevalence is seen among Blacks (ranges from 4% to 46.3%) than Whites (34% to 70.2%) [36,37].

Socioeconomic factors also play a pivotal role in determining health outcomes, including the risk and prognosis of HPV-aOC. These factors encompass various elements of an individual's social and economic circumstances, influencing their access to healthcare, health behaviors, and overall well-being. Socioeconomic status (SES) often dictates an individual's access to healthcare services, including routine check-ups, cancer screenings, and HPV vaccination. Those with lower socioeconomic status may face barriers such as limited healthcare coverage, lack of transportation, or inadequate healthcare facilities, delaying diagnosis and treatment [38,39]. In the US, poor health-related quality of life outcomes are strongly correlated with lower SES; this correlation may be due in part to older persons from lower-income families having less access to healthcare [40]. Additionally, socioeconomic disparities can impact the uptake of the vaccines; as individuals from lower-income backgrounds may have less access to vaccination programs while lower vaccination rates in underserved populations can contribute to a higher risk of HPV-aOC. Socioeconomic factors can influence health literacy and awareness [41], regarding HPV and its association with oropharyngeal cancer. As such, individuals with lower education levels may be less informed about preventive measures, including vaccination and safe sexual practices. Socioeconomic disparities can lead to differences in lifestyle choices, including tobacco and alcohol use, which are additional risk factors for oropharyngeal cancer. People with limited resources may be more likely to engage in high-risk behaviors due to stressors and coping mechanisms. Socioeconomic factors are often linked to geographic disparities in healthcare access and infrastructure. Rural and underserved areas may lack specialized cancer treatment centers, making it difficult for residents to receive timely and appropriate care. Income inequality within a society can exacerbate disparities in oral cancer outcomes [42] and as such, higher-income individuals may have better access to early detection and treatment options, leading to improved survival rates. Socioeconomic disadvantages such as low income, savings, or education level can expose individuals to psychosocial stressors, which may weaken the immune system and potentially contribute to the progression of HPV infections to cancer [40]. Nevertheless, an increased incidence of HPV-aOC is also linked to higher SES [43], which perhaps explains its higher prevalence in developed countries like USA and UK than developing

countries like sub-Saharan African countries [44-48]. As posited by Blumberg, et al. this low prevalence stems from the limited practice of oral sex in the region [48].

### Immunocompromised population

Immunocompromised populations, including individuals with weakened immune systems due to various medical conditions or treatments, face unique challenges and heightened risks when it comes to HPV-aOC [49]. HPV infections, including high-risk types like HPV 16, can persist longer and lead to a higher likelihood of cancer development in immunocompromised individuals [50]. People living with HIV/AIDS and solid organ transplant recipients of immunosuppressive medications often have compromised immune systems, which may make them more susceptible to HPV infections and their complications, including oropharyngeal cancer [49,51,52]. Regular screening and early detection are critical for this population, as they may experience faster disease progression. Routine monitoring and HPV vaccination before transplantation can help reduce the risk. Cancer treatments like chemotherapy and radiation therapy can also suppress the immune system temporarily, increasing the risk of HPV-aOC. Early diagnosis of these conditions and appropriate medical management are crucial to reducing the risk of HPV-aOC.

### Awareness Level of HPV-aOC

Awareness of HPV is a very important factor as it helps in the early diagnosis of HPV. The raised awareness may potentially be a significant factor in raising vaccination rates, thereby, reducing the mortality rates and improving the sexual health of the public. A study identified males, individuals over the age of 65, those with poor levels of education, and current smokers all had a lack of understanding of HPV [53]. Only 29.2% of those who had heard of HPV and Oropharyngeal cancer in the survey had any knowledge of the link between the two. Only 49.7% of people were aware that an HPV vaccine was available. Also, Parsel, et al. found that the percentage of people in the general public and medical professionals who were familiar with HPV ranged from 16% to 75% and 21% to 84%, respectively [54]. Health care practitioners (HCPs) had higher awareness of HPV-aOC, ranging from 22% to 100%, than the public, which had a range of 7% to 57%. Furthermore, Osazuwa-Peters, et al. discovered that the knowledge of HPV-aOC decreased by 5.0% for every year of age increase, and that this decline was worse in men, black people compared to white people, and those with a high school diploma or less compared to college graduates [55]. The results of these surveys indicate that the public awareness of HPV and its association with oropharyngeal cancer is lacking. With these studies it has been established that people with lower levels of education have little to no knowledge on HPV. It has also been noted that as much as more healthcare workers are aware (though not an

impressive number of them) of the HPV and its dangers there is still a large gap in the awareness of the general public. This gives a call for improvement of awareness of HPV-aOC especially in schools by creating brochures, integrating it into school curriculum, special day or monthly awareness dedicated to educating the general public on HPV, engaging community organizations, partnering with HCPs and celebrity endorsements to raise awareness on social media platforms, establish an enabling environment for the community to be able to give feedbacks and ask questions pertaining HPV and sexual health. These will go a long way in improving the awareness of HPV in teenagers and adults alike and among the public thereby improving sexual behavior, vaccination rate and the overall health of the general public.

### Attitude towards HPV Vaccine Uptake

A vaccine is defined as a biological preparation that enhances active acquired immunity to a particular disease. A person's immune system interprets the virus-like particles (VLPs) present in HPV vaccines as invaders after receiving the vaccine [56]. The immune system thus produces antibodies that are focused on these VLPs. These antibodies stay in the body and provide resistance by recognizing and neutralizing the virus if the person is exposed to the actual HPV virus [57,58]. To be most effective, HPV vaccination must be given before potential HPV exposure, which is typically before being sexually active. The HPV vaccine is commonly given among young adolescents, mostly between the ages of 11 and 12. Vaccination is recommended for both boys and girls. For older people who have not been vaccinated, catch-up vaccinations may be recommended [59,60].

Oropharyngeal cancer, in addition to other HPV cancers, can be prevented with the use of the three FDA approved HPV vaccines: Gardasil®, Gardasil-9®, and Cervarix®. The potential use of the HPV vaccine could be for two purposes, namely, prophylactically (when there is no HPV infection), therapeutically (for the treatment of an already infected person), or both [61,62]. HPV vaccine uptake varies significantly from country to country. There are some countries with higher immunization rates than others due to factors including price, availability, public awareness, and immunization policies that vary by country. In comparison to other countries, some have lower HPV vaccination coverage rates in their national immunization programs. In the last 12 years, national HPV vaccination programs have been implemented in over 80 countries, the majority of which are high- or upper-middle-income nations. In contrast, the introduction of vaccines is most difficult in low- and lower-middle-income nations [63].

HPV vaccine uptake is negatively impacted by several myths, practices, attitudes, and beliefs thereby leading to lower vaccination rates [64]. We look at some non-

vaccination-related issues that have drawn particular attention, such as mistrust due to the perceived "newness" of HPV vaccines and worries about sexual risk compensation, insufficient vaccination advice from healthcare professionals, and concerns about sexual risk compensation [64]. Parental consent is also a factor militating the uptake of the HPV vaccine. This is because some parents lack awareness of the HPV vaccine's safety and efficacy [59]. A study found that knowledge of HPV and the vaccination significantly increased vaccine acceptance, with healthcare professionals, families, and familiarity with vaccine recipients serving as effective information sources. Therefore, perceptions of safety and efficacy, knowledge and awareness, recommendations from medical professionals, and information sources all have an impact on attitudes toward HPV vaccine uptake [65]. Higher understanding of vaccines, obtaining childhood vaccinations, being older, having health insurance, using healthcare more frequently, having a healthcare practitioner as a source of information, and having positive attitudes toward vaccination were all linked to higher vaccine uptake [66].

### Risky Sexual Behaviours associated with HPV-aOC

High-risk sexual behaviour is the primary risk factor for the development of HPV-related cancers and the acquisition and persistence of HPV infection [67]. The virus is primarily transmitted through sexual contact, making sexually active individuals more vulnerable. High-risk sexual behaviors, such as having multiple sexual partners, not practicing safe sex, early sexual debut - both age at first vaginal or first oral intercourse, casual travel sex, infidelity, engaging in oral-genital contact also increases the likelihood of HPV transmission [16,68,69]. These behaviours can lead to a higher exposure to the virus and subsequently oropharyngeal cancer. Men who have sex with men are also at a high risk due to the higher prevalence of HPV in this population [70]. The growing incidence of HPV-associated oropharyngeal cancer, which has surpassed cervical cancer as the most common HPV-associated malignancy, is particularly attributed to oral sex behaviours and is connected to oral sexual practices (Chung, et al. 2014; D'Souza, et al. 2009). Increase in the number of recent oral sex partners or open-mouthed kissing partner leads to increase in oropharyngeal cancer [16]. Also, high-risk HPV infection was > 50% higher in women who use oral contraceptives [71]. Thus, oral contraceptive use suggests an incidence of high-risk sexual behaviours.

### Recommendations for Behavioural Modifications and Risk Reduction Strategies

One way to prevent HPV-aOC is through prophylactic HPV vaccination, while the other way is to stop the disease from progressing by finding it early and treating it. A proof-of-principle trial showed excellent vaccine efficacy against a single detection of oral HPV 16/18

infection, suggesting that immunization is a promising primary preventive strategy [72]. Oropharyngeal HPV prevalence has been found to be less common among those who have had vaccinations than among those who have not. In the current and future vaccination cohorts of boys and girls, the impacts of the vaccination program will result in a considerable decrease in the risks of HPV-aOC. Therefore, because immunization confers collective immunity against oropharyngeal HPV, adolescents and all other eligible people should receive the HPV vaccine, ideally before sexual activity. Although vaccination is still the best defense against HPV infection and diseases linked to HPV, alternative approaches offer varying degrees of protection [73]. To assist in the fight against oropharynx malignancies, screening, test, and examination intended to discover cancer in persons without symptoms, can be done [74]. The foundation of screening is a diagnostic method that seeks to enhance survival by detecting disease at an earlier stage than it would otherwise be [75]. Medical professionals and the government should support and offer screening programs for those who engage more in oral sex with more partners or start oral sexual activity at a young age. Additionally, for immunocompromised patients, a three-dose regimen rather than the normal two-dose regimen is recommended [51].

Furthermore, barriers such as male condoms, dental dams, and plastic food wrap should be promoted to stop oropharyngeal transmission of other STIs, such as gonorrhoea and HIV [76]. People who are not immunized should use condoms, avoid unprotected oral sex, and other high-risk sexual activity. Public health campaigns and awareness activities should be implemented to caution young teens against having intercourse without a condom.

Additionally, smoking should be avoided because it raises the incidence of oropharyngeal HPV. This can be avoided by monitoring the populace for tobacco use, counseling, educating them, and offering those who use tobacco products cessation intervention [77]. Other behavioral modifications for oropharyngeal cancer include limiting the number of oral sexual partners, being open and truthful with partners about sexual history and HPV, seeking support or counseling if you or your partner have been diagnosed with an HPV-related condition, avoiding risky sexual behaviors like unprotected oral sex with partners who have unknown or high-risk sexual histories, and getting regular health checks (Table 1).

### Conclusion

In conclusion, the high prevalence of HPV-aOC necessitates urgent action, with a critical focus on risky sexual behaviors, notably oral sex. This analysis illuminates the pressing need for targeted awareness campaigns, emphasizing the link between oral sex and HPV transmission. Educating individuals,

**Table 1:** Recommendations for Reduced HPV-aOC Prevalence.

Factors associated with increased HPV-aOC	
Oral sex	<ul style="list-style-type: none"> <li>• Use of protective barriers</li> <li>• Reduction in number of oral sex partners</li> </ul>
Smoking	<ul style="list-style-type: none"> <li>• Cessation of smoking</li> </ul>
Vaccine hesitancy	<ul style="list-style-type: none"> <li>• Increased vaccine uptake through public health awareness</li> </ul>
Poor Awareness of HPV-aOC	<ul style="list-style-type: none"> <li>• Increased public health education especially by health professionals</li> </ul>

especially the youth, about the risks associated with multiple sexual partners and unprotected oral sex is paramount. Encouraging responsible sexual behavior and advocating for protection during oral activities are central to prevention strategies. Equitable access to HPV vaccination and regular screenings, coupled with fostering open dialogues about sexual health, are pivotal in curbing HPV-aOC. Collaborative efforts must prioritize addressing oral sex as a significant risk factor, shaping a future where informed choices lead to reduced HPV-aOC prevalence.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Funding Source

No funding was received for the preparation of this manuscript.

### Author's Declaration

CEA and UEC developed the concept for the paper. All the authors were involved in drafting the full manuscript.

### References

- Du J, Nordfors C, Åhrlund-Richter A, Sobkowiak M, Romanitan M, et al. (2012) Prevalence of oral human papillomavirus infection among youth, Sweden. *Emerg Infect Dis* 18: 1468-1471.
- Parkin DM, Bray F, Ferlay J, Pisani P (2005) Global Cancer Statistics, 2002. *CA Cancer J Clin* 55: 74-108.
- CDC (2023) U.S. Adult Tobacco Product Use Decreased from 2019 to 2020. CDC Online Newsroom.
- CNN (2023) US cigarette smoking rate falls to historic low, but e-cigarette use keeps climbing.
- Ryerson AB, Peters ES, Coughlin SS, Chen VW, Gillison ML, et al. (2008) Burden of potentially human papillomavirus-associated cancers of the oropharynx and oral cavity in the US, 1998-2003. *Cancer* 113: 2901-2909.
- Chaturvedi AK, Engels EA, Anderson WF, Gillison ML (2008) Incidence trends for human papillomavirus-related and -unrelated oral squamous cell carcinomas in the United States. *J Clin Oncol* 26: 612-619.
- Shiboski CH, Schmidt BL, Jordan RCK (2005) Tongue and tonsil carcinoma: Increasing trends in the U.S. population ages 20-44 years. *Cancer* 103: 1843-1849.
- CDC (2023) HPV, the Vaccine for HPV, and Cancers Caused by HPV.
- Sheedy T, Heaton C (2019) HPV-associated oropharyngeal cancer. *J Am Acad Physician Assist* 32: 26-31.
- Lechner M, Liu J, Masterson L, Fenton TRV (2022) HPV-associated oropharyngeal cancer: epidemiology, molecular biology and clinical management. *Nat Rev Clin Oncol* 19: 306-327.
- Schache AG, Powell NG, Cuschieri KS, Robinson M, Leary S, et al. (2016) HPV-related oropharynx cancer in the United Kingdom: An evolution in the understanding of disease etiology. *Cancer Res* 76: 6598-6606.
- Gillison ML, Chaturvedi AK, Anderson WF, Fakhry C (2015) Epidemiology of human papillomavirus-positive head and neck squamous cell carcinoma. *J Clin Oncol* 33: 3235-3242.
- Senkomago V, Jane Henley S, Thomas CC, Mix JM, Markowitz LE, et al. (2019) Human Papillomavirus-Attributable Cancers-United States, 2012-2016. *MMWR Morb Mortal Wkly Rep* 68: 724-728.
- Bahl A, Kumar P, Dar L, Mohanti BK, Sharma A, et al. (2013) Prevalence and trends of human papillomavirus in oropharyngeal cancer in a predominantly north Indian population. *Head Neck* 36: 505-510.
- D'Souza G, Kreimer AR, Viscidi R, Pawlita M, Fakhry C, et al. (2007) Case-control study of human papillomavirus and oropharyngeal cancer. *N Engl J Med* 356: 1944-1956.
- D'Souza G, Agrawal Y, Halpern J, Bodison S, Gillison ML (2009) Oral sexual behaviors associated with prevalent oral human papillomavirus infection. *J Infect Dis* 199: 1263-1269.
- Dahlstrom KR, Li G, Tortolero-Luna G, Wei Q, Sturgis EM (2011) Differences in history of sexual behavior between patients with oropharyngeal squamous cell carcinoma and patients with squamous cell carcinoma at other head and neck sites. *Head Neck* 33: 847-855.
- Maria Salavastru C, Cristina Niculescu M, Zota A, Nicola G, Morariu HS, et al. (2014) Epidemiological aspects of genital warts in Romania - a 2012 retrospective survey. *Maedica* 9: 144-150.
- Škamperle M, Kocjan BJ, Maver PJ, Seme K, Poljak M (2013) Human papillomavirus (HPV) prevalence and HPV type distribution in cervical, vulvar, and anal cancers in central and eastern Europe. *Acta Dermatovenerol Alp Pannonica Adriat* 22: 1-5.
- Voidăzan S, Tarcea M, Morariu SH, Grigore A, Dobreanu M (2016) Human papillomavirus vaccine - Knowledge and attitudes among parents of children aged 10-14 years: A cross-sectional study, Tirgu Mureș, Romania. *Cent Eur J Public Health* 24: 29-38.
- Boda D, Neagu M, Constantin C, Voinescu RV, Caruntu C, et al. (2016) HPV strain distribution in patients with genital warts in a female population sample. *Oncol Lett* 12: 1779-1782.
- Shah UK (2020) Acute and chronic infections of the oral cavity and pharynx. *Pediatric Otolaryngology* 2007: 138-150.
- Mirabello L, Clarke M, Nelson C, Dean M, Wentzensen N, et al. (2018) The intersection of HPV epidemiology, genomics

- and mechanistic studies of HPV-mediated carcinogenesis. *Viruses* 10: 80.
24. Cervical Cancer Causes, Risk Factors, and Prevention - NCI (2023) National Cancer Institute.
25. Yang Z, Sun P, Dahlstrom KR, Gross N, Li G (2023) Joint effect of human papillomavirus exposure, smoking and alcohol on risk of oral squamous cell carcinoma. *BMC Cancer* 23: 457.
26. Anantharaman D, Muller DC, Lagiou P, Ahrens W, Holcátová I, et al. (2016) Combined effects of smoking and HPV16 in oropharyngeal cancer. *Int J Epidemiol* 45: 752-761.
27. Kumar R, Rai AK, Das D, Das R, Kumar RS, et al. (2015) Alcohol and Tobacco Increases Risk of High Risk HPV Infection in Head and Neck Cancer Patients: Study from North-East Region of India. *PLoS One* 10: e0140700.
28. Lai YH, Su CC, Wu SY, Hsueh WT, Wu YH, et al. (2022) Impact of Alcohol and Smoking on Outcomes of HPV-Related Oropharyngeal Cancer. *J Clin Med* 11: 6510.
29. Gearhart PA (2020) Human papillomavirus (HPV): Practice essentials, background, pathophysiology. *Medscape*.
30. Osazuwa-Peters N, Adjei Boakye E, Rohde RL, Ganesh RN, Moyadi AS, et al. (2019) Understanding of risk factors for the human papillomavirus (HPV) infection based on gender and race. *Sci Rep* 9: 297.
31. Rettig EM, Fakhry C, Khararjian A, Westra WH (2018) Age Profile of Patients with Oropharyngeal Squamous Cell Carcinoma. *JAMA Otolaryngol Head Neck Surg* 144: 538-539.
32. Tota JE, Best AF, Zumsteg ZS, Gillison ML, Rosenberg PS, et al. (2019) Evolution of the oropharynx cancer epidemic in the United States: Moderation of increasing incidence in younger individuals and shift in the burden to older individuals. *J Clin Oncol* 37: 1538-1546.
33. Mahal BA, Catalano PJ, Haddad RI, Hanna GJ, Kass JI, et al. (2019) Incidence and demographic burden of hpv-associated oropharyngeal head and neck cancers in the United States. *Cancer Epidemiol Biomarkers Prev* 28: 1660-1667.
34. Zumsteg ZS, Cook-Wiens G, Yoshida E, Shiao SL, Lee NY, et al. (2016) Incidence of oropharyngeal cancer among elderly patients in the United States. *JAMA Oncol* 2: 1617-1623.
35. Chaturvedi AK, Zumsteg ZS (2018) A snapshot of the evolving epidemiology of oropharynx cancers. *Cancer* 124: 2893-2896.
36. Faraji F, Rettig EM, Tsai H, Asmar MI, Fung N, et al. (2019) The prevalence of human papillomavirus in oropharyngeal cancer is increasing regardless of sex or race, and the influence of sex and race on survival is modified by human papillomavirus tumor status. *Cancer* 125: 761-769.
37. Settle K, Posner MR, Schumaker LM, Tan M, Suntharalingam M, et al. (2009) Racial survival disparity in head and neck cancer results from low prevalence of human papillomavirus infection in black oropharyngeal cancer patients. *Cancer Prev Res* 2: 776-781.
38. Lazar M, Davenport L (2018) Barriers to health care access for low income families: A review of literature. *J Community Health Nurs* 35: 28-37.
39. Labban M, Chen CR, Frego N, Nguyen DD, Lipsitz SR, et al. (2023) Disparities in travel-related barriers to accessing health care from the 2017 national household travel survey. *JAMA Netw Open* 6: e2325291.
40. McMaughan DJ, Oloruntoba O, Smith ML (2020) Socioeconomic status and access to healthcare: Interrelated drivers for healthy aging. *Front Public Heal* 8: 231.
41. Yilmazel G, Cetinkaya F (2016) The importance of health literacy for community health. *TAF Prev Med Bull* 15: 69.
42. Johnson NW, Warnakulasuriya S, Gupta PC, Dimba E, Chindia M, et al. (2011) Global oral health inequalities in incidence and outcomes for oral cancer: causes and solutions. *Adv Dent Res* 23: 237-246.
43. Liederbach E, Kyrillos A, Wang CH, Liu JC, Sturgis EM, et al. (2017) The national landscape of human papillomavirus-associated oropharynx squamous cell carcinoma. *Int J Cancer* 140: 504-512.
44. Ndiaye C, Alemany L, Diop Y, Ndiaye N, Diémé MJ, et al. (2013) The role of human papillomavirus in head and neck cancer in Senegal. *Infect Agent Cancer* 8: 14.
45. Oga EA, Schumaker LM, Alabi BS, Obaseki D, Umana A, et al. (2016) Paucity of HPV-related head and neck cancers (HNC) in Nigeria. *PLoS One* 11: e0152828.
46. Rettig EM, Gooi Z, Bardin R, Bogale M, Rooper L, et al. (2019) Oral human papillomavirus infection and head and neck squamous cell carcinoma in rural Northwest Cameroon. *OTO Open* 3: 2473974X18818415.
47. Kofi B, Mossoro-Kpinde CD, Mboumba Bouassa RS, Péré H, Robin L, et al. (2019) Infrequent detection of human papillomavirus infection in head and neck cancers in the Central African Republic: a retrospective study. *Infect Agent Cancer* 14: 9.
48. Blumberg J, Monjane L, Prasad M, Carrilho C, Judson BL (2015) Investigation of the presence of HPV related oropharyngeal and oral tongue squamous cell carcinoma in Mozambique. *Cancer Epidemiol* 39: 1000-1005.
49. Hewavisenti RV, Arena J, Ahlenstiel CL, Sasson SC (2023) Human papillomavirus in the setting of immunodeficiency: Pathogenesis and the emergence of next-generation therapies to reduce the high associated cancer risk. *Front Immunol* 14: 1112513.
50. Fontaine J, Hankins C, Money D, Rachlis A, Pourreaux K, et al. (2008) Human papillomavirus type 16 (HPV-16) viral load and persistence of HPV-16 infection in women infected or at risk for HIV. *J Clin Virol* 43: 307-312.
51. Garland SM, Brotherton JML, Moscicki AB, Kaufmann AM, Stanley M, et al. (2017) HPV vaccination of immunocompromised hosts. *Papillomavirus Res* 4: 35-38.
52. Reusser N, Downing C, Guidry J, Tying S (2015) HPV carcinomas in immunocompromised patients. *J Clin Med* 4: 260-281.
53. Verhees F, Demers I, Schouten LJ, Lechner M, Speel EJM, et al. (2021) Public awareness of the association between human papillomavirus and oropharyngeal cancer. *Eur J Public Health* 31: 1021-1025.
54. Parsel SM, Barton BM, Beatty S, Friedlander PL (2020) Knowledge gaps among patients and providers in hpv-related oropharyngeal cancer: A systematic review. *Otolaryngol Head Neck Surg* 162: 612-621.
55. Osazuwa-Peters N, Boakye EA, Chen BY, Clancy J, Vallot PL, et al. (2017) Sociodemographic factors associated with knowledge and risk perception of human papillomavirus and human papillomavirus-associated oropharyngeal squamous cell carcinoma among a predominantly black population. *JAMA Otolaryngol Neck Surg* 14: 117-124.
56. Roldão A, Mellado MCM, Castilho LR, Carrondo MJ, Alves PM (2010) Virus-like particles in vaccine development. *Expert Rev Vaccines* 9: 1149-1176.

57. Grgacic EVL, Anderson DA (2006) Virus-like particles: Passport to immune recognition. *Methods* 40: 60-65.
58. Wu X, Ma X, Li Y, Xu Y, Zheng N, et al. (2019) Induction of neutralizing antibodies by human papillomavirus vaccine generated in mammalian cells. *Antib Ther* 2: 45-53.
59. Brabin L, Roberts SA, Farzaneh F, Kitchener HC (2006) Future acceptance of adolescent human papillomavirus vaccination: A survey of parental attitudes. *Vaccine* 24: 3087-3094.
60. Takla A, Wiese-Posselt M, Harder T, Meerpohl J, Röbl-Mathieu M, et al. (2018) Background paper for the recommendation of HPV vaccination for boys in Germany. *Bundesgesundheitsblatt Gesundheitsforsch Gesundheitsschutz* 61: 1170-1186.
61. Takes RP, Wierzbicka M, D'Souza G, Jackowska J, Silver CE, et al. (2015) HPV vaccination to prevent oropharyngeal carcinoma: What can be learned from anogenital vaccination programs? *Oral Oncol* 51: 1057-1060.
62. Casswell G, Gough K, Drosdowsky A, Bressel M, Coleman A, et al. (2021) Sexual health and interpersonal relationships after chemoradiation therapy for human papillomavirus-associated oropharyngeal cancer: A cross-sectional study. *Int J Radiat Oncol Biol Phys* 110: 382-393.
63. Gallagher KE, LaMontagne DS, Watson-Jones D (2018) Status of HPV vaccine introduction and barriers to country uptake. *Vaccine* 36: 4761-4767.
64. Zimet GD, Rosberger Z, Fisher WA, Perez S, Stupiansky NW (2013) Beliefs, behaviors and HPV vaccine: Correcting the myths and the misinformation. *Prev Med* 57: 414-418.
65. Cocchio S, Bertoncetto C, Baldovin T, Fonzo M, Bennici SE, et al. (2020) Awareness of HPV and drivers of HPV vaccine uptake among university students: A quantitative, cross-sectional study. *Heal Soc Care Community* 28: 1514-1524.
66. Kessels SJM, Marshall HS, Watson M, Braunack-Mayer AJ, Reuzel R, et al. (2012) Factors associated with HPV vaccine uptake in teenage girls: A systematic review. *Vaccine* 30: 3546-3556.
67. Rettig E, Kiess AP, Fakhry C (2015) The role of sexual behavior in head and neck cancer: implications for prevention and therapy. *Expert Rev Anticancer Ther* 15: 35-49.
68. Antonsson A, de Souza MMA, Panizza BJ, Whiteman DC (2022) Sexual debut and association with oral human papillomavirus infection, persistence and oropharyngeal cancer-An analysis of two Australian cohorts. *Int J Cancer* 151: 764-769.
69. Sikström B, Hellberg D, Nilsson S, Brihmer C, Mårdh PA (1996) Sexual risk behavior in women with cervical human papillomavirus infection. *Arch Sex Behav* 25: 361-372.
70. Mistry HB, Lebelo RL, Matshonyonge F, Nchabeleng M, Mathebula M, et al. (2022) Oral and oropharyngeal high-risk HPV prevalence, HIV status, and risk behaviours in a cohort of South African men who have sex with men. *AIMS Public Heal* 9: 129-141.
71. Cotton SC, Sharp L, Seth R, Masson LF, Little J, et al. (2007) Lifestyle and socio-demographic factors associated with high-risk HPV infection in UK women. *Br J Cancer* 97: 133-139.
72. Kreimer AR (2014) Prospects for prevention of HPV-driven oropharynx cancer. *Oral Oncol* 50: 555-559.
73. Dahlstrom KR, Day AT, Sturgis EM (2021) Prevention and screening of HPV malignancies. *Semin Radiat Oncol* 31: 297-308.
74. Vlantis AC (2016) Human papilloma virus and oropharyngeal carcinoma - lessons from history. *Chinese J Dent Res* 19: 9-16.
75. Kreimer AR, Shiels MS, Fakhry C, Johansson M, Pawlita M, et al. (2018) Screening for human papillomavirus-driven oropharyngeal cancer: Considerations for feasibility and strategies for research. *Cancer* 124: 1859-1866.
76. Gupta A, Perkins RB, Ortega G, Feldman S, Villa A (2019) Barrier use during oro-genital sex and oral Human Papillomavirus prevalence: Analysis of NHANES 2009–2014. *Oral Dis* 25: 609-616.
77. Timbang MR, Sim MW, Bewley AF, Farwell DG, Mantravadi A, et al. (2019) HPV-related oropharyngeal cancer: a review on burden of the disease and opportunities for prevention and early detection. *Hum Vaccin Immunother* 15: 1920-1928.