

Oral sex and oropharyngeal cancer

The role of the primary care physicians

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Abstract

Background: We aimed to study the prevalence of oral sex and its possible association with human papillomavirus (HPV) 16 infection in the development of oropharyngeal cancer in the US population for possible prevention.

Methods: We conduct a systemic review on the prevalence of oral sex among Americans among different age groups, the prevalence of HPV 16 infection reported in oropharyngeal cancer, and correlation between oral sex and oropharyngeal cancer.

Results: Oral sex is prevalent among adolescents and sexually active adults. Sixty percent of oropharyngeal cancer reported in the United States is associated with HPV 16 infections. Individuals who practiced oral sex with multiple partners are at risk for developing oropharyngeal cancer and need to be informed about practicing safe sex or getting vaccination.

Conclusion: Family physicians will play a key role in prevention and educating the public about the risk of oral sex.

Abbreviations: CIN = cervical intraepithelial neoplasia, CIS = carcinoma in situ, HIV = human immunodeficiency virus, HPV = human papilloma virus, ISH = in situ hybridization, NHANES = national health and nutritional examination survey, PCR = polymerase chain reaction, SEER = Surveillance, Epidemiology, and End Results, STD = sexually transmitted disease.

Keywords: HPV 16, oral sex, oropharyngeal cancer, prevention

1. Introduction

In the United States, the number of people between 20 and 44 years of age is estimated to be 107 million in 2010. This number is projected to increase to 118 million in 2015 based on the United Nations Population Division.^[1] This specific age group constitutes the bulk of the work force supporting the American economy and its increasing number of retirees. Thus, any disease affecting this segment of the population is expected to have lasting and serious consequences on the US economy. Recently, a report from Surveillance, Epidemiology, and End Results (SEER)

data demonstrated a statistically significant increase of oropharyngeal cancers affecting young people between the age of 20 and 44 years, encompassing all American ethnic groups.^[2,3] The incidence of tonsillar carcinoma increased at an alarming pace in the young (50 years or younger).^[4] Hence, oropharyngeal carcinoma is now recognized as a specific disease affecting the young.^[5]

The rise of oropharyngeal carcinoma in the United States has been reported to be linked with human papillomavirus (HPV) 16 infection.^[6,7] Presence of the virus DNA can be identified in oropharyngeal cancer biopsy specimens.^[8,9] Transmission of HPV 16 in head and neck cancer was reported to be through deep kissing and orogenital sex.^[10,11] The popularity of oral sex among young adults may have led to an increase of HPV 16 infection, which may be the cause for the current rise of HPV-associated oropharyngeal cancers in the United States and worldwide. The purpose of this review is to assess the prevalence of oral sex and the prevalence of HPV 16-associated oropharyngeal cancers in the US population. Understanding the factors associated with HPV epidemiology in head and neck cancer may help clinicians develop strategies to cope with this specific clinical entity in terms of treatment and prevention.

2. Methods

2.1. Literature search strategy

Electronic searches were performed in the following databases: PubMed, Embase, ISI Web of Knowledge (Web of Science), and Google Scholar. In PubMed, the term “Oral Sex” as both key words and Medical Subject Headings (MeSH) term, and the results were combined with searches for the MeSH terms HPV16, oropharyngeal cancer, and US. All “Related Citations” for results

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found in PubMed were searched as well. Embase, Web of Science, and Google Scholar were searched using the keywords noted earlier. All identified article titles were then entered into the Web of Knowledge individually, resulting in a list of articles citing the originally identified articles. This list was then culled for the inclusion in the set of articles to be reviewed.

2.2. Selection criteria

Eligible studies for the present review included those in which patients with histologically proven oropharyngeal cancer and HPV 16 infection were reported in the United States. All studies reporting the prevalence of oral sex in all age groups, heterosexual, and ethnic groups in the United States were reported. All studies reported outside of the United States were excluded. However, selected studies outside the United States may be relevant in the Discussion section but were not reported in the Results section. Abstract, case reports, conference presentations, editorials, and expert opinions were excluded. Studies reporting the prevalence of oral sex among homosexual and sex workers were also excluded as the study targets the frequency of oral sex in the general US population. All duplicated studies were also excluded.

2.3. Data extraction and critical appraisal

The findings from the initial searches were used to decide the clinical outcome of the present review. The primary outcomes were to assess the prevalence of oral sex in the United States and the prevalence of HPV 16 infection in oropharyngeal cancer in the United States. Data was extracted to analyze each article for: prevalence of oral sex in the United States from the 90's when the first study was conducted until 2015, prevalence of HPV 16 in the cancer biopsy specimen from the 90's when it was first reported in the United States until 2015. The technique of HPV 16 detection in the study was also reported as in situ hybridization (ISH) may be less sensitive than polymerase chain reaction (PCR) to identify the virus in the biopsy specimen. Under-reporting the prevalence of HPV 16 virus in oropharyngeal cancer was a possible bias associated with the method of detection. As oral sex may be a taboo subject and may not be disclosed depending on age, cultural, ethnic, and socioeconomic groups, all studies reporting oral sex were analyzed to have a crude approximation of the frequency of oral sex in the United States. As oral sex may be associated with oropharyngeal cancer, all studies linking oral sex to HPV 16-induced oropharyngeal cancer are analyzed to identify individuals at risk for developing oropharyngeal cancer.

The University of Arizona Institutional Review Board approved the study as it is a review of the literature and does not require patient consent.

3. Results

3.1. Quantity of trials

A total of 359 references were reported worldwide during the period studied through the 4 search engines after exclusion of duplicate or irrelevant references. A total of 308 were excluded after reviewing the abstract. Fifty-one full articles were assessed. Sixteen articles assessed the prevalence of oral sex. Twenty-three reported the prevalence of HPV 16 in biopsy specimens and 9 linked the prevalence of oral sex to the development of oropharyngeal cancer. After applying the selection criteria, only 23 remained for assessment. A total of 74 references were reported worldwide about the presence of HPV 16 in the biopsy

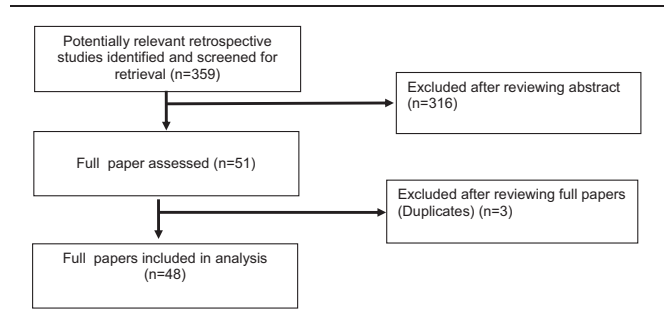


Figure 1. Prisma flow diagram of included studies.

specimen. After applying the selection criteria, only 23 remained for assessment. A total of 9 references linking oral sex to HPV-induced oropharyngeal cancer were analyzed. Figure 1 summarizes the search. As all studies were retrospective, bias could not be excluded.

3.2. Prevalence of oral sex in the United States

In 1993, Janus et al^[12] reported the first study of oral sex in America. A survey of 2765 adult men and women reported that 10% of men and 18% of women were engaged in oral genital sex. The following year, Laumann et al^[13] conducted a survey of 3432 Americans aged between 18 and 59 years regarding their sexual practice. Only 27% of the men and 19% of women reported having oral sex during the last sexual event. In 2002, Mosher et al^[14] conducted a similar survey of 12,571 people 15 to 44 years of age in the United States. This revealed that 90% of men and 88% of women had oral sex with an opposite sex partner. Orogenital sexual activity involved all ages and ethnicities. In another survey of 618 adolescents recruited from 2 California public high schools in 9th and 10th grade, 275 (44%) admitted to have oral sex only or both oral and vaginal sex.^[15] Oral sex can begin early, even in middle school children. In a study of 1279 students in this demographic, age 12 to 14 years, 101 (7.9%) reported to have oral sex.^[16] Thirty students (2.6%) had participated in oral sex when they were younger than 10 years. Among those engaged in oral sexual activity, two-third had >1 partner.^[16] Furthermore, oral sex increases progressively with age. In a survey of 12,571 American men and women aged 15 to 44 years, over 75% had oral sex.^[17] Oral sex prevalence was <50% and >80% for the 15- to 19-year-old group and older than 20 years' group, respectively. Importantly, <10% of the people practicing oral sex used condoms regardless of the age group.^[17] A recent trend among college age students is the hook up phenomenon wherein oral sex occurred in 38.4% sexual partners with no romantic attachment.^[18,19] Other studies have corroborated the strong relationship between oral sex and age.^[20-27] Table 1 summarizes oral sex prevalence according to age in the United States.^[12-27]

3.3. Prevalence of HPV 16 infection in oropharyngeal carcinoma reported in the United States

Using ISH technique or PCR, HPV 16 DNA was demonstrated in oropharyngeal cancer biopsies.^[6,8,11,28-47] Among 2824 oropharyngeal cancers reported in 23 US studies, HPV 16 was detected in 60.2% of the patients (range: 40%–87%). Table 2 summarizes the prevalence of HPV 16-induced oropharyngeal cancer in the United States.^[6,8,11,28-47]

Table 1
Prevalence of oral sex according to age in US population.

Study	No. of subjects	Age, y	Prevalence	Period of study
Janus and Janus ^[12]	2765	>18	10%–18%	1993
Lauman et al ^[13]	3432	18–59	19%–27%	1994
Mosher et al ^[14]	12,571	15–44	88%–90%	2002
Brady and Halpern-Felsher ^[15]	618	Adolescents (NS)	44%	2007
Markham et al ^[16]	1279	12–14	7.9%	2009
Lechlitter et al ^[17]	12,571	15–44	75%	2007
Lewis et al ^[18]	1468	18–25	38.4%	2010
Fielder et al ^[19]	483	18–21	40%	2012
Gates and Sonenstein ^[20]	1297	15–19	49%	2000
Bersamin and Walker ^[21]	1105	12–16	10.9%	2006
Lindberg et al ^[22]	2271	15–19	54%–55%	2008
Halpern-Felcher et al ^[23]	580	14.54 (mean)	19.6%	2005
Boekeloo and Howard ^[24]	335	12–15	18%	2002
Hans et al ^[25]	477	18–41	89%	2007
Chandra et al ^[26]	13,495	15–44	89%	2008
Copen et al ^[27]	42,099	15–24	66% (females), 65% (males)	2010

NS = not specified.

3.4. Correlation between oral sex and HPV16-induced oropharyngeal cancer

Oral sex has been implicated in the development of HPV16-induced oropharyngeal cancer. Individuals with a history of oral sex, multiple partners, and oral HPV 16 infection are at increased risk for developing cancer.^[11,36,38,40,48–51] This is highlighted by a case study of 240 patients with oropharyngeal cancer. HPV 16-positive and HPV 16-negative patients had distinct risk factors profiles. Patients positive for HPV 16 had a history of oral sex and multiple oral sex partners. In contrast, HPV-negative patients had no history of oral sex and a strong history of smoking and drinking.^[38] This is also corroborated in another

study of 356 patients with oropharyngeal cancers. Among the ones who were HPV-positive (n=315), mean life time oral sex partners were 12.8 compared to 6 for HPV-negative patients (n=41).^[42] Individuals with multiple life-time oral sex partners are particularly vulnerable to the development of HPV-induced oropharyngeal cancer. Using PCR, ISH, and serology to identify patients with and without HPV 16-induced oropharyngeal cancer, patients with viral-induced cancer had a history of ≥4 life-time oral sex partners compared to the ones without viral infection. Men may be at more risk for developing oropharyngeal cancer compared to women because of the higher number of life-time oral sex partner.^[51] Table 3 summarizes the correlation

Table 2
Prevalence of human papilloma virus 16 infection in oropharyngeal cancer reported by American institutions.

Study	No. of patients	Age	Technique	Prevalence	Year reported
Ernster et al ^[6]	72	mean 53.6	PCR	69%	2007
D'Souza et al ^[8]	100	NS	PCR	72%	2007
Smith et al ^[11]	67	NS	PCR	34%	2004
Nichols et al ^[28]	44	NS	ISH	61%	2009
Westra et al ^[29]	21	NS	ISH	57%	2008
Strome et al ^[30]	52	mean 61	PCR	40%	2002
Kong et al ^[31]	49	NS	PCR	67%	2009
Ji et al ^[32]	97	NS	PCR	72%	2009
Cohen et al ^[33]	35	mean 55.8	PCR	68%	2008
Kumar et al ^[34]	42	median 55	PCR	64%	2007
Weinberger et al ^[35]	107	median 61	PCR	61%	2004
Begum et al ^[36]	45	NS	ISH	82%	2005
Ritchie et al ^[37]	45	mean 52	PCR	42%	2003
Gillison et al ^[38]	240	NS	ISH	38%	2008
Singhi and Westra ^[39]	175	NS	ISH	87%	2010
Sivathamparam et al ^[40]	43	mean: 57	ISH	74%	2013
Jordan et al ^[41]	235	NS	PCR	67%	2012
Dahlstrom et al ^[42]	356	median: 56	ISH, PCR	87%	2015
Salazar et al ^[43]	65	median: 64	PCR	35%	2014
Worsham et al ^[44]	118	NS	PCR	43%	2013
Isayeva et al ^[45]	102	NS	ISH, PCR	55%	2013
Liu et al ^[46]	185	median: 55	PCR	40%	2015
Goodman et al ^[47]	529	NS	PCR	71%	2015
Total	2824			60.2%	

ISH = in situ hybridization, NS = not specified, PCR = polymerase chain reaction.

Table 3
Studies suggesting correlation between oral sex and HPV-16 induced oropharyngeal cancer.

Study	No. of patients	Technique of HPV detection	No. of lifetime oral sex partners
Smith et al ^[11]	67	PCR	≥4
Ritchie et al ^[36]	19	PCR	≥6
Gillison et al ^[38]	240	ISH	≥6
Sivasithamparam et al ^[40]	43	ISH	≥5
Dahlstrom et al ^[42]	315	ISH, PCR	≥12
Furniss et al ^[48]	78	Serology	≥10
Schwartz et al ^[49]	55	PCR	≥5
Herrero et al ^[50]	26	PCR	Not specified but individuals at risk often practiced oral sex
Chaturvedi et al ^[51]	9480	PCR	25 (men), 10 (women)
Total	10,323		≥7

HPV = human papilloma virus, ISH = in situ hybridization, PCR = polymerase chain reaction.

between oral sex and HPV 16-induced oropharyngeal cancer.^[11,36,38,40,42,48–51]

4. Discussion

To our knowledge, this is the first review on prevalence of oral sex and the emergence of oropharyngeal cancer affecting young American adults through HPV 16 infection. From 1993 to 2002, the percentage of American men and women who admitted to having oral sex increased from 10% to 18% to 88% to 90%. The reported increase in oral-genital contacts affects all ethnic groups, regardless of age, sex, and rural or urban areas.^[12–27] Hooking up, that is, sexual interaction between partners who are not dating or in a romantic relationship often involves oral sex because of its convenience. In a study of 483 female college students, 34% admitted to hooking up before college admission. During their first college year, 40% had hooking experience involving oral sex.^[19] More ominously, oral sex is becoming popular among adolescents and middle school children who are still psychologically immature and do not grasp the full consequences of their action.

Even though the prevalence of HPV 16 oral infection remains unknown among sexually active adolescents, epidemiologic studies in cervical cancer suggest that they are at highest risk to develop cancer as vaginal sex at young age predisposes to viral infection and development of cervical cancer.^[52]

Behavioral studies of adolescents and young adults suggest that this age group is the most vulnerable to sexually transmitted diseases because they tend to have both multiple and older partners and do not practice safe sex.^[53–54] In a study of 18,984 adolescents aged 13 to 17 years, 56% of the respondents reported >2 partners, 54% had concurrent partners, 69% had sex with older partners, and 35% had sex outside of their ethnic group.^[53] The risk of HPV genital infection is also much higher for males who started vaginal intercourse at a young age compared to older males, thus exposing their partners to oral infections if they also practiced oral sex.^[55] Condom use was infrequent among adolescents who had multiple partners and a previous history of a sexually transmitted disease.^[53–54] Therefore, it is not surprising that among youths who practiced oral sex regularly, condom use was practically nonexistent perhaps because of the misconception that oral sex is relatively safe.^[56] In a study of 867 adolescents attending a New York City public high school, 91.8% had a high knowledge about HIV transmission and prevention. However, 40% of these students thought that sexually transmitted disease (STD) germs were harbored only in the vagina or the penis and 20% did not know that condoms

could prevent transmission of venereal diseases.^[56] Increased awareness of HIV transmission through vaginal intercourse and the low risk of HIV infection through saliva make oral sex a convenient method to engage with multiple partners without the added fear of pregnancy.^[23–25] Casual attitudes among adolescents and young adults that oral sex is not real sex leads to carelessness, engaging in cunnilingus-fellatio acts with >1 partner with no or little protection.^[16,17] Among 12,571 Americans of all ethnic groups aged 15 to 44 years, only 6.4% of the men and 5.7% of the women recalled of using condoms at their last oral sex encounter.^[17] Married men and women, individuals with nonmonogamous partners or a higher number of sex partners in one's life time were less likely to use condoms during oral sex.^[17] Male sexual partners of women with genital HPV infection and carriers of HPV 16 are often asymptomatic.^[57] If these individuals engage in oral sex with multiple partners without protection, the risk of HPV transmission increases significantly. Conversely, men with multiple sex partners will most likely acquire HPV infection creating a vicious circle linked to sexual promiscuity.^[58]

Despite multiple studies on HPV infection in the genital area, little is known about the prevalence of oral HPV infection. D'Souza et al's^[6] is the first study demonstrating that oral HPV infection rates increase with deep kissing and multiple sex partners suggesting that saliva is a favorable medium for HPV transmission. Even though HPV infection is usually self-limited, in individuals with recent (<6 months) history of oral sex with multiple partners, the infection may not clear up.^[59] As an illustration, the prevalence of oral HPV infection is low (0.9%) among 334 patients with genital HPV infection.^[60] However, the rate of oral infection can increase significantly if one practice oral sex. In a study of 43 women with genital HPV 16 infection, 53% developed oral infection if they provided (fellatio) and received (cunnilingus) oral sex from their partners suggesting a strong correlation between oral sex and oral HPV infection.^[61] Long-term follow-up of women diagnosed with oral HPV infection demonstrated that 55% to 60% of the individuals infected remained infectious at 6 months' follow-up.^[62] The risk of long-term persistent HPV infection is also corroborated in a study of 148 female college students who had persistent genital infection 12 to 28 months later if they had >1 sexual partners.^[63] Thus, individuals who practice unprotected oral sex with multiple partners may be at risk for persistent infection. To date, the most compelling evidence linking oral sex and persistence of HPV 16 in the oral mucosa comes from the National Health and Nutritional Examination Survey (NHANES). The study included 2116 men and 2140 women aged 20 to 69 years who answered a survey on

sexual behavior and provided oral-rinse sample for HPV 16 detection.^[64] Oral sexual behavior was the primary determinant for oral HPV infection regardless of age, race, sex, or sexual preference. Interestingly, young men (30–44 years) had the most life time oral sexual partners and had the highest risk of HPV 16 oral infection compared to women, which raises the hypothesis that performing oral sex on a woman increased the chance for infection.^[64] More studies need to be done to investigate whether there is relationship between oral sex, oral HPV16 infection, and late development of cancer.

HPV 16 has a special predilection for the tonsillar crypts.^[65,66] Its DNA becomes integrated in the host cells inducing tonsillitis.^[67] The mechanism of malignant transformation has yet to be elucidated but has been postulated to occur through dysregulation of cell cycle check points in head and neck cancer studies.^[68,69] Among 2295 oropharyngeal cancers reported in the United States, 59.7% contained HPV 16 virus. If one postulates that oral sex started to gain popularity in the 90's because of HIV fear and the average time from HPV infection to cancer development is 12 years,^[70] one should see an increased incidence of oropharyngeal cancer in early 2000's, which would rise rapidly in the next decades as the number of people infected with oral HPV increases.

Epidemiologic studies in the United States support that hypothesis. Both SEER data from and 1973 to 2004 have confirmed the rise of oropharyngeal carcinoma, particularly tonsillar carcinoma, affecting all ethnic groups in the United States compared to other head and neck sites.^[2,4,71] Compared to older individuals, young patients (younger than 50 years) are at increased risk of developing tonsillar carcinoma. The incidence of tonsil carcinoma increased from 15% in 1974 to 1983 to 55% in 1994 to 2003 for young patients compared to 26% and 37% for older patients over the same time period.^[4] Improvement in cancer-specific survival for tonsillar cancer patients younger than 50 years suggests that the rise in oropharyngeal cancer in the young may be associated with HPV infection.^[4] In another study, the rise of tonsillar carcinoma from 1998 to 2003 in the United States was associated with a decrease of head and neck cancer in other sites.^[72] As the rate of HPV-positive oropharyngeal cancer increased by 225% from 1988 to 2004, it was estimated that the annual number of HPV-positive oropharyngeal cancers in the United States will exceed the annual number of cervical cancers by the year 2020 if the current trend continues.^[73] If one considers that the cost owing to HPV-related cervical cancer in women is already prohibitive because of years of life lost and mortality-related productivity cost,^[74] the cost owing to HPV-associated oropharyngeal cancer would be much higher because it affects both sexes and the lack of awareness that it may be associated with oral sex.

There could be a worldwide epidemic linked to oral sex as HPV-associated oropharyngeal cancer is also increasing in other countries. Nasman et al^[75] reported a steady increase in HPV-associated tonsillar carcinoma in Sweden. The incidence of HPV-positive tumors were respectively 68%, 77%, and 93% for the period reported in 2000 to 2002, 2003 to 2005, and 2006 to 2007. The increase in HPV-positive tumors was also associated with a decrease in prevalence of HPV-negative tumor in the same period suggesting an epidemic of virus-associated carcinoma.

Increased popularity of oral sex and infrequent use of condoms during fellatio may be associated with HPV infection and other orally transmitted sexual disease.^[76,77] A survey of 1373 students aged 16 to 18 years in the United Kingdom revealed that 56% had experienced fellatio or cunnilingus. Only 2% of individuals

engaged frequently in oral sex reported consistent use of condom.^[76] As a result, the incidence of other sexually transmitted disease is also rising through oral sex. A survey of European countries demonstrated a steady rise of oral syphilis from 1999 to 2007.^[77] An international study of 5642 head and neck cancer patients confirmed the hypothesis that oropharyngeal cancers were associated with the practice of oral sex.^[78] Individuals with ≥ 4 lifetime oral sex partners were at increased risk for developing oropharyngeal cancer. Men with an earlier age at sexual debut (< 18 years) were particularly vulnerable of developing tonsillar cancer. Women who practiced oral sex were at risk for developing base of tongue cancer.^[78] Therefore, unless public health measures are taken to educate the public about the risks of oral sex, prevention of oral HPV transmission, and possibly the need of HPV vaccination for both males and females adolescents, we predict a steady rise of oropharyngeal cancers in the United States and internationally. Simple measures such as use of condoms should significantly reduce the risks of HPV transmission and cancer development.^[79,80]

Vaccination should be considered in young individuals practicing oral sex as it has been proven effective in reducing the risk of HPV-induced genital warts.^[81] Family physicians will play an increasing role in educating patients about the danger of oral sex and for possible vaccination of individuals at risk. In a study of 2775 females aged 9 to 59 years, only 15.2% of individuals aged 11 to 26 years received vaccination.^[82] If efforts for HPV prevention were to be successful, both sexes should get vaccination at a young age if they practice oral sex.

HPV 16 vaccination has been proven effective to reduce the rate of genital infection and subsequent development of cervical carcinoma in situ (CIS), which is often the precursor of invasive cervical carcinoma in young women. A meta-analysis of 20,583 sexually active women aged 15 to 23 years who were randomized between placebo ($n = 10,292$) or vaccine ($n = 10,291$) demonstrate a significant reduction of grade 2 to 3 cervical intra-epithelial neoplasia (CIN) and CIS among patients who received the vaccine.^[83] Other studies also corroborated the vaccine efficacy to reduce pathogenic HPV infection and cervical cancer in young women of all ethnic groups.^[84–86] In the United States, a significant reduction of HPV-associated high-grade CIN has been observed in the period following introduction of the vaccine.^[87] Vaccination was most effective to prevent grade 3 CIN among the age group 15 to 17 years suggesting that if a similar policy is to be implemented for prevention of oropharyngeal HPV infection and cancer development, adolescents of both sexes would benefit the most from the vaccination.^[85] Preliminary study suggests that HPV 16 vaccination may decrease the risk of persistent HPV oral infection. Herrero et al^[88] reported a study of 7466 women aged 18 to 25 years who were randomized to receive HPV 16/18 vaccine or hepatitis A as placebo. Among 5840 participants who provided an oral sample for HPV 16 infection, only 1 had infection in the vaccine group compared to 15 in the control group, for an estimated vaccine efficacy (VE) of 93.3%. Corresponding efficacy against prevalent cervical HPV 16 infection for the same cohort was 72% suggesting that the vaccine may be effective to prevent both oral and cervical HPV infection. Even though the primary endpoint of the study was to assess VE for prevention of cervical carcinoma, the study raised interesting question whether it may also be effective for oropharyngeal carcinoma as 3611 participants who gave oral sample for HPV testing admitted to have oral sex with single ($n = 2105$) or multiple lifetime oral sex partners ($n = 1516$). Future

Table 4

Postulated mechanism linking oral sex to HPV 16-associated oropharyngeal cancer development and possible interventions to reduce the cancer rates in the future.

Cancer development sequence	Interventions
Personal belief: oral sex is not real sex leading to prosmicuity. Individuals at risks: multiple partners, genital HPV 16 infection, couples practicing both fellatio and cunnilingus, young age (<18 y).	Public education: oral sex is real sex with the dangers of sexually transmitted diseases.
Oral HPV 16 infection with special predilection for tonsillar crypts	Protection during oral sex (example: condoms)
Latency period	Vaccination of individuals at risks
Development of oropharyngeal cancer in young individuals	Physician awareness for early detection and treatment. Oral sex history should be elicited in young patients with tonsillar mass or neck nodes.

HPV = human papilloma virus.

studies should be performed to assess the effectiveness of the HPV vaccine to prevent cervical and oropharyngeal carcinoma.

We would like to emphasize that the public should be aware that oral sex is real sex with its danger of STDs. In a survey of 1105 youths aged 12 to 16 years, 70% of the participants believed that boys and girls retained their virginity if they engaged in oral sex and 33% considered oral sex as abstinence.^[89] Among high school students who considered themselves virgins (never had vaginal intercourse), 10% practiced oral sex regularly.^[90]

Among 599 college students in the 90's, 59% of those surveyed reported oral-genital contact as not having sex.^[91] In another survey of 477 college students reported in 2007, the percentage of students who believed that oral sex is not sex was 80%.^[25] The casual attitude about oral sex may explain why 89% of the students surveyed reported oral sex with multiple partners without protection (mean: 3 partners) and the popularity of oral sex among premarital couples with strong religious beliefs.^[23,92] A recent report of increased HPV 16 oral infection among men practicing oral sex with multiple partners may be the consequence of the public ignorance about the danger of oral sex.^[93] Despite the fact that men are at increased risk for oral HPV infection when they practice oral sex, a survey of 303 adult men participating in a screening survey for head and neck cancer reported that only 29.9% were aware of the link of HPV infection and oropharyngeal cancer. Among the persons who knew the infection risk, only 25.1% received their information from their health care practitioner, thus highlighting again the important role of the primary care physicians in educating the public for disease prevention.^[94]

We postulate in Table 4 the sequence of events possibly linking oral sex to oropharyngeal cancer development and possible measures to reduce the rates of HPV 16-associated oropharyngeal cancer in the future. We cannot exclude the possibility that factors besides pattern of sexual practices may have contributed to the increased incidence. Although the association of HPV with cancer is known, the carcinogenic process of HPV is still under investigation. Furthermore, only a small fraction of people with oral HPV infection develops oropharyngeal cancer and hence other factors are clearly at play. Notwithstanding putative mechanisms, we argue that simple but important measures such as use of condoms should significantly reduce the risk of HPV transmission and cancer development.

5. Conclusion

The prevalence of oral sex has become a threat for both the American population and worldwide because of the risk of oropharyngeal carcinoma associated with HPV 16 infection. Unless public health measures are taken to educate the public

about the risks of oral sex, an epidemic of oropharyngeal cancer affecting the young may ensue with serious outcomes. Family physicians will play a crucial role in the fight against oropharyngeal cancer.

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