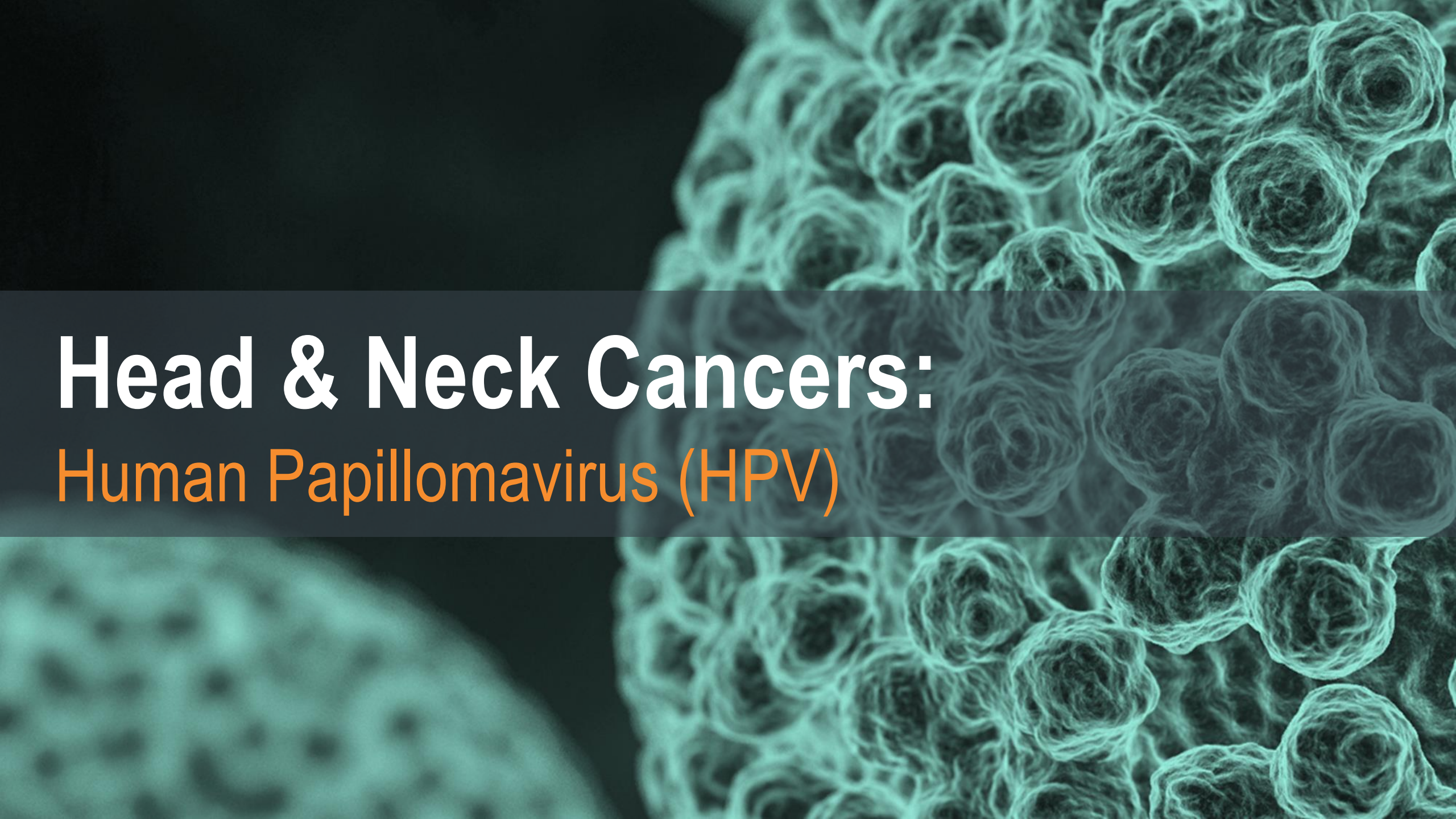

Head & Neck Cancers:

Human Papillomavirus (HPV)

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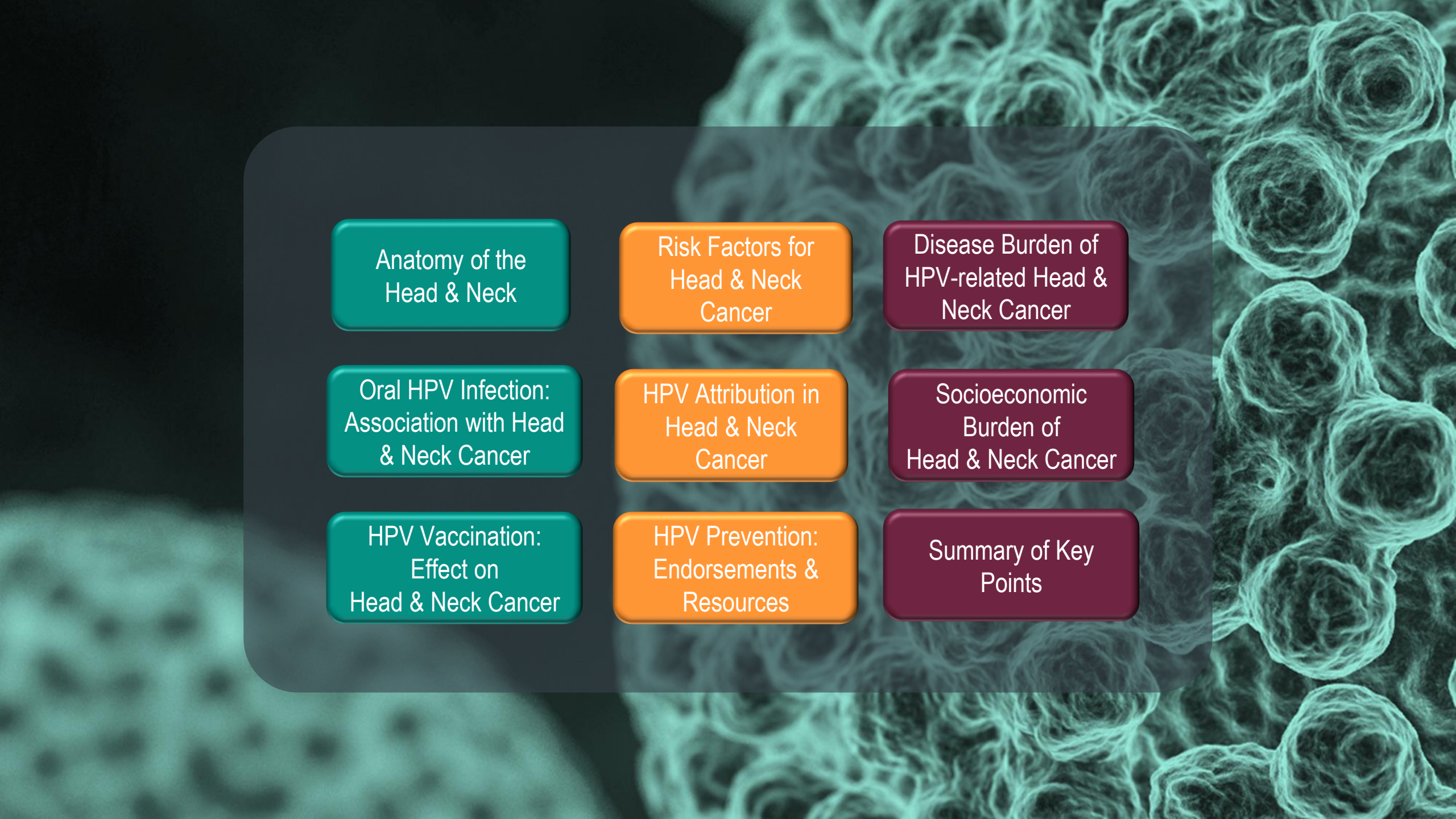
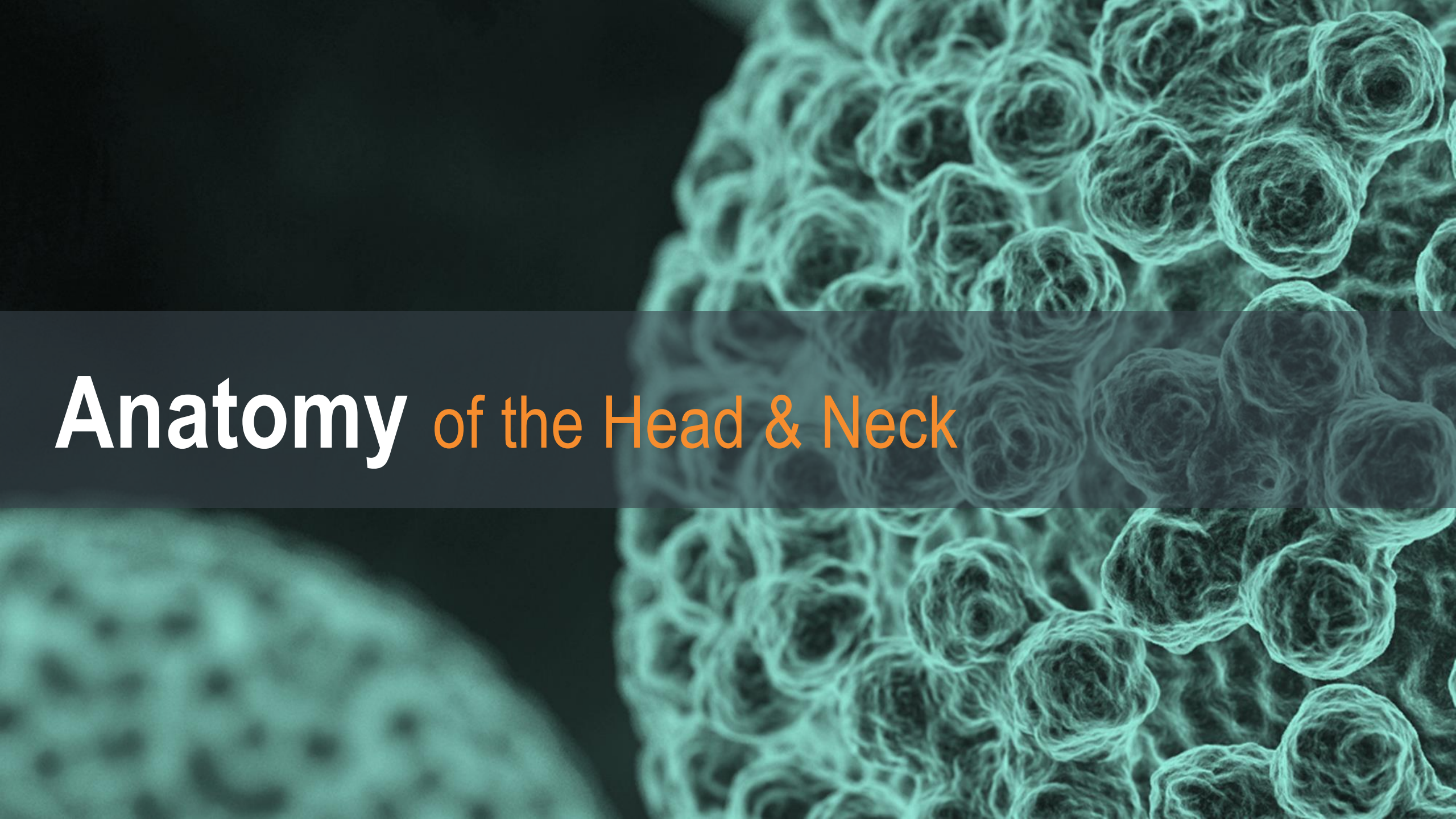
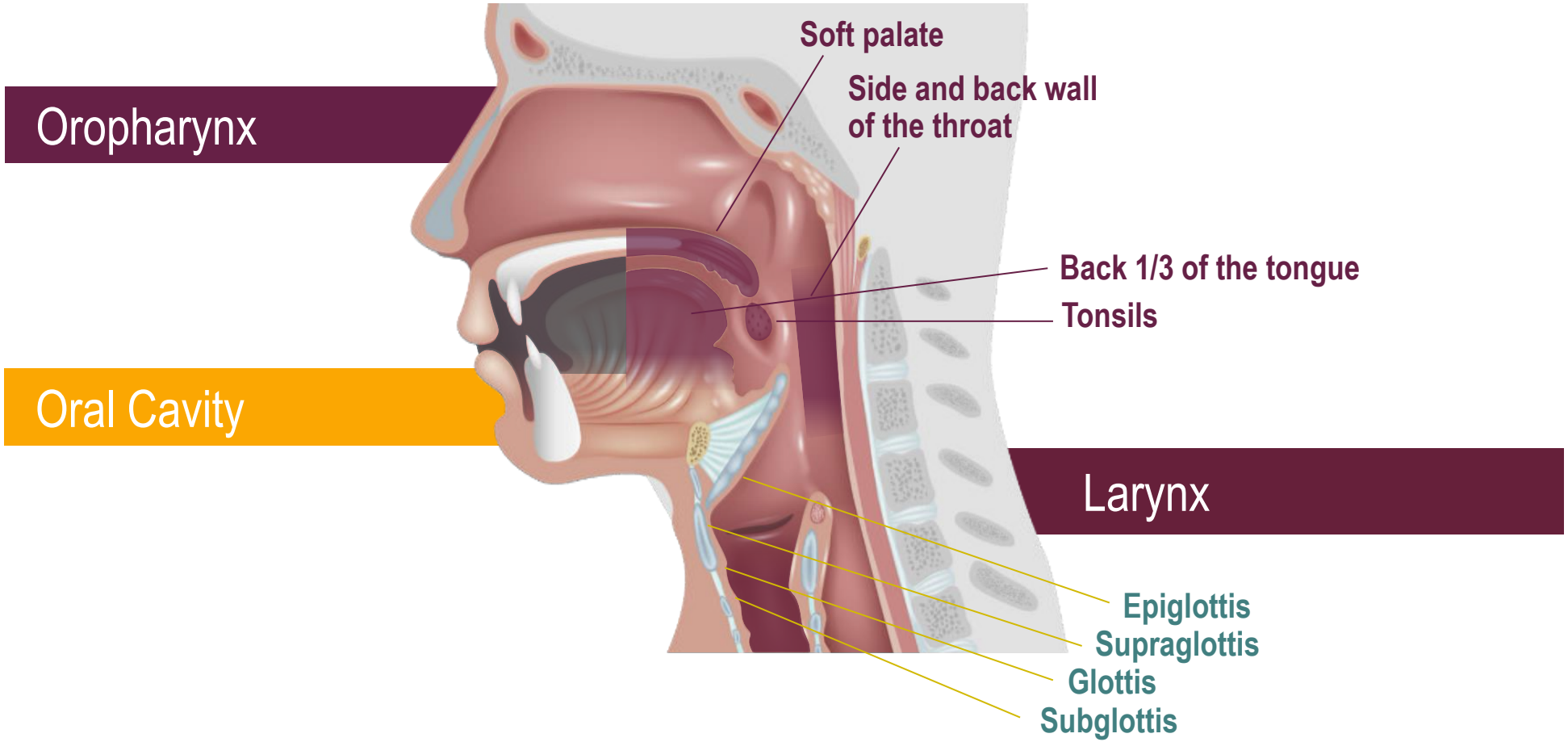

Anatomy of the Head & Neck
Risk Factors for Head & Neck Cancer
Disease Burden of HPV-related Head & Neck Cancer
Oral HPV Infection: Association with Head & Neck Cancer
HPV Attribution in Head & Neck Cancer
Socioeconomic Burden of Head & Neck Cancer
HPV Vaccination: Effect on Head & Neck Cancer
HPV Prevention: Endorsements & Resources
Summary of Key Points



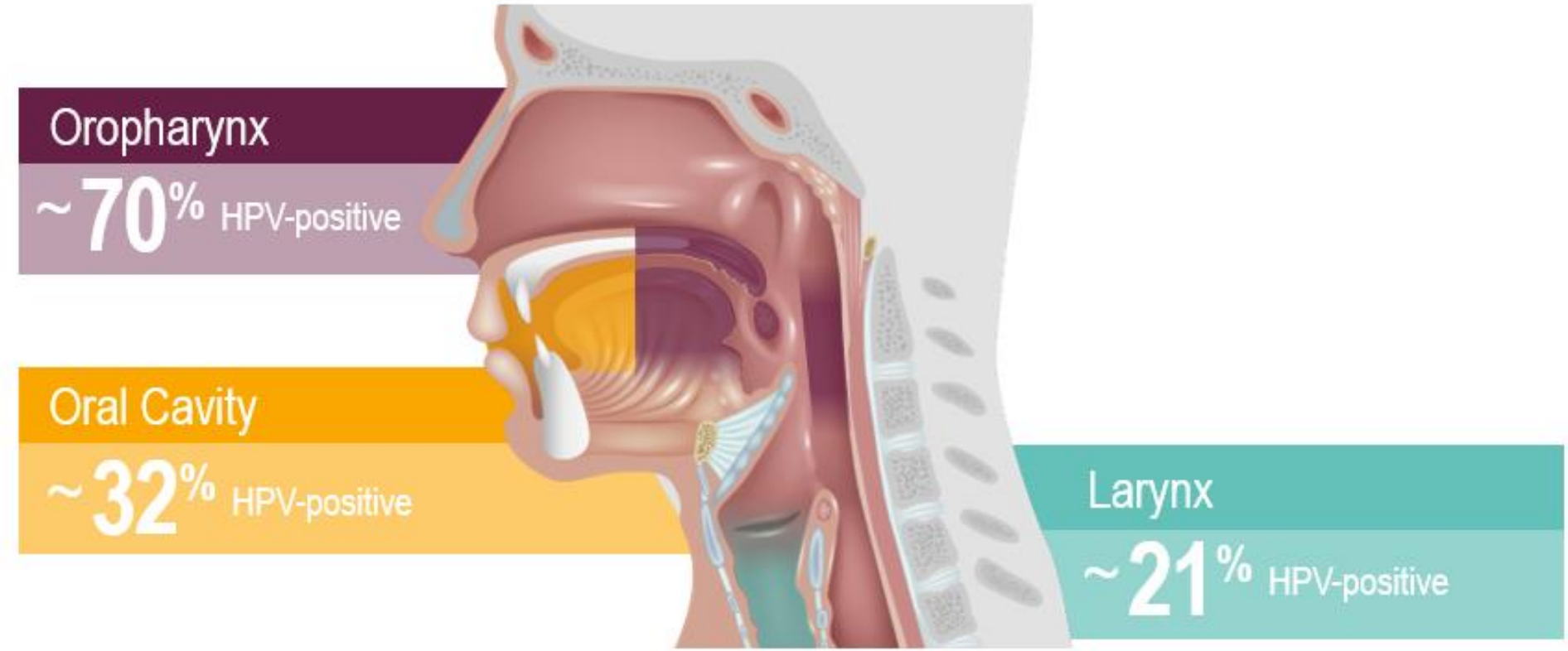
Anatomy of the Head & Neck

Anatomical Locations of Selected Head and Neck Cancers



1. NCI website. Last updated November 21, 2019. Accessed February 26, 2020. https://www.cancer.gov/types/head-and-neck/patient/adult;
2. NCI website. Last updated November 21, 2019. Accessed February 25, 2020. https://www.cancer.gov/types/head-and-neck/patient/adult/oropharyngeal-treatment-pdq;
3. NCI website. Last updated November 21, 2019. Accessed February 26, 2020. https://www.cancer.gov/types/head-and-neck/patient/adult/laryngeal-treatment-pdq

HPV DNA Detection by Anatomic Location of Certain Head and Neck Cancers



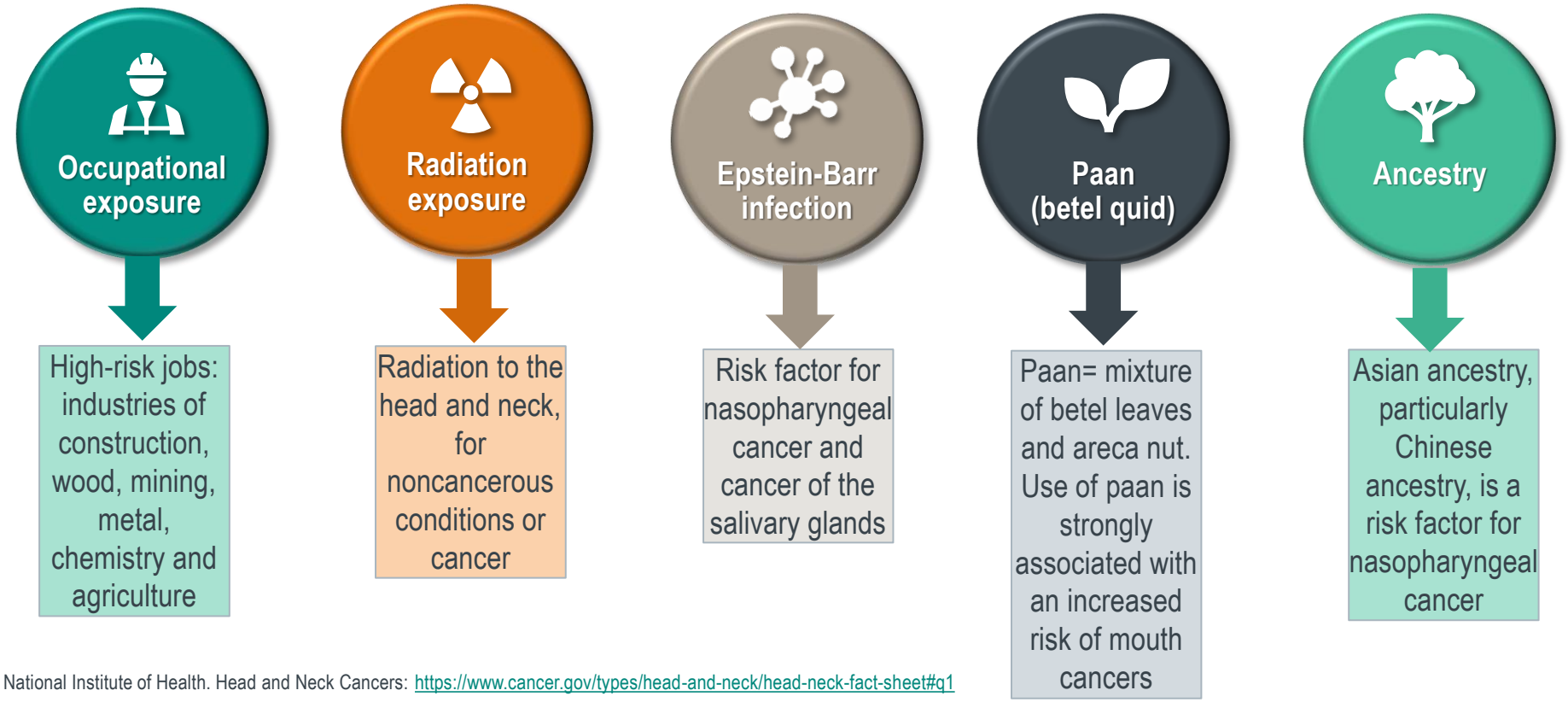
DNA, deoxyribonucleic acid; HPV, human papillomavirus

1. Saraiya M et al. *J Natl Cancer Inst.* 2015;107(6):djv086;
2. NCI website. Last updated November 21, 2019. Accessed February 25, 2020. https://www.cancer.gov/types/head-and-neck/patient/adult/oropharyngeal-treatment-pdq

Risk Factors for Head & Neck Cancer

Risk Factors for Head & Neck Cancers

- **Alcohol** and **tobacco use**, including smokeless tobacco, are important risk factors for head and neck cancers,
  - especially cancers of the oral cavity, oropharynx, hypopharynx, and larynx
- **Other risk factors include:**



National Cancer Institute, National Institute of Health. Head and Neck Cancers: https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet#q1

Risk Factors for Oropharyngeal Cancers

- Most oropharyngeal cancers are still related to alcohol and tobacco use, however this is changing in economically developed areas of the world[1]
- Infection with oncogenic **human papillomavirus (HPV),** especially Type 16, is a risk factor for some types of head and neck cancers, particularly **oropharyngeal** cancers that involve the tonsils or the base of the tongue[2]

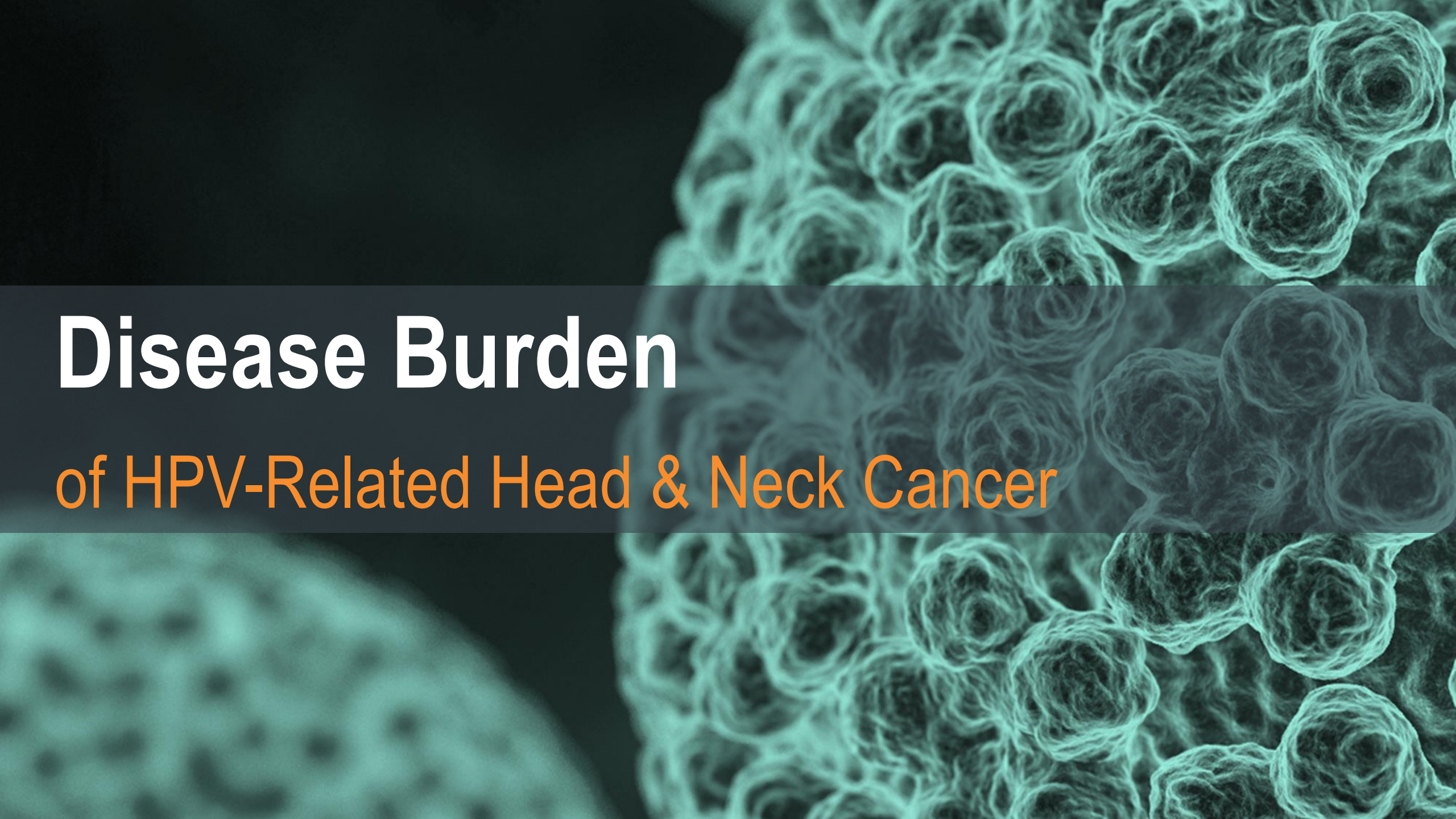
The overwhelming majority of oral HPV infections are sexually acquired[3]

Sexual behavior is now established as the most strong and consistent risk factor for oropharyngeal cancer[3]

Lifetime number of oral sexual partners seems to be the behavioral measure most strongly, consistently, and specifically associated with **oropharyngeal** cancer[3]

1. de Martel C, Plummer M, Vignat J, Franceshi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *Int J Cancer*. 2017;141:664-670. https://www.ncbi.nlm.nih.gov/pubmed/28369882

2. National Cancer Institute, National Institute of Health. Head and Neck Cancers: https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet#q1 3. Gillison ML, et al. Epidemiology of Human Papillomavirus-Positive Head and Neck Squamous Cell Carcinoma. J Clin Oncol. 2015;33(29):3235–3242. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4979086/

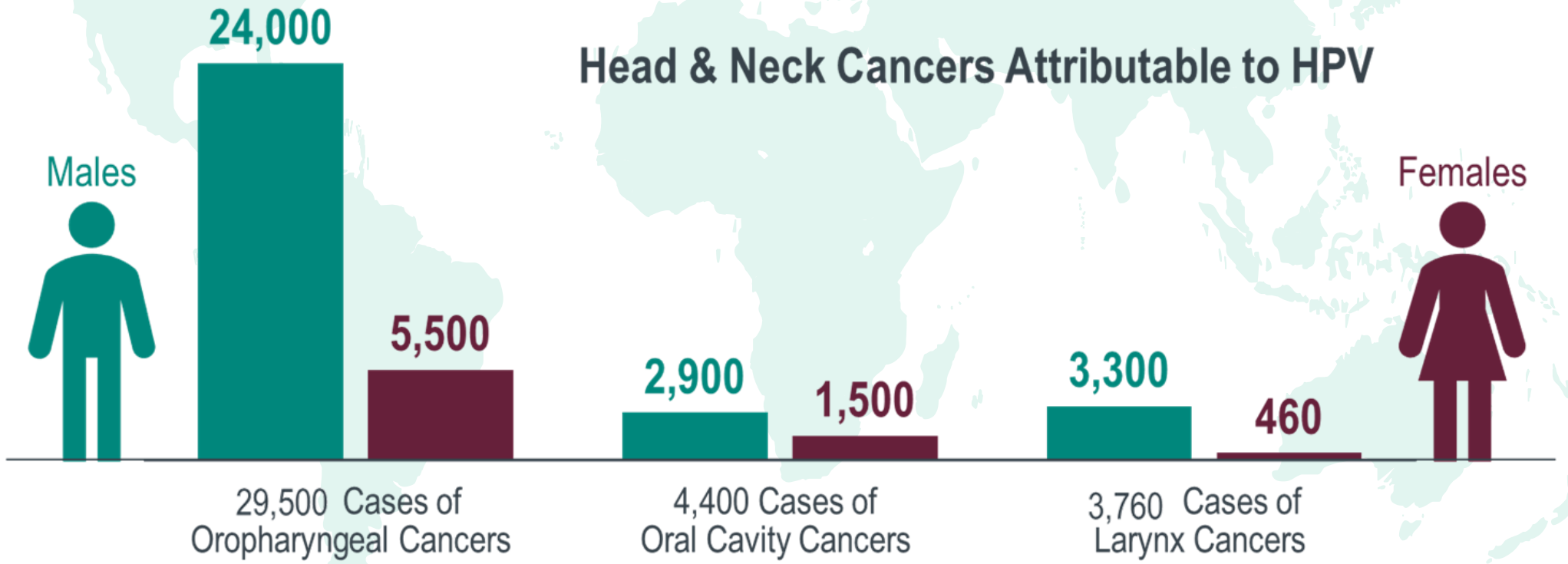


Disease Burden

of HPV-Related Head & Neck Cancer

Disease Burden of HPV-Related Head & Neck Cancers:
Global

The most recent global data from GLOBOCAN 2012 found that around 30% of oropharyngeal cancers are caused by HPV; however, this varies greatly worldwide, being highest in more developed countries (over 40% in Europe, Northern America, Australia, New Zealand, Japan and Republic of Korea), but much lower (<20%) in less-developed countries



de Martel C, Plummer M, Vignat J, Franceshi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *Int J Cancer*. 2017;141:664-670. https://www.ncbi.nlm.nih.gov/pubmed/28369882

Disease Burden of HPV-Associated Head & Neck Cancers: United States

Oropharyngeal squamous cell carcinoma is currently the **most common HPV-associated* cancer** in the US[1,2]

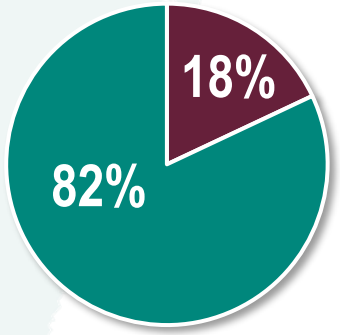
HPV-related **cervical cancer** incidence rates

decreased 1.6% per year

while the rate of HPV-related oropharyngeal cancer incidence **increased significantly** by an average annual percentage change

In **2015,** oropharyngeal squamous cell carcinoma was the **most common** HPV-associated cancer

with
15,479
cases in males



and
3,438
cases in females

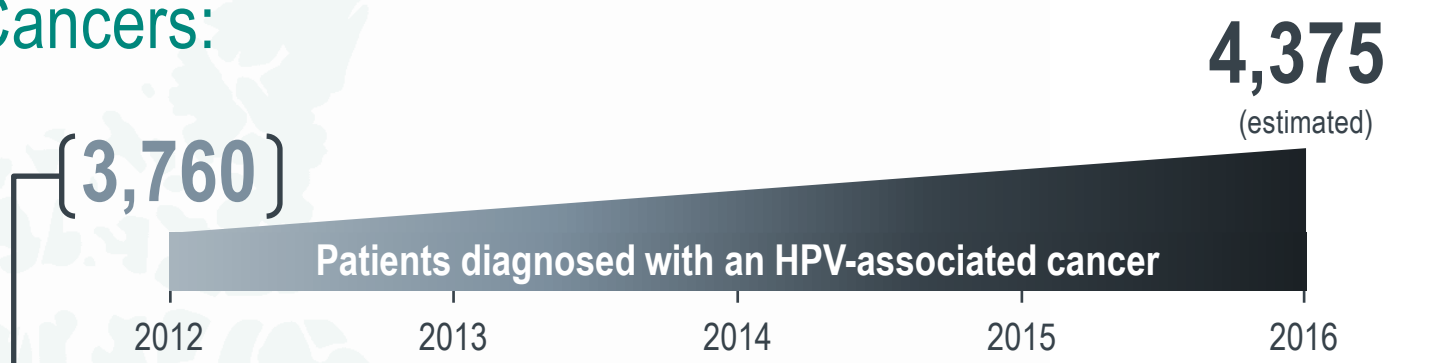
*__HPV-associated cancer__ was defined as an invasive malignancy in which HPV DNA was frequently found in special studies and was microscopically confirmed.

1. Senkomago V, Henley SJ, Thomas CC, et al. Human Papillomavirus-Attributable Cancers - United States, 2012-2016.; MMWR 2019. 2. Van Dyne EA, Henley SJ, Saraiya M, Thomas CC, Markowitz LE, Benard VB. Trends in Human Papillomavirus-Associated Cancers - United States, 1999-2015. MMWR *Morb Mortal Wkly Rep*. 2018 Aug 24;67(33):918-924. https://www.ncbi.nlm.nih.gov/pubmed/30138307

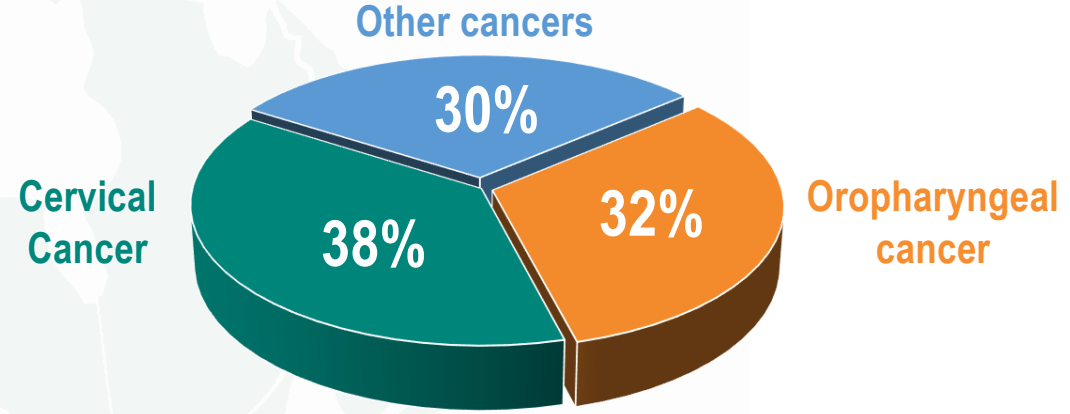
Disease Burden Head & Neck Cancers: Canada

HIGHLIGHTS

- The incidence rate of HPV-associated oropharyngeal cancer (OPC) was **4.5x higher** in males than females in 2012
- The incidence rate of OPC increased in both sexes, but at **a much faster rate among males**



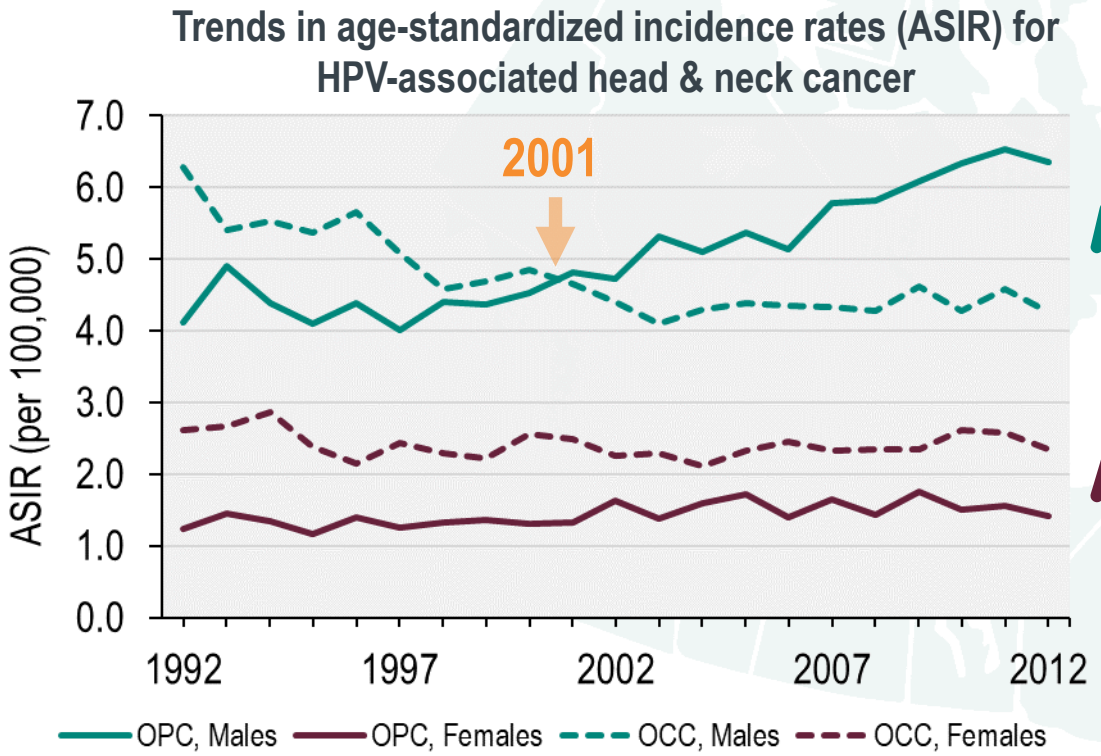
The **most common** types of HPV-associated cancer in 2012 were **oropharyngeal cancer (1335 cases)** and cervical cancer (1300 cases), followed by anal cancer (475 cancers)



Proportion of HPV-associated cancer deaths (2012)

Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2016.

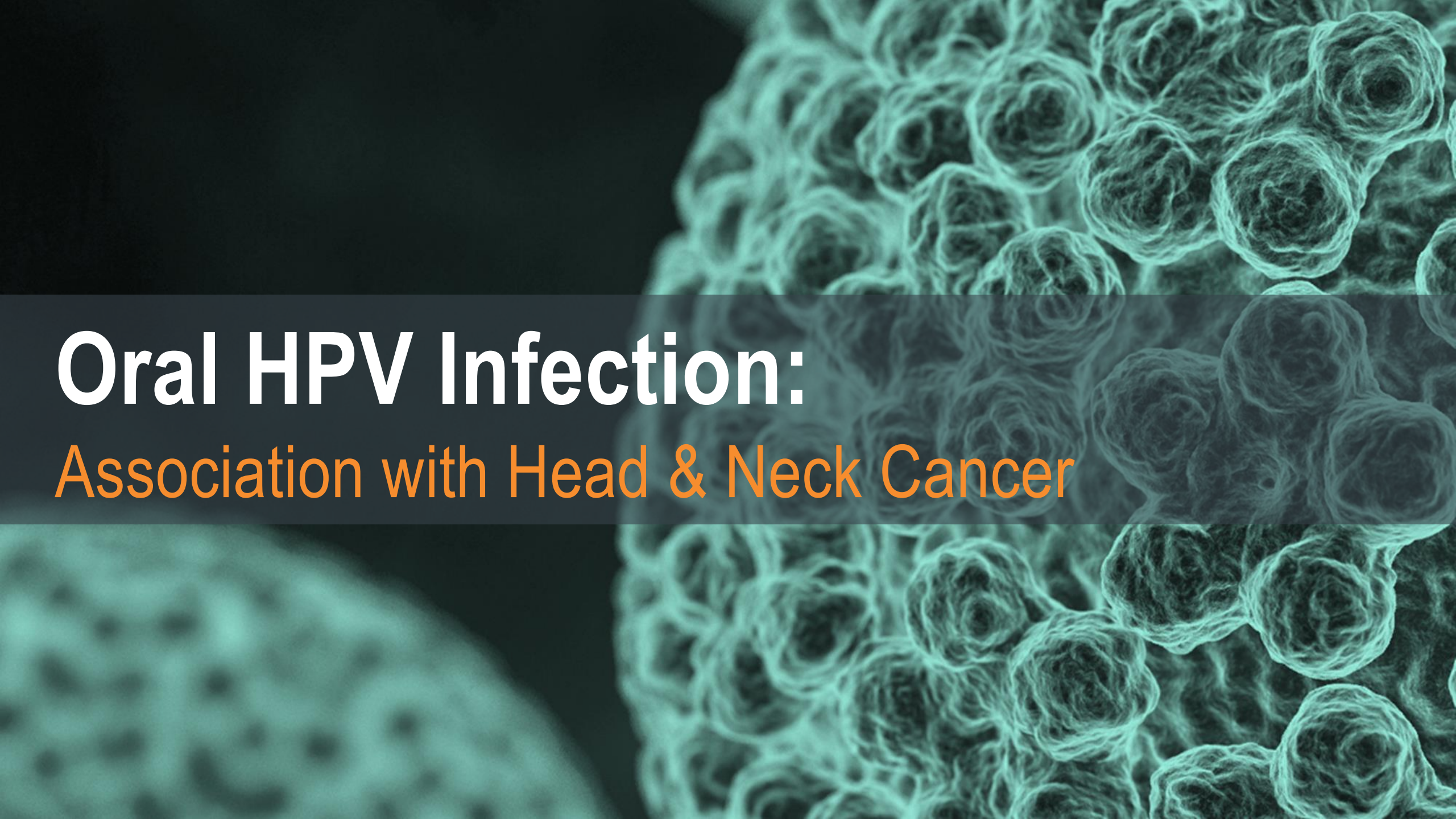
Incidence Rate of Oropharyngeal Cancer Over Time: Canada



In **MALES**, the incidence of **Oropharyngeal Cancer (OPC)** **surpassed** the incidence of **Oral Cavity Cancer (OCC)** in 2001.

In **FEMALES**, the incidence of **Oral Cavity Cancer (OCC)** is relatively stable and continues to be higher than the incidence of **Oropharyngeal Cancer (OPC)**.

Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2016.



Oral HPV Infection:

Association with Head & Neck Cancer

Epidemiology of Oral HPV Infection:
Association with Head & Neck Cancer

Over a decade of evidence has determined that human papillomavirus (HPV) is **the principal cause of an increase in incidence** of certain head and neck squamous cell cancers in some regions of the world.

Case-control studies have **established oral HPV infection as the principal risk factor** for HPV-positive oropharyngeal cancer

Gillison ML, Chaturvedi AK, Anderson WF, Fakhry C. Epidemiology of Human Papillomavirus-Positive Head and Neck Squamous Cell Carcinoma. *J Clin Oncol*. 2015;33(29):3235–3242.
https://www.ncbi.nlm.nih.gov/pubmed/26351338

Epidemiology of Oral HPV Infection: Association with Head & Neck Cancer

An analysis of the National Health and Nutrition Examination Survey (NHANES) data from the 2009-2010 and 2011-2012 cycles was performed; cancer incidence rates for the year 2011 from nine cancer registries covered by the National Cancer Institute's SEER program (1973 to 2011) were utilized. Oropharyngeal cancers were defined to include the base of tongue, lingual tonsil, soft palate, uvula, tonsil, oropharynx, and Waldeyer's ring.

The results found that:

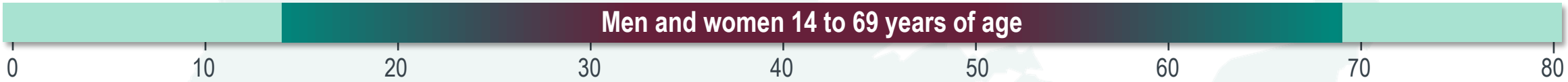
Oral oncogenic HPV infection prevalence was shown to **peak at ages 25 to 30 years and 55 to 60 years**, and the median age at oropharyngeal cancer diagnosis was 63 years; 58 years for HPV-positive cases

From this, the authors estimated an **average latency period** for HPV-positive oropharyngeal cancer of **approximately 10 to 30 years**, assuming either peak in prevalence could contribute to risk

The **disease relevance of either of the two peaks** for oral oncogenic HPV infection, however, **is unknown**

Gillison ML, Chaturvedi AK, Anderson WF, Fakhry C. Epidemiology of Human Papillomavirus-Positive Head and Neck Squamous Cell Carcinoma. *J Clin Oncol*. 2015;33(29):3235–3242.
https://www.ncbi.nlm.nih.gov/pubmed/26351338

Oral HPV Infection: Prevalence
United States



A cross-sectional study was conducted as part of NHANES 2009-2010 with **5,579 men and women aged 14 to 69 years** provided a 30-second oral rinse for HPV DNA testing

The prevalence of oral HPV infection among **men and women aged 14 to 69 years was 6.9%** (95% CI, 5.7%-8.3%) and prevalence of HPV Type 16 was 1.0% (95% CI, 0.7%-1.3%)

Oral HPV infection followed a bimodal pattern with respect to age, with peak prevalence among **individuals aged 30 to 34 years and 60 to 64 years**

Infection was less common among **those without vs those with a history of any type of sexual contact,** (*P*<0.001); and increased with number of sexual partners (*P*<0.001 for trend) and cigarettes smoked per day (*P*<0.001 for trend)

Men had a **significantly higher prevalence than women** for any oral HPV infection, (*P*<0.001)

Gillison ML, Broutian T, Pickard RK, et al. Prevalence of oral HPV infection in the United States, 2009-2010. *JAMA*. 2012;307(7):693–703. https://www.ncbi.nlm.nih.gov/pubmed/22282321

HPV Attribution in Head & Neck Cancer

HPV Types Associated with Head & Neck Cancers: Global

An analysis of data from GLOBOCAN 2012 demonstrated that worldwide, among cases of HPV-related head and neck cancers

HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 combined

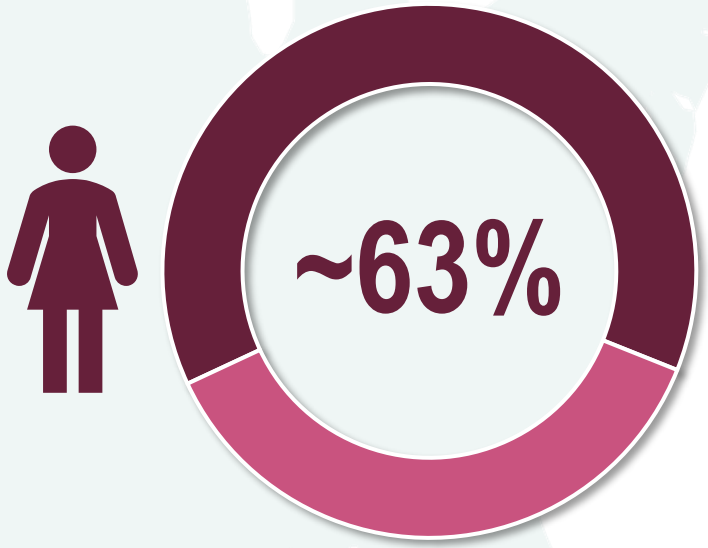
were responsible for

de Martel C, Plummer M, Vignat J, Franceshi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *Int J Cancer*. 2017;141:664-670. https://www.ncbi.nlm.nih.gov/pubmed/28369882

HPV Attribution in Head & Neck Cancers:
United States

The Centers for Disease Control and Prevention (CDC) estimates that **~70% of oropharyngeal cancer cases overall** are probably caused by HPV

of oropharyngeal **cancer cases in males** are probably caused by HPV

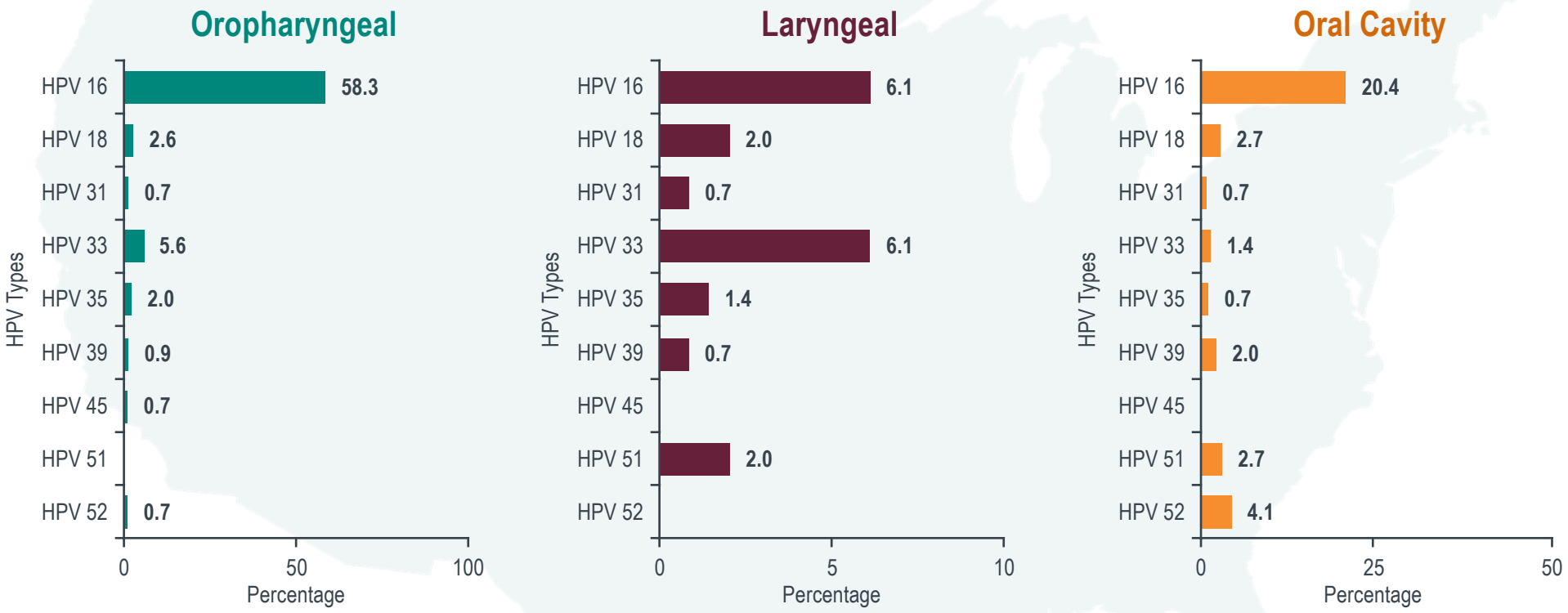


of oropharyngeal **cancer cases in females** are probably caused by HPV

CDC. 2018 HPV & Cancer. How Many Cancers are Linked to HPV Each Year?. https://www.cdc.gov/cancer/hpv/statistics/cases.htm

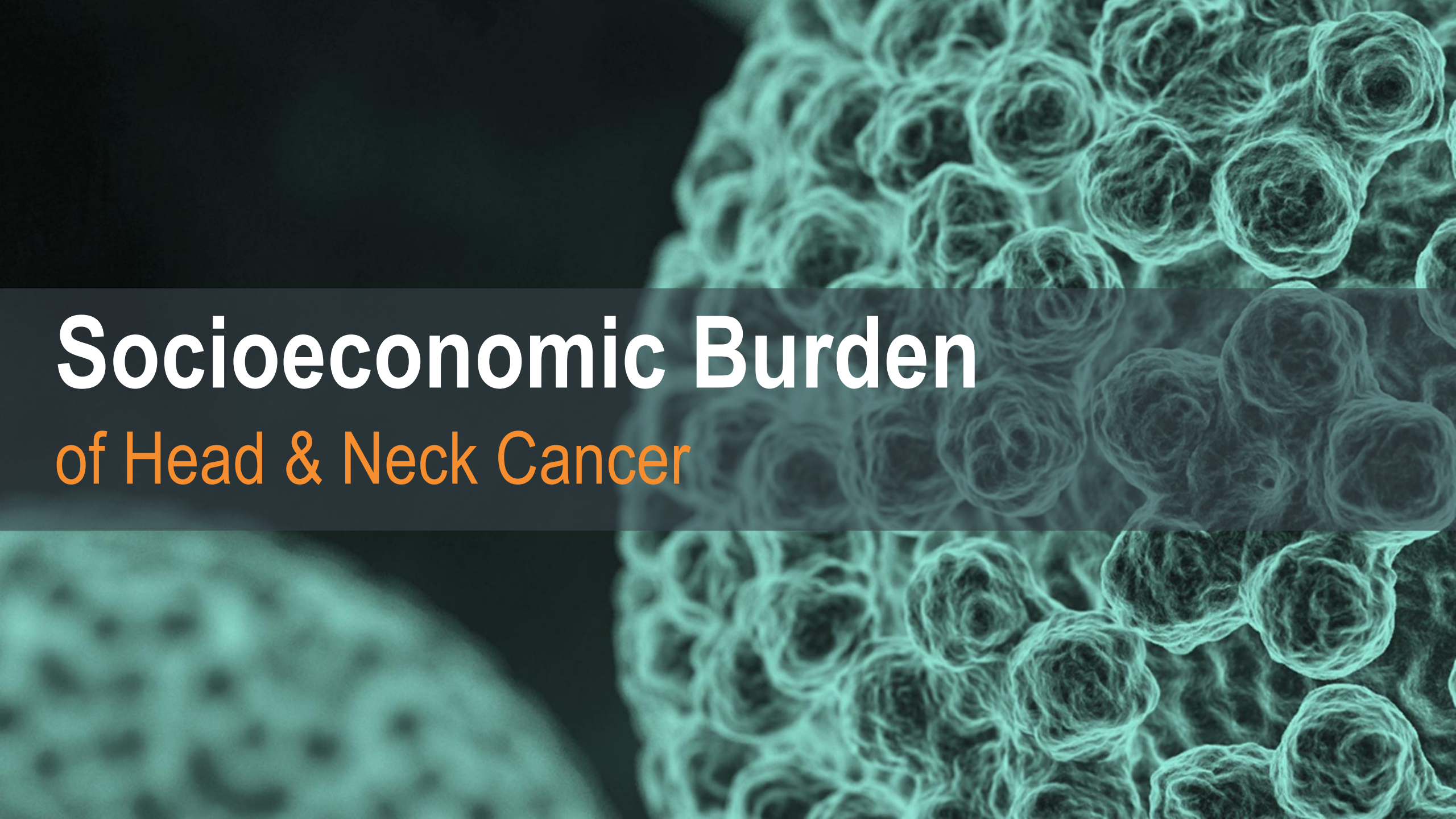
HPV Attribution in Head & Neck Cancers
United States

Attribution of Most Common Oncogenic HPV Genotypes Detected in Head & Neck Cancers



HPV 16 was the most common type found in oropharyngeal cancers

Saraiya M, Unger ER, Thompson TD, et al. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. *J Natl Cancer Inst*. 2015;107(6):djv086. https://pubmed.ncbi.nlm.nih.gov/25925419



Socioeconomic Burden

of Head & Neck Cancer

Socioeconomic Burden of HPV-Related Head & Neck Cancers: United States

A literature search found **6 studies published between 2012-2018 that provided updated medical cost estimates for 5 HPV-associated cancers**

The annual burden of each cancer type was calculated as **the estimated annual number of cases multiplied by percentage of cases with HPV and cost per case estimates**

Cancers included in the analysis were **anal, cervical, oropharyngeal, vaginal, and vulvar**

In the studies that evaluated **oropharyngeal cancer**, the estimated cost per case was ranged from

$21,200 to **$64,700** in 2008

The estimated cost per case of **oropharyngeal cancer** ranged from

$65,000 to **$146,100** in 2018

Chesson, H. W., et al. (2019). Updated medical care cost estimates for HPV-associated cancers: implications for cost-effectiveness analyses of HPV vaccination in the United States. *Hum Vaccin Immunother* 15(7-8): 1942-1948. https://www.ncbi.nlm.nih.gov/pubmed/31107640.

Socioeconomic Burden of HPV-Related Head & Neck Cancers: Canada

Data used several Manitoba Health clinical and administrative databases to identify **all persons diagnosed with an HPV-related disease** in Manitoba

Direct Medical Costs of Diseases Associated with HPV Infection:
all costs incurred in relation to the diagnosis and treatment

TREATMENT COST
One episode of
cervical dysplasia
$220

One episode of
cervical carcinoma in situ
$1,300

TREATMENT COST
One case of
Cervical cancer
$15,000

One case of
Oral cancer
$33,000

Righolt C H et al. (2018) The Direct Medical Costs of Diseases Associated with Human Papillomavirus Infection in Manitoba, Canada. Appl Health Econ Health Policy. https://doi.org/10.1007/s40258-017-0367-1

Psychosocial Impact

of Head & Neck Cancer

Risk of Suicide for Head & Neck Cancer Survivors: United States

An analysis of SEER data for over 4 million cancer survivors from 2000-2014 found that for survivors of head & neck cancers :

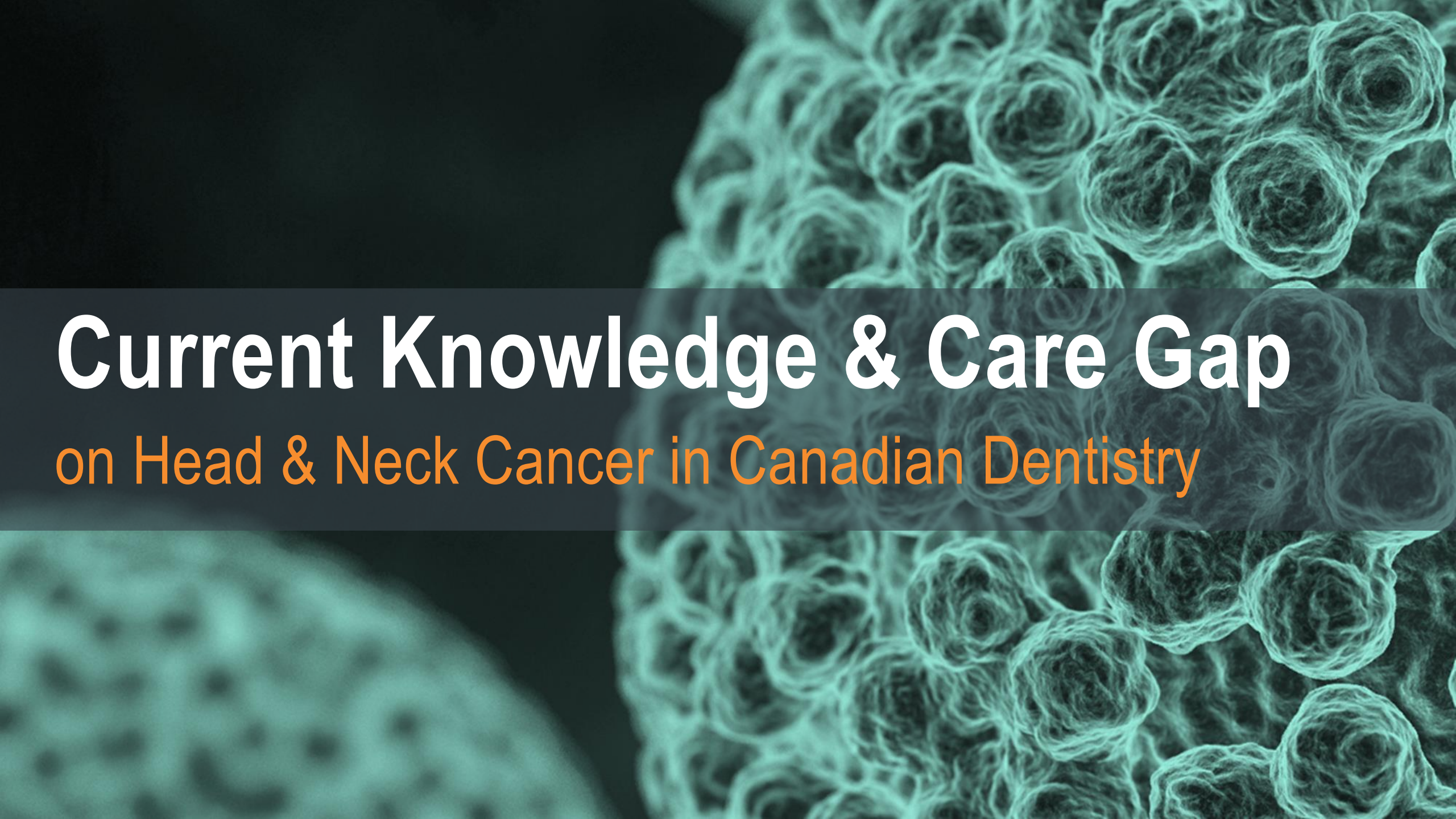
- There was a **27% increase in the risk of suicide** in 2010-2014 compared with 2000-2004
- Suicide rates were **twice as high** (63.4/100,000) as for other cancers (23.6/100,000)

- Sources of distress unique to head & neck cancer survivors that may result from treatment:

- facial disfigurement
- difficulty swallowing
- loss of taste or smell

- difficulty speaking
- depression

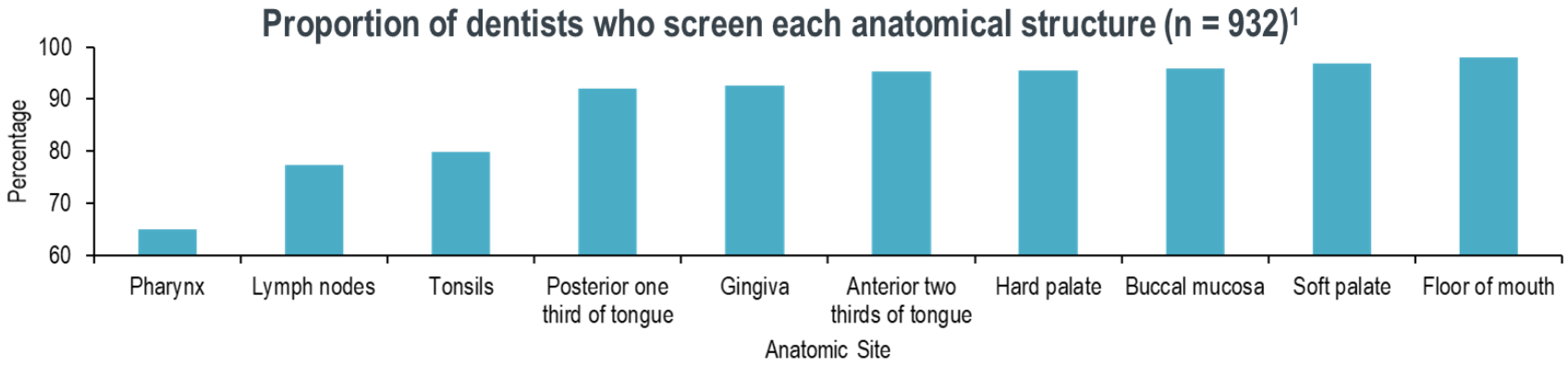
Osazuwa-Peters N, Simpson MC, Zhao L, et al. Suicide risk among cancer survivors: Head and neck versus other cancers. *Cancer.* 2018;124(20):4072-4079. https://www.ncbi.nlm.nih.gov/pubmed/30335190

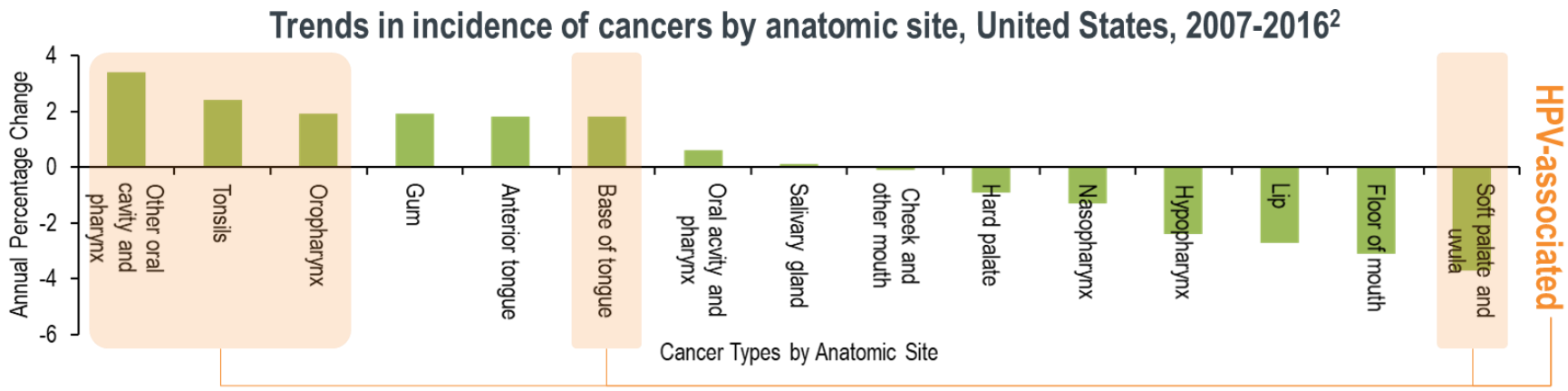


Current Knowledge & Care Gap

on Head & Neck Cancer in Canadian Dentistry

Dentists' Capacity to Mitigate the Burden of Oral Cancers:
Ontario, Canada





92.4%

believed that they are adequately trained to recognize the early signs and symptoms of oral cancer[1]

35.4%

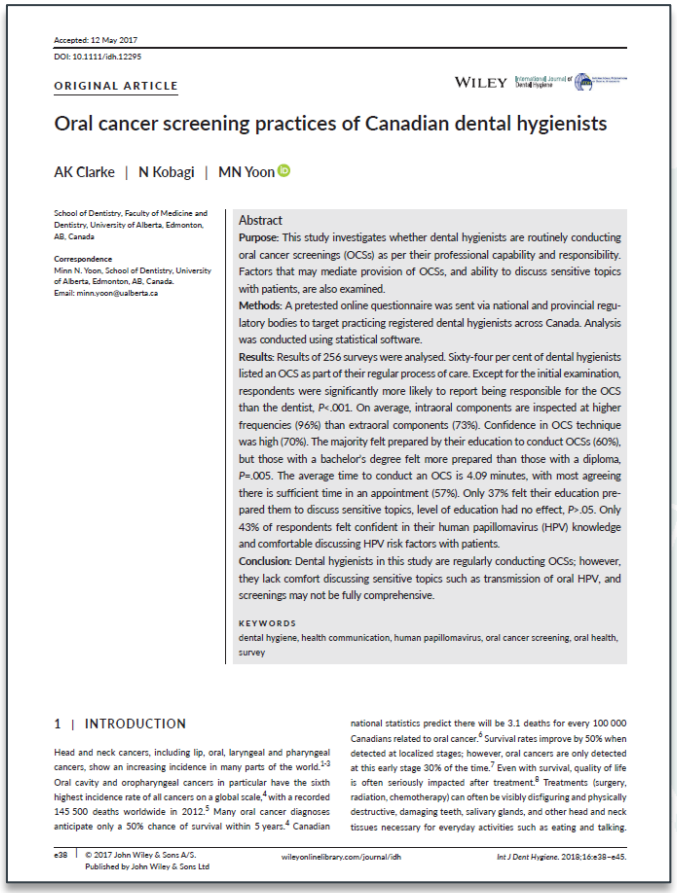
believed said that they are adequately trained to obtain biopsy samples from suspected lesions[1]

<40%

believed said that they are adequately trained to address relevant risk factors (smoking, alcohol use, HPV)[1]

1. J Can Dent Assoc. 2020 Feb;86:k2. **2.** MMWR Morb Mortal Wkly Rep. 2020 Apr 17;69(15):433-438.

Oral Cancer Screening Practices of Canadian Dental Hygienists: Canada



Accepted: 12 May 2017
DOI: 10.1111/idh.12295

ORIGINAL ARTICLE

WILEY International Journal of Dental Hygiene

Oral cancer screening practices of Canadian dental hygienists

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Email: minn.yoon@ualberta.ca

Abstract

Purpose: This study investigates whether dental hygienists are routinely conducting oral cancer screenings (OCSs) as per their professional capability and responsibility. Factors that may mediate provision of OCSs, and ability to discuss sensitive topics with patients, are also examined.

Methods: A pretested online questionnaire was sent via national and provincial regulatory bodies to target practicing registered dental hygienists across Canada. Analysis was conducted using statistical software.

Results: Results of 256 surveys were analysed. Sixty-four per cent of dental hygienists listed an OCS as part of their regular process of care. Except for the initial examination, respondents were significantly more likely to report being responsible for the OCS than the dentist, $P<.001$. On average, intraoral components are inspected at higher frequencies (96%) than extraoral components (73%). Confidence in OCS technique was high (70%). The majority felt prepared by their education to conduct OCSs (60%), but those with a bachelor's degree felt more prepared than those with a diploma, $P=.005$. The average time to conduct an OCS is 4.09 minutes, with most agreeing there is sufficient time in an appointment (57%). Only 37% felt their education prepared them to discuss sensitive topics, level of education had no effect, $P>.05$. Only 43% of respondents felt confident in their human papillomavirus (HPV) knowledge and comfortable discussing HPV risk factors with patients.

Conclusion: Dental hygienists in this study are regularly conducting OCSs; however, they lack comfort discussing sensitive topics such as transmission of oral HPV, and screenings may not be fully comprehensive.

KEYWORDS
dental hygiene, health communication, human papillomavirus, oral cancer screening, oral health, survey

1 | INTRODUCTION

Head and neck cancers, including lip, oral, laryngeal and pharyngeal cancers, show an increasing incidence in many parts of the world.[1-3] Oral cavity and oropharyngeal cancers in particular have the sixth highest incidence rate of all cancers on a global scale,[4] with a recorded 145 500 deaths worldwide in 2012.[5] Many oral cancer diagnoses anticipate only a 50% chance of survival within 5 years.[4] Canadian national statistics predict there will be 3.1 deaths for every 100 000 Canadians related to oral cancer.[6] Survival rates improve by 50% when detected at localized stages; however, oral cancers are only detected at this early stage 30% of the time.[7] Even with survival, quality of life is often seriously impacted after treatment.[8] Treatments (surgery, radiation, chemotherapy) can often be visibly disfiguring and physically destructive, damaging teeth, salivary glands, and other head and neck tissues necessary for everyday activities such as eating and talking.

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64% dental hygienists listed an oral cancer screening as part of their regular process of care

Intraoral Components

are inspected at higher frequencies (96%) than extraoral components (73%)

The average time to conduct an oral cancer screening

4.09 minutes

37% felt their education prepared them to discuss sensitive topics

43% felt confident in their HPV knowledge and comfortable discussing HPV risk factors with patients

Dental hygienists (n=256) in this study regularly conducts oral cancer screenings; however, they lack comfort discussing sensitive topics such as oral HPV, and screenings may not be fully comprehensive.

Int J Dent Hyg. 2018 May;16(2):e38-e45.

HPV Vaccination:

Effect on Head & Neck Cancer

HPV Vaccination:
Effect on Head & Neck Cancer

There are **currently no data** from clinical studies evaluating the efficacy and safety of the 4-valent or 9-valent HPV vaccines in the prevention of head and neck cancers.

However,

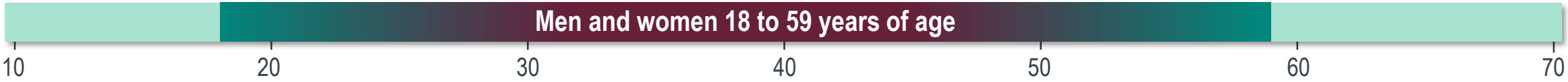
Population-level impact studies have evaluated the correlation of HPV vaccination with the prevalence of oral HPV infection[1,2]

Data for these studies was extracted from the National Health and Nutrition Examination Survey (NHANES): a cross-sectional, stratified, multistage probability sample of the civilian US population

1. Chaturvedi AK, Graubard BI, Broutian T, et al. Prevalence of Oral HPV Infection in Unvaccinated Men and Women in the United States, 2009-2016. *JAMA*. 2019;322(10):977–979. https://www.ncbi.nlm.nih.gov/pubmed/31503300

2. Chaturvedi AK, Graubard BI, Broutian T, et al. Effect of prophylactic human papillomavirus (HPV) vaccination on oral HPV infections among young adults in the United States. *J Clin Oncol*. 2018 Jan 20;36(3):262-267. https://www.ncbi.nlm.nih.gov/pubmed/29182497

HPV Vaccination: Effect on Oral HPV Infection



An analysis was conducted across 4 cycles of NHANES in the US during 2009-2016 using data from 13,676 individuals 18-59 years of age. Comparisons of oral HPV prevalence for 4 vaccine HPV types (16, 18) and 33 nonvaccine types.

HPV vaccination rates increased from **0% to 5.8% in men**

and from **7.3% to 15.1% in women**

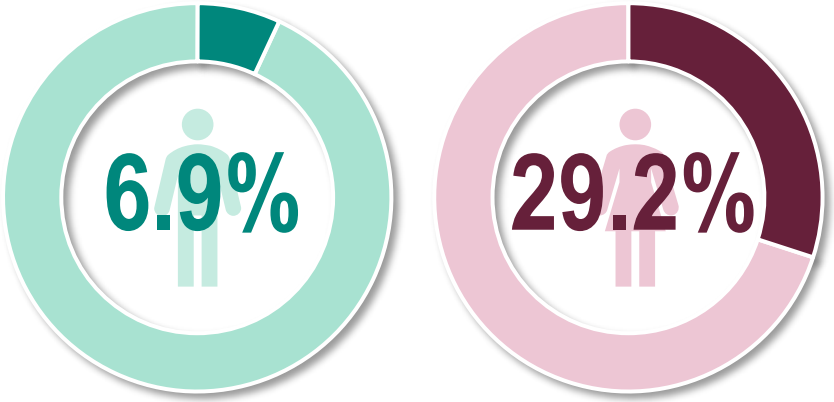
Demographic and behavioral characteristics were unchanged in men and women

- Vaccine-type oral HPV prevalence **declined by 37%** between 2009-2010 and 2015-2016 in **unvaccinated US men aged 18 to 59 years,** suggesting herd protection against oral HPV infections
- Prevalence of nonvaccine-type oral HPV infections **remained unchanged in unvaccinated men**
- In **unvaccinated women aged 18 to 59 years,** oral HPV prevalence **remained unchanged for vaccine types** (0.6% in 2009-2010 vs 0.5% in 2015-2016); **and for nonvaccine types** (2.6% in 2009-2010 vs 3.3% in 2015-2016)

Chaturvedi AK, Graubard BI, Broutian T, et al. Prevalence of Oral HPV Infection in Unvaccinated Men and Women in the United States, 2009-2016. *JAMA*. 2019;322(10):977–979. https://www.ncbi.nlm.nih.gov/pubmed/31503300

HPV Vaccination: Effect on Oral HPV Infection Among Young Adults United States

Cross-sectional study: Population–level effect of prophylactic HPV vaccination on the burden of oral HPV infection

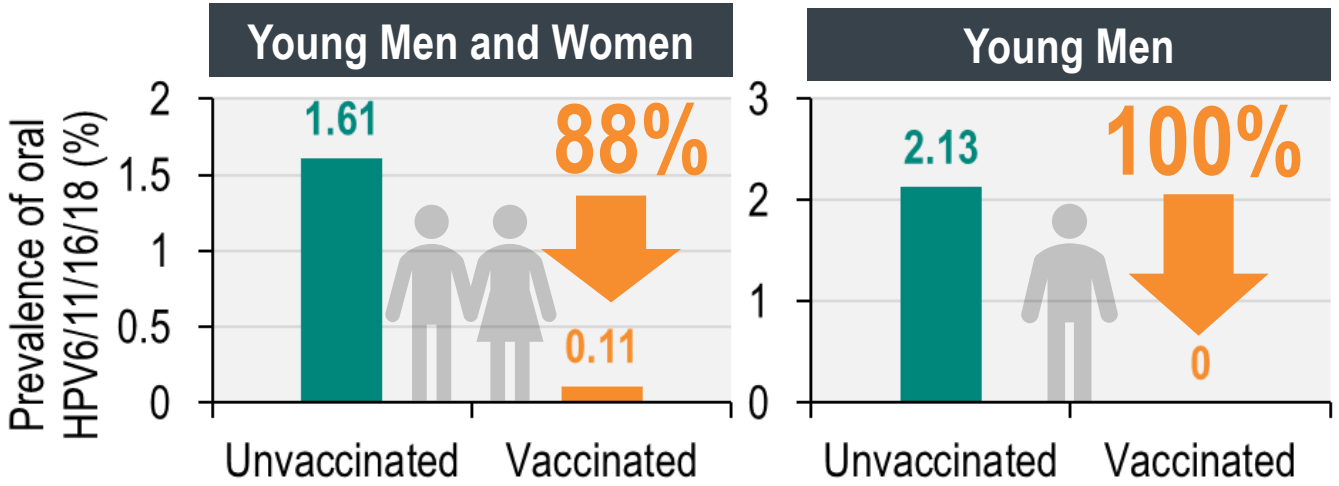


Between 2011 and 2014,

6.9% Men 29.2% Women

18 to 33 years of age

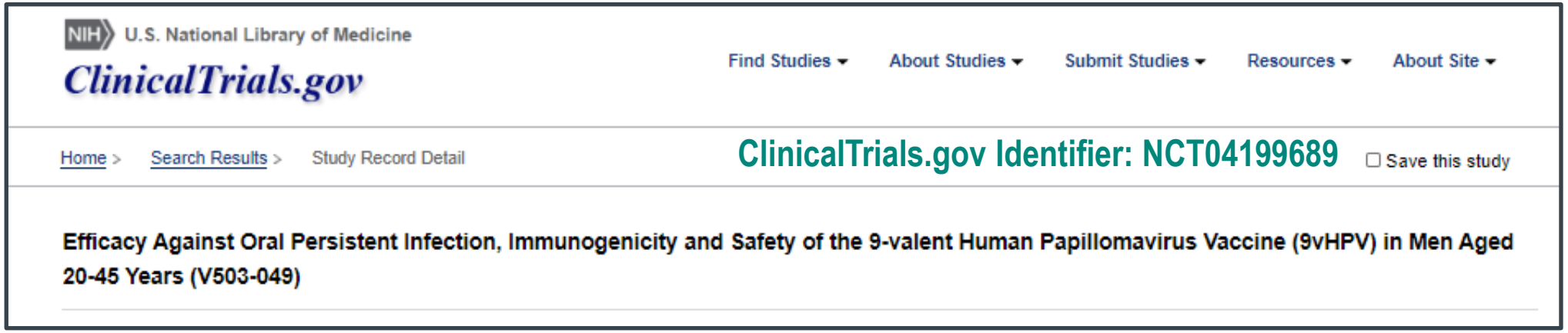
reported receipt of at least one dose of the 4-valent HPV vaccine before the age of 26 years



HPV vaccination was associated with an estimated **88% reduction** in the prevalence of HPV 6/11/16/18–related oral infections **among vaccinated young adults** and **100% reduction in vaccinated men**

Chaturvedi AK, Graubard BI, Broutian T, et al. Effect of prophylactic human papillomavirus (HPV) vaccination on oral HPV infections among young adults in the United States. *J Clin Oncol*. 2018 Jan 20;36(3):262-267. https://www.ncbi.nlm.nih.gov/pubmed/29182497

HPV Vaccination: Clinical Trial on Oral Persistent Infection in **Men** Aged 20-45 Years: Ongoing



Study Type: Interventional (Clinical Trial)
Estimated Enrollment: **6000 participants**
Allocation: Randomized, Placebo Controlled
Masking: Triple (Participant, Care Provider, Investigator)

Primary Purpose: Prevention
Actual Study Start Date: **February 27, 2020**
Estimated Primary Completion Date: **July 15, 2024**
Estimated Study Completion Date: **July 15, 2024**

*Similar to what has been demonstrated for HPV-related anogenital infection and disease, if oral persistent infection is prevented via HPV vaccination, then it can be inferred that head and neck cancer caused by the 7 high-risk HPV types in the 9-valent HPV vaccine can also be prevented.

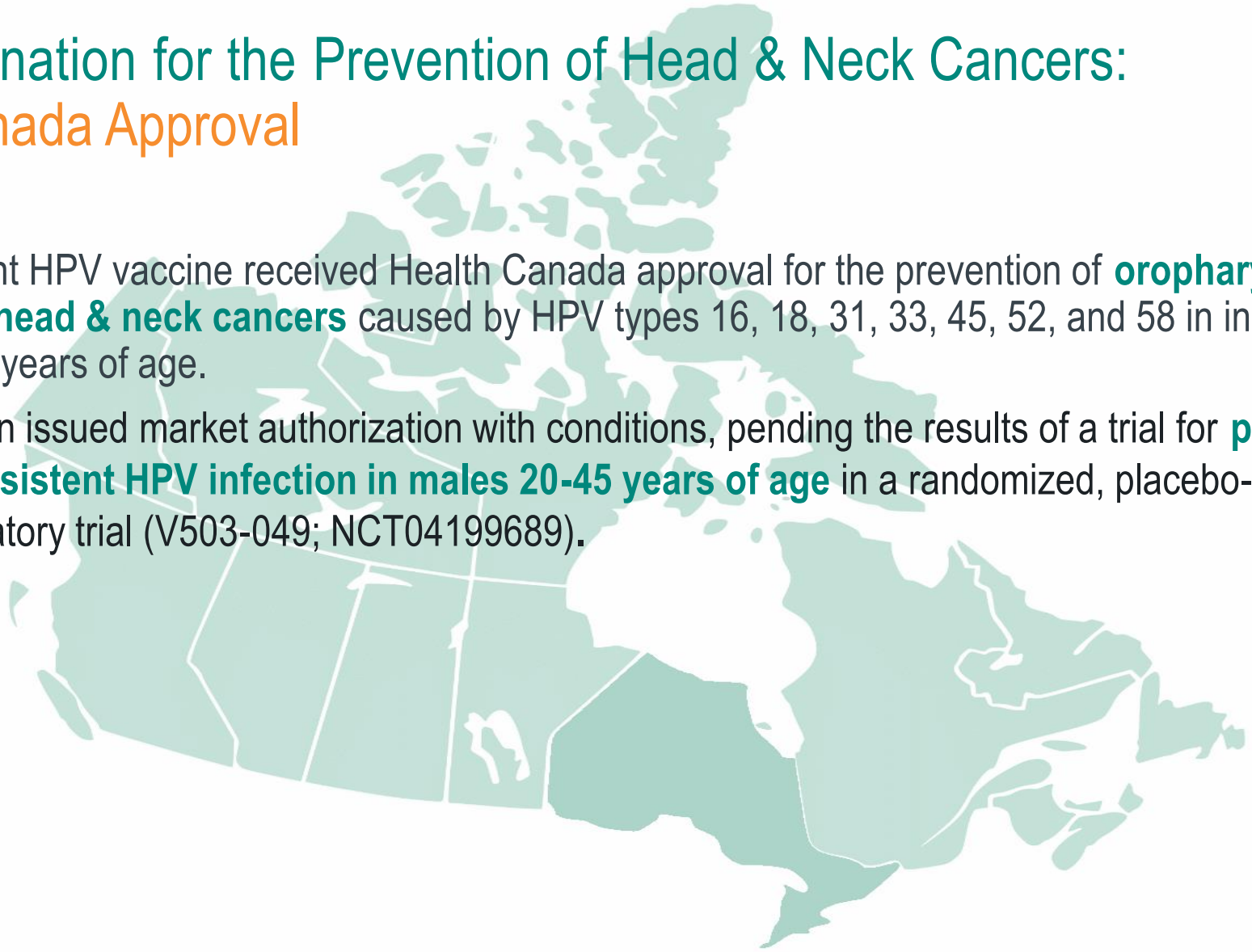
https://clinicaltrials.gov/ct2/show/NCT04199689;
*WHO Primary end-points for prophylactic HPV vaccine trials. International Agency for Research on Cancer (IARC) Working Group Report 2014

HPV Vaccination for the Prevention of Head & Neck Cancers: US FDA Approval

- The 9-valent HPV vaccine has received accelerated approval in the United States for the prevention of **oropharyngeal cancer and other head & neck cancers** caused by HPV types 16, 18, 33, 45, 52, and 58.
  - And is currently being investigated for the **prevention of oral persistent HPV infection in males 20-45 years of age** in a randomized, placebo-controlled confirmatory trial (V503-049; NCT04199689).

https://www.fda.gov/vaccines-blood-biologics/vaccines/gardasil-9

HPV Vaccination for the Prevention of Head & Neck Cancers:
Health Canada Approval



- The 9-valent HPV vaccine received Health Canada approval for the prevention of **oropharyngeal cancer and other head & neck cancers** caused by HPV types 16, 18, 31, 33, 45, 52, and 58 in individuals 9 through 45 years of age.
  - has been issued market authorization with conditions, pending the results of a trial for **prevention of oral persistent HPV infection in males 20-45 years of age** in a randomized, placebo-controlled confirmatory trial (V503-049; NCT04199689).

Gardasil 9 Product Monograph. https://www.merck.ca/static/pdf/GARDASIL_9-PM_E.pdf

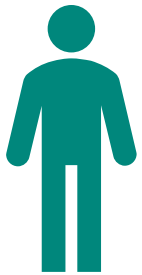
HPV Prevention:

Recommendations and Position Statements

NACI: National Advisory Committee on Immunization

Government of Canada

- 2vHPV, 4vHPV or 9vHPV recommended for **FEMALES** age 9-26 years old
- May be used in females over age 26 years old **(no upper age limit)**
- **Is recommended for those with current or past history of pap abnormalities, cervical cancer and EGW**



- 4vHPV or 9vHPV vaccine recommended for **MALES** age 9-26 years old for prevention of EGW, AIN, anal cancer, PIN and penile cancer
- 4vHPV or 9vHPV vaccine may be used in males over age 26 years old **(no upper age limit)**

National Advisory Committee on Immunization (NACI), March 2017; National Advisory Committee on Immunization (NACI), July 2016.

Office of the Chief Dental Officer of Canada

Government of Canada

OVERVIEW

Human papillomavirus and oral health

Office of the Chief Dental Officer of Canada[1]

Abstract

Canada is among the world leaders in oral health. Despite this, there are growing concerns about the rising rates of HPV-related mouth and throat cancers. The link between human papillomavirus (HPV) and cervical cancer is well established; fortunately, thanks to detection and vaccination, Canada has one of the lowest incidence rates of cervical cancer in the world. The HPV-related mouth and throat cancers, however, present a different picture. In Canada, about 25% to 35% of mouth and throat cancers are related to oral HPV infection; and in 2012, the incidence rate of HPV-associated oropharyngeal cancer was more than 4.5 times higher in males than females. Furthermore, HPV vaccination uptake in Canada is higher among females than males. Physicians and nurses in public health and clinical settings have a role to play in the fight against HPV transmission, as do oral health professionals. Oral health professionals can play a key role in preventing HPV infection and HPV-related oropharyngeal cancers by raising awareness, educating and offering counselling to their clients, and promoting evidence-based preventive and diagnostic interventions.

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Keywords: HPV, oral cancer, oral sex, awareness, oral health professionals

Introduction

Canada is considered to be among the world leaders in oral health (1). Oral health is defined by the Canadian Dental Association as "a state of the oral and related tissues and structures that contribute positively to physical, mental and social well-being and the enjoyment of life's possibilities, by allowing the individual to speak, eat and socialize unhindered by pain, discomfort or embarrassment" (2). It might come as a surprise to most Canadians that there are growing concerns about the rise in numbers of human papillomavirus (HPV)-related mouth and throat cancers (3). Sexually transmitted infections (STIs) are a significant public health concern in Canada (4). However, when one first thinks about STIs, their impact on oral health is often not top of mind. HPV infection is a good example of such an overlooked connection. HPV is both very common and very contagious; and different types of HPV are transmitted through sexual activities. More than 70% of sexually active Canadian men and women will have a sexually transmitted HPV infection at some point in their lives (5). While most people will contract this virus in their genital area, it can also be contracted in the mouth and throat (3). People are generally unaware of this fact, and of the potential consequences of an oral HPV infection (6). This overview will provide a synopsis of HPV, HPV-related oropharyngeal cancer (OPC), and how oral health professionals can contribute to reducing the burden of OPC on individuals and health care.

Human papillomavirus epidemiology

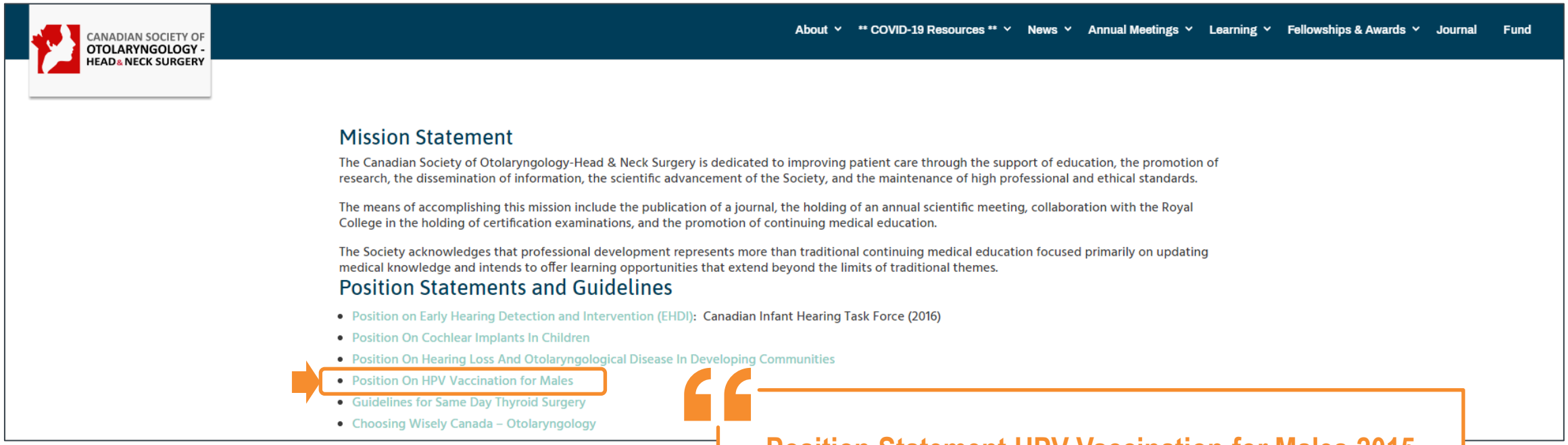
There are over 100 types of HPV and the virus can infect different parts of the body (5). Low-risk strains cause minor ailments, such as warts, whereas high-risk strains can cause cancer (7). HPV is the most common STI in Canada and around the world, and most sexually active Canadians will eventually become infected with the virus (5). In many cases, the infection will disappear on its own, but in the small portion of cases, where the infection remains, it may lead to the development of cancers of the cervix, vagina, penis, anus, mouth or throat (8). It can take years before an infection by the high-risk persistent form of the virus can develop, in some cases, into cancer. Therefore, preventing transmission and immunizing pre-adolescents, teenagers, young adults and other potentially vulnerable groups is important (9).

The causal relation between HPV and cervical cancer is well established (10). HPV is the cause for nearly all cervical cancer (11). Indeed, according to a recent article, "cervical cancer continues to be a major public health problem affecting middle-aged women, particularly in less-resourced countries" (12). According to the World Health Organization, cervical cancer is the fourth most frequent cancer in women worldwide (13). In Canada however, we have seen a sharp decline in both incidence and mortality over time, with one of the lowest incidence rates of cervical cancer in the world (14). The combination of an early adoption of wide-spread screening tests and the introduction of the HPV vaccine played a key role in that decline (15).

> Oral health professionals can play a key role in preventing HPV infection and HPV-related oropharyngeal cancers by raising awareness, educating and offering counselling to their clients, and promoting evidence-based preventive and diagnostic interventions.
>
> *November 5, 2020*

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2020-46/issue-11-12-november-5-2020/human-papillomavirus-oral-health.html

Position statements:
Canadian Society of Otolaryngology-Head & Neck Surgery



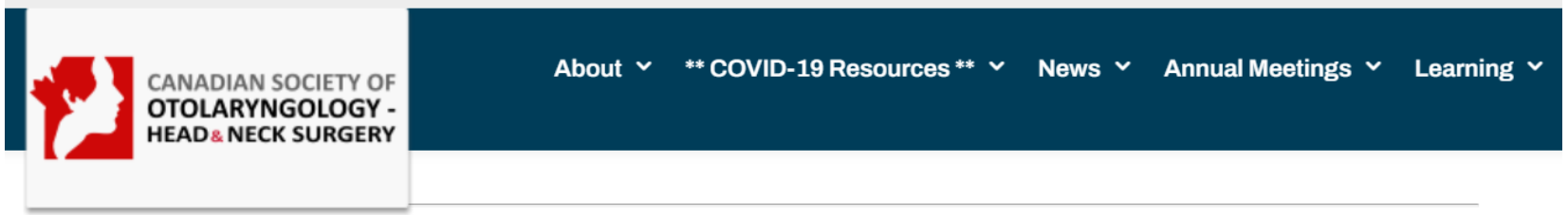
Position Statement HPV Vaccination for Males 2015

Recognizing that human papillomavirus (HPV) is the most common sexually transmitted infection in men and women and that males suffer from the consequences of being infected with HPV, the CSOHNS calls on the Canadian Government to fund HPV vaccination programs for boys and men.

https://www.entcanada.org/cso/position-statements/position-statement-hpv-vaccination-for-males/

Joint statement

Canadian Society of Otolaryngology-Head & Neck Surgery, Society of Obstetrics and Gynecology and Canadian Society of Gynecologic Oncology



GOC
LA SOCIÉTÉ DE GYNÉCO-ONCOLOGIE DU CANADA
THE SOCIETY OF GYNECOLOGIC ONCOLOGY OF CANADA

Positions, Statements and Guideline Links

Bethesda Position FNA

HPV Prevention Statement

Our Ongoing and Neglected HPV Cancer Challenge

Vaccination, Screening and Early Detection will Eliminate HPV-associated Cancers (2021)

THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA

Our Ongoing and Neglected HPV Cancer Challenge

Vaccination, screening and early detection will eliminate HPV-associated cancers

A statement from concerned medical societies in Canada:

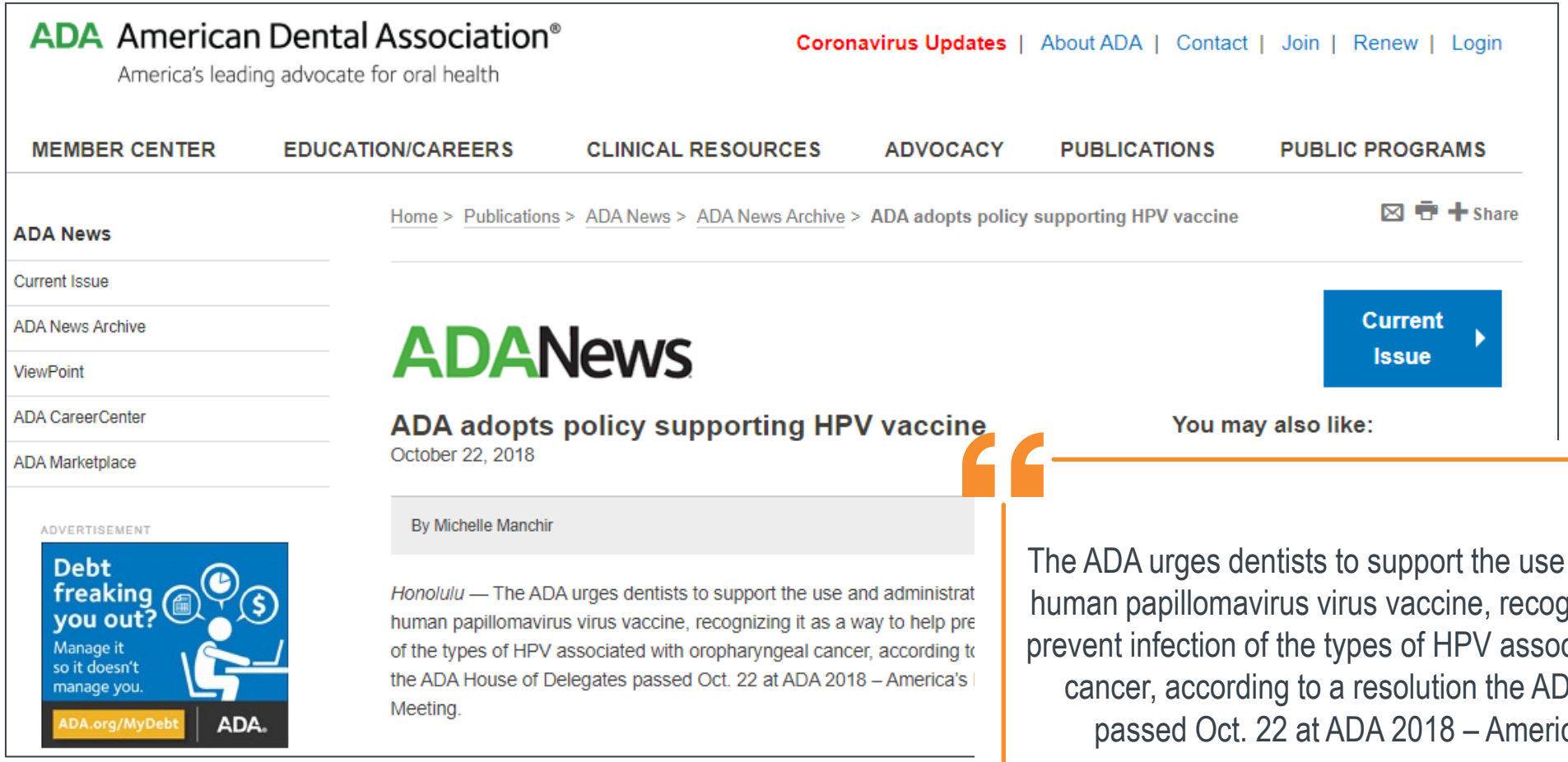
We encourage:

o HPV vaccination of all males and females aged 9 to 45, or any age with on-going risk of exposure to HPV

Position statements:
Alberta Dental Association & College

https://www.dentalhealthalberta.ca/preventing-hpv-positive-oropharyngeal-cancer/

Position statements:
American Dental Association



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By Michelle Manchir

Honolulu — The ADA urges dentists to support the use and administrat
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of the types of HPV associated with oropharyngeal cancer, according t
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Meeting.

> The ADA urges dentists to support the use and administration of the human papillomavirus virus vaccine, recognizing it as a way to help prevent infection of the types of HPV associated with oropharyngeal cancer, according to a resolution the ADA House of Delegates passed Oct. 22 at ADA 2018 – America's Dental Meeting.

https://www.ada.org/en/publications/ada-news/2018-archive/october/ada-adopts-policy-supporting-hpv-vaccine

Resources provided by associations

Ontario Dental Association & Dental Hygienists Association

Patient Fact Sheet

Ontario Dental Association

HPV-Positive Oropharyngeal Cancer

Common questions & answers about HPV-positive oropharyngeal squamous cell cancer (HPV-OSCC)

A fact sheet for patients with HPV-positive oropharyngeal cancer and their families.

Additional Information
A comprehensive list of references is available in:
Fakhry C. and D'Souza G. Discussing the diagnosis of HPV-OSCC: Common Questions and Answers. *Oral Oncology*. 2013

Reprinted with permission from Fakhry C, D'Souza G. Discussing the diagnosis of HPV-OSCC: Common Questions and Answers, *Oral Oncol* (2013), http://dx.doi.org/10.1016/j.oraloncology.2013.06.002

What is Human Papillomavirus (HPV)?

- HPV is a sexually transmitted infection that can infect the oropharynx (tonsils and back of throat), anus, and genitals.
- There are many types of HPV. HPV can cause cancer, warts or have no effect.
- HPV is very common in the U.S. and Canada. Over two million Canadians have some type of genital or oral HPV infection.
- In some people, oral HPV infection leads to HPV-OSCC after many years.

What causes oropharyngeal cancer?

- HPV now causes most oropharyngeal cancers in the U.S. and Canada.
- It is recommended that oropharyngeal tumors be tested for HPV.
- Smoking and alcohol use can also cause oropharyngeal cancer.

How did I get an oral HPV infection?

- HPV is transmitted to your mouth by oral sex. It may also be possible to get oral HPV by other ways.
- Performing oral sex and having many oral sex partners can increase your chances of oral HPV infection.
- Having an oral HPV infection does not mean your partner was/is unfaithful and does not suggest promiscuity.
- Many people with HPV-OSCC have only had a few oral sex partners in their life.

Who has oral HPV infection?

- Many people will likely be exposed to oral HPV in their life.
- Around 10% of men and 3.6% of women in the U.S. and Canada have HPV in their mouths and HPV infection is more commonly found with older age.
- Most people clear the infections on their own within a year or two, but in some people HPV infection persists.

Can I transmit oral HPV infection to others?

Family and Friends:
- Oral HPV is not casually transmitted by sharing drinks or kissing on the cheek.
- We do not know if open mouth kissing can transmit HPV.

Partners of people with HPV-OSCC:
- You have already likely shared whatever infections you have.
- You do not need to change your sexual behaviour.
- Female partners should have regular cervical Pap screening.

New sexual partners in the future:
- Many patients with HPV-OSCC no longer have HPV detectable in their mouth after treatment, while others do.
- With new partners, discuss protection methods (e.g. condoms and barrier protection).

When did I get this infection?

- We do not know the time from first oral HPV infection to cancer but it takes many years.
- We know that some people have infection 15 years or more before cancer.

What does having HPV in my tumor mean?

- Oropharyngeal cancer patients with HPV in their tumor live longer, on average, than people without HPV (i.e. HPV-positive tumors usually respond well to therapy).
- However, patients who currently smoke tobacco or have smoked for a long time in the past do not live as long as patients who never smoked. Patients who are current smokers should consider quitting.

Will the HPV vaccine help me?

- The HPV vaccine prevents people from getting new HPV infections.
- The vaccine will not help you clear an infection you already have.
- The vaccine is recommended for people ages nine to 26 years old.

Will my spouse/partner also get HPV-OSCC?

- The risk of HPV-OSCC may be slightly higher among spouses of HPV-OSCC but this cancer remains rare among spouses.
- There are no recommended screening tests for HPV-OSCC.

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DENTAL HYGIENE FACTS

odha Ontario Dental Hygienists' Association

Human Papillomavirus (HPV) & Oral Care

Recent data show that HPV is contributing to a growing number of head and neck cancers. The incidence of HPV-associated oropharyngeal cancers – cancers of the tonsil, throat and base of the tongue – has been increasing over the last 30 years. It is considered the sixth leading cause of cancer deaths in the world. Studies suggest that the rise could be attributed to changing lifestyles and sexual behaviours, specifically an increase in the number of young people having oral sex with many partners.

ABOUT HPV

HPV is one of the most common sexually transmitted viruses. About 70 per cent of all oropharyngeal cancers are caused by HPV infection. The virus infects the mucous membranes – the moist linings of the body cavity – such as the mouth, nose, throat, tongue, tonsils, vagina, penis and anus. HPV is extremely contagious. It is transmitted from person to person by skin-to-skin contact.

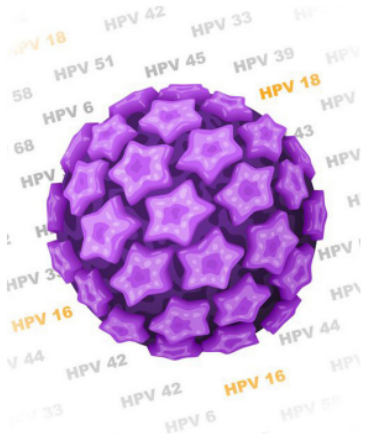
Some facts to consider:

- At least 70 per cent of sexually active men and women will have at least one HPV infection during their lifetime.
- Approximately three to nine million Canadians are infected with HPV. Most HPVs are non-cancerous and easily treated.
- While there are many different high-risk mucosal types of HPV, the most common types of infection associated with cancer are HPV-16 and HPV-18.
- HPV-18 and HPV-16 cause most of the cervical cancers.
- A large percentage of the HPV-positive oropharynx cancers are caused by HPV-16, a strain targeted by Gardasil and Cervarix, the two vaccines currently on the market to prevent cervical cancer.

CLINICAL IMPLICATIONS

Once the mucous membrane is infected with HPV, the virus multiplies throughout the body. Lesions may appear within weeks, months or years. Often individuals don't even know they are infected with HPV.

HPV infections causing genital warts are very contagious and can be contracted through sexual activity with the infected person. This includes kissing and/or touching



the skin of the infected area – like the scrotum, vagina, vulva and anus – and having intercourse. Although HPV is more likely to be transmitted when lesions or warts are visible, transmission is possible even when warts aren't visible.

SIGNS AND SYMPTOMS

- Genital warts are small, flat or cauliflower-shaped lesions that appear in the genital area, including the vagina, cervix, vulva, penis, scrotum and anus. They are usually painless but they can bleed, itch or have some discharge.
- Precancerous lesions or cervical dysplasia are abnormal cells in the cervix. These are painless and can only be detected with a Pap test.
- Infection in the oral cavity can be detected by:
  - A sore throat that doesn't respond to antibiotics
  - Hoarseness of voice
  - Pain when swallowing or chewing
  - A lump in the throat
  - Bleeding in the mouth
  - Oral lesions that don't heal

Dental Hygienists: Your Partners in Oral Health

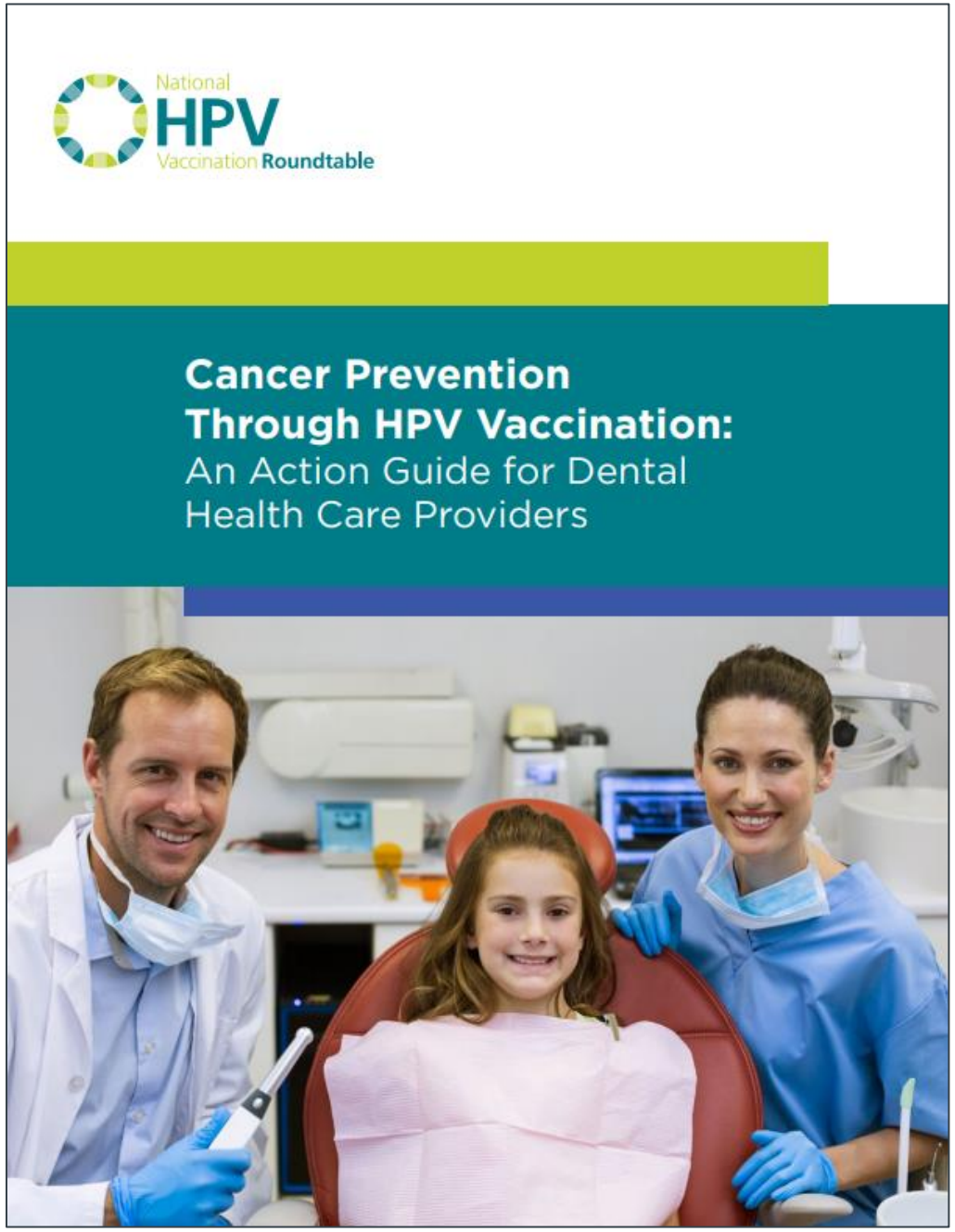
www.odha.on.ca

Resources provided by organizations
HPV Vaccination Roundtable

National HPV Vaccination Roundtable

The HPV Vaccination Roundtable is a national coalition created by the American Cancer Society (ACS), with funding from the Centers for Disease Control and Prevention, to be a trusted source of information on HPV vaccination.

https://hpvroundtable.org/action-guides/



Summary of Key Points

Summary: HPV-Related Head & Neck Cancers

- Infection with **human papillomavirus (HPV)** is a risk factor for some types of head and neck cancers, particularly **oropharyngeal** cancers that involve the tonsils or the base of the tongue

- Globally, oropharyngeal cancer incidence rates are **higher** and have increased more sharply **among men** than women

- In Canada, the incidence of HPV-related oropharyngeal cancers (OPC) has been on the rise since the mid-1990s, and in 2012, these were reported to have surpassed the number of cervical cancers.

- **Worldwide**, among cases of HPV-related head and neck cancers,

HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 combined

were responsible for

Summary: HPV-Related Head & Neck Cancers

- Incidence of HPV-Related oropharyngeal cancers is **increasing** while cancers typically related to smoking and drinking are **decreasing**

- Development of head and neck squamous cell carcinoma from an HPV transforming infection may take more than

10 years

- Non-cervical cancers account for a substantial proportion of the **global economic burden** of **HPV-related cancers**

Summary: HPV Vaccination for the Prevention of Head & Neck Cancers

- The 9-valent HPV vaccine has been approved by Health Canada for the prevention of **oropharyngeal cancer and other head & neck cancers** caused by HPV types 16, 18, 33, 45, 52, and 58.
  - And is currently being investigated for the **prevention of oral persistent HPV infection in males 20-45 years of age** in a randomized, placebo-controlled confirmatory trial (V503-049; NCT04199689).