

HPV Affects Men Differently than Women: is prevention the same for both?



Panellist: Dr. Anthony Zeitouni MD, MSc, FRCSC

Associate Professor of Otolaryngology and Head and Neck Surgery: McGill University
Director (OTL-HNS) Skull Base Program: McGill University
Chair, Head and Neck Tumour Board, McGill University Health Centre



Panellist: Dr. Cecilia Dong DMD, BSc (Dent), MSc (Prosthodontics), FRCDC(C)

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Cross-appointments in the Departments of Pathology and Laboratory Medicine, & Otolaryngology - Head and Neck Surgery;
Centre Affiliate, Centre for Education Research and Innovation (CERI)



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Chair, 19 To Zero
Public Health and Preventive Medicine Physician
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Physician, Cleveland Clinic Canada
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Moderator: Dr. Marc Steben MD, CCFM, FCFM

Chair of the Canadian Network on HPV Prevention
Co-President, HPV Global Action
School of Public Health, Université de Montréal
Board Member & Education Committee Chair, International Papillomavirus Society



Organizer: George Wurtak BSc, MED

Executive Director, Consortium for Infectious Disease Control
Director, Canadian Network on HPV Prevention
Founding Chair, International Indigenous HPV Alliance

Webinar Objectives

- Summarize the burden of HPV and differences in natural history of HPV-associated diseases
- Compare HPV-related disease impacts between male and female patients
- Propose methods to increase patient awareness of head and neck cancer issues and for HPV prevention overall
- Elaborate on the ways that different specialties can improve HPV awareness and prevention

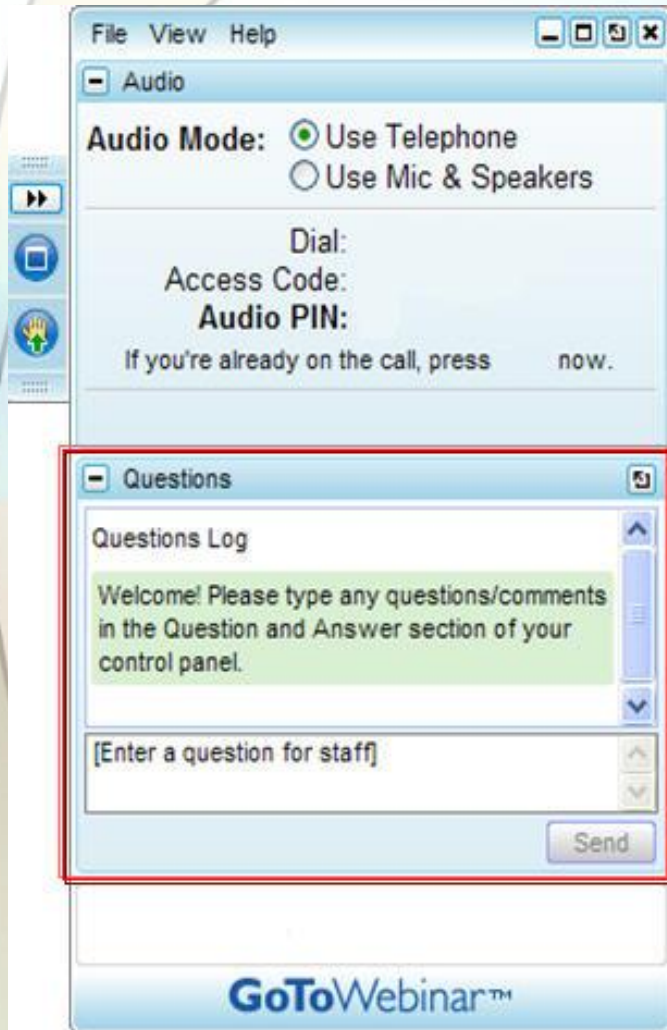
Administrative Information

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- Submit questions at any time by typing in the "Questions" pane on the control panel & click 'Send' button
- Questions will be answered at the end of the presentation

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Moderator



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- Chair, Canadian Network on HPV Prevention
- Co-President, HPV Global Action
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- Board Member & Education Committee Chair, International Papillomavirus Society
- 2023 president elect, International society for STD research

Presenter



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OROPHARYNX CANCER

Anthony Zeitouni, MD, FRCSC

Associate Professor, Otolaryngology Head & Neck Surgery

McGill University



Centre universitaire de santé McGill
McGill University Health Centre



McGill

HEAD AND NECK CANCER

- 6.5% of annual cancer cases worldwide
- 2/3 men
- 1/3 women
- 5000 new cases in Canada per year
- One of the top 10 cancers for men



HPV ASSOCIATED HEAD AND NECK CANCERS

- Epidemiology of this emerging epidemic
- Clinical manifestations and diagnosis
- Overview of treatment options
- Burdon of this cancer
 - Physical
 - Psychological

HEAD AND NECK SURGERY

- Squamous cell cancer of the upper aerodigestive region
- Parotid and salivary gland cancers
- Skin cancers
- Thyroid cancers
- Sino-nasal cancers
- Skull Base tumors

SQUAMOUS CELL CANCER OF THE UPPER AERODIGESTIVE SPHERE

- Squamous cell cancers
- Change a person's ability to interact in society
- Speaking
- Eating
- Swallowing
- Appearance

HEAD AND NECK SQUAMOUS CELL CANCER

- Oral Cavity

- **Oropharynx**

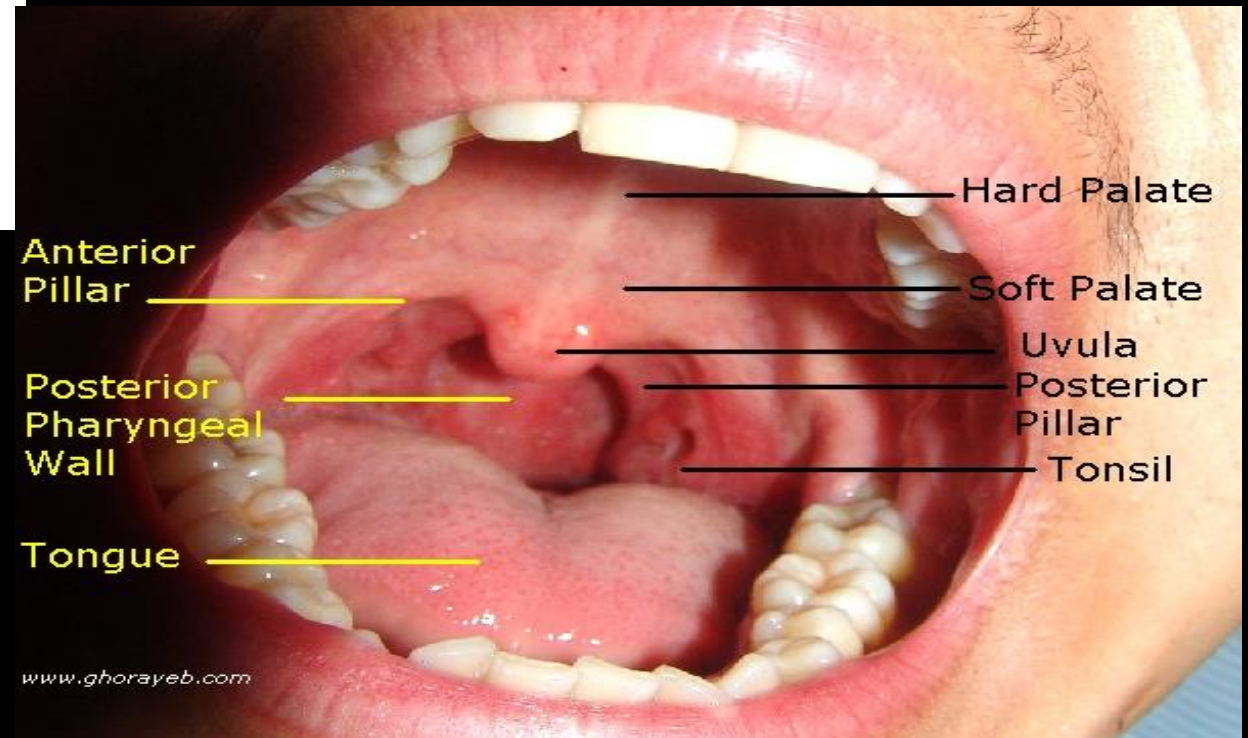
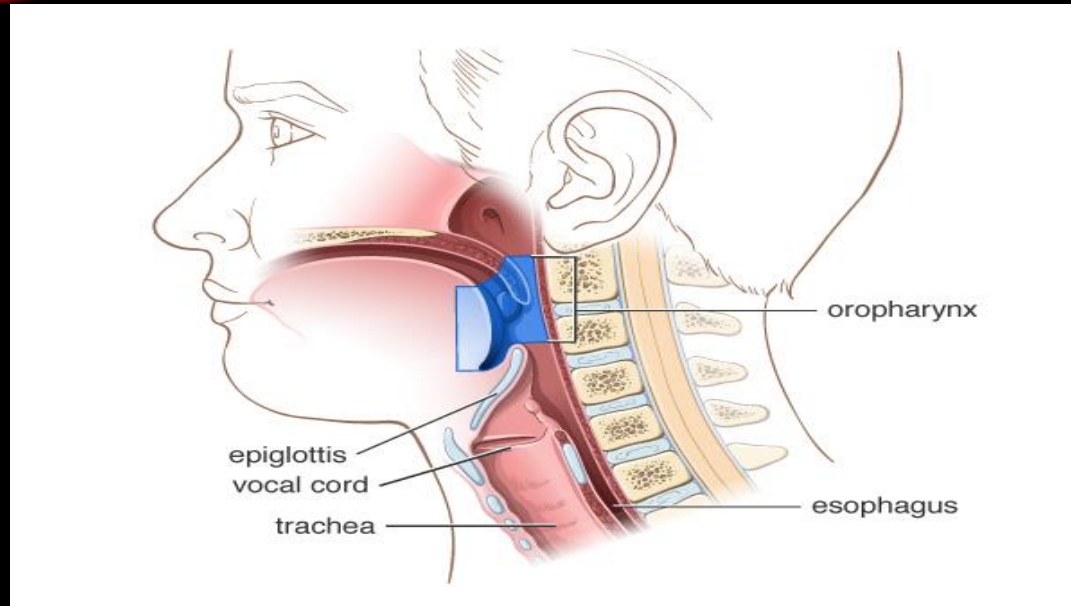
- Larynx

- Nasopharynx

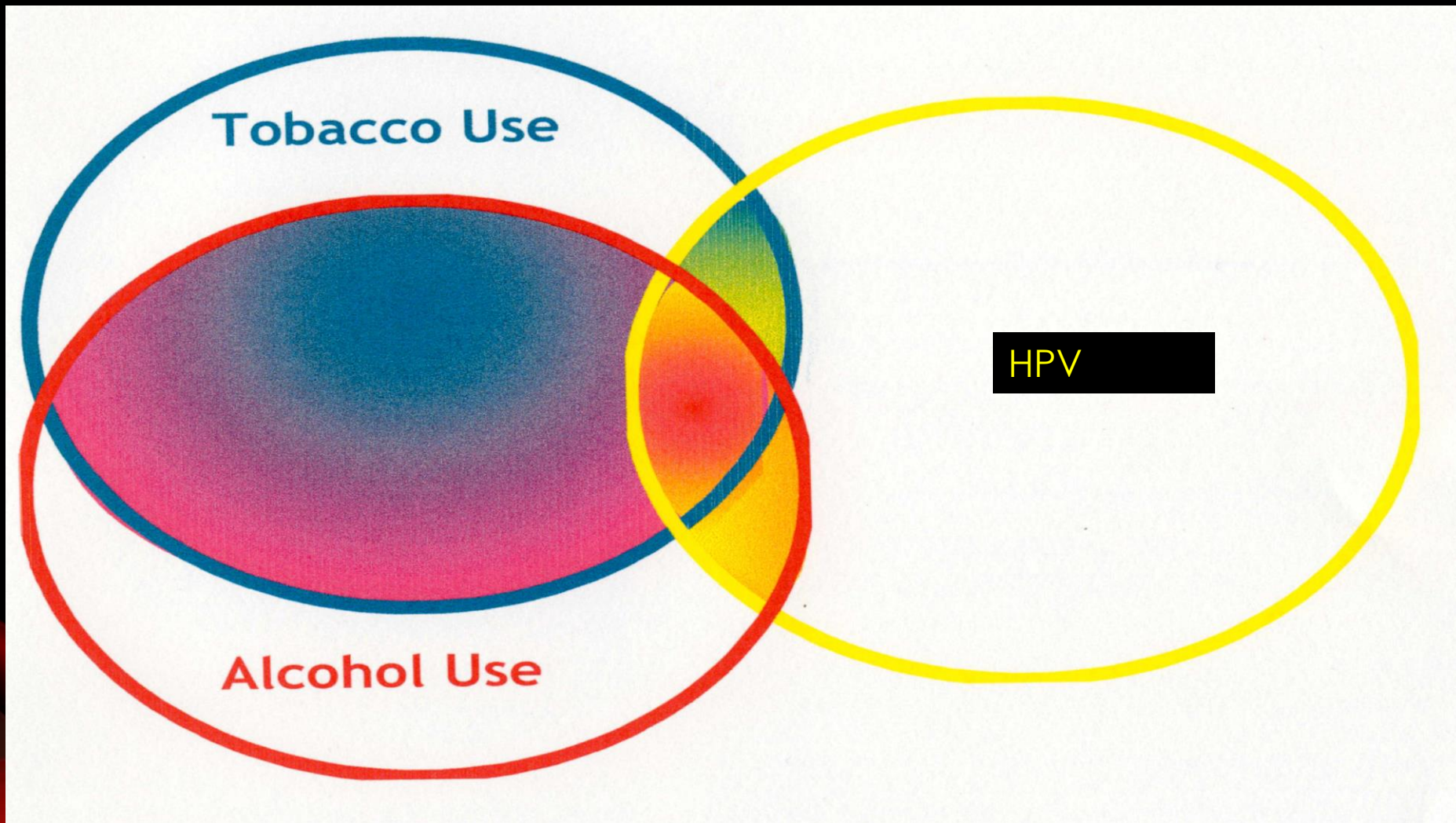
OROPHARYNGEAL SITES

- The oropharynx begins where the oral cavity stops.
- Base of tongue (the back third of the tongue),
- soft palate,
- tonsils and tonsillar pillars,
- the back wall of the throat.

OROPHARYNX



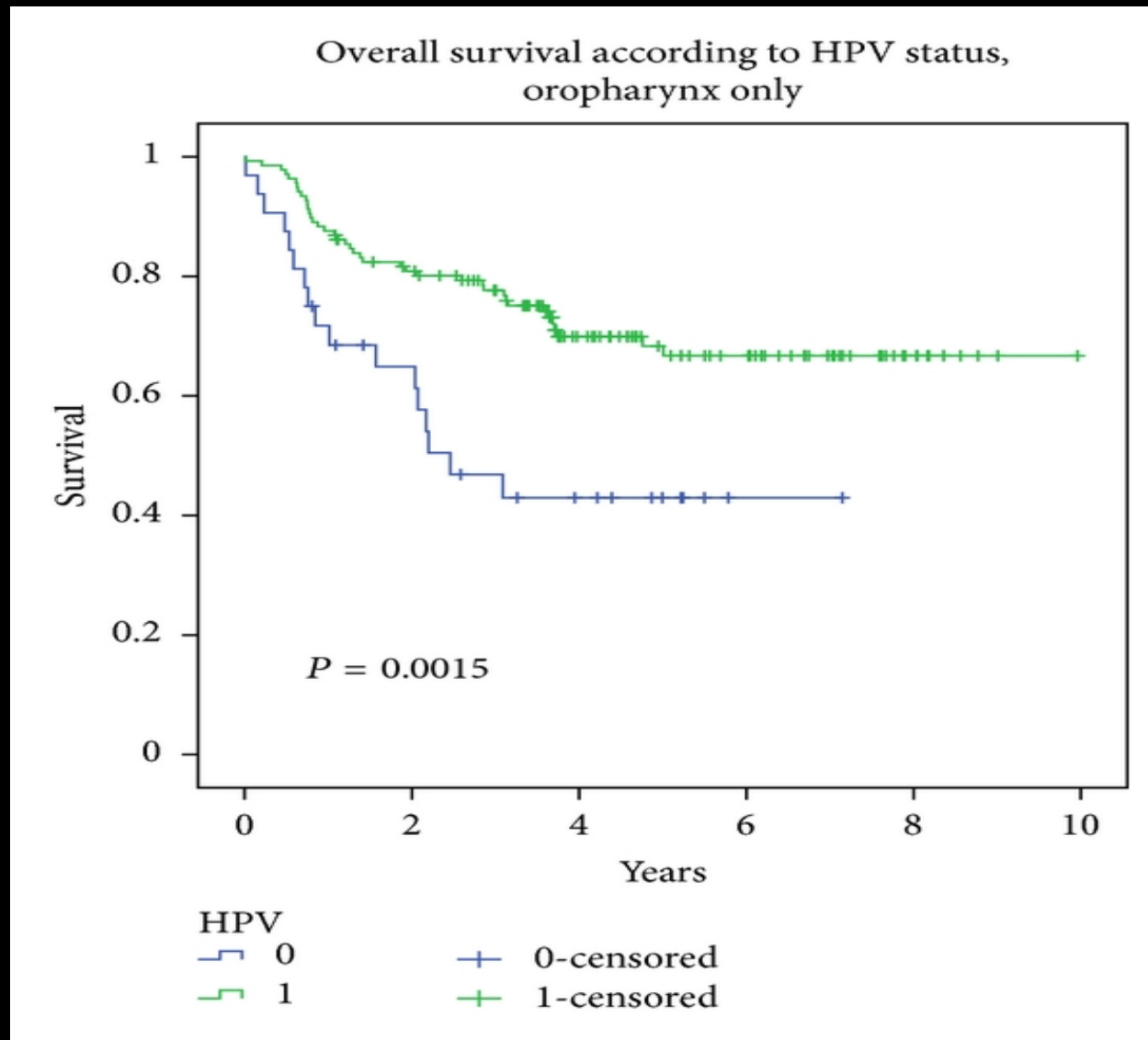
Head and Neck Cancer Risk Factors



OROPHARYNX SCCA: TWO DISTINCT DISEASES

	HPV POSITIVE	HPV NEGATIVE
Histology	Basaloid	Keratinized
Age	Younger	Older
Gender	3:1 men	3:1 men
SE status	High	low
Risk Factors	Sexual Behaviour	ETOH, Tobacco
Cofactors	Marijuana, immunosupp	ETOH, Tobacco
Incidence	Rising	Falling
Survival	Better	Worse

Overall survival according to HPV status



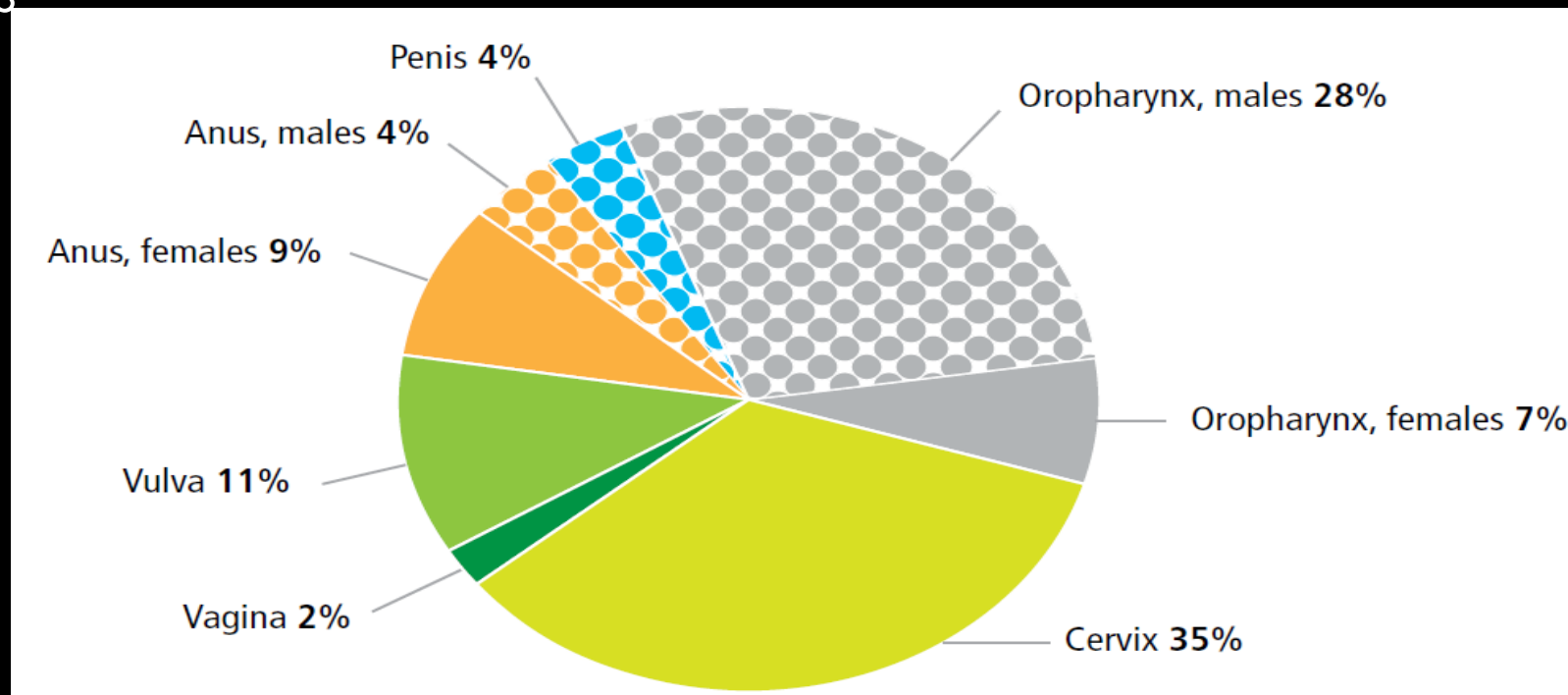


Incidence of HPV-associated cancers

- 3760 cases were diagnosed in 2012 (64% in females ; 36% in males)
- OPC and cervical cancers were the most commonly diagnosed, followed by anal and vulvar cancers

Proportion (%) of new cases for selected HPV-associated cancers, Canada 2012*

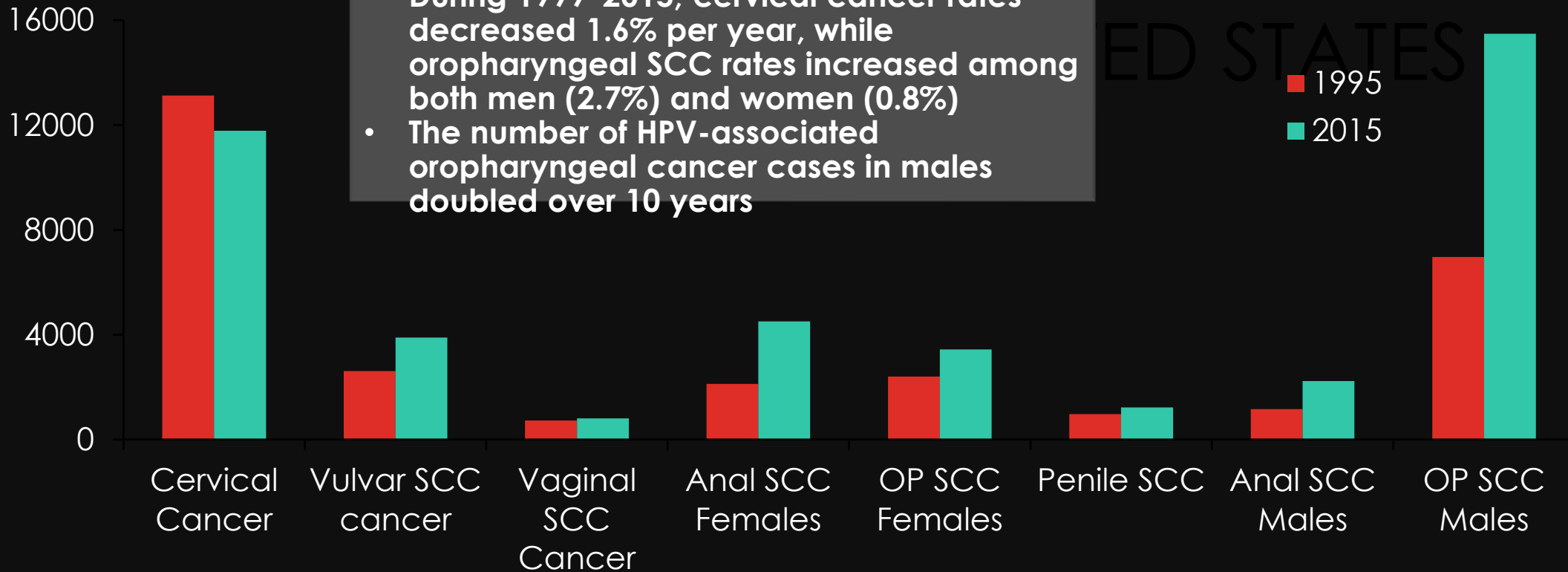
*Quebec data are from 2010



TRENDS IN HPV-ASSOCIATED CANCERS

1999-2015

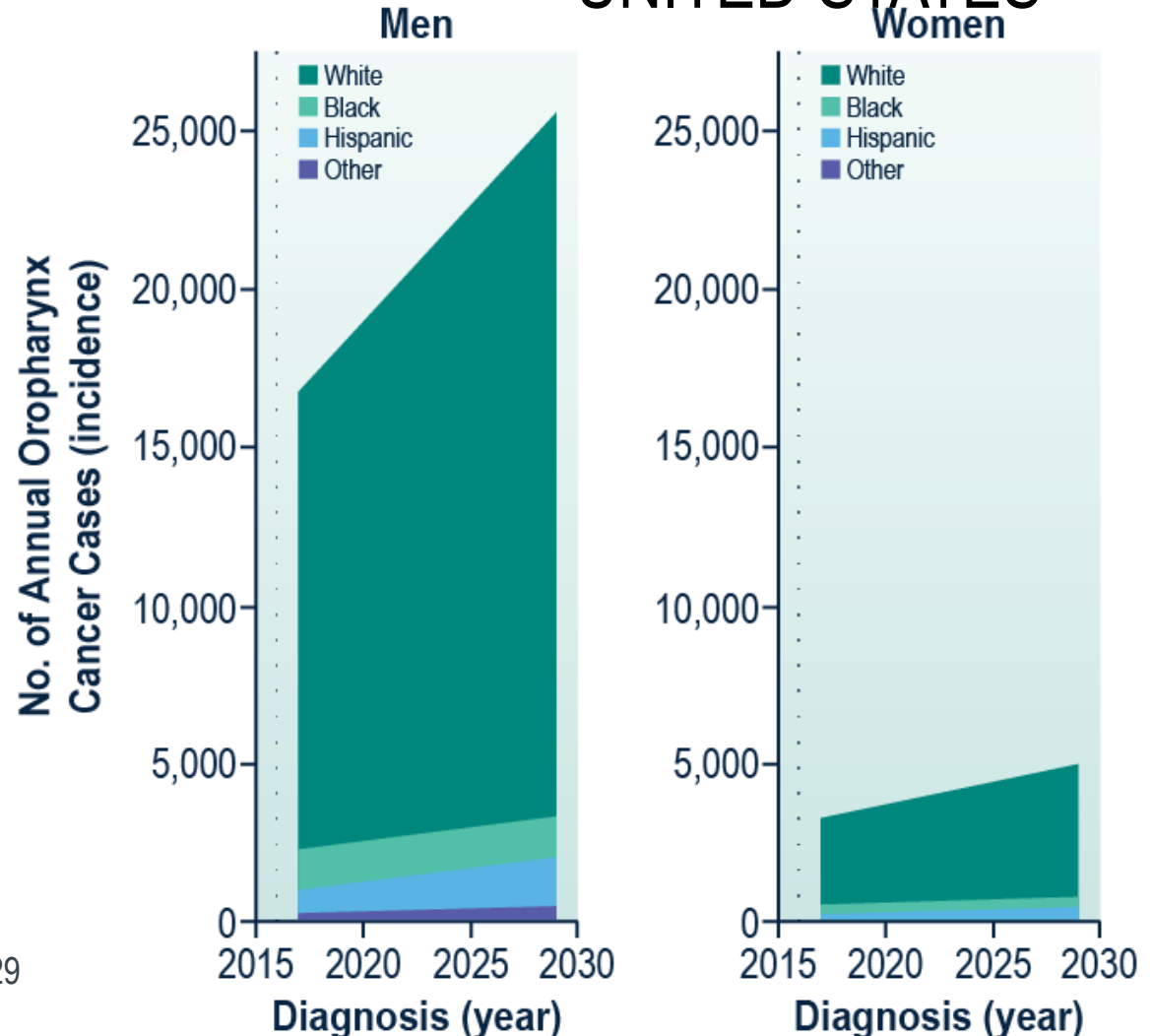
UNITED STATES



OP: Oropharyngeal; SCC: Squamous Cell carcinoma

PROJECTED OROPHARYNGEAL CANCER RATES: UNITED STATES^A

- Analysis projects a dramatic increase in annual number of oropharyngeal cancer cases in the US:
 - From **20,124 cases** in 2016 to **30,629 cases** in 2029
- **Increase is primarily driven by**
 - Older white males and females ≥ 65 years of age
- Most dramatic increase projected to be in **older white males**



An analysis forecasted the future burden of oropharynx cancers through 2029 by projecting the observed cohort-specific age-specific incidence rates.

HPV: THE MOST COMMON SEXUALLY TRANSMITTED DISEASE

- Most individuals will have at least one infection
- Infection occur via oral sex
- Infection is usually cleared in 6-12 months
 - Men mount lower antibody response
 - Accounting for risk factors men have 2.3 x oral HPV infection
- Infections usually resolve
- Very rarely lead to cancer
- Cancer develops over many decades

WHY MORE FREQUENT IN MEN?

- Higher number of partners
- Only explains part of the difference in prevalence
- Per partner risk is 3-4 times higher in men than women
- Chaturvedi et al: data consistent with higher transmission when oral sex performed on a woman by a man
- Differences in immune response between genders

DIAGNOSES

- Oropharynx cancer presentation different HPV – vs HPV+
- HPV –
 - Present most often with a sore throat x months
- HPV +
 - Present with a neck node or persistent sore throat
 - Unilateral painful tonsil



The McGill Head & Neck Cancer Fund
Fonds de recherche McGill des cancers tête et cou
 Department of Otolaryngology - Head and Neck Surgery
 Département d'Oto-rhino-laryngologie et de chirurgie cervico-faciale

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Michael Douglas

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MICHAEL





DIAGNOSIS:
NECK NODES





UNILATERAL TONSIL
SWELLING
WITHOUT ULCER



BASE OF TONGUE MASS



PRIMARY CAN BE VARIABLE IN SIZE. TONSIL, BASE OF TONGUE PALATE

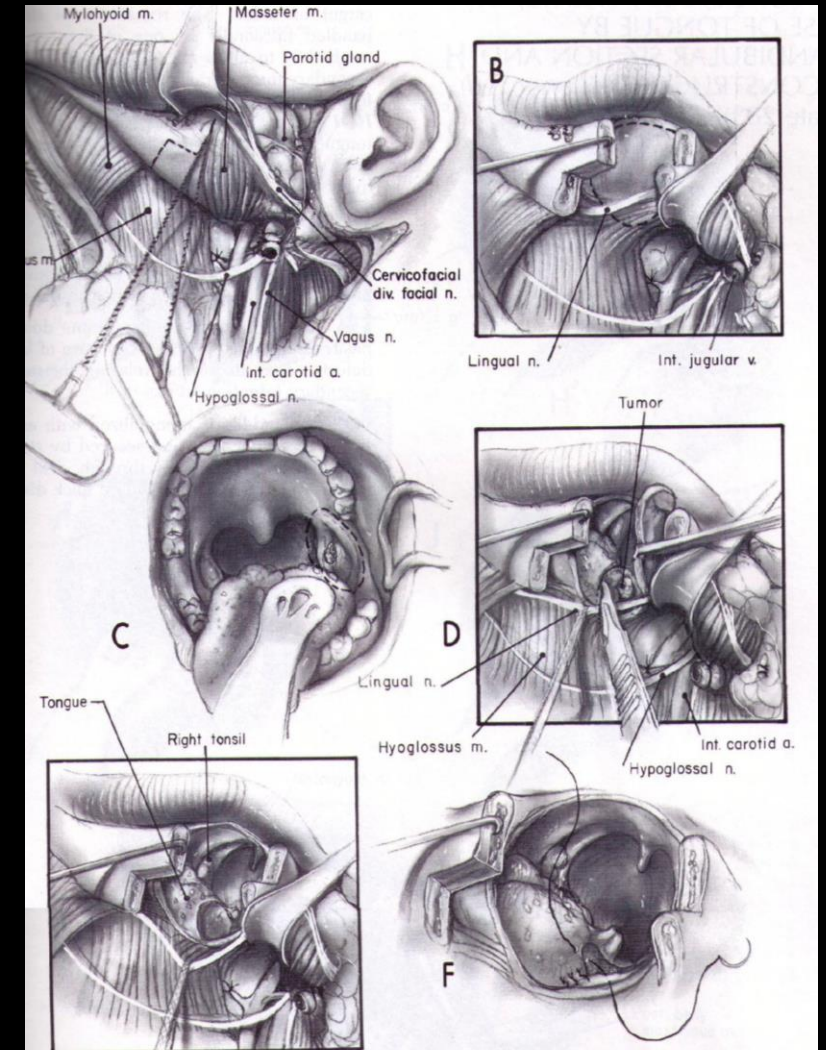
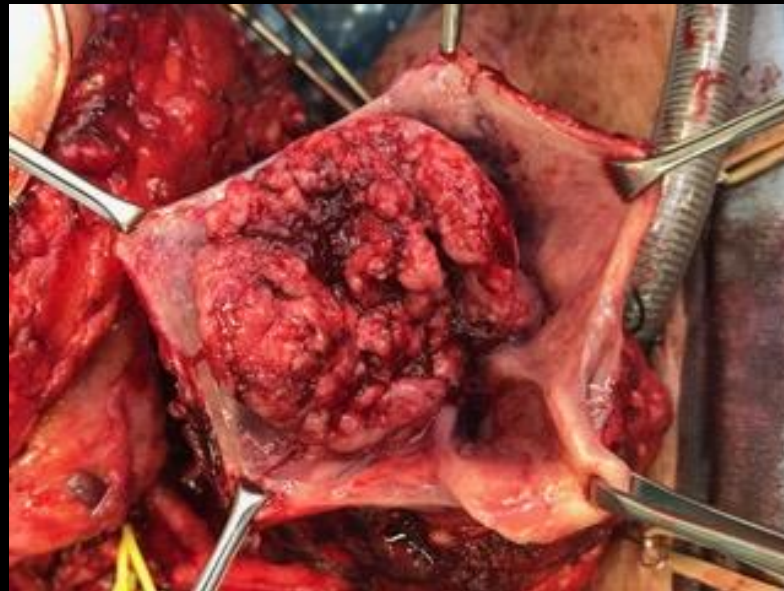


TREATMENT

- Surgical
- Radiation
- Chemo
- Psycho-oncological

TREATMENT

- In 1970-90
- Open surgical approaches
- Followed by radiation
- Effective but surgery led to significant morbidity



TREATMENT

- Chemo-radiation
- High dose of radiation with chemotherapy to augment the effect of xrt
- Worked well in eradicating disease
- High morbidity
- 10-30 % of patients could not swallow after
- PEG dependence
- Dry mouth, dental disease...

ROBOTICS



ROBOTIC SURGERY

- Transoral resection
- 5 yr local control >90%
- 14% temporary trach
- 4% permanent G tube





COMPLICATIONS

- Psycho-social
- Physical

PSYCHOLOGICAL COMPLICATIONS

- Secondary to having a head and neck cancer
 - Disfigurement
 - Loss of functions related to speech and eating
 - Highest rates of anxiety and depression
 - Highest rates of suicide ideation
- Secondary to having a HPV, thus sexually transmitted cancer
 - Fear, shame, guilt
 - Issues of infidelity

COMPLICATIONS- PSYCHOLOGICAL

- Sexually transmitted nature of this cancer
- Disfigurement
 - Very high in Head and Neck cancer patients
- Depression
 - Highest level of any cancer site
- suicide risk
 - Head and neck patients have the highest risk of any cancer site

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



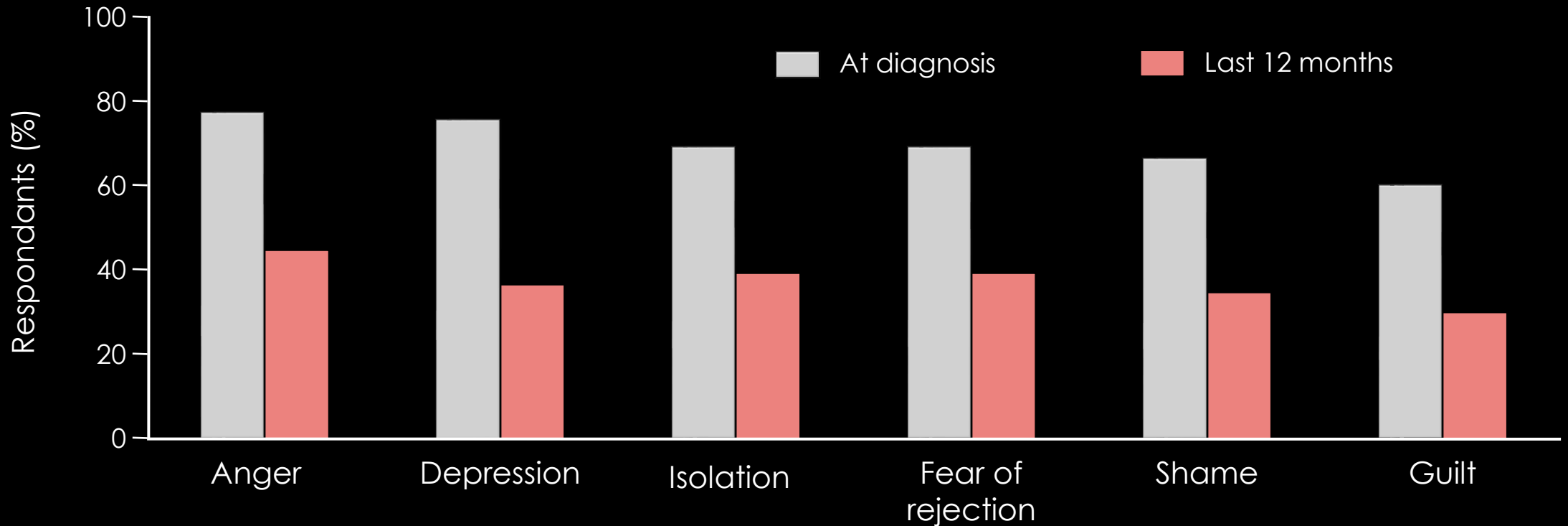
•difficulty speaking
•depression



IMPACT OF HPV-POSITIVE STATUS ON PATIENTS WITH OPC AND THE NEED FOR COUNSELING

- The psychosocial burden of an HPV diagnosis has been well documented among women with cervical cancer.
- Limited study measuring the impact of HPV-positive status of patients with OPC.
- Patients within these populations all share the same risk factors.
- It is necessary to extrapolate from the wealth of available data on women with HPV-induced cellular lesions

PSYCHOSOCIAL REACTION TO DIAGNOSES OF HPV



n = 454

COMPLICATIONS: PHYSICAL

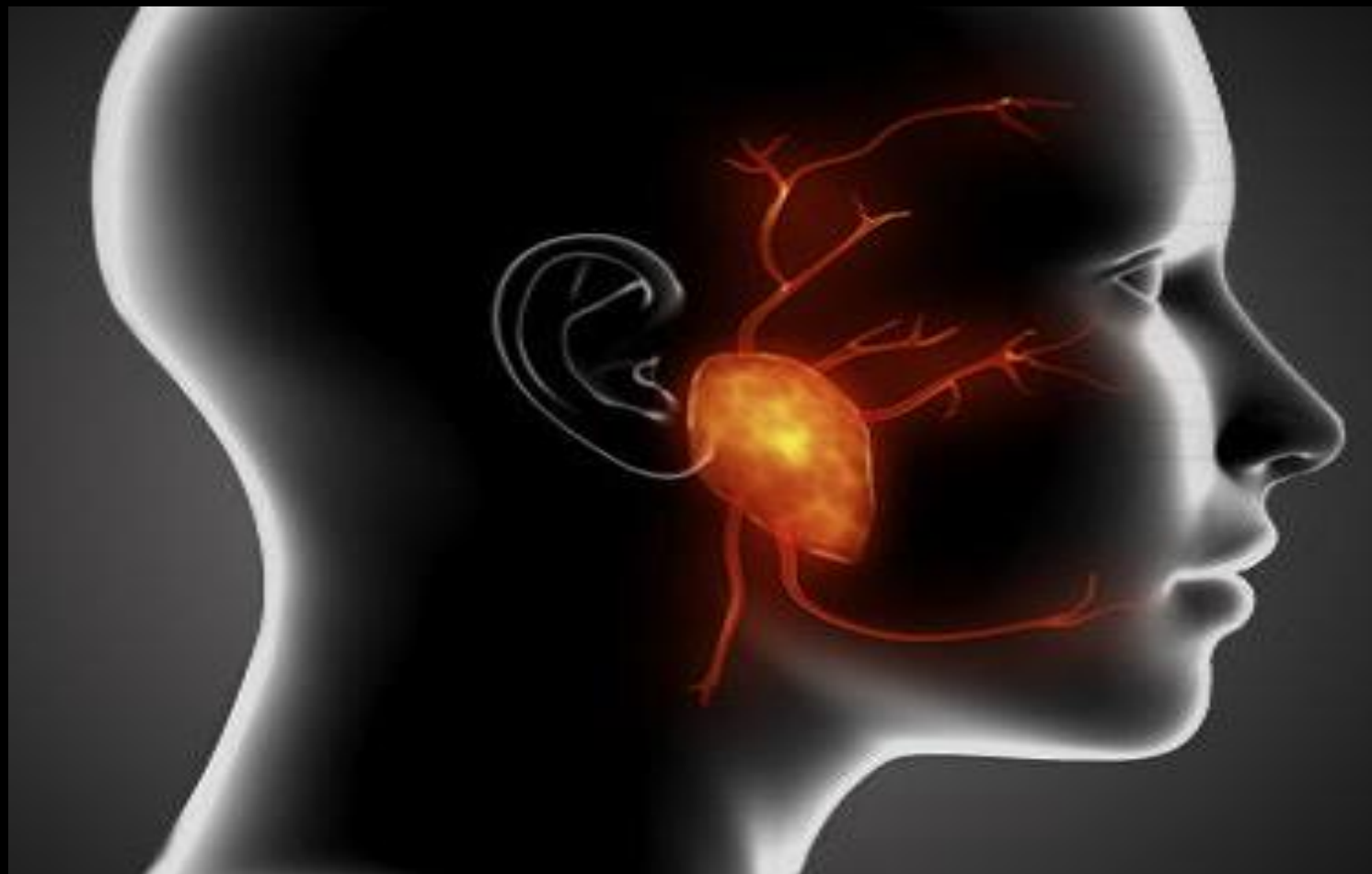
- Skin
 - Scars, contracture
 - lymphedema
- Mucosal
 - XRT leads to loss of salivary function
 - Dental problems
 - Xerostomia
 - Dysphagia and scarring
- Trismus:
- Endocrine: loss of thyroid function
- Unable to eat by mouth = 30%



HPV ASSOCIATED HEAD AND NECK CANCERS

- Epidemiology of this emerging epidemic
- Clinical manifestations and diagnosis
- Overview of treatment options
- Burdon of this cancer
 - Physical
 - Psychological

THANK YOU



Presenter



Dr. Cecilia Dong DMD, BSc (Dent), MSc (Prosthodontics), FRCD(C)

- Assistant Professor, Division of Prosthodontics, Schulich School of Medicine and Dentistry: Western University
- Cross-appointment in the Department of Pathology and Laboratory Medicine
- Cross-appointment in the Department of Otolaryngology - Head and Neck Surgery
- Centre Affiliate, Centre for Education Research and Innovation (CERI)

Speaker

DR. CECILIA DONG

Dr. Cecilia Dong completed a two-year pre-dentistry program at Brandon University, was awarded a DMD degree and a BSc(Dent) degree from the University of Manitoba, and practiced general dentistry in Brandon, Manitoba before earning a MSc(Prosthodontics) degree from the University of Toronto. She was a full-time academic at the University of Manitoba and worked part-time in private practice as a prosthodontist. Her experience with HPV-related head and neck cancer developed while working as a part-time dental consultant at CancerCare Manitoba and conducting a chart review study on patient-reported symptoms from oropharyngeal cancer patients.

Dr. Dong joined the Schulich School of Medicine and Dentistry, Western University in August 2019. She has developed prosthodontic curriculum for dental students and is involved in interprofessional education. She has research collaborations with colleagues in the Department of Oral Pathology and Laboratory Medicine as well as the Department of Otolaryngology – Head and Neck Surgery. Her passion for quality dental education and quality patient care aligns with her connection to the Centre for Education Research and Innovation (CERI).

She initiated a connection with Merck Canada in early 2020 and has been involved on the ground floor opening up HPV vaccination to the dental community. She is an examiner for the Royal College of Dentists of Canada and Chair of the Education Committee for the Canadian Society for Disability and Oral Health.

A microscopic view of cells, likely showing a cluster of cells with a teal overlay. The cells are arranged in a somewhat regular pattern, and the teal color highlights the cell boundaries and internal structures. The background is dark, making the teal cells stand out.

Impact of HPV-Related Head & Neck Cancers

May 12, 2023

Cecilia Dong, DMD, BSc (Dent), MSc (Prosthodontics), FRCD(C)

DISCLOSURE

- While I have accessed resources from Merck Canada to develop this presentation, the perspective from which I present is my own.
- I have received honoraria from Merck Canada for educational presentations.

OBJECTIVES

1. To describe the **impact of HPV-related disease**.
2. To compare the impact of HPV-related disease between **male and female** patients to **inform prevention strategies**.

A microscopic view of HPV particles, showing numerous spherical, multi-layered structures with a distinct outer shell and a darker core. The particles are densely packed and appear to be interacting with a surface, possibly a cell membrane. The background is dark, making the glowing green particles stand out.

The Impact of HPV-Related Disease

Anatomy of the Head and Neck

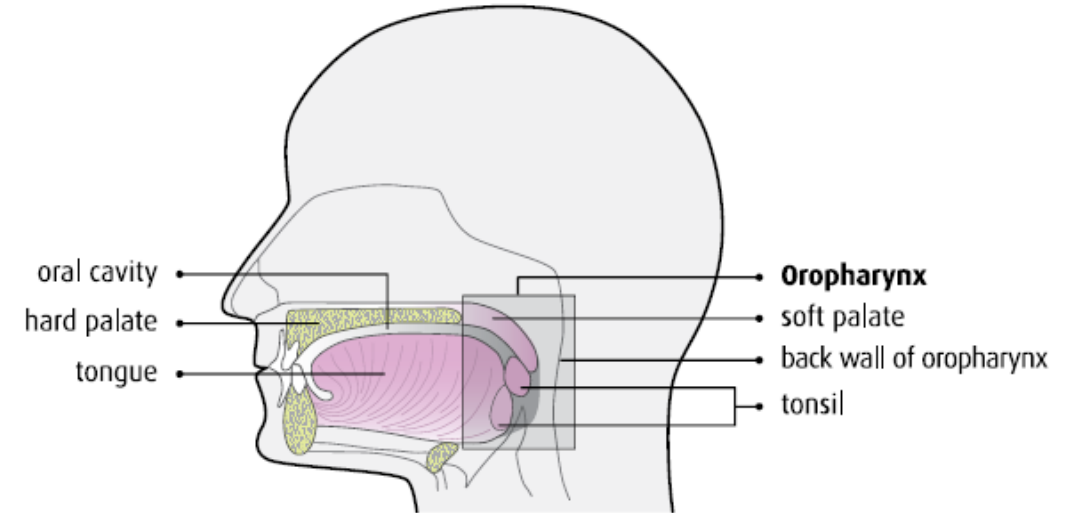
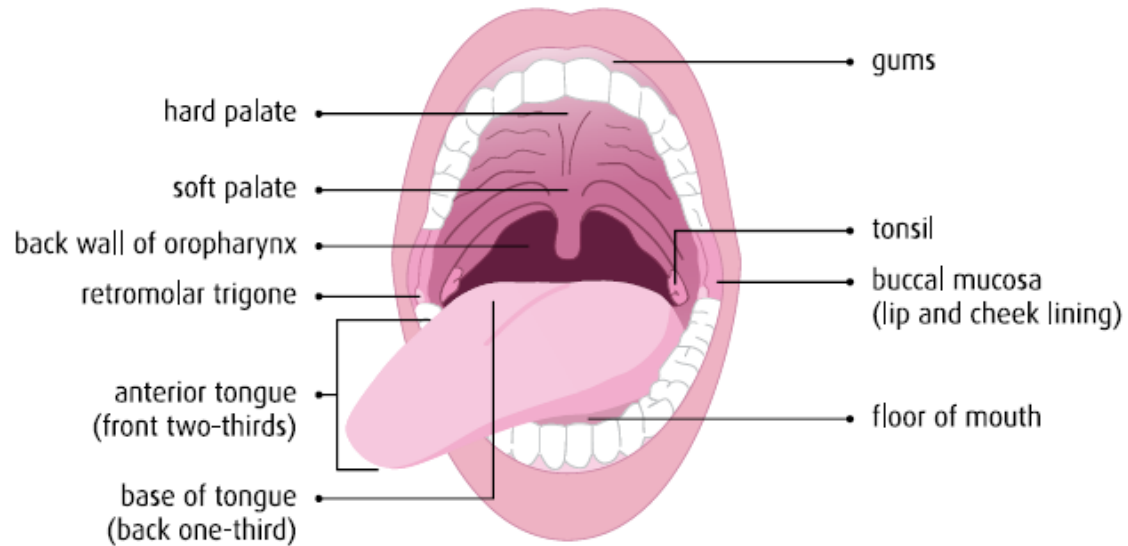


Figure 7.7: Selected anatomical sites of the oropharynx and oral cavity created by Canadian Cancer Society

Oropharyngeal cancers (OPC)

Head and neck cancers at sites known to be related to HPV (mainly the base of the tongue, tonsils and other oropharynx)

Oral cavity cancers (OCC)

Cancers of oral sites that show a stronger association with tobacco and alcohol

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

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



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



EMPLOYMENT & RETURN TO WORK

Background: Human papillomavirus (HPV)-positive oropharyngeal cancer primarily affects working-age adults. Chemotherapy and radiation (CTRT) used to treat this disease may adversely impact a survivors' ability to work after treatment.

Methods: We surveyed participants with HPV-positive oropharyngeal cancer who completed CTRT regarding employment. We examined the associations between 1) sociodemographic and clinical factors and employment outcomes, and 2) health-related quality of life and satisfaction with ability to work.

Results: 102 participants were employed full-time at diagnosis for pay and surveyed at a median of 23 months post-CTRT (range 12–57 months). The median age at diagnosis was 57 years (range 25–76 years). During CTRT, 8 % stopped working permanently, 89 % took time off or reduced responsibility but later returned, and 3 % reported no change. For those who took time off but returned, median time to return to work was 14.5 weeks. In multivariable analysis, younger age predicted for needing more than the median time off. At time of survey, 85 % participants were working, 7 % had retired, and 8 % were not working for other reasons. Seventeen percent of participants were not satisfied with their current ability to work, which was associated with poorer health-related quality of life and persistent treatment toxicities ($p < 0.001$).

Conclusions: CTRT interrupts employment in the majority of working patients with HPV-positive oropharyngeal cancer but most return. However, treatment-related toxicities might lead to dissatisfaction with ability to work.

Baxi SS, Salz T, Xiao H, Atoria CL, Ho A, Smith-Marrone S, Sherman EJ, Lee NY, Elkin EB, Pfister DG. Employment and return to work following chemoradiation in patient with HPV-related oropharyngeal cancer. *Cancers Head Neck*. 2016 Jun 3;1:4. doi: 10.1186/s41199-016-0002-0. PMID: 31093334; PMCID: PMC6457145.

Purpose: Human papillomavirus (HPV)-associated oropharyngeal cancer (OPC) commonly affects people of working age, yet there is limited data regarding the return-to-work experience in this cohort. This study aimed to investigate the proportion of survivors currently working after completion of radiation therapy and to explore potential facilitators and barriers to working after treatment.

Methods: A cross-sectional, single-institutional study was undertaken at the Peter MacCallum Cancer Centre, a comprehensive cancer center in Melbourne, Victoria, Australia. Eligible participants were 18 to 65 years old at diagnosis, were employed at or within the 3 months before diagnosis, and had completed curative treatment for HPV-associated OPC ≥ 4 months before enrollment. Participants completed a paper-based survey to assess baseline demographics, employment status, and quality of life (QOL; Functional Assessment of Cancer Therapy Head and Neck). Open-ended questions explored factors affecting return to work. Associations between current employment status and various disease, treatment, and demographic variables and with QOL were examined. Free-text items were analyzed by summarizing content analysis.

Results: Of 93 participants approached, 68 responded (73.1%). Mean age was 54.1 years (range, 39-64 years), and 89.7% were male. Most participants (67.6%) had stage II disease and were treated with chemoradiation (85.3%). Mean time after treatment was 2.6 years (range, 0.3-9.1 years). Fifty-eight of 68 participants (85.3%) were working at enrollment; median time to return to work was 6.0 months (interquartile range, 4-10 months); 45 (77.6%) were in the same role and 35 (60.3%) worked the same number of hours. Ten participants were not working, 3 had retired, 5 reported persistent and significant treatment toxicity preventing employment. Survivors currently working reported higher physical, functional, and global QOL scores. Access to leave and support from treating doctors were facilitators for return to work, whereas fatigue was frequently reported as a barrier to returning to work.

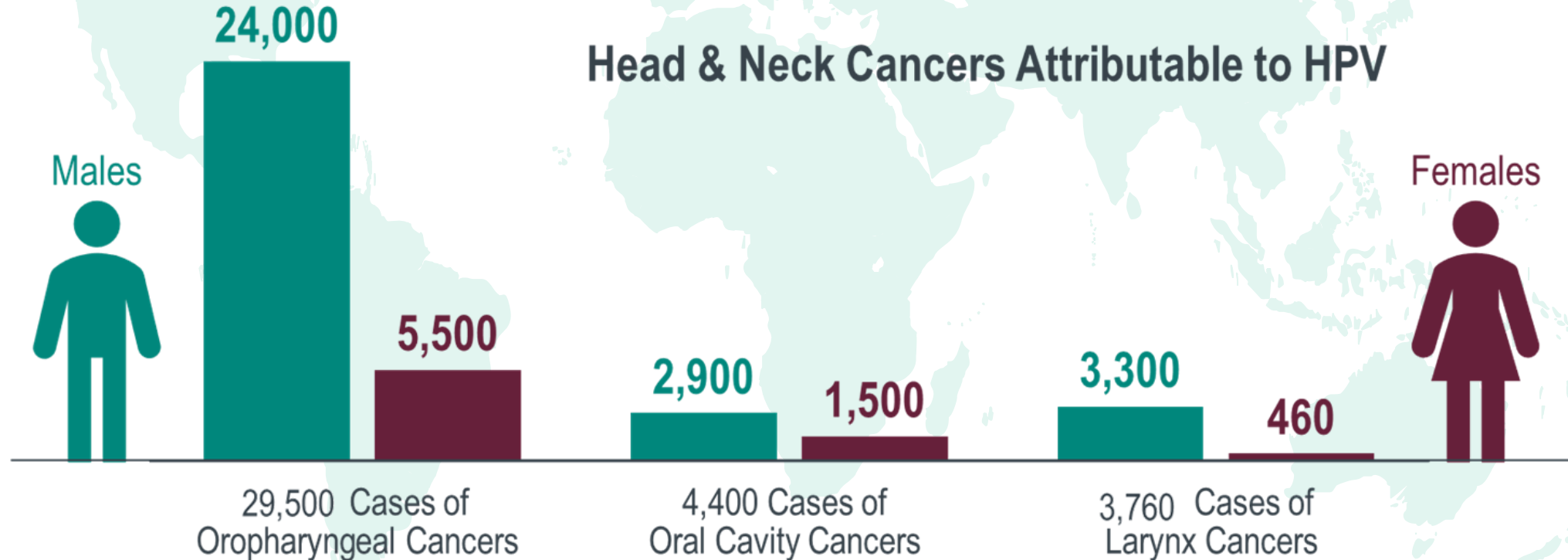
Conclusion: With time, the majority of participants with HPV-associated OPC will return to work after radiation therapy. Attention to symptom management and support from the workplace may enable more successful return to work.

The Impact of HPV-Related Disease



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

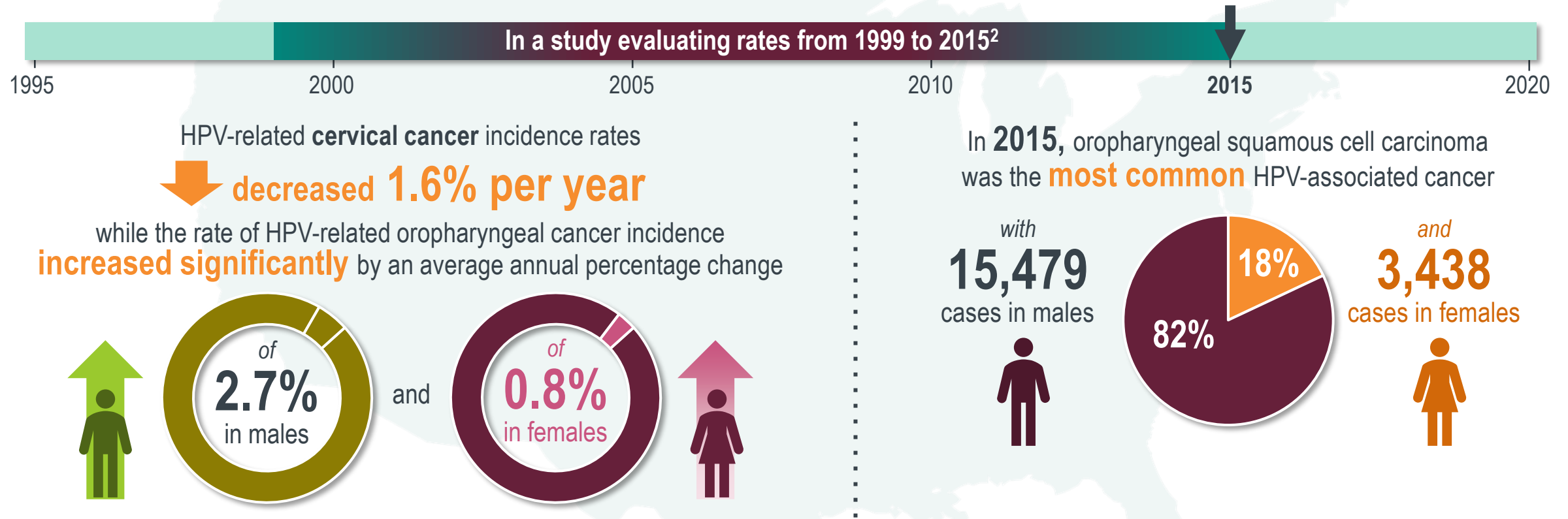
The most recent global data from GLOBOCAN 2012 found that around 30% of oropharyngeal cancers are caused by HPV; however, this varies greatly worldwide, being highest in more developed countries (over 40% in Europe, Northern America, Australia, New Zealand, Japan and Republic of Korea), but much lower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



de Martel C, Plummer M, Vignat J, Franceschi 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**

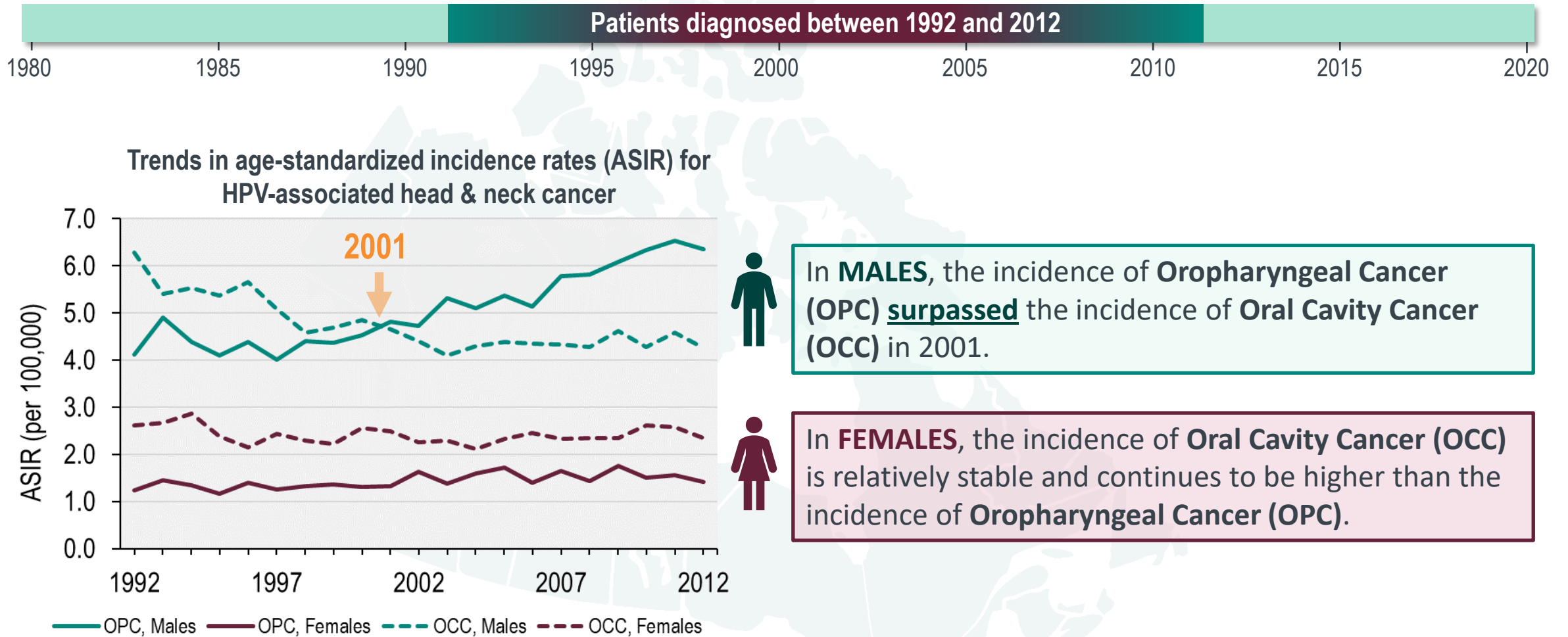
Oropharyngeal squamous cell carcinoma is currently the **most common HPV-associated*** cancer in the US^{1,2}



*HPV-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>

Incidence Rate of Oropharyngeal Cancer Over Time: **Canada**



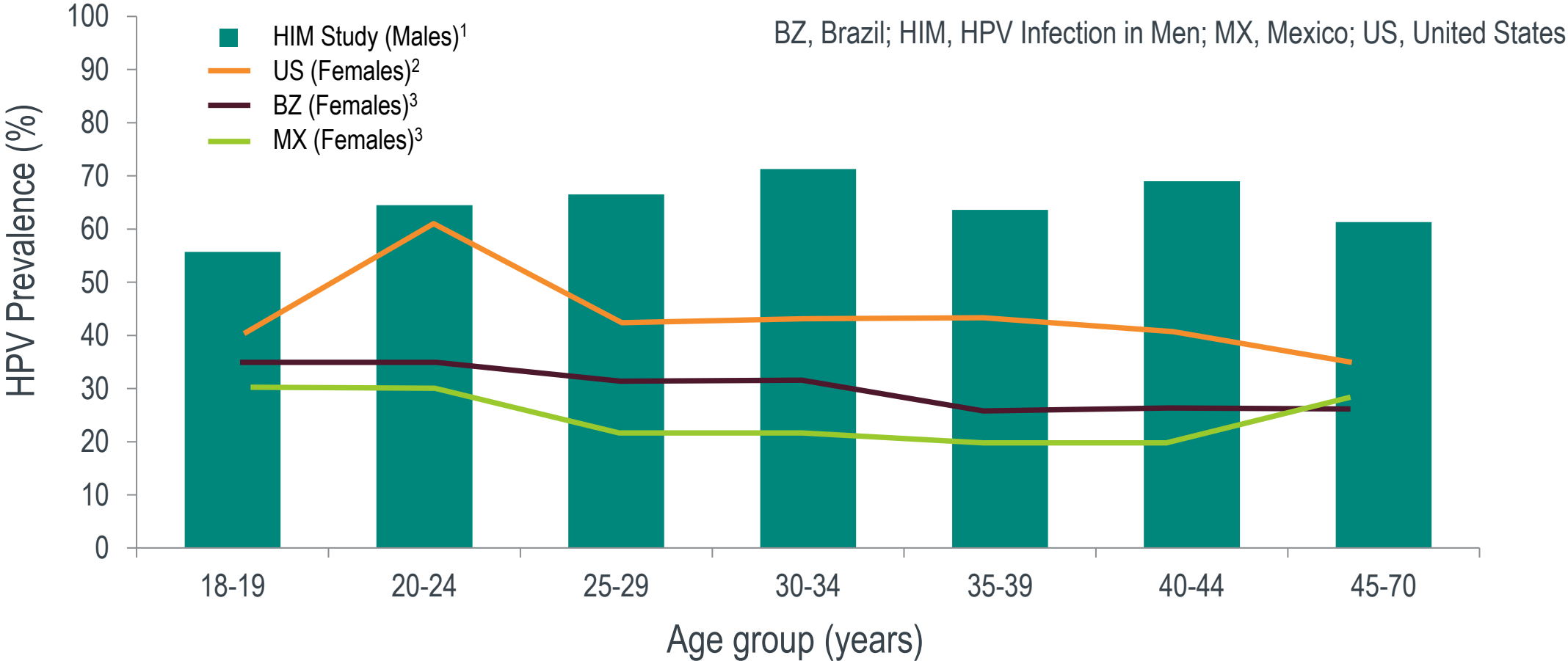
HPV Types Associated with Head & Neck Cancers: **Global**

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

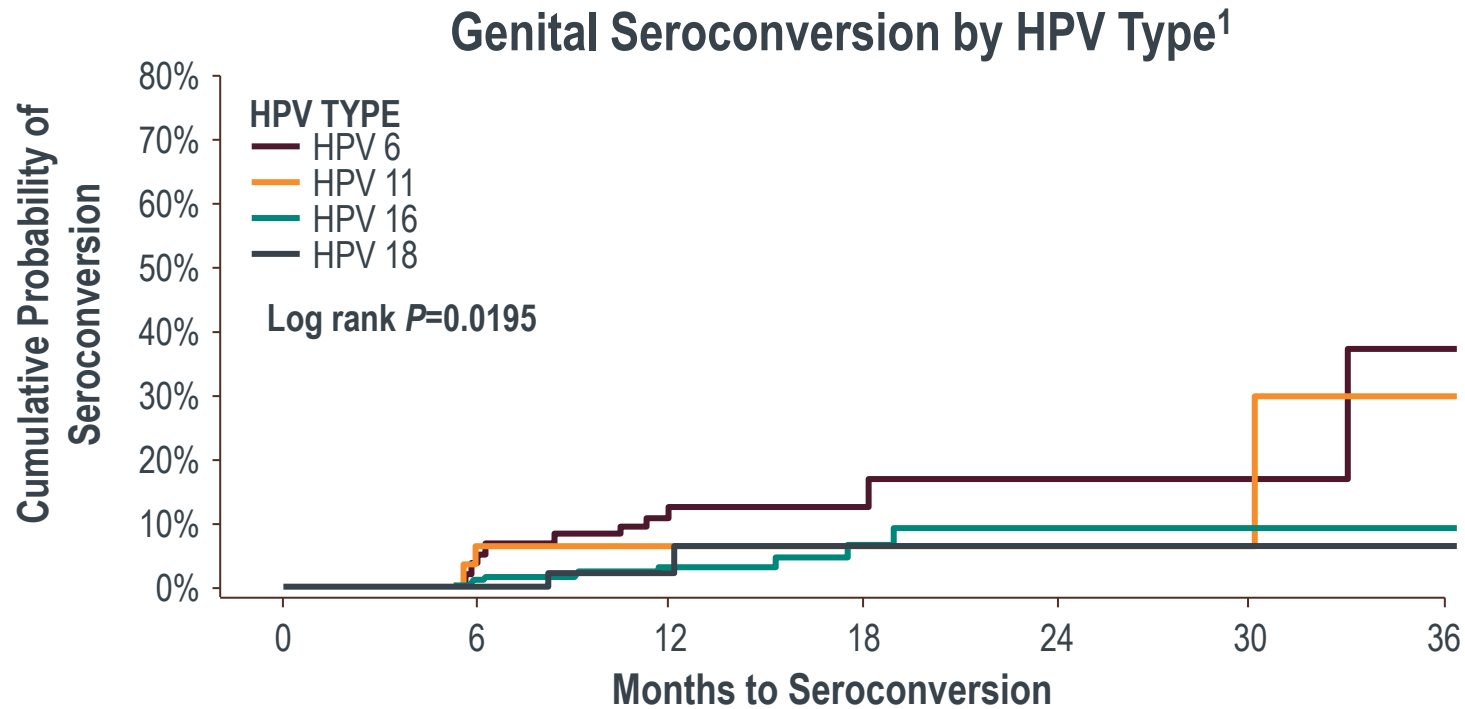


Genital HPV Prevalence is Higher in Males than Females Across all Age Groups



1. Giuliano AR et al. *Cancer Epidemiol Biomarkers Prev.* 2008;17:2036-43; 2. Dunne EF et al. *JAMA.* 2007;297:813-19; 3. ICO/IARC HPV Information Centre on HPV and Cancer. <http://www.hpvcentre.net/datastatistics.php>. Accessed June 4, 2018.

Males have a Low Rate of Seroconversion Following Genital HPV Infection



% Seroconversion		
Type	Males ¹	Females ²
HPV6	19.3%	68.8%
HPV11	8.6%	NA
HPV16	3.6%	59.5%
HPV18	3.4%	54.1%

1. Giuliano AR et al. *Papillomavirus Res.* 2015;1:109-15.; 2. Carter et al. *J Infect Dis.* 2000 Jun;181(6):1911-9.

Protection - The Role of Natural infection is Modest

The Journal of Infectious Diseases

MAJOR ARTICLE



Natural Acquired Immunity Against Subsequent Genital Human Papillomavirus Infection: A Systematic Review and Meta-analysis

Daniel C. Beachler, Gwendolyn Jenkins, Mahboobeh Safaeian, Aimée R. Kreimer, and Nicolas Wentzensen

Division of Cancer Epidemiology, and Genetics, National Cancer Institute, Bethesda, Maryland

Beachler et al. J Infect Dis. 2016 May 1;213(9):1444-54.

Results:

- 14 studies included >24,000 individuals from 18 countries
- Protection against subsequent infection was:

- With HPV 16; RR, (0.65; 95% CI .50-.80)

35%

- With HPV 18; RR, (0.70; 95% CI .43-.98)

30%

- No reduction was seen for males for HPV 16 or 18

Conclusion:

HPV antibodies acquired through natural infection provide modest protection against subsequent cervical HPV infection

Vaccine is Effective in Patients Previously Exposed to HPV

Meta Analysis

8 Studies
9569
Sero+ DNA-
Participants

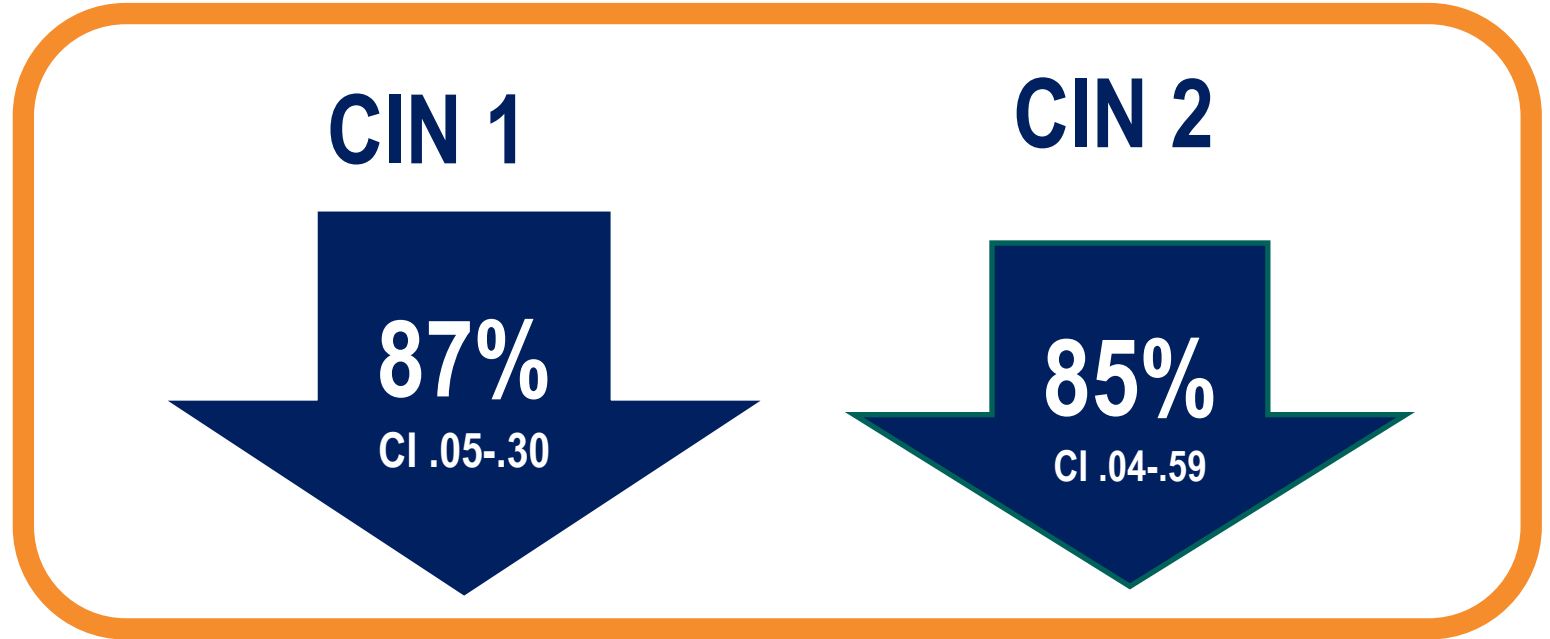
6 mth Persistent
Infection



12 mth Persistent
Infection



VACCINE EFFICACY



Conclusion:

“Women without DNA evidence of HPV 16/18 infection should be offered prophylactic HPV vaccination regardless of prior exposure history”

4vHPV Vaccination After Treatment Reduces Risk of CIN2+ Recurrence

Systematic Review & Meta-Analysis on 10 Studies

Independent from HPV Types

59%

Risk Reduction of recurrent CIN2+ After HPV Vaccination

RR=0.41
95% CI [0.27; 0.64]

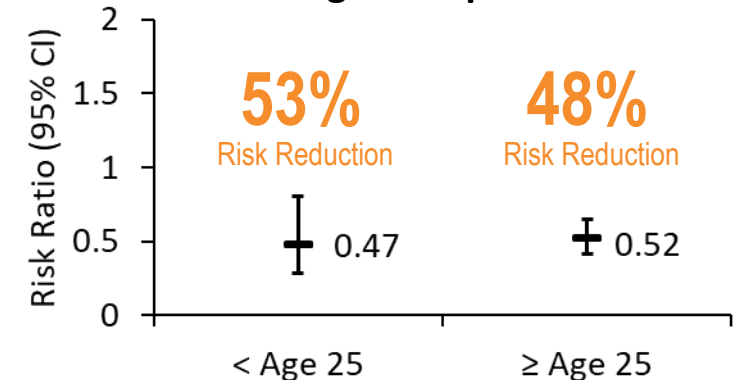
HPV 16/18-related

63%

Risk Reduction of recurrent CIN2+ After HPV Vaccination

RR=0.37;
95% CI [0.17; 0.80]

Risk Reduction Did not Vary Across Different Age Groups



Risk of recurrent CIN2+ was significantly reduced after surgical excision and HPV vaccination compared to surgical excision only

Efficacy of 4vHPV Vaccine in Females 24 - 45 Years Old

British Journal of Cancer (2011) 105, 28–37
© 2011 Cancer Research UK. All rights reserved 0007-0924/11
www.bjancer.com

End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24–45 years of age

X Castellsagué^{1,2}, N Muñoz³, P Pitakittithum³, D Ferris⁴, J Monsonego⁵, K Ault⁶, J Luna², E Myers⁷, S Mallary⁸, OH Bautista⁹, J Bryan², S Vuocolo², RM Haupt¹⁰ and A Saah¹¹

¹Unit of Infections and Cancer, Cancer Epidemiology Research Program, IDIBELL, Institut Català d'Oncologia ICO, CIBER ESP, L'Hospitalet de l'ebre, Catalonia 08907, Spain; ²National Institute of Cancer, Bogotá, Colombia; ³Faculty of Tropical Medicine, Vaccine Trial Center, Mahidol University, Bangkok, Thailand; ⁴Departments of Family Medicine and Obstetrics and Gynecology, Medical College of Georgia, Augusta, GA, USA; ⁵Department of Gynaecology, Fédération Mutualiste Parisienne, Paris, France; ⁶Department of Obstetrics and Gynecology and the Emory Vaccine Center, Emory University School of Medicine, Atlanta, GA, USA; ⁷Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, NC, USA; ⁸Merck & Co. Inc., North Wales, PA, USA

BACKGROUND: Previous analyses from a randomised trial in women aged 24–45 years have shown the quadrivalent human papillomavirus (qHPV) vaccine to be efficacious in the prevention of infection, cervical intraepithelial neoplasia (CIN), and external genital lesions (EGLs) related to HPV 6/11/16/18. In this report, we present end-of-study efficacy, safety, and immunogenicity data with a median follow-up time of 4.0 years.

METHODS: We enrolled 3819 24–45-year-old women with no history of cervical disease or genital warts in the past 5 years. Women received quadrivalent vaccine or placebo at day 1, and at months 2 and 6. Ascertainment of CIN/EGL was accomplished through Pap testing, genital inspection, and cervicovaginal sampling (every 6 months). The main analysis was conducted in a per-protocol efficacy population (that received three doses, was naive to the relevant HPV types at day 1, and remained free of infection through month 7). Efficacy was also estimated in other naive and non-naive populations.

RESULTS: Vaccine efficacy against the combined incidence of persistent infection, CIN/EGL related to HPV6/11/16/18 in the per-protocol population was 88.7% (95% CI: 78.1, 94.8). Efficacy for women who were seropositive and DNA negative for the relevant vaccine HPV type at the time of enrolment who received at least 1 dose was 66.9% (95% CI: 4.3, 90.6). At month 48, 91.5, 92.0, 97.4, and 47.9% of vaccinated women were seropositive to HPV 6/11/16/18, respectively. No serious vaccine-related adverse experiences were reported.

CONCLUSIONS: The qHPV vaccine demonstrated high efficacy, immunogenicity, and acceptable safety in women aged 24–45 years, regardless of previous exposure to HPV vaccine type.

British Journal of Cancer (2011) 105, 28–37. doi:10.1038/bjc.2011.185 www.bjancer.com
Published online 31 May 2011
© 2011 Cancer Research UK

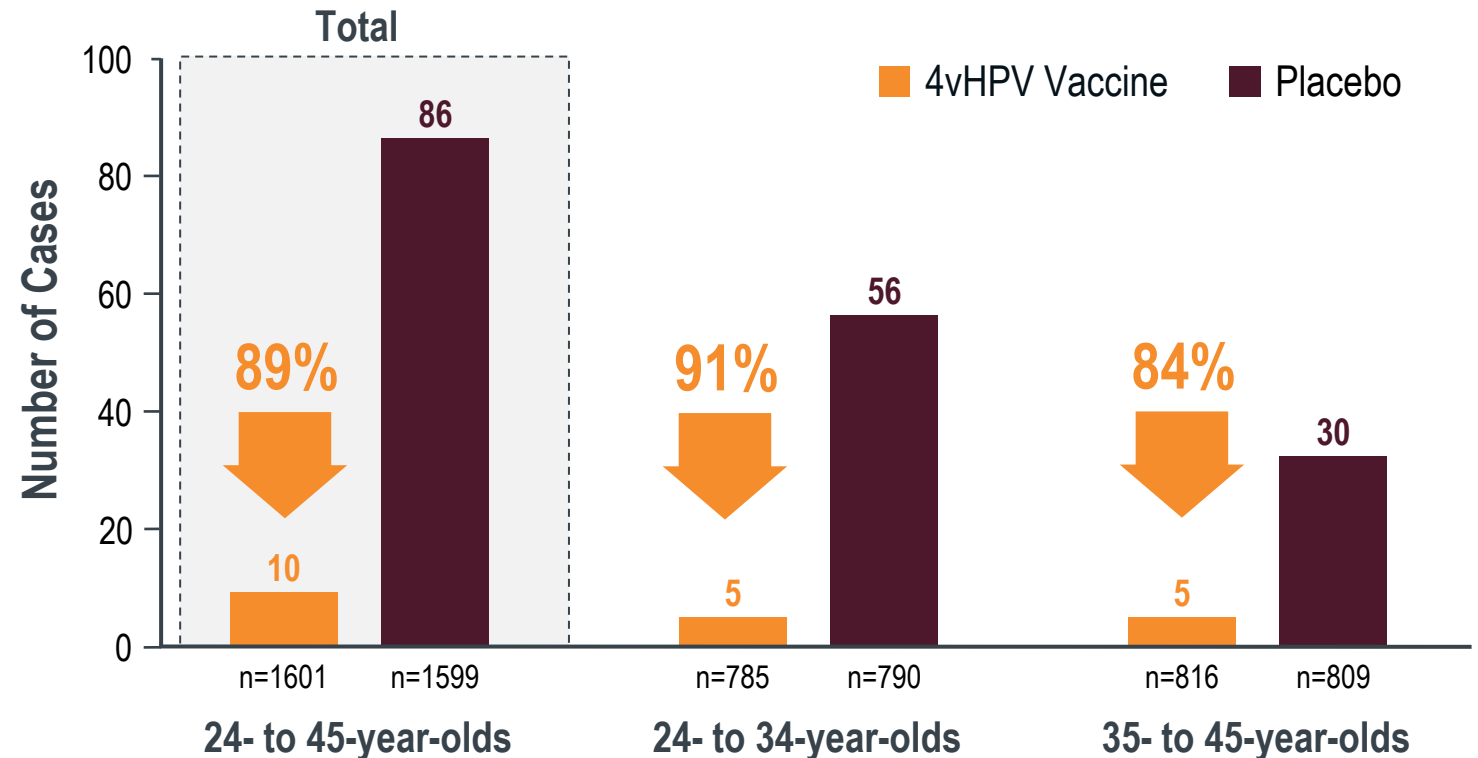
Keywords: HPV; vaccine; cervical; adult

Persistent infection of the uterine cervix by 15–20 carcinogenic human papillomavirus (HPV) genotypes leads to the vast majority of cervical cancers (Walboomers *et al.*, 1999; Muñoz *et al.*, 2003) and related precursor lesions (International Agency for Research on Cancer Working Group, 2007). Although most sexually active women are at risk of HPV infection, the incidence of HPV infection peaks soon after the onset of sexual activity in most populations (Jacobs *et al.*, 2000; Schiffman and Kjaer, 2003; Dunne *et al.*, 2007). Although incidence rates tend to decline thereafter, women older than age 25 years also remain at risk for acquisition of new HPV infections (Castellsagué *et al.*, 2009; Muñoz *et al.*, 2009).

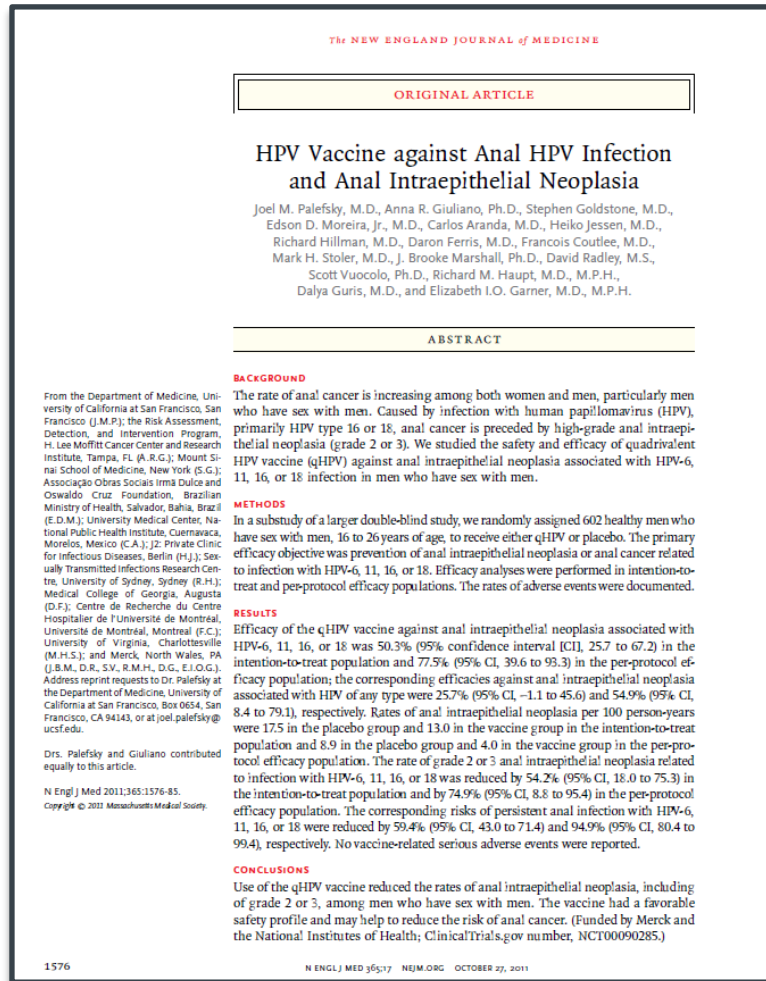
Data from Colombia show that the 5-year cumulative risk of incident cervical HPV infection decreased from 42.5% in females aged 15–19 years to 30% in those aged 25–29 years, and to 22% in those aged 30–44 years (Muñoz *et al.*, 2004). However, a second peak in HPV DNA prevalence has been observed in women in the fourth and fifth decades of life (de Sanjose *et al.*, 2007). Whether this second peak is due to new infections, viral reactivation, waning immunity, or another mechanism is unclear. The cohort study from Colombia supports the possibility of new infections, as the curve of incident high-risk HPV infections is also bimodal with a first peak in women under 25 years of age and a second peak after menopause (Muñoz *et al.*, 2004). Conflicting evidence with respect to a bimodal infection peak is provided by Rodríguez *et al.* (2010), although these two studies are not directly comparable. Previous studies have demonstrated that the prophylactic quadrivalent HPV (qHPV) vaccine is highly effective in preventing HPV 6, 11, 16, or 18-related high-grade cervical, vulvar, or vaginal intraepithelial neoplasia (CIN, VIN, or VaIN, respectively).

*Correspondence: Dr X Castellsagué. Email: xcastellsagué@iconcoliguanet or castellsaguex@gmail.com
Received 3 February 2011; revised 18 April 2011; accepted 26 April 2011; published online 31 May 2011

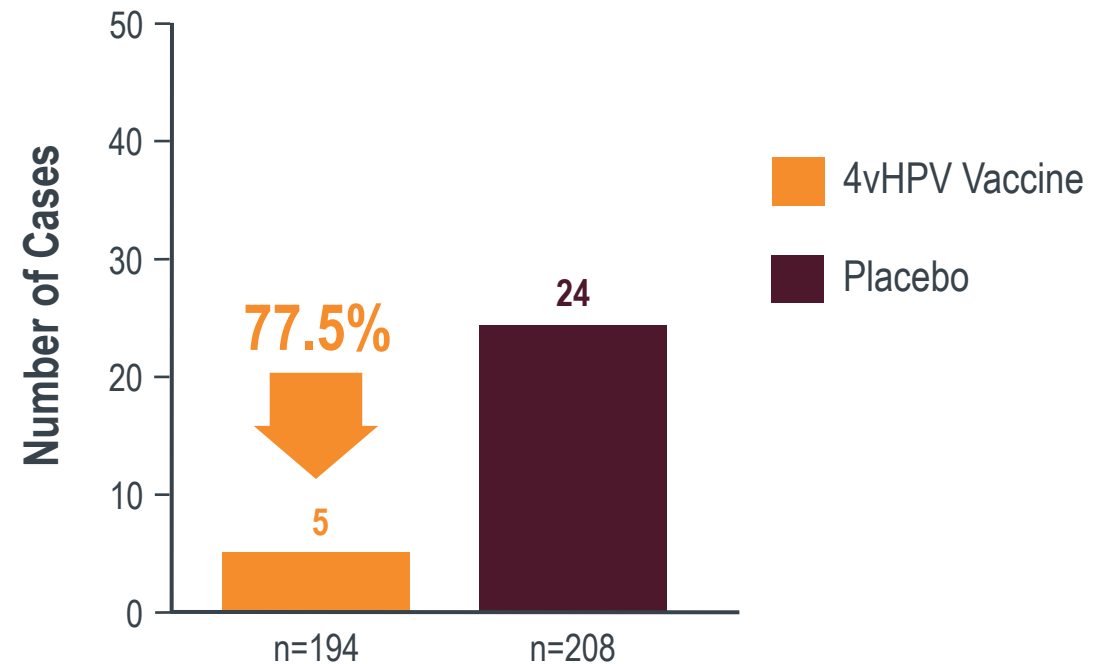
Vaccine Efficacy Against HPV 6/11/16/18-related Persistent Infection, CIN (Any Grade), and EGL (Per-protocol)



4vHPV Vaccine Reduces Anal Neoplasia in Males 16-26 Years Old



Vaccine Efficacy Against HPV 6/11/16/18-related Anal Neoplasia in MSM (Per-protocol)



n = number of subjects who have at least 1 follow-up visit after month 7
MSM: men who have sex with men

Decline of Oral HPV Infections Among US Adults 18-33 Years Old Post-Vaccination

VOLUME 36 • NUMBER 3 • JANUARY 20, 2018

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Effect of Prophylactic Human Papillomavirus (HPV) Vaccination on Oral HPV Infections Among Young Adults in the United States

Anil K. Chaturvedi, Barry I. Graubard, Tarek Broutian, Robert K.L. Pickard, Zhen-Yue Tong, Weihong Xiao, Lisa Kahle, and Maura L. Gillson

ABSTRACT

Purpose
The incidence of human papilloma virus (HPV)-positive oropharyngeal cancers has risen rapidly in recent decades among men in the United States. We investigated the US population-level effect of prophylactic HPV vaccination on the burden of oral HPV infection, the principal cause of HPV-positive oropharyngeal cancers.

Methods
We conducted a cross-sectional study of men and women 18 to 33 years of age (N = 2,627) within the National Health and Nutrition Examination Survey 2011 to 2014, a representative sample of the US population. Oral HPV infection with vaccine types 16, 18, 6, or 11 was compared by HPV vaccination status, as measured by self-reported receipt of at least one dose of the HPV vaccine. Analyses accounted for the complex sampling design and were adjusted for age, sex, and race. Statistical significance was assessed using a quasi-score test.

Results
Between 2011 and 2014, 18.3% of the US population 18 to 33 years of age reported receipt of at least one dose of the HPV vaccine before the age of 26 years (29.2% in women and 6.9% in men; $P < .001$). The prevalence of oral HPV16/18/6/11 infections was significantly reduced in vaccinated versus unvaccinated individuals (0.11% v 1.61%; $P_{adj} = .008$), corresponding to an estimated 88.2% (95% CI, 5.7% to 98.5%) reduction in prevalence after model adjustment for age, sex, and race. Notably, the prevalence of oral HPV16/18/6/11 infections was significantly reduced in vaccinated versus unvaccinated men (0.0% v 2.13%; $P_{adj} = .007$). Accounting for vaccine uptake, the population-level effect of HPV vaccination on the burden of oral HPV16/18/6/11 infections was 17.0% overall, 25.0% in women, and 6.9% in men.

Conclusion
HPV vaccination was associated with reduction in vaccine-type oral HPV prevalence among young US adults. However, because of low vaccine uptake, the population-level effect was modest overall and particularly low in men.

J Clin Oncol 36:262-267. © 2017 by American Society of Clinical Oncology

INTRODUCTION

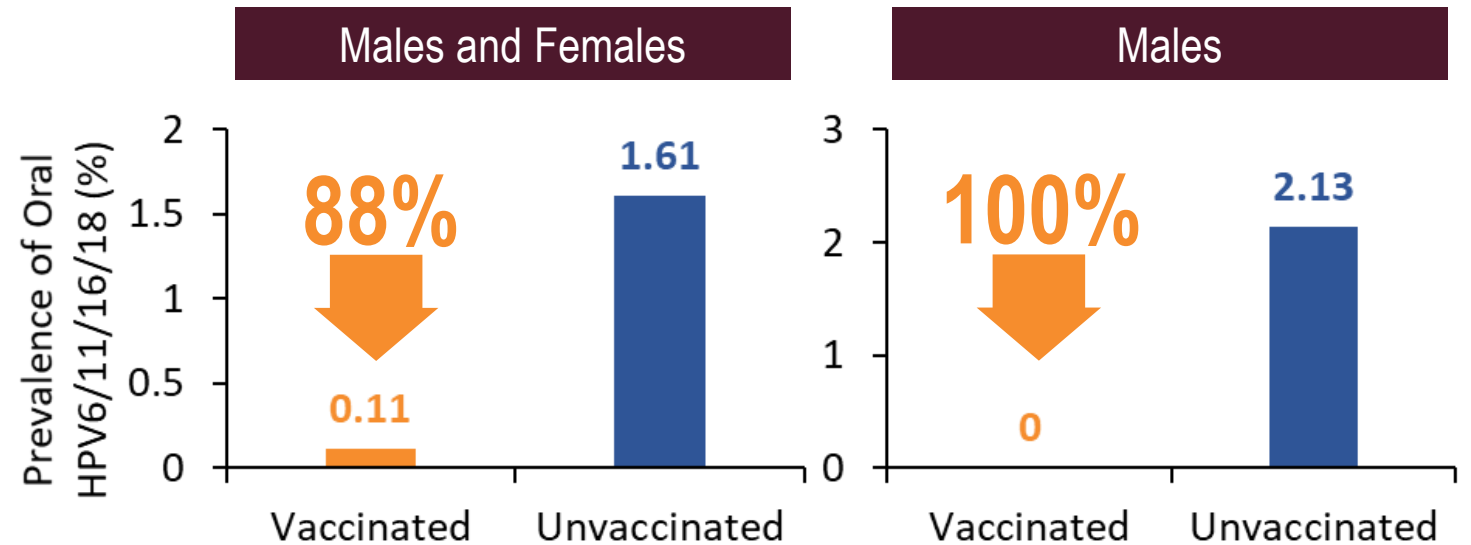
The incidence of oropharyngeal cancer caused by human papillomavirus (HPV) infection has increased rapidly in recent decades in men in the United States as well as numerous other developed countries worldwide.¹ Furthermore, HPV-positive oropharyngeal cancer is projected to become the most common HPV-caused cancer in the United States by 2020, with the majority of the burden in men.¹ More than 70% of the approximately 12,000 oropharyngeal cancers diagnosed annually in the United States are caused by HPV, with approximately 90% of HPV-positive oropharyngeal cancers caused by HPV16 and the remainder caused by other oncogenic HPV types.²⁻³ Given the absence of screening and secondary prevention strategies, prophylactic HPV vaccination has the greatest potential to prevent HPV-positive oropharyngeal cancers.⁴

Prophylactic HPV vaccination with the bivalent (HPV16/18), quadrivalent (HPV16/18/6/11), or nonavalent (HPV16/18/6/11/31/33/45/52/58) vaccine is currently recommended for US females and males (quadrivalent and nonavalent) ages 9 to

ASSOCIATED CONTENT

Appendix
DOI: <https://doi.org/10.1200/JCO.2017.750141>
DOI: <https://doi.org/10.1200/JCO.2017.750141>

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Currently no HPV vaccines outside of the US and Canada are approved for the prevention of oropharyngeal cancer and other head & neck cancers caused by HPV types 16, 18, 33, 45, 52, and 58.

HPV Vaccination: Effect on Oral HPV Infection

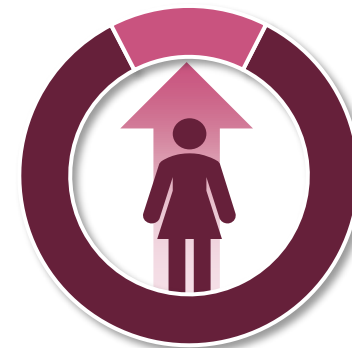


An analysis was conducted across 4 cycles of NHANES in the US during 2009-2016 using data from 13,676 individuals 18-59 years of age. Comparisons of oral HPV prevalence for 4 vaccine HPV types (16, 18) and 33 nonvaccine types.

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)

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).

HPV-Related Head and Neck Cancers in Male Patients

- The patient profile has changed from older males from low socioeconomic backgrounds to younger non-smoking non-drinkers from high socioeconomic backgrounds.
- Data shows that previous exposure from multiple partners increase to risk of HPV acquisition and it does not offer protection from future disease.
- HPV vaccines have been shown to be effective in males and Canada has recently changed the indication to include males up to 45 years old and has issued a specific indication for HPV-related head and neck cancer.

HPV-Related Cancer in Female Patients

- Women with a history of CIN are at higher risk of recurrent CIN or invasive cervical cancer.
 - 37 vs. 6 cancers per 100 000 women-years in those with a history of CIN vs. controls, respectively.
 - A study from Toronto found that women who undergo procedure for CIN3 have a 10-fold risk of cervical cancer in 5 years.
- One infection site can be a reservoir for an anatomically distant location.

KEY DISCUSSION POINTS

Opportunity

- **Highly effective vaccine to protect against HPV-related cancers**

Male Patients

- Anal, penile, and increasing incidence of head and neck cancers
- Unpleasant warts and procedure(s) to remove them
- Transmission of genital warts and cancers

Female Patients

- At risk for more serious disease and future procedures
- Natural exposure provides at best limited protection from recurrent disease so 9-valent HPV vaccine provides additional benefits
- Transmission of genital warts and cancers

Presenter



Dr. Jia Hu MD, MSc, CCFP, FRCPC

- Chair, 19 To Zero
- Public Health and Preventive Medicine Physician and Family Physician
- Physician, Cleveland Clinic Canada
- Adjunct Professor, University of Calgary



Increasing awareness of HPV-related disease

**CIDC Webinar
May 12, 2023**



Presenter background & disclosures

Background:

- Public health specialist and family physician
- CEO, 19 To Zero
- Corporate Medical Director, Cleveland Clinic Canada
- Adjunct Professor, University of Calgary
- Board Member, Partners in Health Canada

I have the following disclosures:

- Advisory Board/Speakers Bureau – Sanofi, Merck, GSK, Pfizer, Moderna, Seqirus
- Research/Clinical Trials: CIHR, PHAC, Alberta Innovates, Sanofi, Merck, GSK, Pfizer, Moderna



**Canada's largest multi-sector coalition
addressing health behaviour changes**

19 To Zero is a non-profit coalition of health experts, behavioural scientists, community organizations, academics, marketing professionals, and others working to **understand and promote key health behaviors like vaccination** through **research, community engagement, education, and intervention.**

A Multimodal Approach for **Health Behaviour Change**

Primary Research

We conduct market research and social media listening to understand perceptions and discourse surrounding vaccines and public health



Advocacy

We advocate for policies at federal, provincial, and health system levels that will improve healthcare delivery and outcomes for Canadians



Community Engagement

We are a trusted partner of a large network of groups representing communities and organizations of all types across Canada



Health Advisory & Strategy

We advise industry and health systems partners on best practices to improve health outcomes, particularly with respect to vaccine uptake



Behaviour Change & Education Campaigns

We develop, design, and execute targeted educational and marketing interventions to improve public health



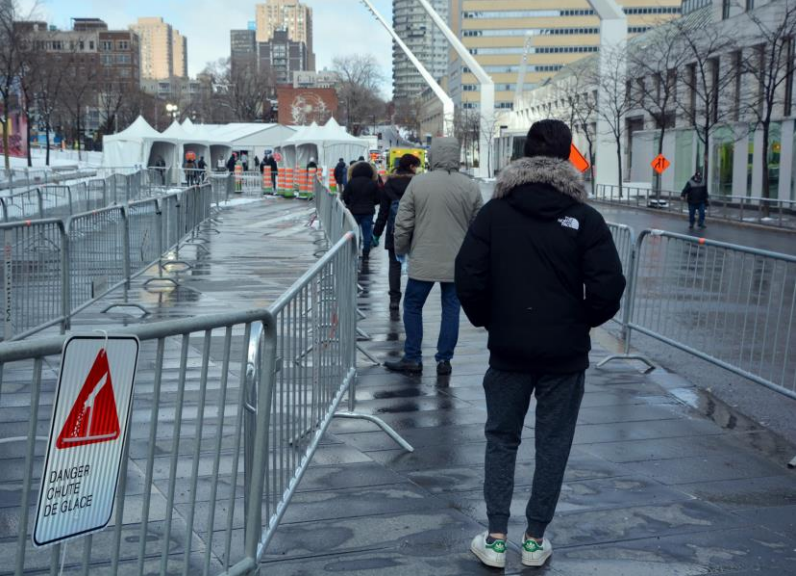
Healthcare Worker Engagement

We engage a pan-Canadian network of healthcare professionals (physicians, nurses, pharmacists) to understand their needs and provide tailored resources to improve their practices





Approaching Behaviour Change



Targeting Behavior isn't sufficient

If we target the underlying belief -- how seriously they take an illness -- this will influence everything else around decision-making (e.g., seeking more information, seeking a vaccine, etc.)



Creating a sense of urgency around the issue

- Generally speaking, **there is low awareness** that HPV is a major cause of head and neck cancer (both among patients and providers) and that vaccination is the key action to prevent this from happening
- Raising awareness is much easier if we can create a bit of a ‘burning platform’ that articulates how much of a problem this is from the perspective of:
 - Overall **morbidity/mortality**
 - Perceived **severity (e.g., cancer sounds bad to people)**
 - Perceived **newness**

Build a coalition

Many players are (potentially) involved in raising awareness about this topic.
Having some champions is also useful

Groups we normally work with:

- Healthcare groups (physicians, pharmacists, dentists?)
- Public health organizations
- Academics / researchers

Groups we don't always work with:

- *Industry*
- *Community organizations / NGOs (especially for harder to reach populations)*
- *Employers*

Examples of organizations we have worked with to promote vaccinations across different populations



Joint statement

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



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)



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: American Dental Association

The screenshot shows the ADA website header with the logo and tagline 'America's leading advocate for oral health'. Navigation links include 'Coronavirus Updates', 'About ADA', 'Contact', 'Join', 'Renew', and 'Login'. A menu bar contains 'MEMBER CENTER', 'EDUCATION/CAREERS', 'CLINICAL RESOURCES', 'ADVOCACY', 'PUBLICATIONS', and 'PUBLIC PROGRAMS'. The breadcrumb trail is 'Home > Publications > ADA News > ADA News Archive > ADA adopts policy supporting HPV vaccine'. A 'Share' button is visible. The article title is 'ADA adopts policy supporting HPV vaccine' with a date of 'October 22, 2018' and author 'By Michelle Manchir'. The article text states: 'Honolulu — 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.' An advertisement for 'Debt freaking you out?' is on the left. A 'Current Issue' button is on the right. A quote box on the right contains the article's main message.

ADA American Dental Association®
America's leading advocate for oral health

[Coronavirus Updates](#) | [About ADA](#) | [Contact](#) | [Join](#) | [Renew](#) | [Login](#)

[MEMBER CENTER](#) [EDUCATION/CAREERS](#) [CLINICAL RESOURCES](#) [ADVOCACY](#) [PUBLICATIONS](#) [PUBLIC PROGRAMS](#)

Home > Publications > ADA News > ADA News Archive > ADA adopts policy supporting HPV vaccine [Share](#)

ADA News

Current Issue

ADA News Archive

ViewPoint

ADA CareerCenter

ADA Marketplace

ADA News

ADA adopts policy supporting HPV vaccine
October 22, 2018

By Michelle Manchir

Honolulu — 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.

Debt freaking you out?
Manage it so it doesn't manage you.
ADA.org/MyDebt | ADA

Current Issue

You may also like:

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>

Understand the population

Identify the target population(s) and learn a few things about them

- **What do they know** about the issue currently
- What factors would lead them to **change their behaviour** around the issue
- What are some **barriers** around changing their behaviour
- Where do they **obtain their information** (i.e., channels)
- How could I **segment** this population
- Are there **special populations** I really want to chase down (e.g., older men, gay men, etc.)

How?

Usually a combination of surveys, focus groups/interviews, social media analytics

Our research shows **four effects** most important to consider in public health behaviour change efforts

CEILING EFFECT



Preaching to the converted doesn't work

BUBBLE EFFECT



Public health messages are stuck in an echo chamber

CONSTELLATION EFFECT

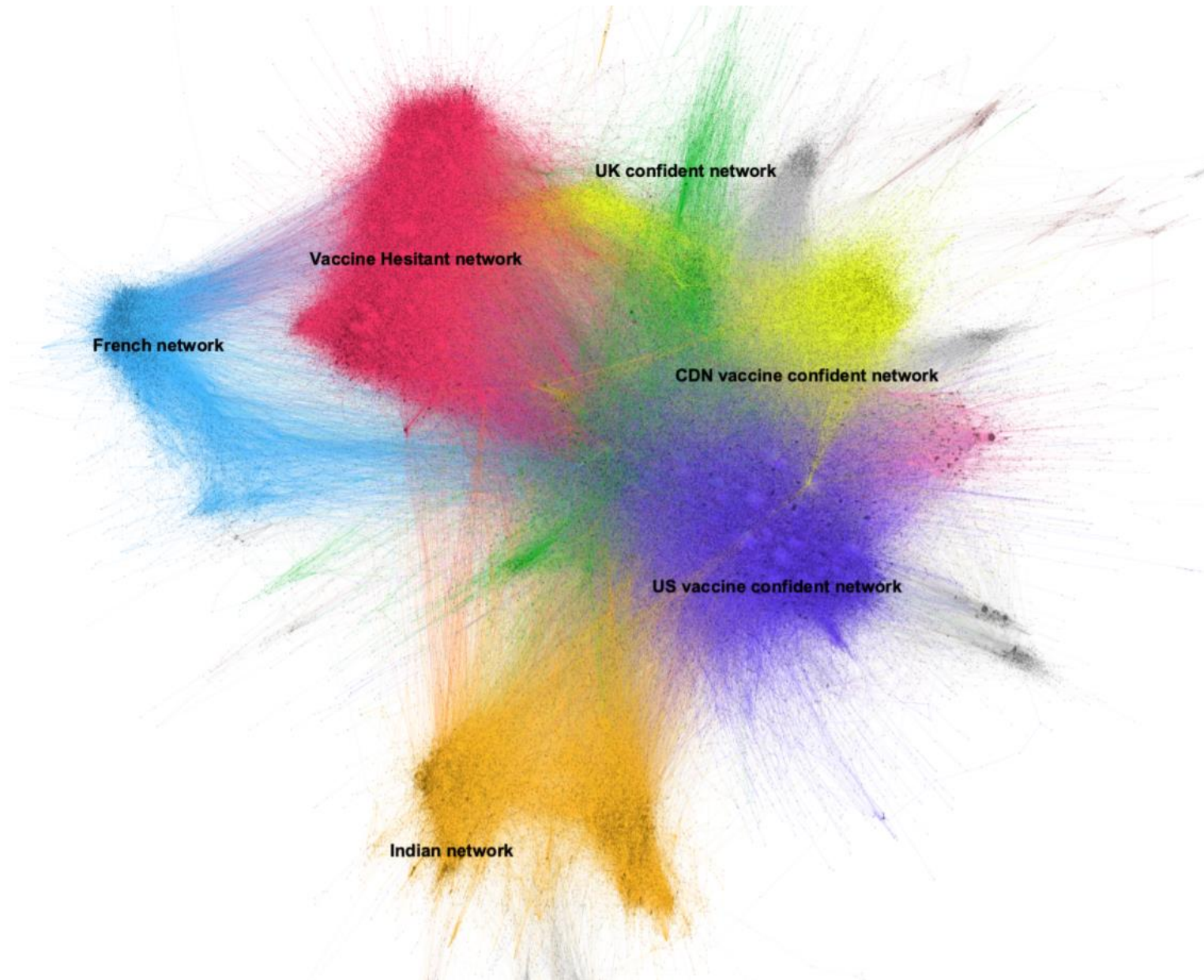


People have different reasons for hesitancy / confidence

CHANNEL EFFECT



You have to reach people where they are



Bubble Effect: Public health messages are stuck in an echo chamber

Vaccine hesitant people aren't part of the same media and social media ecosystems as vaccine confident people.

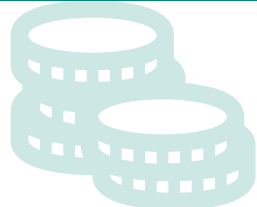


BARRIERS TO VACCINATION



Barrier to Vaccination among Canadian Physicians¹

1



PERCEIVED BARRIERS OF COST

Cost was seen as the number one barrier by **92% to 95%** of physicians. Perceived barriers of cost may **limit recommendations for vaccination**, particularly among older women or men.



Barrier to Get Vaccinated among Canadian Adults²

1



LACK OF PHYSICIAN RECOMMENDATION

The number one reported barrier to vaccination for the general public was **not having a recommendation from a doctor**. **Cost** was seen as a barrier by **only 18% (male)** and **20% (female)** of participants.

HEALTHCARE PROFESSIONAL'S RECOMMENDATION



Communication¹

Explaining the need for immunization



Clearly conveying the risk

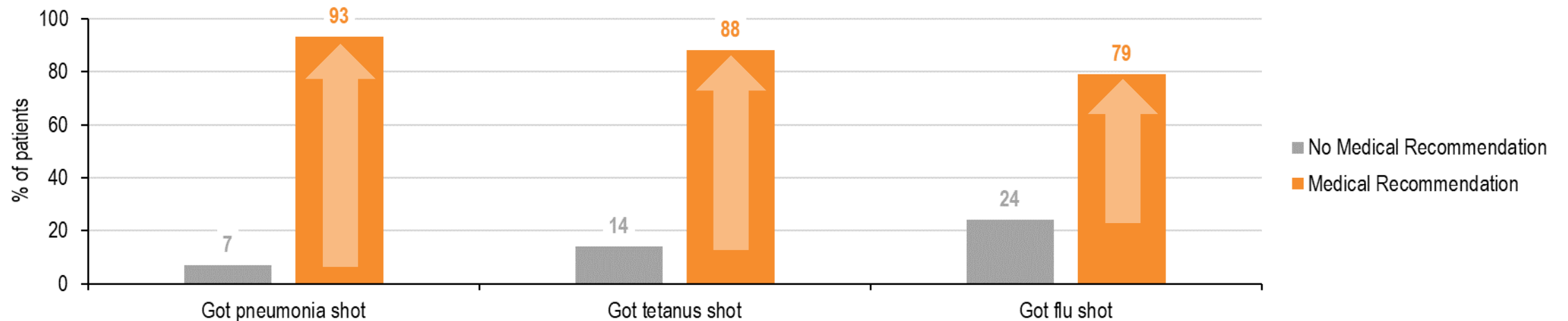


Strong physician/provider recommendation



Recommendation is critical²

Medical recommendations make huge differences



Intervene in the population

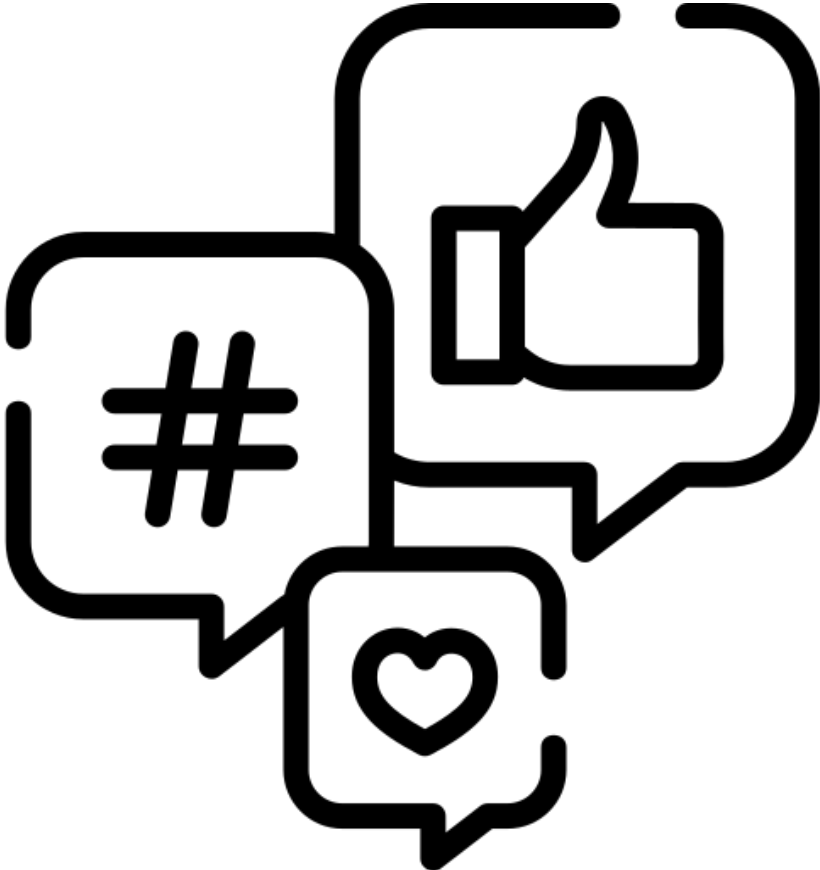
The best interventions are informed by **what channels are most likely to reach a target audience** and **multimodal** (e.g., multiple channels influencing)



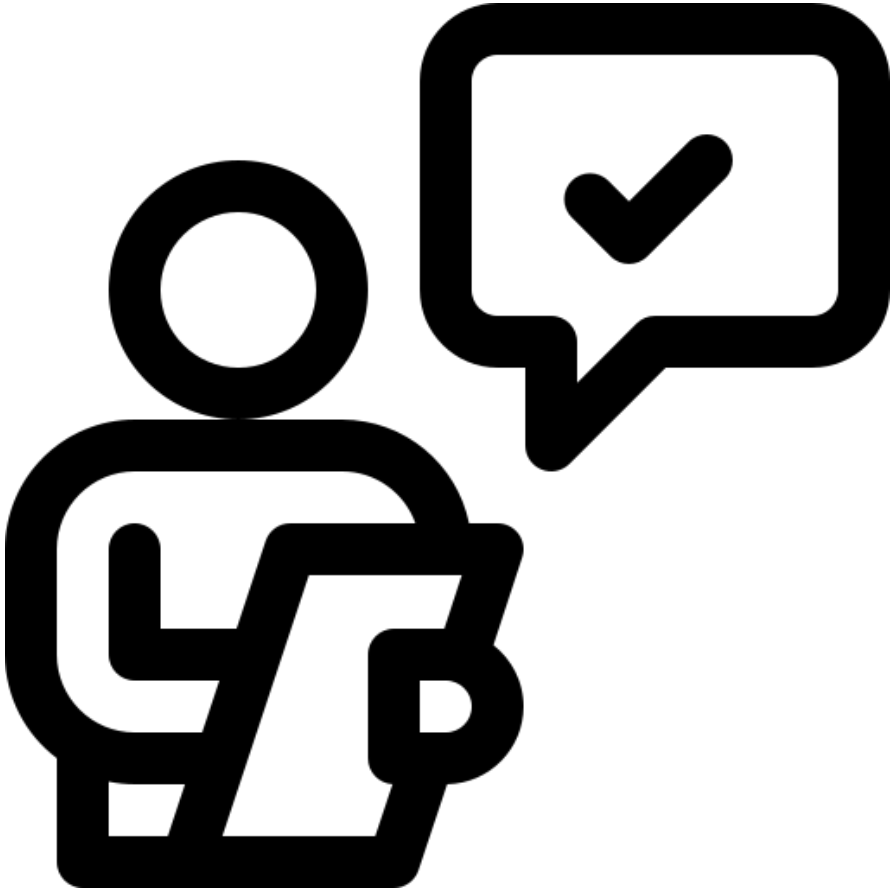
A Case Study – HPV vaccine ‘catch-up’ campaign in Ontario



Data Collection Methodology



Social Media Analytics



Survey

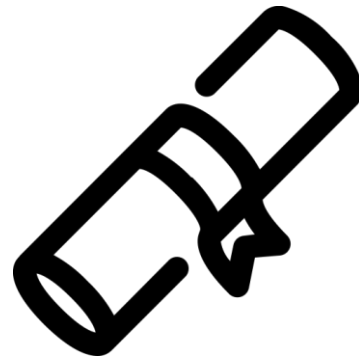
Survey Insights



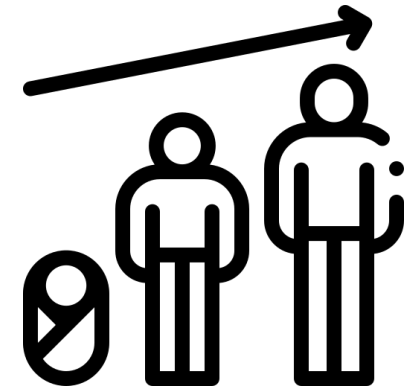
n=778 Ontarians with children between the ages of 10 and 18 (inclusive) were surveyed over the period of July 5th to 25th, 2022.



62% Female



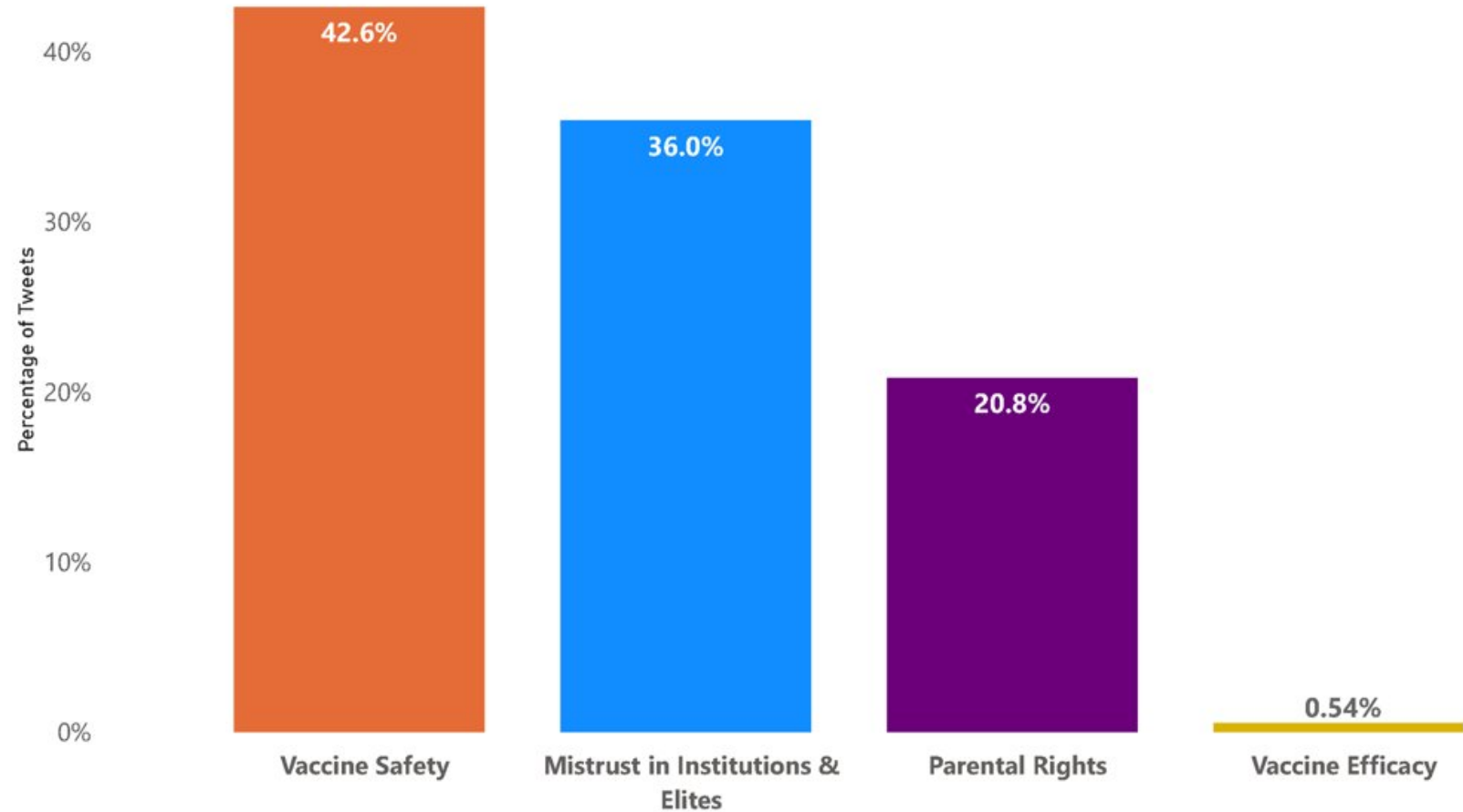
45% had a Bachelor's degree



Age Median = 42

Social Media Insights

- Collected tweets globally using Twitter API on HPV from January 2019 – May 2021
- Key terms used to collect HPV school-based vaccine tweets from Parents:
 - HPV, Gardasil, Cervarix, kid, child, daughter, son, girl, boy, school, parent, daughter, father mother, dad, mom
- Vaccine hesitant network:
 - 30,368 Tweets
 - 10,220 Accounts
- 4 main topics of concern:
 - Safety, mistrust, rights and efficacy



FOUR Creative Concepts

Back
to School
Checklist

1

BACK TO SCHOOL



AGENDA



NOTEBOOK



**SCHOOL BASED
VACCINES**

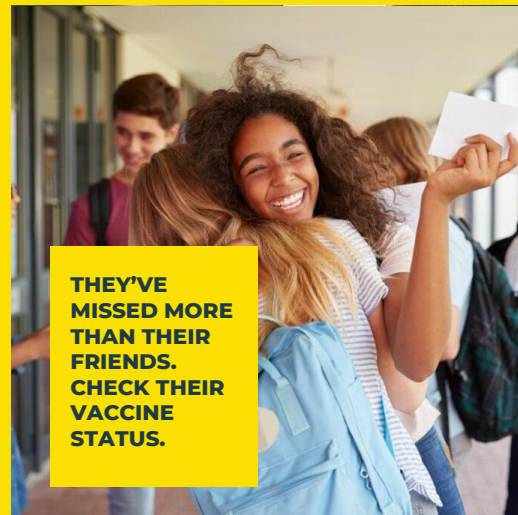
A Lot Can
Happen
in 2 Years

2



What's
Missing?

3



You Can't
Protect Them
From Everything

4



What's Missing? - Campaign Overview

SOCIAL MEDIA



VIDEO



NEWSLETTER



A reach of over **30 million** in top-tier outlets including the Globe & Mail, Toronto Star, Global News, and CBC.

Syndicated coverage across Ontario outlets, highlighting local vaccine catch-up clinics.

Routine vaccination rates for children, teens in Canada dropped dramatically since start of COVID-19 pandemic

CARLY WEEKS > HEALTH REPORTER
PUBLISHED AUGUST 30, 2022



Rates of routine student vaccines are 'alarmingly low.' Here's why doctors are concerned

"The rationale for immunizations remains very clear," said Dr. Noah Ivers, noting recent meningitis outbreak that saw one person die after infection.

By **Alessia Passafiume** Staff Reporter
Tue., Aug. 30, 2022 | 4 min. read



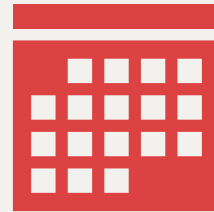
Paid media strategy



Our paid media buy focused on Facebook and Google Search to drive audiences to their respective PHU. Leveraging creative developed by Emergence, our campaigns launched at the end of September and ran for 8 weeks throughout the fall.



Campaign goal:
**Traffic to PHU
websites**



Duration:
September 27 – November 13



Allocated Spend:
\$100,000

Google Search: Overall Metrics and by Region



On Google Search, we received over 34.7K impressions and 4.7K clicks to our target PHUs during the campaign. We saw strong performance of our ads in all regions and exceeded industry benchmarks for the Click Through Rate (CTR).

The table below highlights the breakdown of each region by our performance metrics.

Region	Impressions	Link Clicks	CTR	CPC
Toronto	16,448	2,341	14.23%	\$0.93
Peel	9,511	1,521	15.99%	\$1.15
York	3,191	450	14.10%	\$1.52
Ottawa	5,621	481	8.56%	\$1.71
Total	34,771	4,793	13.22%	\$1.33

*Metrics highlighted in yellow indicated campaign performance better than industry benchmarks

Google Healthcare industry benchmark for CTR: 3.27%

Facebook: Overall Metrics and by Region



On Facebook and Instagram, we received over 10.7M impressions and 59.6K clicks to our target PHUs during the campaign. We saw strong performance of our ads in all regions and exceeded industry benchmarks for the Cost Per Click (CPC).

The table below highlights the breakdown of each region by our performance metrics.

Region	Impressions	Reach	Video Views	Link Clicks	CTR	CPC
Peel	3,414,368	206,240	42,751	21,228	.62%	\$1.27
York	2,869,794	162,848	99,298	14,843	.52%	\$1.55
Toronto	1,936,553	166,945	54,134	11,375	.59%	\$1.12
Ottawa	1,660,210	97,504	52,966	8,332	.50%	\$1.35
Ontario	875,448	155,135	25,014	3,985	.48%	\$0.78
Total	10,756,373	788,672	274,163	59,673	0.54%	\$1.21

*Metrics highlighted in yellow indicated campaign performance better than industry benchmarks

Facebook Healthcare industry benchmark for CPC: \$1.32

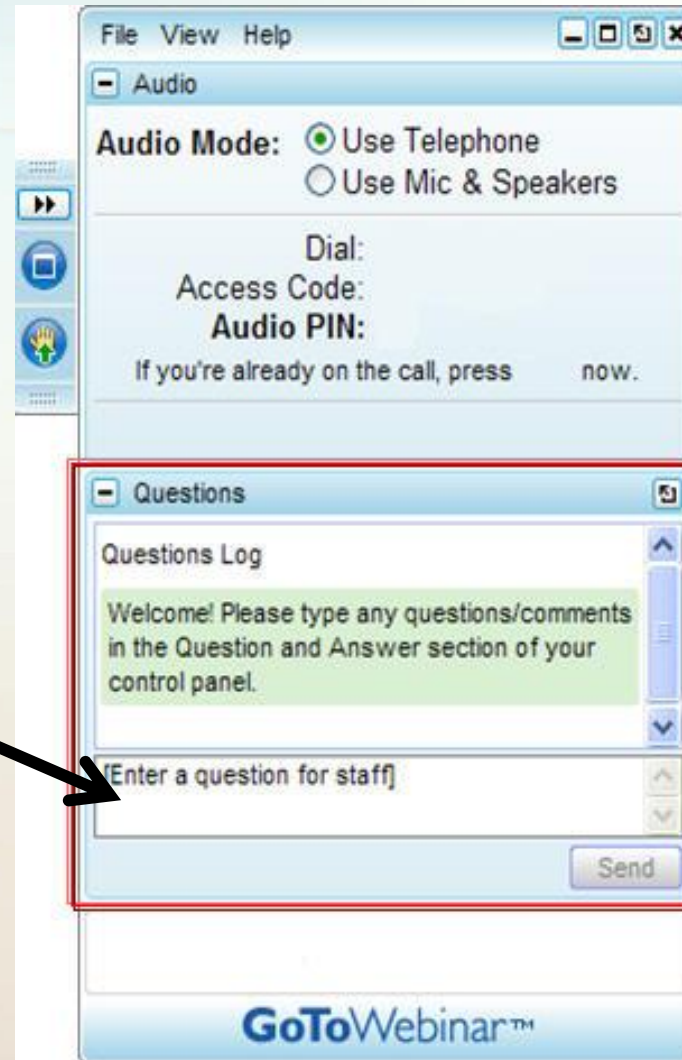
Thank you - Questions



Question & Answer Period

On a computer, submit your text question using the Questions pane

NOTE: On a mobile device, tap on the “?” or “Questions” to open the questions pane



HPV Affects Men Differently than Women: is prevention the same for both?

Evaluation: <https://bit.ly/3GYVGfQ>

- Slide Set, Video recording, HPV documents at:
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Thank you for participating!

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