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HPV Global Action
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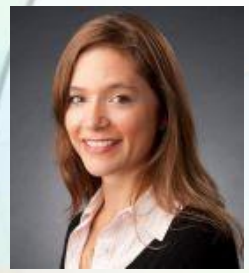
Consortium for Infectious Disease Control
Presents

www.CIDCgroup.org

The rate of HPV head & neck cancers is rapidly rising:
what more can be done in prevention?



Presenter: Dr. Melissa Henry PhD
- Associate Professor and FRQS Senior Clinician-Scientist, Gerald Bronfman Department of Oncology, McGill University
- Director, International Psycho-Oncology Society (IPOS)

Presenter: Dr. Denis Soulieres MD, MSc, FRCPC
- Hematologist and Medical Oncologist, Centre Hospitalier de l'Université de Montréal
- Clinical researcher
- Molecular Biologist

Presenter: Dr. John-Peter Bradford
BA, MA, ABD, PhD
- Head and Neck Cancer Thriver & Advocate
- Co-founder, LSTN (Life-Saving Therapies Network)

•Moderator: Dr. Marc Steben MD,CCFM, FCFM
Co-President, HPV Global Action
- Chair, Canadian Network on HPV Prevention
- Board Member, International Papillomavirus Society

This educational program is made possible through the support of **Merck Canada**

July27, 2023

Moderator

Dr. Marc Steben MD,CCFM, FCFM

- Co-President, HPV Global Action
- Chair, Canadian Network on HPV Prevention
- Board Member, International Papillomavirus Society

Webinar Objectives

1. Describe the burden of disease of head and neck cancers in Canadians
2. Explain the complexity of challenges for patients with head and neck cancer
3. Review the efficacy of HPV vaccine to lower burden of head and neck HPV cancers
4. Recognize signs and symptoms of head and neck cancer
5. Discuss potential screening methods
6. Develop a better understanding of the perspectives of a head and neck cancer patient

Administrative Information

How to participate:

- You can hear the audio for today's webinar via your computer by selecting "Use Mic & Speakers"
- 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

NOTE: For mobile device users:

- To open the questions pane, tap on the "?" or "Questions"
- To change your audio setting, tap on the "Settings" icon

Note: A recording of the presentation will be made available at www.CIDCgroup.org and hpvglobalaction.org

Evaluation

Complete the Evaluation Survey at:

https://forms.gle/FYPTFDRYnPsN6CKk9

Completion of survey is requested to receive a certificate of participation

– all registered participants will receive an email with this link

Slides and Video Recording

The webinar **Slides and Recording** will be archived at:

hpvglobalaction.org and www.CIDCgroup.org

Presenter

Dr. Melissa Henry PhD

- Associate Professor and FRQS Senior Clinician-Scientist, Gerald Bronfman Department of Oncology, McGill University
- Director, International Psycho-Oncology Society (IPOS)

HPV head and neck cancers : We need a control strategy now! The case for better clinical awareness and a stronger preventive agenda

Dr. MELISSA HENRY, McGill University

Associate Professor, Gerald Bronfman Department of Oncology

McGill University

McGill

Acknowledgements

FRQS Senior Clinician-Scientist Salary Award

Fonds de recherche Santé Québec

Head and neck SCC arise from the mucosal epithelium of the:

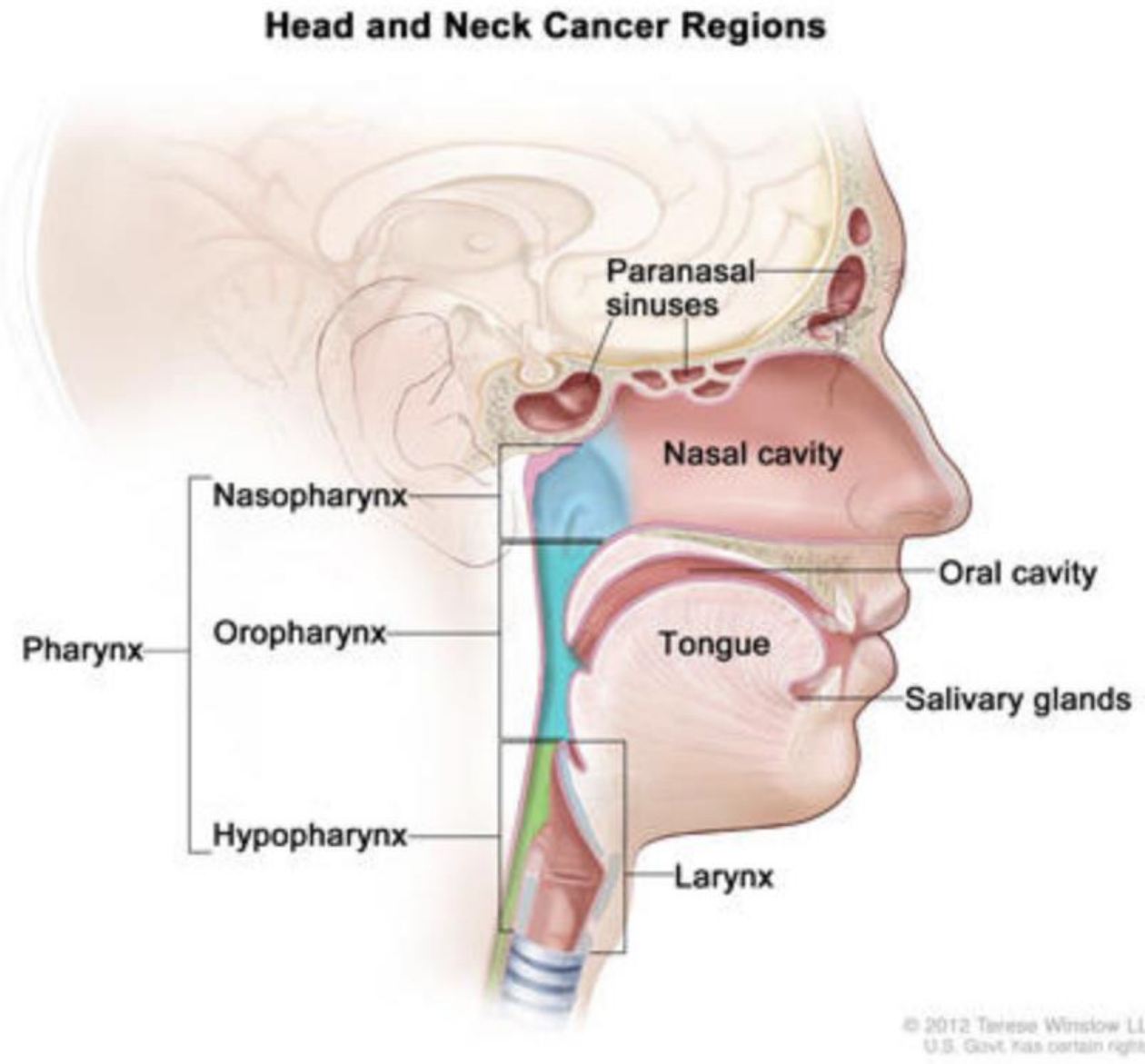
Oral cavity – lips, buccal mucosa, anterior tongue, hard palate, floor of mouth, and retromolar trigone;

Nasopharynx;

Oropharynx – tonsils, base of tongue, soft palate, uvula, and posterior pharyngeal wall;

Hypopharynx; and

Larynx



Cancer Statistics

HNC is the 7th most common cancer

- In Canada → 7,500 new cases and 2,100 deaths annually

HNC incidence continues to rise, with a 30% increase annually by 2030

- Increased incidence attributed to rise in oropharyngeal cancer, linked to HPV infection
- Over next 20 years → majority of HNC will be HPV-positive

Gormley et al., 2022; Canadian Cancer Society, 2022

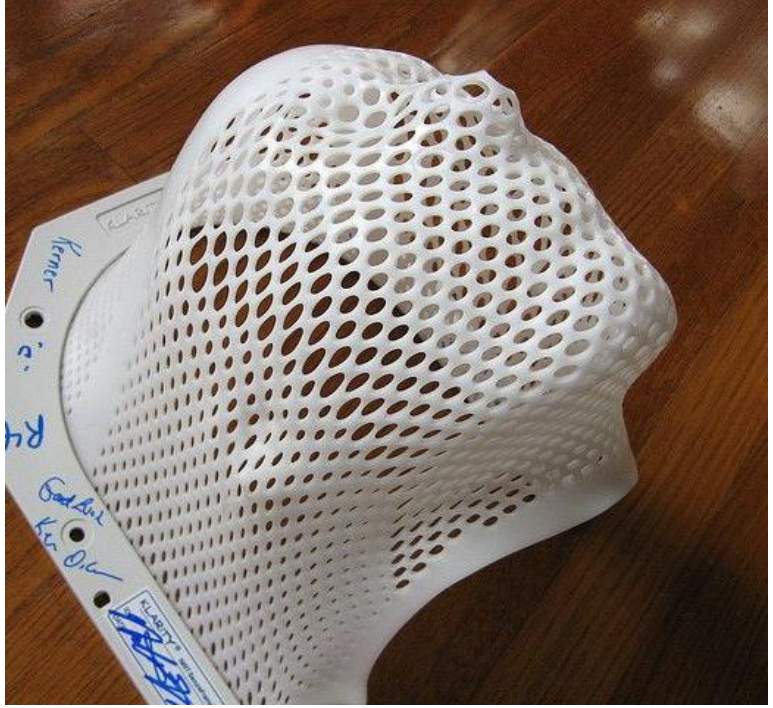
Cancer Statistics

While HNC represent only 4% of newly diagnosed cancers, they generally have a poorer prognosis

- Mean age at diagnosis is 63 years; 74% male
- 60-70% newly diagnosed in advanced disease
- 50% 5-year survival rates on average
- 80% Surgery; 15% w/ microvascular free-flap reconstruction
- 70% radiotherapy with IMR, w/ or without chemo as adjunct
  - 6 weeks daily XRT + 6 weeks weekly chemo

Major risk factors for HNC

- Tobacco smoking alone and in combination with alcohol consumption → accounting for 72% of cases
- The human papillomavirus (HPV) in oropharyngeal cancer
- Clearly socioeconomically patterned → Not explained entirely by smoking and alcohol
- Diet, physical activity, and oral hygiene → minor risk factors



HNC-P → at-risk for social disparities, psychological distress, and suicide

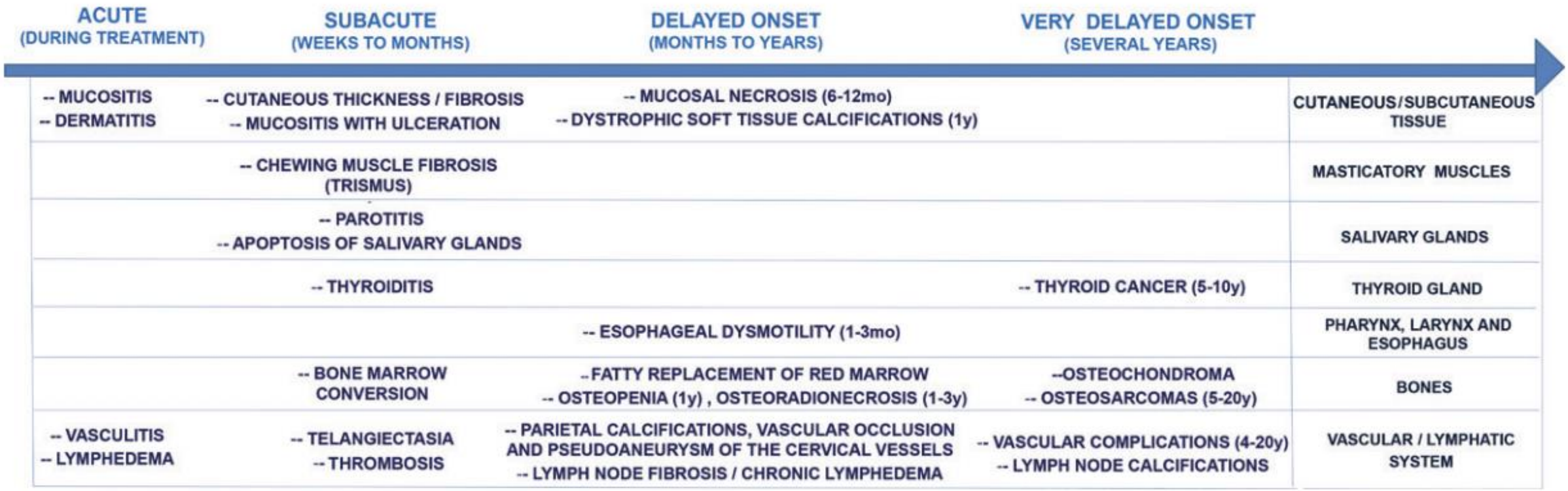
Invasive treatments involving pain, disfigurement, and compromised function in vital and visible areas of eating, speech, and breathing.

- Particularly affecting the social/interpersonal domain

Treatment recovery takes on average 12-36 months

Long term sequalae

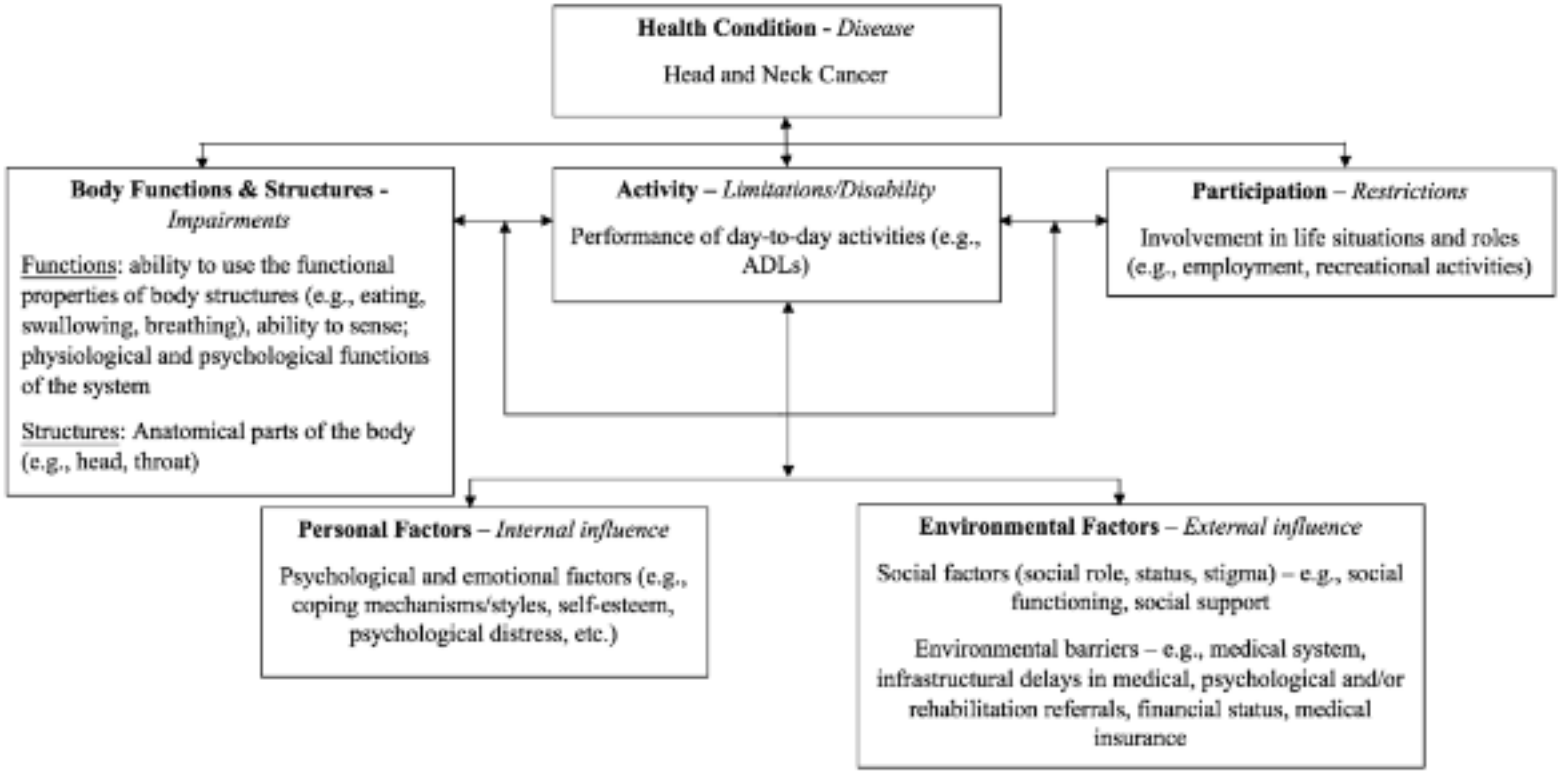
Main side effects from treatment



ACUTE (DURING TREATMENT)	SUBACUTE (WEEKS TO MONTHS)	DELAYED ONSET (MONTHS TO YEARS)	VERY DELAYED ONSET (SEVERAL YEARS)	
-- MUCOSITIS -- DERMATITIS	-- CUTANEOUS THICKNESS / FIBROSIS -- MUCOSITIS WITH ULCERATION	-- MUCOSAL NECROSIS (6-12mo) -- DYSTROPHIC SOFT TISSUE CALCIFICATIONS (1y)		CUTANEOUS/SUBCUTANEOUS TISSUE
	-- CHEWING MUSCLE FIBROSIS (TRISMUS)			MASTICATORY MUSCLES
	-- PAROTITIS -- APOPTOSIS OF SALIVARY GLANDS			SALIVARY GLANDS
	-- THYROIDITIS		-- THYROID CANCER (5-10y)	THYROID GLAND
		-- ESOPHAGEAL DYSMOTILITY (1-3mo)		PHARYNX, LARYNX AND ESOPHAGUS
	-- BONE MARROW CONVERSION	-- FATTY REPLACEMENT OF RED MARROW -- OSTEOPENIA (1y) , OSTEORADIONECROSIS (1-3y)	--OSTEOCHONDROMA -- OSTEOSARCOMAS (5-20y)	BONES
-- VASCULITIS -- LYMPHEDEMA	-- TELANGIECTASIA -- THROMBOSIS	-- PARIETAL CALCIFICATIONS, VASCULAR OCCLUSION AND PSEUDOANEURYSM OF THE CERVICAL VESSELS -- LYMPH NODE FIBROSIS / CHRONIC LYMPHEDEMA	-- VASCULAR COMPLICATIONS (4-20y) -- LYMPH NODE CALCIFICATIONS	VASCULAR / LYMPHATIC SYSTEM

Rocha et al., 2022

What is function?

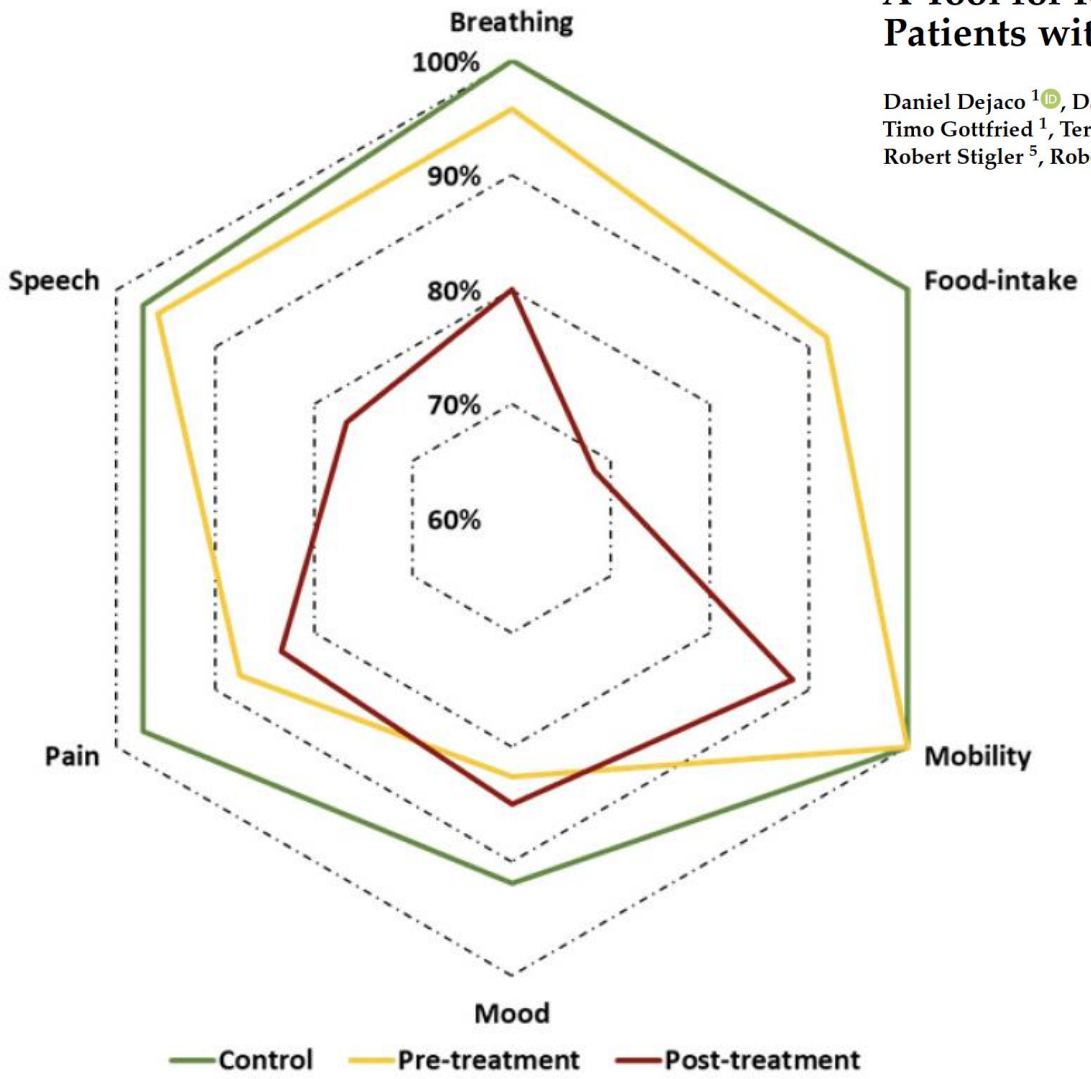


Adapted with permission, from the World Health Organization (WHO), *Towards a common language for functioning, disability and health: ICF (The International Classification of Functioning, Disability and Health)*, p.9, Retrieved January 4, 2018 from http://www.who.int/classifications/icf/training/icfbeginnersguide.pdf.

cancers

MDPI

Figure 1



Star plot showing the percentages of normal and near-normal scores (functional integrity; scores 3 and 4) for controls (green line), HNC patients before therapy (yellow line), and HNC patients after therapy (red line). The star axes represent the percentages of study participants with functional integrity for the functional domains breathing, food intake, neck and shoulder mobility, mood, pain, and speech.

Article

A Tool for Rapid Assessment of Functional Outcomes in Patients with Head and Neck Cancer

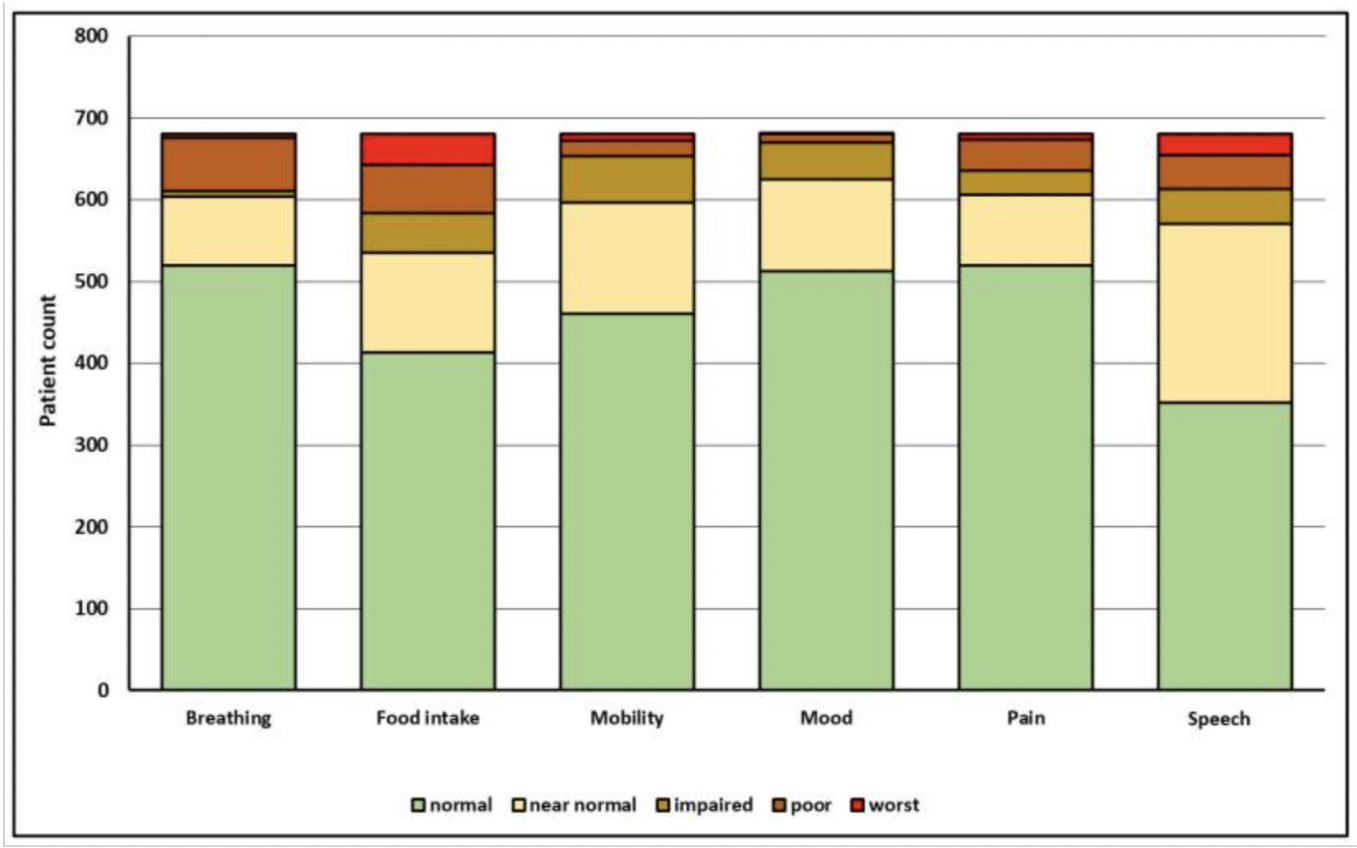
Daniel Dejaco [1], David Riedl [2,*], Sebastian Gasser [1], Volker Hans Schartinger [1], Veronika Innerhofer [1], Timo Gottfried [1], Teresa Bernadette Steinbichler [1], Felix Riechelmann [3], Roland Moschen [2], Oliver Galvan [4], Robert Stigler [5], Robert Gassner [5], Gerhard Rumpold [2], Anna Lettenbichler-Haug [1] and Herbert Riechelmann [1]

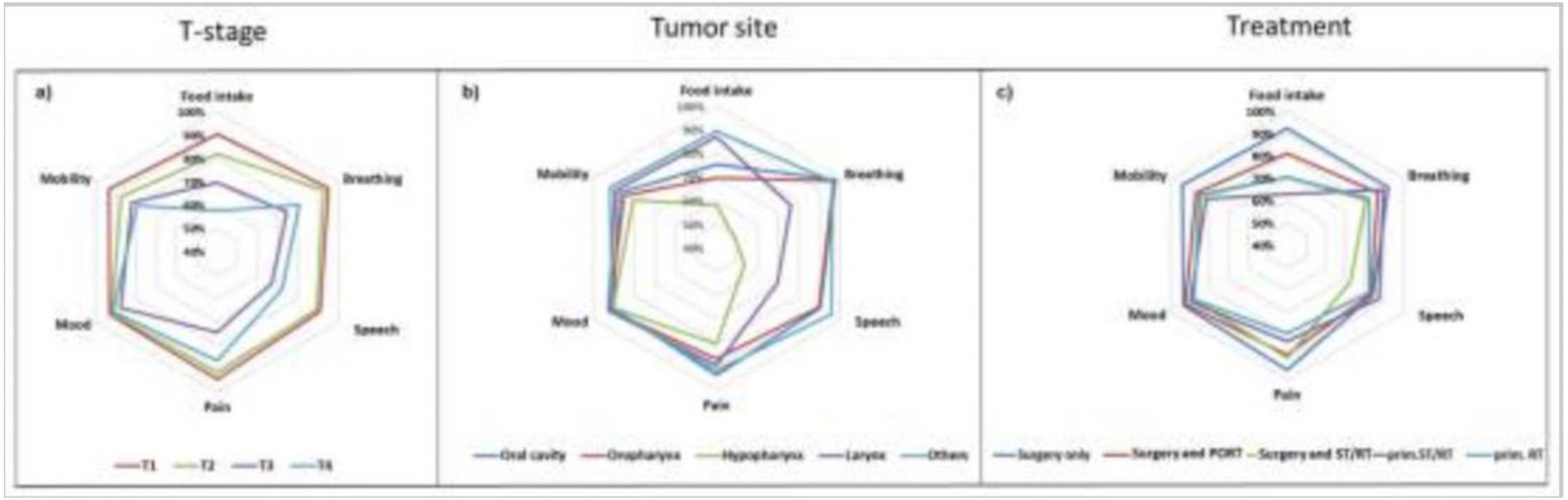
Long-term functional consequences

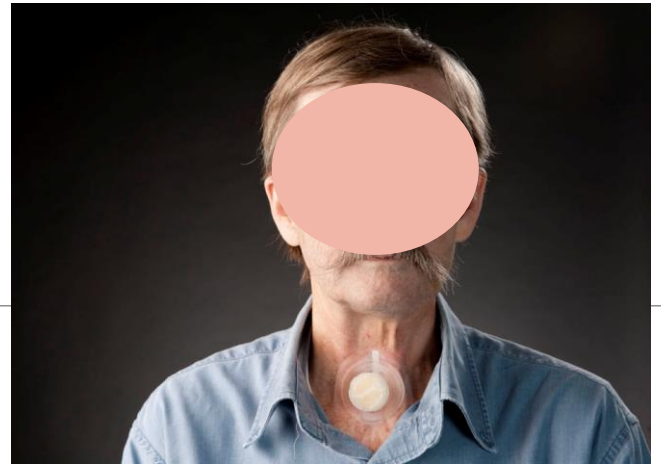
N=681 patients with HNC – Median=3years post-initial diagnosis

Severe limitations most frequently affected the functional domain of **food intake (21.5%)**, followed by **speech (16.3%)**.

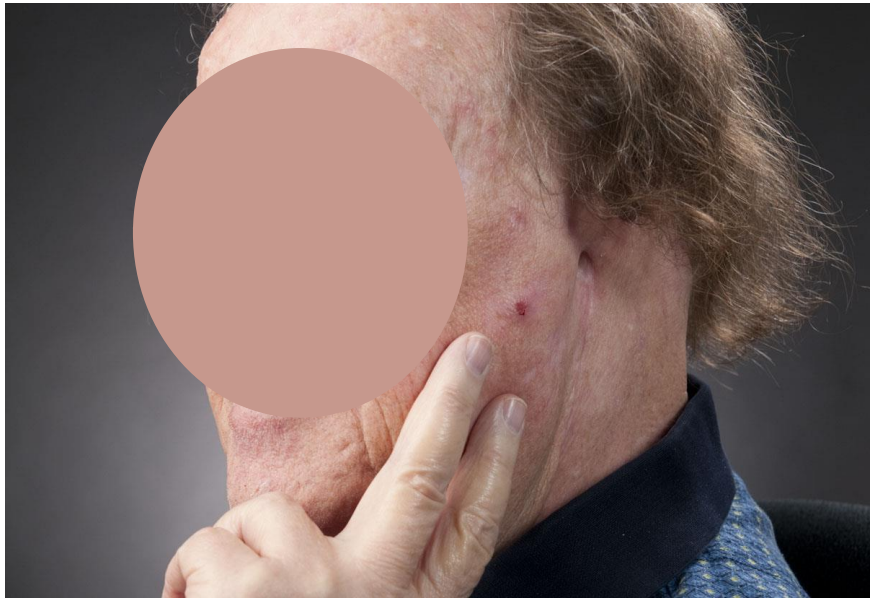
Lifestyle changes → 14.3% depend on a gastrostomy or feeding tube, 10.2% on a tracheotomy, 10% not able to communicate by telephone, 6.7% depend on opioids, 8.2% are on antidepressants, and 4.1% are not able to drive a car or comb their hair due to head and neck stiffness.

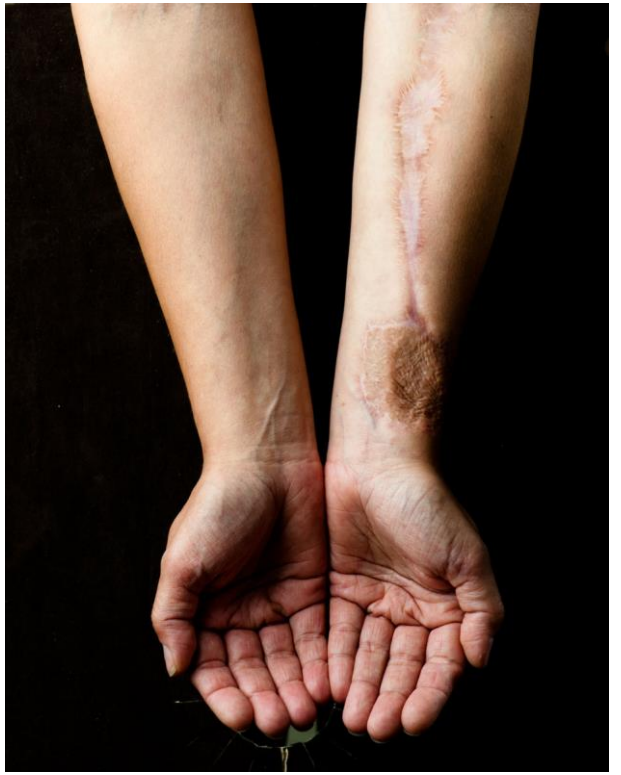



T-stage
Tumor site
Treatment
a)
b)
c)
Food intake
Breathing
Speech
Pain
Mood
Mobility
T1
T2
T3
T4
Oral cavity
Oropharynx
Hypopharynx
Larynx
Others
Surgery only
Surgery and PORT
Surgery and ST/RT
prim.ST/RT
prim. RT



↓survival, disease free status, post operative function, nutritional status/weight loss, tx compliance, ↑recurrence, medical expenditures, narcotics, tobacco/alcohol





Cancer Care Continuum

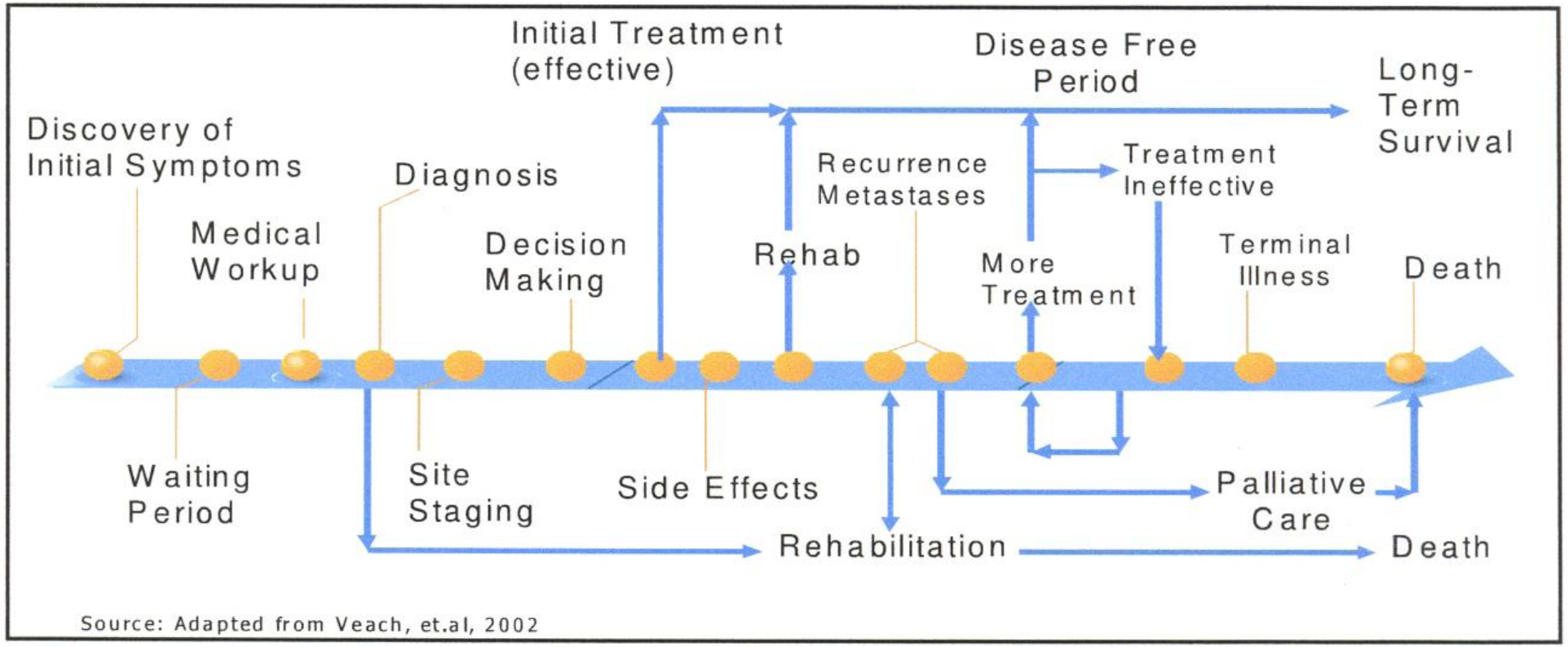


Figure 1: Cancer Care Continuum: Points of Assessment

A research program to identify and better conceptualize early determinants of mental health in patients with head and neck cancer

McGill

Hôpital général juif
Jewish General Hospital

Centre universitaire de santé McGill
McGill University Health Centre

Douglas
INSTITUT UNIVERSITAIRE EN SANTÉ MENTALE
MENTAL HEALTH UNIVERSITY INSTITUTE

Acknowledgements

Quebec Health Research Fund (FRQS) Grant

FRQS Clinician-Scientist Salary Awards

Co-Investigators:

- Drs. Zeev Rosberger, Saul Frenkiel, Michael Hier, Anthony Zeitouni, Martin Black, Nader Sadeghi, Alexander Mlynarek, Karen Kost, Keith Richardson, Marco Mascarella, Christina MacDonald, Gabrielle Chartier, Xun Zhang, AM Rodriguez, Francois Chiocchio, Sylvie Lambert, Franco Carnevale, Michael Meaney, Kieran O'Donnell, Phil Gold, Celia Greenwood

Residents, students and staff:

- Lawrence Chen, Thi Thu Thao Nguyen, Han-Tin Kao, Raphaelle Harvey, Emily Arnovitz, Eleonora Sargi, Ali Alias, Maria Cherba, Claudia Woronko, Fabienne Fuehrmann, Justin Desroches, Avina De Simone, Clara Bolster-Foucault, Lia Bertrand, Christina Klassen, Alexandra Cohen, Lola Ianovski, Kelly Chang, Ala Bdira, Laura Anne Habib, Mathew Morrison, Ji Wei Yang, Xuejiao Joanna Li, Shiru Lin, Angela Ho, Sonalia Amarasekera, Cassie Chaloux, Maria Cherba, Clara-Bolster Foucault, Judy Fung, Goda Galinyte, Deniz Keskinel, Dr. Marco Mascarella, Camille Texier, Nabila Zuberi

Cancer Care Continuum

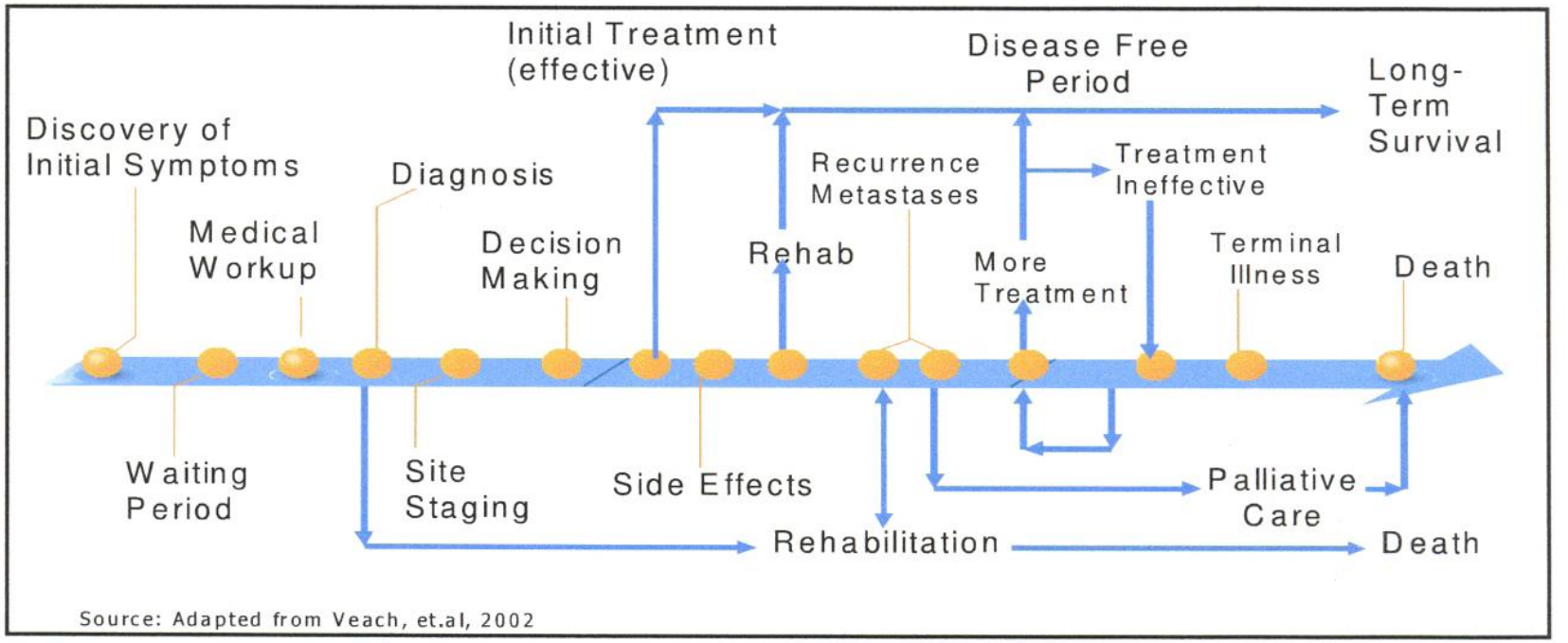
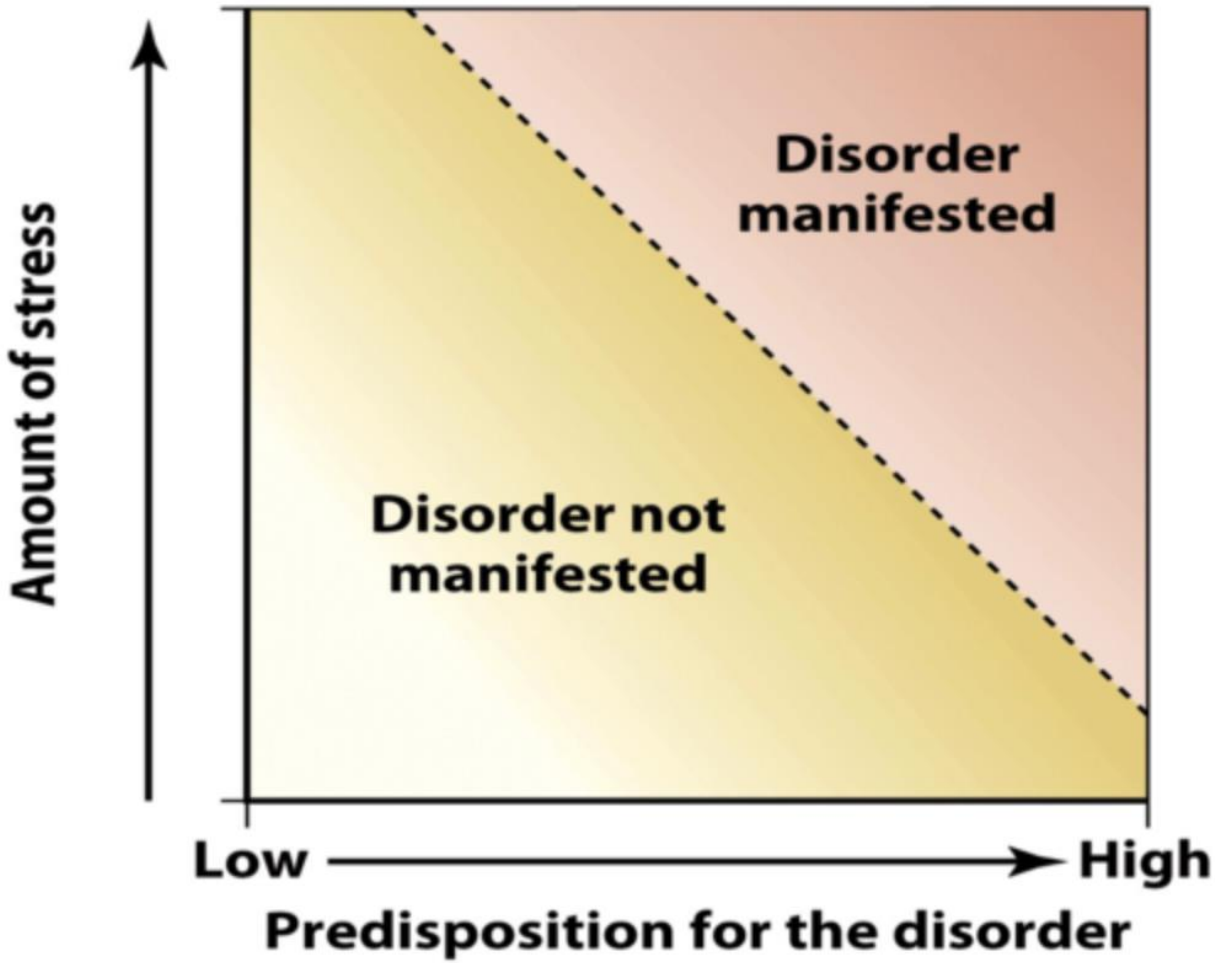


Figure 1: Cancer Care Continuum: Points of Assessment

Diathesis-Stress Model, Wilson and Cleary QoL Model and Life Course Approach

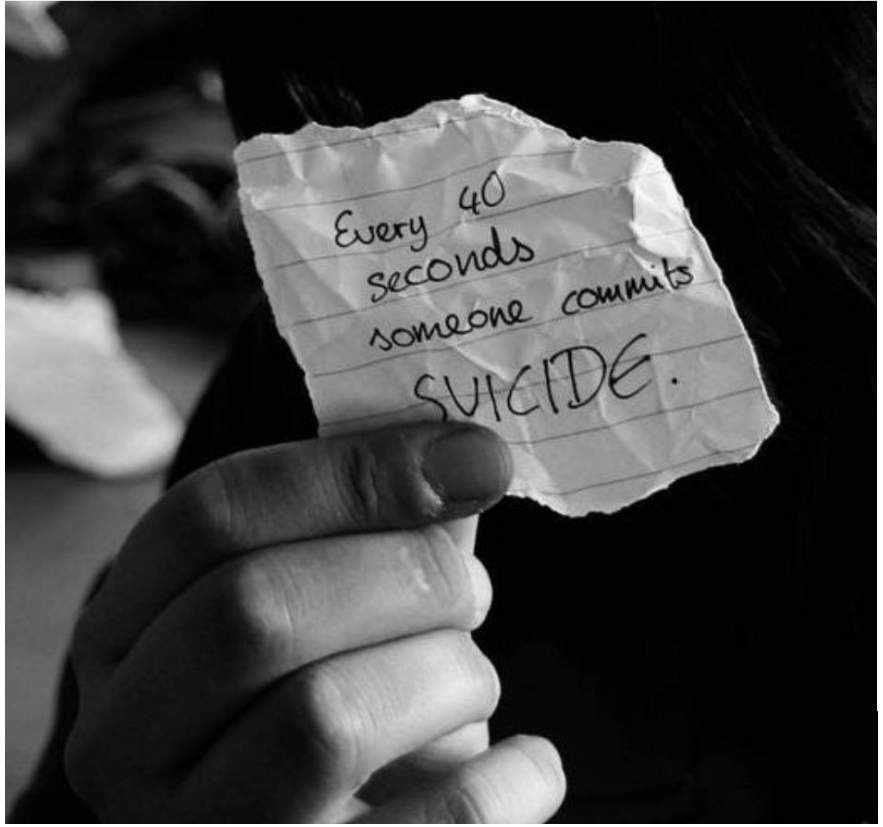
Stress-Diathesis Model



Methods

Prospective longitudinal study of 223 patients newly diagnosed with HNC.

- Structured Clinical Interviews
- Psychometric measures
- Medical chart reviews
- Saliva sample for genetic testing



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Original Research—Head and Neck Surgery

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–
Head and Neck Surgery
2018, Vol. 159(5) 843–852

DOI: 10.1177/0194599818776873
http://otojournal.org
SAGE

Prevalence and Risk Factors of Suicidal Ideation among Patients with Head and Neck Cancer: Longitudinal Study

Melissa Henry, PhD[1,2], Zeev Rosberger, PhD[1,2], Lia Bertrand[1], Christina Klassen[2], Michael Hier, MD[1,2], Anthony Zeitouni, MD[1,3], Karen Kost, MD[1,3], Alex Mlynarek, MD[1,2,3], Keith Richardson, MD[1,3], Martin Black, MD[1,2], Christina MacDonald, MSc[2], Xun Zhang, PhD[1,3], Gabrielle Chartier, MSc[2], and Saul Frenkiel, MD[1,2,3]

- Longitudinal study: Prevalence of SI, onset in trajectory from dx to 1 year, predictors of SI

- 16% suicidal <1yr of cancer dx
- 30% moderate to high risk of suicide
- 50/50 onset
- Predictors: prior psychiatric hx & coping with alcohol use
- Poorer QoL, function, HN Sx, complications
- We need to consider the diathesis, not only treatment-related burden
- Importance of suicide prevention in OHNS clinics

Received: 14 November 2017 | Revised: 12 February 2018 | Accepted: 7 March 2018
DOI: 10.1002/pon.4705

PAPER

WILEY

A screening algorithm for early detection of major depressive disorder in head and neck cancer patients post-treatment: Longitudinal study

Melissa Henry[1,2,3,4,5,6,7] | Zeev Rosberger[1,2,4,6,7] | Lola E. Ianovski[4] | Michael Hier[1,3,4,5,6] | Anthony Zeitouni[1,3,8] | Karen Kost[1,3,8] | Alex Mlynarek[1,3,4,5,6,8] | Martin Black[1,3,4,5,6] | Christina MacDonald[5,9] | Keith Richardson[1,3,8] | Xun Zhang[10] | Fabienne Fuhrmann[1,4] | Gabrielle Chartier[5,9] | Saul Frenkiel[1,3,4,5,6,8]

- 20% point prevalence MDD dx-3mo (14.2% 3-mo; 22.6% lifetime) vs. Canada 4.7% & 11.3%
- Predictors:
  - ✓ Advanced stage, OR=4.94, p=0.04
  - ✓ Receiving surgery only, OR=8.73, p=0.04
  - ✓ Lifetime hx AD (SCID-I), OR=6.62, p=0.01
  - ✓ Higher pre-treatment anxiety and depression (HADS), OR=0.45, p=0.05
- MDD compromised QoL over 6 months
- Research implication → Immunological hypothesis – Sickness Behaviour

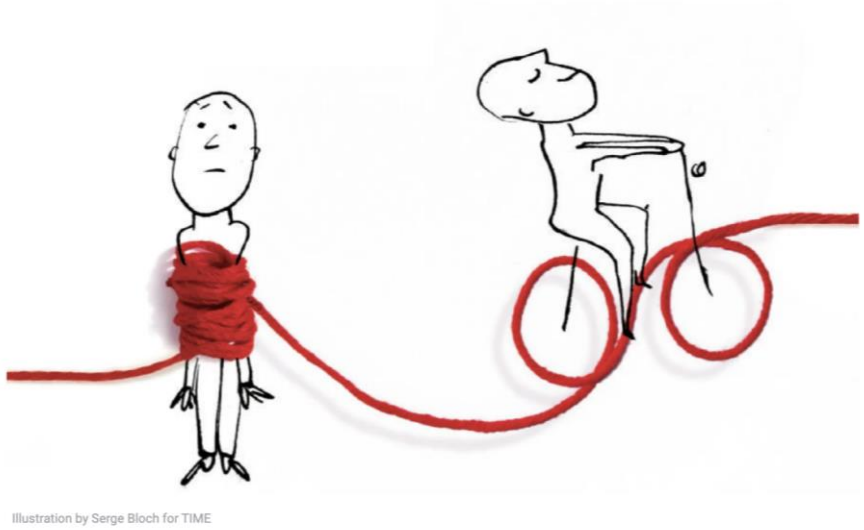
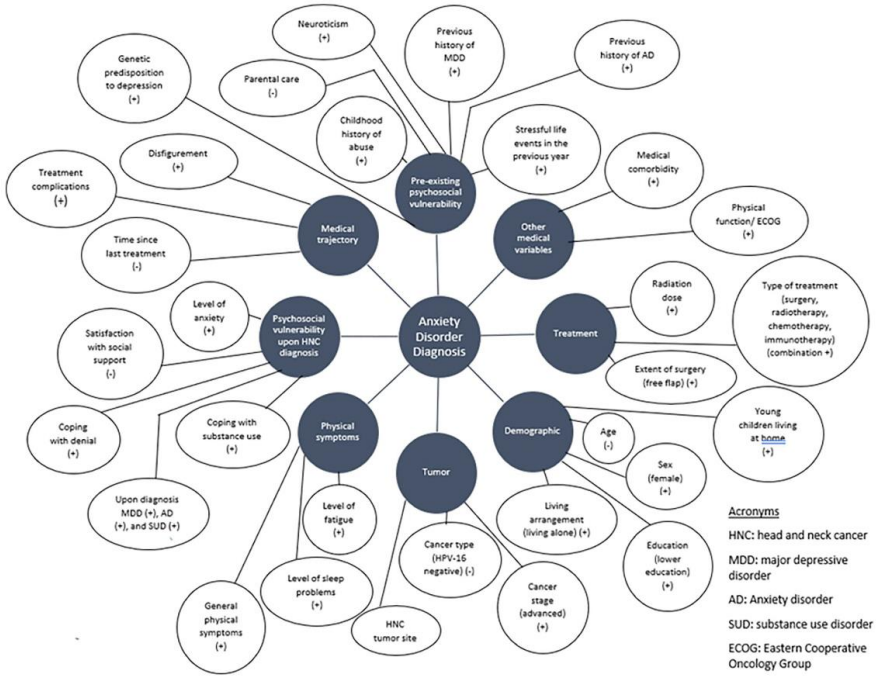


Illustration by Serge Bloch for TIME



Received: 9 May 2021 | Revised: 11 June 2021 | Accepted: 23 June 2021

DOI: 10.1002/pon.5760

WILEY

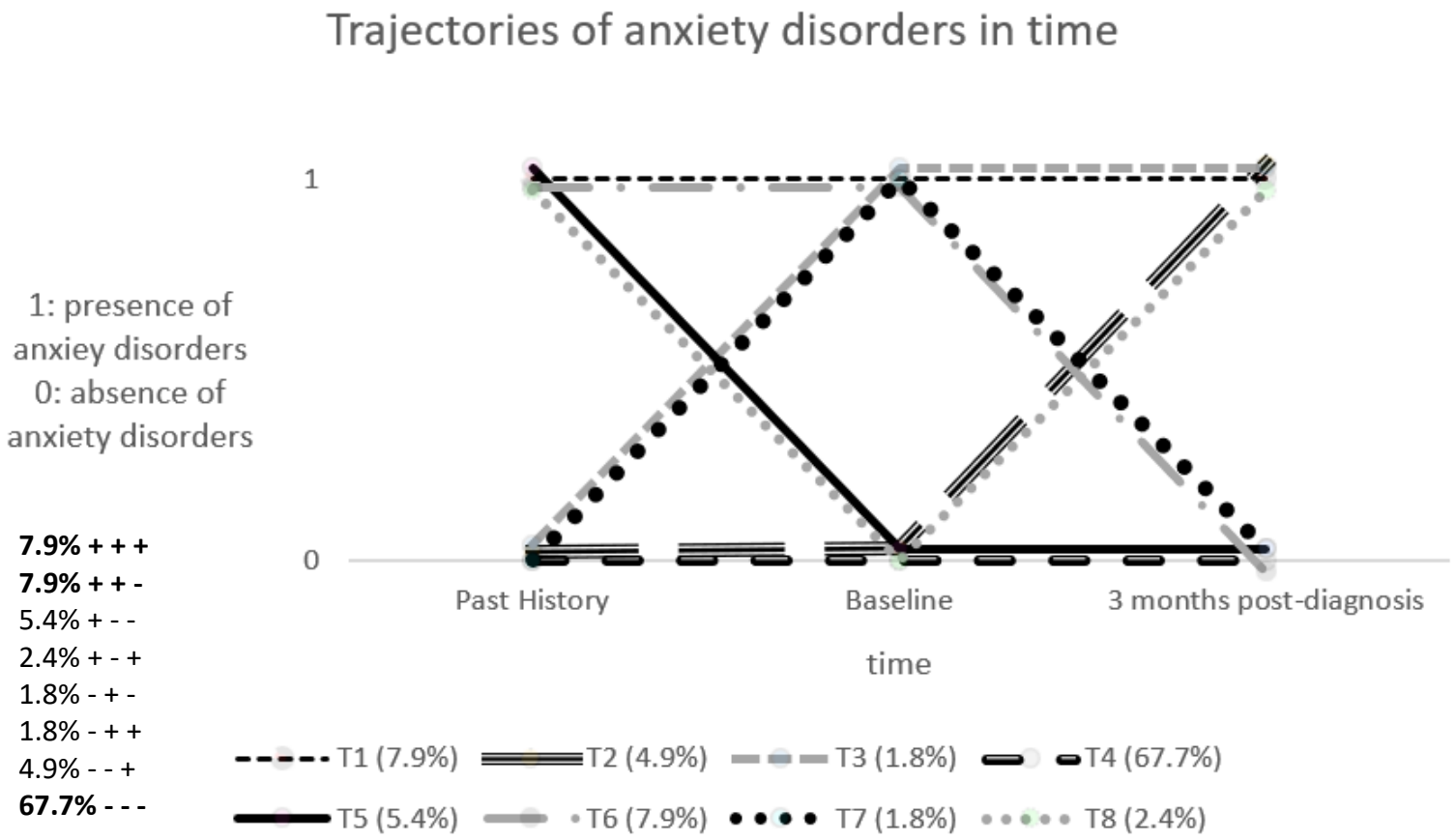
ORIGINAL ARTICLE

Longitudinal study indicating antecedent psychosocial vulnerability as predictor of anxiety disorders post-treatment in people with head and neck cancer

Melissa Henry[1,2,3,4] | Elyonora Sargi[5] | Saul Frenkiel[3,6] | Michael Hier[3,6] | Anthony Zeitouni[6,7] | Karen Kost[6,7] | Alex Mlynarek[3,6,7] | Martin Black[3,6] | Christina MacDonald[3,8] | Keith Richardson[6,7] | Gabrielle Chartier[3,8] | Nader Sadeghi[6,7] | Zeev Rosberger[1,2,9]

Results: Twenty-five percent of patients presented a lifetime AD, 19.4% within 2 weeks of HNC diagnosis, and 16.6% immediately post-treatment; representing 26.7% of patients with AD at any timepoint from the moment of diagnosis to immediately post-treatment. Patients were more likely to present an AD immediately post-treatment when they: were diagnosed with advanced-stage cancer (OR = 3.40, p = 0.006), presented a upon cancer diagnosis AD (OR = 2.45, p = 0.008) and/or experienced childhood abuse (OR = 1.96, p = 0.03).

Anxiety Disorders in patients with HNC

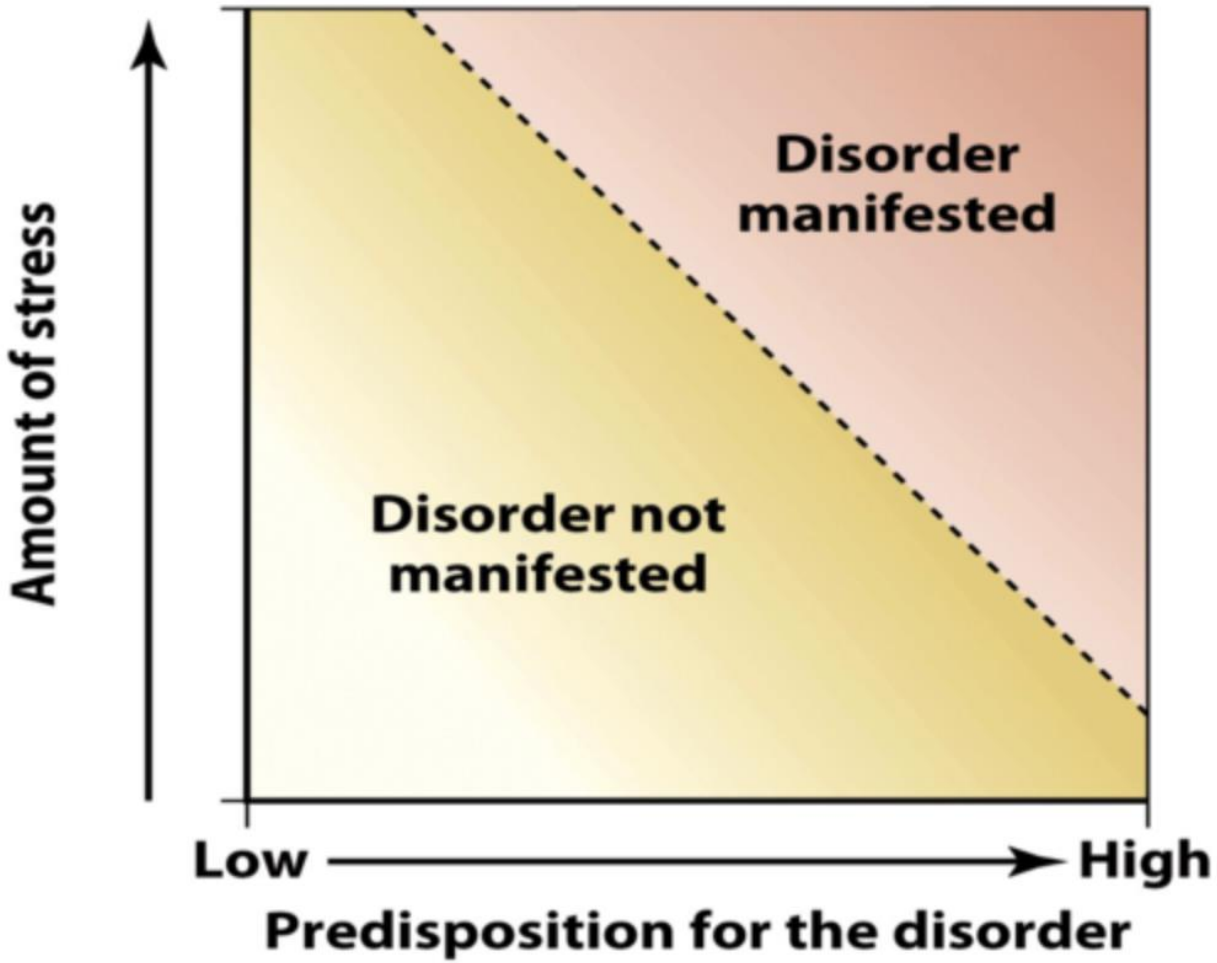


50% Past AD → 66% upon HNC diagnosis → 50% persist immediately post-tx

No AD in the past → 4% developed AD upon HNC dx → 50% remained stable immediately post-tx

Stress-Diathesis Model →

Inter-influence of the medical and larger predisposing context



The role of genetic predispositions

Journal of Affective Disorders 331 (2023) 149–157

Contents lists available at ScienceDirect

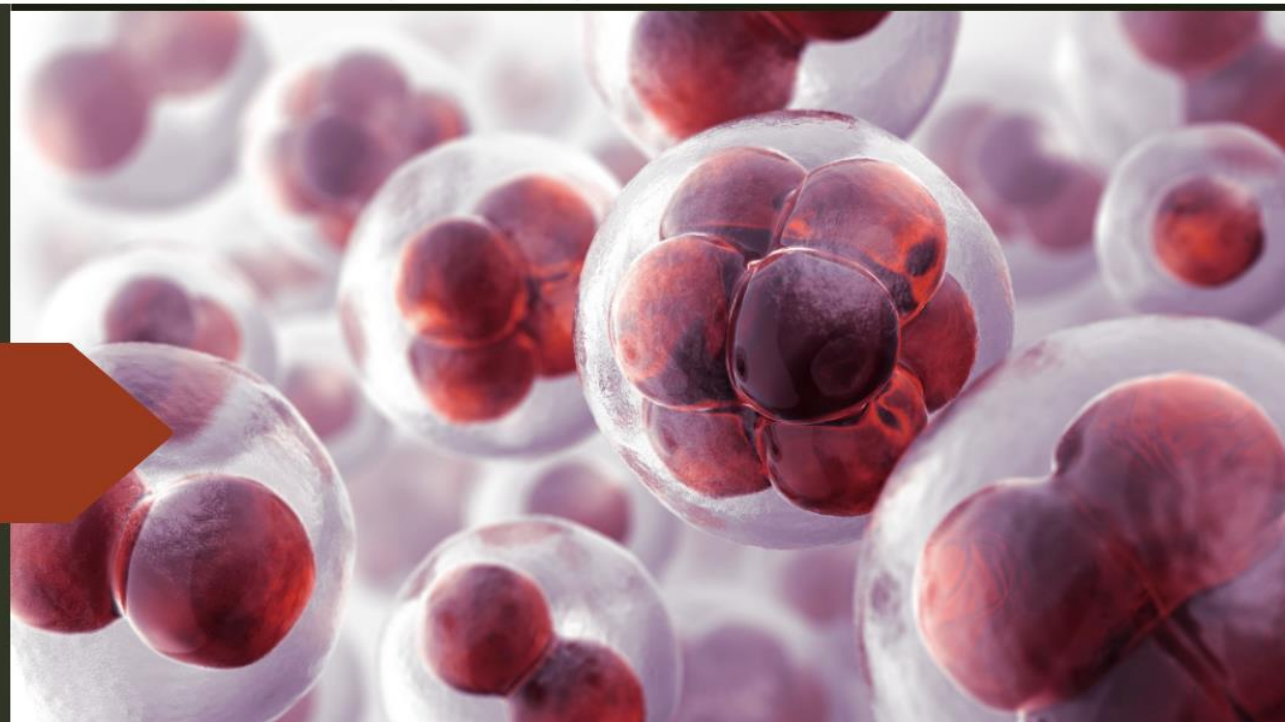
Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Genetic predisposition to depression and inflammation impacts symptom burden and survival in patients with head and neck cancer: A longitudinal study

Melissa Henry [a,b,c,*], Raphaële Harvey [a], Lawrence M. Chen [a,d], Michael Meaney [a,d], Thi Thu Thao Nguyen [a,d], Han-Tin Kao [a,d], Zeev Rosberger [a,b,c], Saul Frenkiel [a,b,d], Michael Hier [a,b,c], Anthony Zeitouni [a,e], Karen Kost [a,e], Alex Mlynarek [a,b,e], Keith Richardson [a,e], Celia M.T. Greenwood [a,c], David Melnychuk [a,b], Phil Gold [a,b], Gabrielle Chartier [b], Martin Black [a,b], Marco Mascarella [a,e], Christina MacDonald [b], Nader Sadeghi [a,e], Khalil Sultanem [a,e], Georges Shenouda [a,e], Fabio Cury [a,e], Kieran John O'Donnell [a,d,f,g]



Genetic predisposition to depression

ARTICLES
https://doi.org/10.1038/s41588-018-0090-3
nature genetics

Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression

Major depressive disorder (MDD) is a common illness accompanied by considerable morbidity, mortality, costs, and heightened risk of suicide. We conducted a genome-wide association meta-analysis based in 135,458 cases and 344,901 controls and identified 44 independent and significant loci. The genetic findings were associated with clinical features of major depression and implicated brain regions exhibiting anatomical differences in cases. Targets of antidepressant medications and genes involved in gene splicing were enriched for smaller association signal. We found important relationships of genetic risk for major depression with educational attainment, body mass, and schizophrenia: lower educational attainment and higher body mass were putatively causal, whereas major depression and schizophrenia reflected a partly shared biological etiology. All humans carry lesser or greater numbers of genetic risk factors for major depression. These findings help refine the basis of major depression and imply that a continuous measure of risk underlies the clinical phenotype.

MDD is a notably complex and common illness[1]. It is often chronic or recurrent and is thus accompanied by considerable morbidity, disability, excess mortality, substantial costs, and heightened risk of suicide[2–8]. Twin studies attribute approximately 40% of the variation in liability to MDD to additive genetic effects (phenotype heritability, h^2)[9], and h^2 may be greater for recurrent, early-onset, and postpartum MDD[10,11]. Genome-wide association studies (GWAS) of MDD have had notable difficulties in identifying individual associated loci[12]. For example, there were no significant findings in the initial Psychiatric Genomics Consortium (PGC) MDD mega-analysis (9,240 cases)[13] or in the CHARGE meta-analysis of depressive symptoms ($n = 34,549$)[14]. More recent studies have proven modestly successful. A study of Han Chinese women (5,303 recurrent MDD cases) identified significant loci[15], a meta-analysis of depressive symptoms (161,460 individuals) identified 2 loci[16], and an analysis of self-reported major depression identified 15 loci (75,607 cases).

There are many reasons why identifying causal loci for MDD has proven difficult[12]. MDD is probably influenced by many genetic loci, each with small effects[17], as are most common diseases[18], including psychiatric disorders[19,20]. Estimates of the proportion of variance attributable to genome-wide SNPs (SNP heritability, h^2_{SNP}) indicate that around

depression (Table 1 and Supplementary Tables 1–3). The methods used by these cohorts were thoroughly reviewed, drawing on the breadth of expertise in the PGC, and we assessed the comparability of the cohorts using genomic data. We use 'MDD' to refer to directly evaluated subjects meeting standard criteria for major depressive disorder and use 'major depression' where case status was determined using alternative methods as well as to the phenotype from the full meta-analysis.

We evaluated the comparability of the seven cohorts by estimating the common variant genetic correlations (r_g) between them. These analyses supported the comparability of the seven cohorts (Supplementary Table 3), as the weighted mean r_g was 0.76 (s.e. = 0.03). The high genetic correlations between the 23andMe and other cohorts are notable. While there was no statistical evidence of heterogeneity in the r_g estimates for pairs of cohorts ($P = 0.13$), the estimate was statistically different from 1, which may reflect etiological heterogeneity. This estimate can be benchmarked against the slightly larger weighted mean r_g between schizophrenia cohorts of 0.84 (s.e. = 0.05)[11].

Given the positive evidence of the genetic comparability of these cohorts, we completed a genome-wide association meta-analysis

Advances in genomics can help delineate the contribution of depression and inflammation to symptom burden and survival in the immediate post-treatment of patients with severe medical diseases, through the study of polygenic risk scores (PRS).

March 2016

Depression and Survival in Patients With Head and Neck Cancer

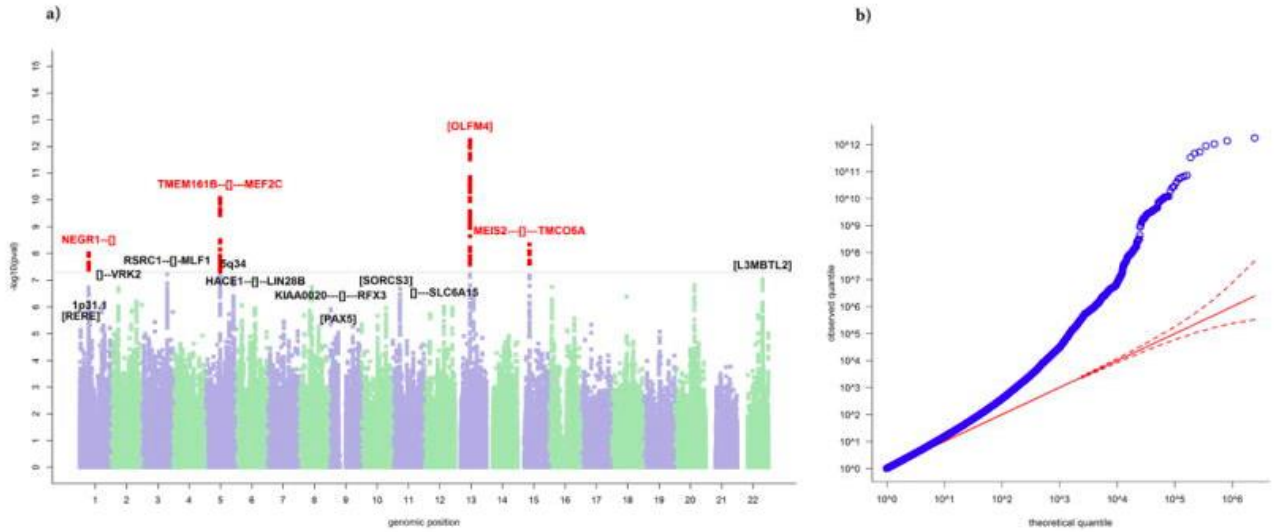
A Systematic Review

JAMA Otolaryngology–Head & Neck Surgery

Brittany Barber, MD[1]; Jace Dergousoff, MD[2]; Linda Slater, MLIS[3]; et al

What is a polygenic risk score (PRS)?

Figure 1



Discovery phase meta-analysis of 23andMe self-report ascertainment of major depression (75,607 cases and 231,747 controls) and PGC MDD (9,240 cases and 9,519 controls). a) Manhattan plot of Discovery phase 23andMe GWAS. LD score regression calculated intercept was used for inflation correction. The threshold for genome-wide significance ($p < 5\times10^{-8}$) is indicated by the purple line. Red dots represent SNPs with p-values smaller than the genome-wide significant threshold. Regions labeled in black denote loci that reached genome-wide significance in the join-analysis. b) Q-Q plot for the 23andMe MDD GWAS.

A number based on variation in multiple genetic loci and their associated weights found in GWAS studies

- 23 and me

Assures prediction of a trait taking into account multiple variation or SNP

Lack of PRS-D studies as it relates to symptom burden and survival in oncology.

HNC affords a unique opportunity

- same high stress situation
- high levels of psychiatric comorbidities pre-cancer → 47%
- high degree of disease- & tx-related burden, and lower survival

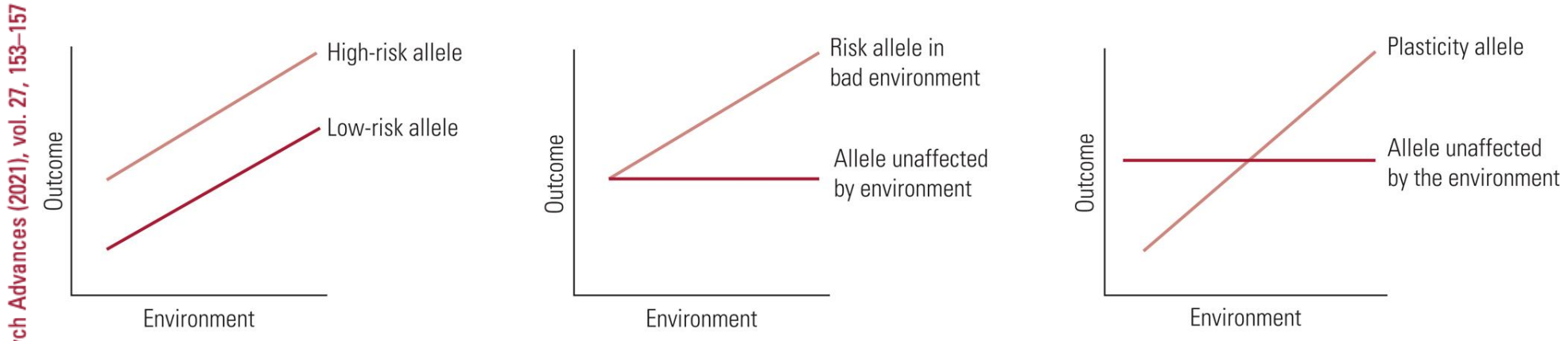


FIG 1 Gene × environment associations. (a) gene and environment effects (additive, no interaction). (b) Diathesis-stress (risk factor). (c) Differential susceptibility (plasticity).

Symptom burden predicted by XRT, medical comorbidities, anxiety, and PRS-D

Variable	Standardized coefficients	Unstandardized coefficients	95% confidence interval	*t*	*p*
Age in years	-0.006	-0.002	-0.06 | 0.05	-0.07	0.94
Cancer stage	-0.10	-0.74	-2.37 | -0.90	-0.90	0.37
HPV-status	0.02	0.12	-1.10 | 1.35	0.20	0.84
Anti-cancer treatment	0.08	0.08	-0.15 | 0.32	0.69	0.49
Total dose of radiotherapy	0.46	0.002	0.001 | 0.003	4.00	<0.001***
Chemotherapy type	-0.06	-0.41	-1.13 | 1.95	0.53	0.60
Medical comorbidity	0.16	0.57	-0.07 | 1.21	1.78	0.08†
Anti-inflammatory medication	0.02	0.18	-1.40 | 1.76	0.23	0.82
Diagnosis of AD	0.23	1.69	0.43 | 2.94	2.67	<0.001***
HADS Anxiety	0.29	0.20	0.07 | 0.34	3.04	0.003**
PRS Inflammation	-0.16	-0.51	-1.06 | 0.05	-1.81	0.07†
PRS Depression – 2018	0.18	0.66	0.003 | 1.32	2.00	0.049*
Baseline SB-total	0.24	0.32	0.07 | 0.57	2.52	0.01*

†trend, ***p<0.001, **p<0.01, *p<0.05; AD=Anxiety Disorder; HADS=Hospital Anxiety and Depression Scale; PRS=Polygenic Risk Score; SB=Sickness Behavior.

Anxiety Dx: 19.4%

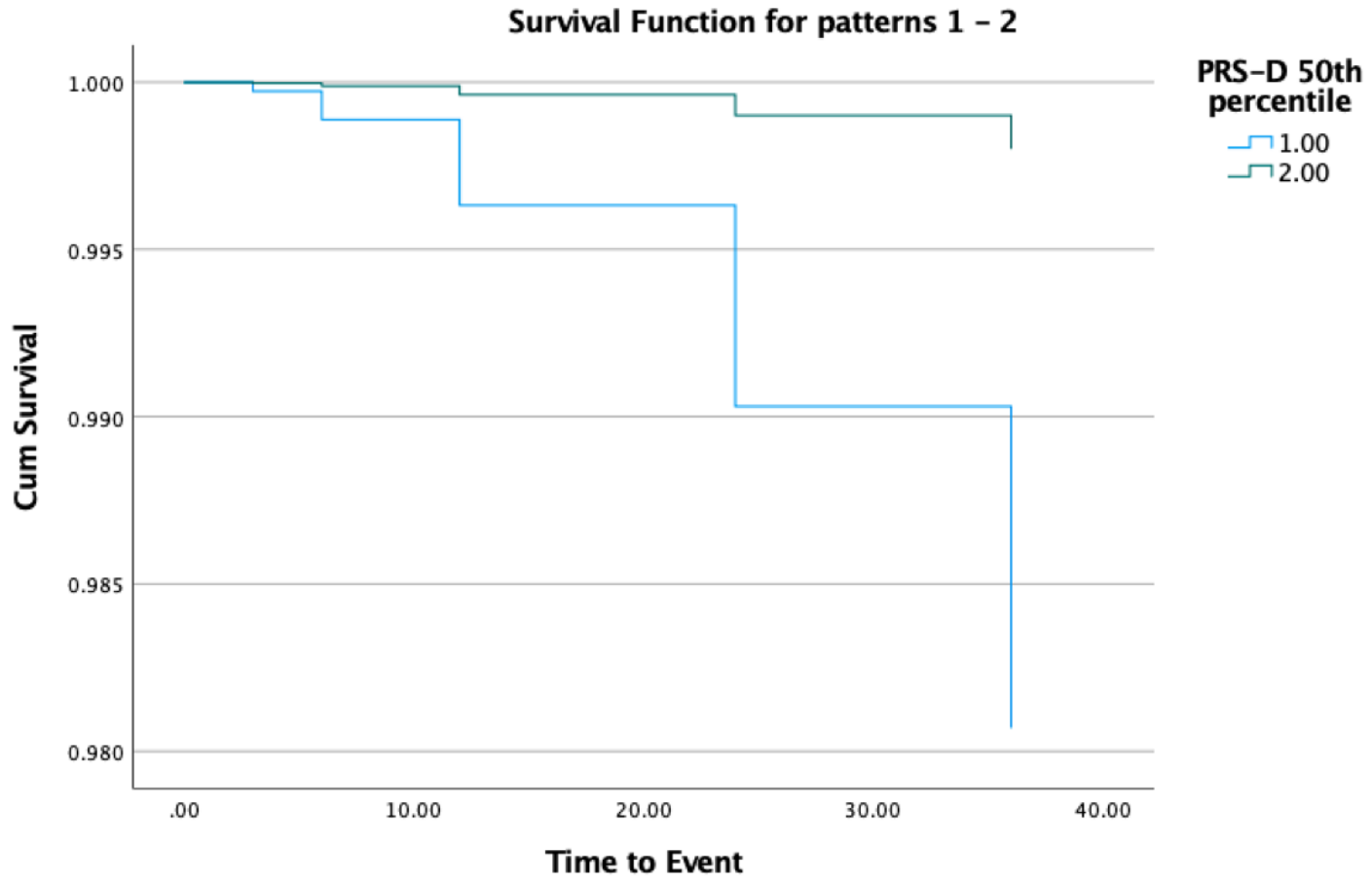
-Agoraphobia w/ or w/out panic dis. (7%)
-Simple phobia (7%)
-Social Phobia (4%)
-PTSD (2%)
-GAD (5%)
-OCD (0.5%)
-Claustrophobia (4%)

Cox proportional hazards survival analysis of 3, 6, 12, 24, and 36 month survival

Variable	B	Exp(B)	95% confidence interval of Exp(B)	*p*
Age	0.06	1.06	0.99 | 1.14	0.11
University Education	0.32	1.38	0.36 | 5.27	0.88
Early cancer stage (I/II)	7.62	2047.15	0.000 | 1.02E+45	0.88
HPV-status	2.17	8.72	1.14 | 66.86	0.037*
Medical comorbidity	0.22	1.24	0.22 | 7.08	0.81
Anti-inflammatory medication	-0.76	0.47	0.13 | 1.77	0.27
Treatment type	-18.52	0.00	0.00 | 1.81E+39	0.98
Early recurrence/progression (3 months)	-13.86	0.00	0.00 | 8.09E+190	0.95
Cigarettes	-2.11	0.12	0.03 | 0.53	0.005**
Alcohol abuse	0.33	1.39	0.87 | 2.21	0.17
Childhood abuse	2.01	7.49	0.66 | 84.43	0.10
Lifetime psychiatric condition	-1.39	0.25	0.03 | 2.42	0.23
Psychiatric medication	2.07	7.91	0.65 | 96.42	0.11
Psychosocial oncology service	-1.21	0.30	0.06 | 1.64	0.16
FACT-G + H&N Module	-0.01	0.99	0.94 | 1.03	0.55
Stressful life events	-0.20	0.82	0.57 | 1.18	0.28
HADS Anxiety	0.27	0.77	0.61 | 0.96	0.02*
HADS Depression	0.07	0.93	0.67 | 1.29	0.66
PRS inflammation	0.14	1.15	1.01 | 1.30	0.03*
PRS depression – 2019	-0.15	0.86	0.47 | 1.57	0.62
PRS depression – 2018	1.75	5.75	1.55 | 21.27	0.009**

†trend, ***p<0.001, **p<0.01, *p<0.05; FACT-G + H&N Module=Functional Assessment of Cancer Therapy – General + Head and Neck Module; HADS=Hospital Anxiety and Depression Scale; PRS=Polygenic Risk Score.

Survival probability <36 months of diagnosis w/ 50th percentile of the 2018 PRS for depression



Gut-Brain Axis

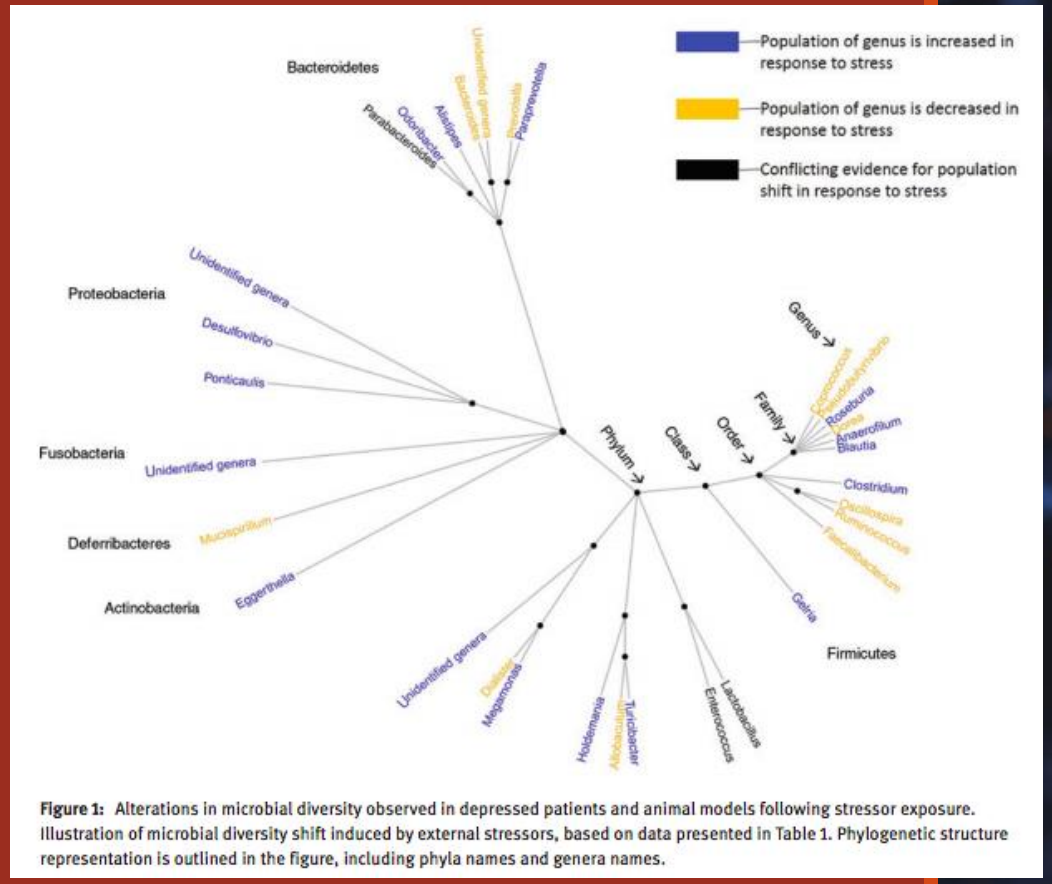


Figure 1: Alterations in microbial diversity observed in depressed patients and animal models following stressor exposure. Illustration of microbial diversity shift induced by external stressors, based on data presented in Table 1. Phylogenetic structure representation is outlined in the figure, including phyla names and genera names.

HPV- vs. non-HPV related head and neck cancers

Psycho-Oncology (2021)

Table 1. Variables associated with anxiety and depression immediately post-HNC diagnosis and immediately post-treatment.

Variable	Unstandardized coefficient B	Standard coefficient Beta	p-value	95% Confidence Interval (CI) for B
Variables associated with anxiety and depression immediately post-HNC diagnosis				
Sex (female)	2.76	0.17	0.07†	-0.23 | 5.74
HPV status	-14.44	-0.92	<0.001***	-20.01 | -8.87
SCID past history of MDD x HPV	3.41	0.37	0.006**	1.02 | 5.81
SCID <2 weeks of HNC diagnosis MDD x HPV	6.35	0.57	<0.001***	3.07 | 9.63
Variables associated with anxiety and depression immediately post-treatment				
Tumor site hypopharyngeal	15.73	0.19	0.009**	4.04 | 27.43
Lifetime pre-cancer history of suicidal ideation	3.51	0.14	0.07†	-0.33 | 7.35
Anxiety and depression <2 weeks of HNC diagnosis (HADS)	0.78	0.80	<0.001***	0.37 | 1.19

* p<0.05; ** p<0.01; ***p<0.001; † 0.05 > p < 0.10; HPV=Human papilloma virus; RAPS4-QF = Rapid Alcohol Problems Screen – Quantity Frequency; SCID=Structured Clinical Interview for DSM; MDD=Major Depressive Disorder; SUD=Substance Use Disorder; HNC=head and neck cancer.

Table 2. Variables associated with quality of life immediately post-HNC diagnosis and immediately post-treatment.

Variable	Unstandardized coefficient B	Standard coefficient. Beta	p-value	95% Confidence Interval (CI) for B
Variables associated with quality of life immediately post-HNC diagnosis				
Education (university)	-0.04	-0.13	0.02*	-0.07 | -0.006
Advanced cancer stage (stages III/IV)	-5.62	-0.11	0.07	-11.70 | 0.45
Tumor site hypopharyngeal	-15.95	-0.11	0.06	-32.68 | 0.77
HPV status	19.12	0.43	0.001**	7.70 | 30.53
SCID <2 weeks of HNC diagnosis MDD x HPV	-8.77	-0.28	0.01**	-15.49 | 2.05
Level of anxiety (HADS)	-2.51	-0.52	<0.001***	-3.13 | -1.88
Variables associated with quality of life immediately post-treatment				
Tumor site hypopharyngeal	-40.42	-0.16	0.04*	-79.61 | -1.22
Smoked cigarettes <30 days of HNC	-9.82	-0.16	0.049*	-19.61 | -0.02
Lifetime pre-cancer history of suicidal ideation	-15.71	-0.19	0.02*	-28.75 |-2.66
Level of anxiety (HADS)	-1.44	-0.28	0.008**	-2.49 | -0.39
Quality of life <2 weeks of HNC diagnosis (FACT-G + HN Module)	0.35	0.31	0.002***	0.13 | 0.57

* p<0.05; ** p<0.01; ***p<0.001; † 0.05 > p < 0.10; HPV=Human papilloma virus; HADS=Hospital Anxiety and Depression Scale; RAPS4-QF = Rapid Alcohol Problems Screen – Quantity Frequency; SCID=Structured Clinical Interview for DSM; MDD=Major Depressive Disorder; SUD=Substance Use Disorder; HNC=head and neck cancer.

Paying attention to sexual aspects

Descriptive studies have found concerns related to the sexually transmitted nature of HPV persisting in long-term survivorship (40%):

- Concerns about infecting one's partner (43%)
- Worry about the causes of infection (17%)
- Reduction in sexual intimacy (28%)
- Effects on intimate relationship (20%)
- HPV status being kept secret for fear of embarrassment or stigma (14%)

D'Souza et al., 2016; Milbury et al., 2013

Clinical practice guidelines

- Recommend that the physician:
  - assess the impact of an HPV diagnosis
  - help the patient understand the diagnosis (why, how, when), and
  - proactively discuss sexuality issues with patients (and refer if needed)

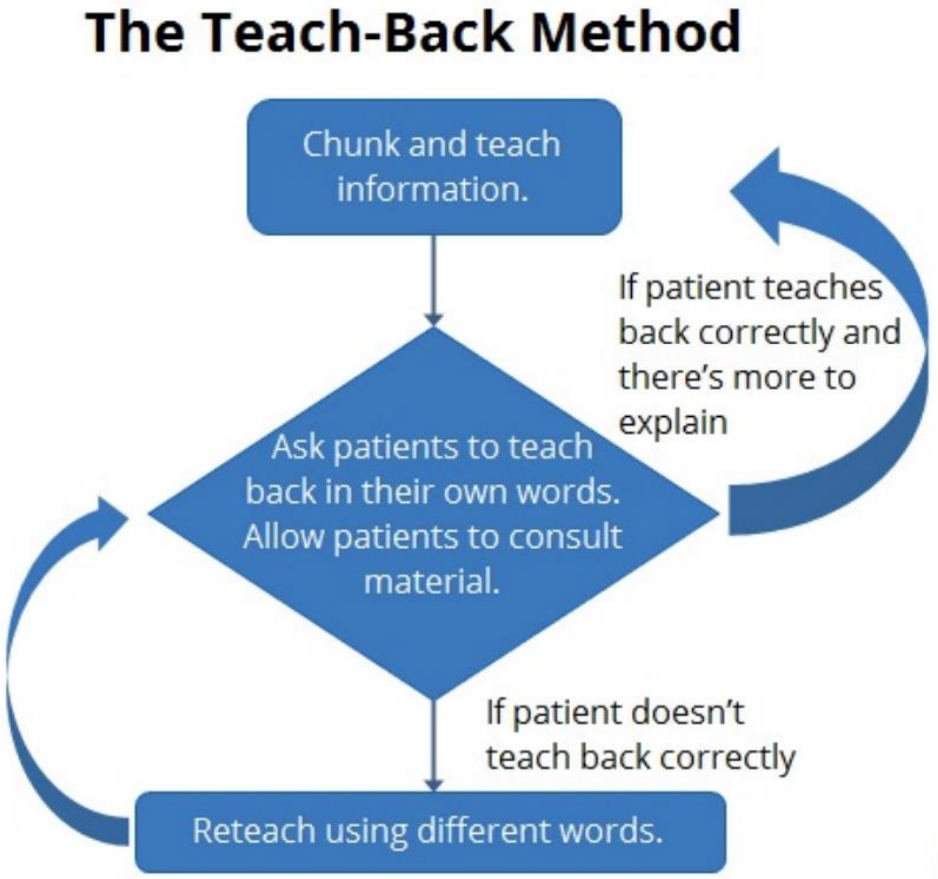
Money DM, Roy M, Scrivener J, Allen L, Brewer M et al. (2007). Canadian consensus guidelines on human papillomavirus. Journal of Obstetrics and Gynaecology Canada, 29(8), S1.

Teach-Back Method

Major challenge →

- Physicians over-estimate their capacity to communicate
- In HNC, they may have a priority list → survival, function, appearance
- Recall of information

Systematic Review → TBM effective in 19 of the 20 studies → learning-related outcomes (e.g. knowledge recall and retention) & objective HR outcomes (e.g. self-care abilities).



In Conclusion – Prehabilitation

Pre-treatment or treatment-concurrent

Targets function to reduce incidence and severity of current and future impairments

In general: Diet, exercise, psychosocial wellbeing

In HNC:

- Mental health
- Exercise (i.e., dysphagia/motion exercises/trismus/swallowing specific (neuromuscular plasticity)
- Alcohol, nicotine, and drug cessation

Health care cost

Loewen et al., 2021

Conclusion

- Mental health → Health disparities and inequalities in HNC
- Screening for distress → routine clinical intake in HNC clinics
- Develop prehabilitation protocols
- Implement collaborative models of care
- Train staff in crisis evaluation & doctor-patient communication
- Keep in mind the MH and PSO diathesis in treatment-response and survival

Thank you!

FLUX Exhibition, International Museum of Surgical Science (IMSS) in Chicago

Presenter

Dr. Denis Soulieres **MD, MSc, FRCPC**

- Hematologist and Medical Oncologist, Centre Hospitalier de l'Université de Montréal
- Clinical researcher
- Molecular Biologist

HPV and HNSCC in Canada. Stats. Facts. Future

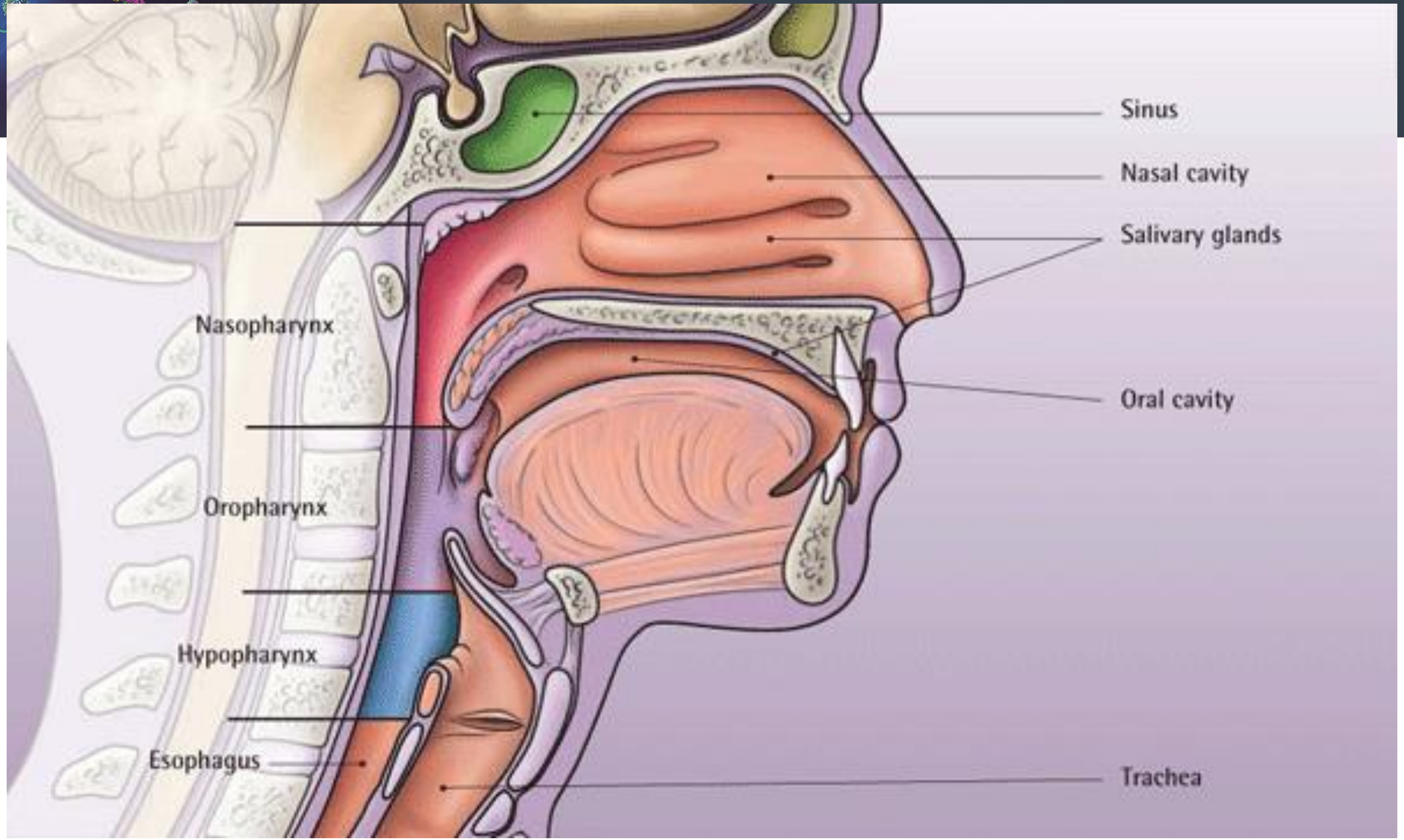
Denis Soulières, MD, MSc, FRCPC

Hematologist and Medical Oncologist

Centre Hospitalier de l'Université de Montréal

Conflicts of interest

- No direct financial interest in Pharma
- Advisor nationally and internationally
  - MSD, Pfizer, Novartis, Ipsen, Eisai, Adlai-Nortye
- Research grants to institution and not to self
  - MSD, Pfizer, Novartis, Adlay-Nortye


Sinus
Nasal cavity
Salivary glands
Nasopharynx
Oral cavity
Oropharynx
Hypopharynx
Esophagus
Trachea

Epidemiology of H&N Cancer in Canada

- Histology of H&N Cancer:
  - 80-85% Squamous Cell Carcinoma
- Site of primary:
  - 60-70%: oropharynx
- HPV prevalence:
  - Oropharynx: 80-90%
  - Other sites: 20-30%

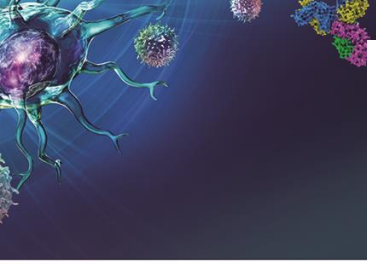


TABLE 1 Relative rankings for selected cancers with respect to incidence, survival, as well as five- and 25-year prevalenc
Canada (excluding Quebec*), selected time frames†

Rank	Incidence (2018)	5-year observed survival (2015–2017)	5-year prevalence (2018)	25-year prevalence (2018)
	Both sexes	Both sexes	Both sexes	Both sexes
1	Breast	Testis	Breast	Breast
2	Lung and bronchus	Thyroid	Prostate	Prostate
3	Prostate	Hodgkin lymphoma	Colorectal	Colorectal
4	Colorectal	Breast	Bladder	Melanoma
5	Bladder	Prostate	Lung and bronchus	Thyroid
6	Non-Hodgkin lymphoma	Melanoma	Melanoma	Bladder
7	Melanoma	Uterus (body, NOS)	Non-Hodgkin lymphoma	Non-Hodgkin lymphoma
8	Uterus (body, NOS)	Cervix	Thyroid	Uterus (body, NOS)
9	Kidney and renal pelvis	Kidney and renal pelvis	Uterus (body, NOS)	Lung and bronchus
10	Thyroid	Bladder	Kidney and renal pelvis	Kidney and renal pelvis
11	Head and neck	Non-Hodgkin lymphoma	Head and neck	Head and neck
12	Leukemia	Head and neck	Leukemia	Leukemia
13	Pancreas	Colorectal	Multiple myeloma	Cervix
14	Stomach	Leukemia	Ovary	Testis
15	Multiple myeloma	Multiple myeloma	Stomach	Ovary
16	Brain/CNS	Ovary	Cervix	Hodgkin lymphoma
17	Ovary	Stomach	Pancreas	Multiple myeloma
18	Liver	Brain/CNS	Testis	Stomach
19	Esophagus	Liver	Brain/CNS	Brain/CNS
20	Cervix	Lung and bronchus	Hodgkin lymphoma	Pancreas
21	Testis	Esophagus	Liver	Liver
22	Hodgkin lymphoma	Pancreas	Esophagus	Esophagus

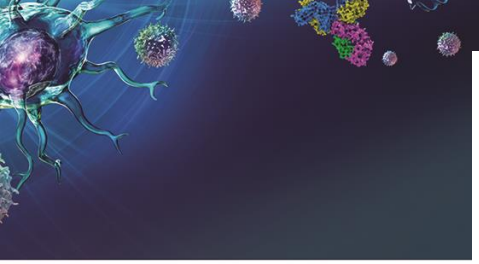


TABLE 2 Person-based prevalence for selected cancers by prevalence duration and sex, Canada,* January 1, 2018

	25-year prevalence (diagnosed since 1993)			5-year prevalence (diagnosed since 2013)			2-year prevalence (diagnosed since 2016)		
	Both sexes	Males	Females	Both sexes	Males	Females	Both sexes	Males	Females
All cancers†	**1,573,960**	**747,875**	**826,085**	**635,185**	**312,540**	**322,645**	**302,300**	**152,005**	**150,300**
Lung and bronchus	67,155	29,090	38,060	42,600	18,910	23,690	25,575	11,740	13,825
Breast	329,805	1,960	327,840	111,795	840	110,955	48,645	405	48,240
Colorectal	188,160	101,340	86,820	76,820	42,755	34,060	34,640	19,340	15,300
Prostate	301,820	301,820	—	96,590	96,590	—	43,740	43,735	—
Bladder	77,625	58,150	19,475	37,315	28,635	8,685	17,595	13,535	4,055
Non-Hodgkin lymphoma	77,180	41,125	36,060	32,915	18,070	14,845	15,320	8,455	6,865
Melanoma	93,895	46,475	47,420	34,715	18,435	16,275	15,555	8,470	7,085
Uterus (body, NOS)	74,900	—	74,900	27,820	—	27,820	12,690	—	12,685
Kidney and renal pelvis	54,295	33,245	21,050	23,035	14,840	8,195	10,590	6,885	3,705
Head and neck	47,700	33,560	14,135	20,350	14,720	5,625	9,875	7,185	2,690
Pancreas	7,500	3,865	3,635	5,375	2,890	2,480	3,845	2,080	1,765
Leukemia	47,055	27,300	19,760	19,310	11,500	7,805	8,590	5,155	3,435
Thyroid	83,915	18,575	65,345	28,925	7,280	21,645	11,160	2,925	8,235
Stomach	13,555	8,375	5,180	6,940	4,465	2,480	3,945	2,590	1,355
Multiple myeloma	15,030	8,475	6,555	9,570	5,495	4,075	4,960	2,865	2,095
Liver	6,825	5,115	1,705	4,265	3,260	1,000	2,485	1,955	530
Brain/CNS	13,385	7,175	6,210	5,075	2,840	2,230	2,875	1,610	1,260
Ovary	20,040	—	20,040	8,100	—	8,100	3,935	—	3,935
Esophagus	5,100	3,810	1,280	3,235	2,470	760	2,170	1,670	495
Cervix	22,235	—	22,235	5,695	—	5,695	2,630	—	2,635
Testis	20,090	20,090	—	5,135	5,135	—	2,135	2,130	—
Hodgkin lymphoma	16,180	8,730	7,455	4,260	2,365	1,890	1,820	1,010	805
All other cancers	104,940	51,260	53,680	49,310	24,670	24,635	25,570	12,940	12,630

FIGURE 1.4 Distribution of new cancer cases for selected cancers, by age group, Canada (excluding Quebec*), 2013–2017

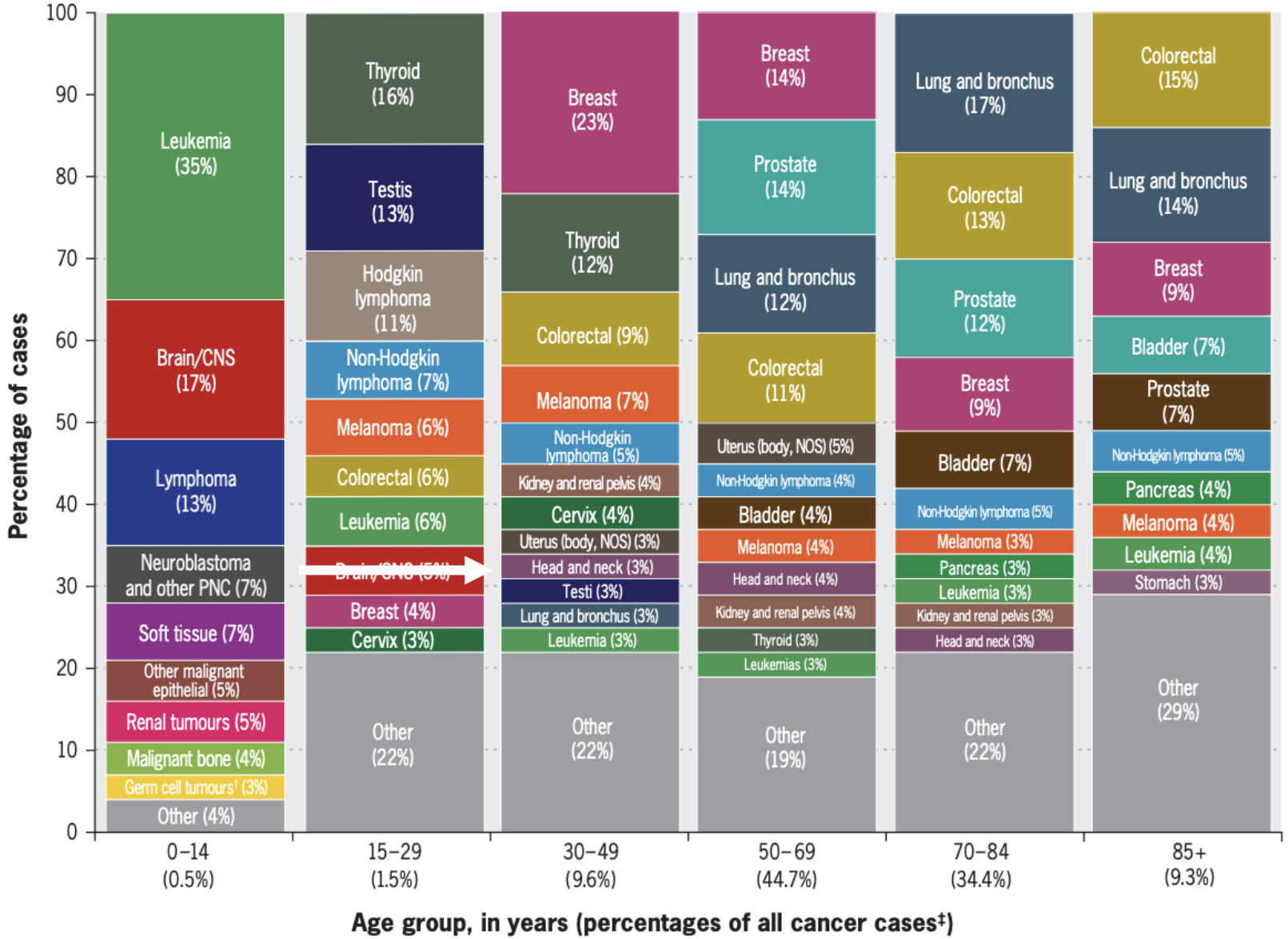
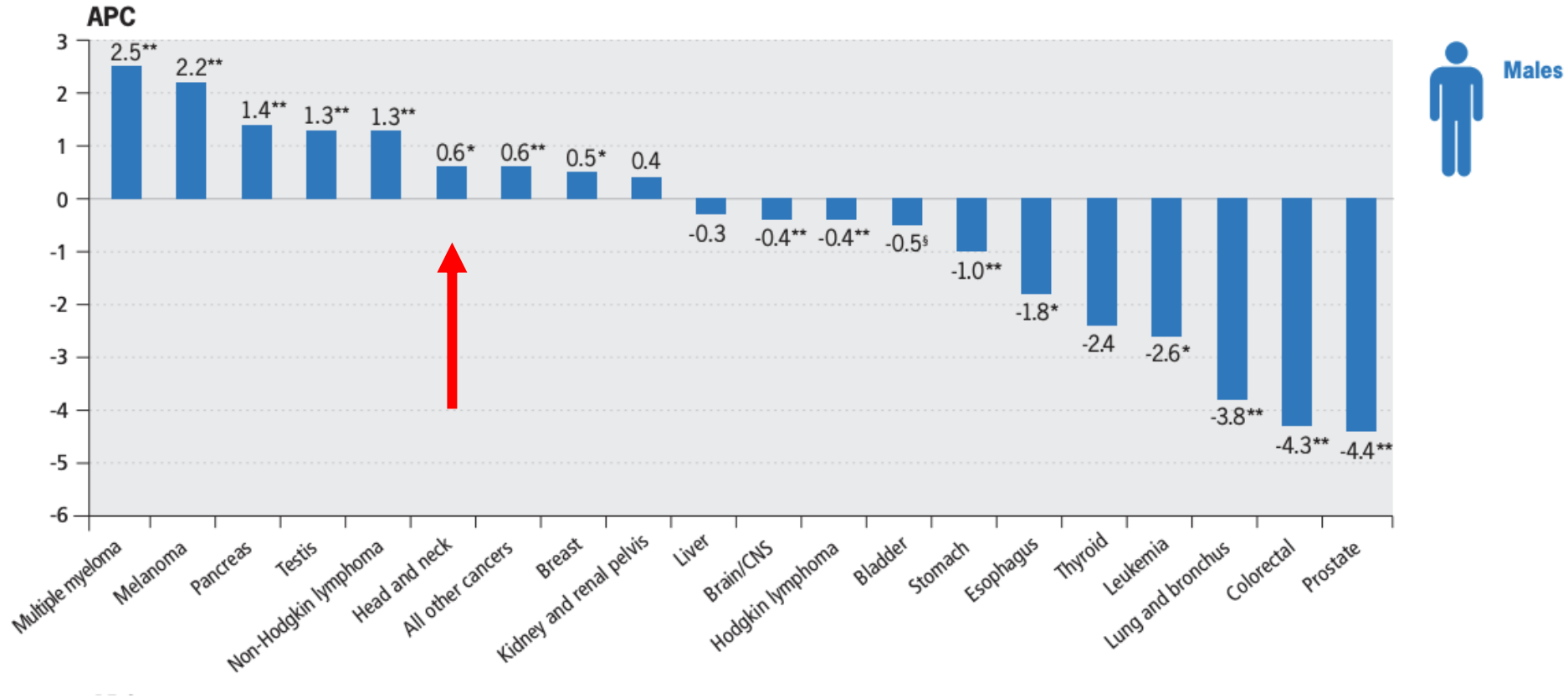
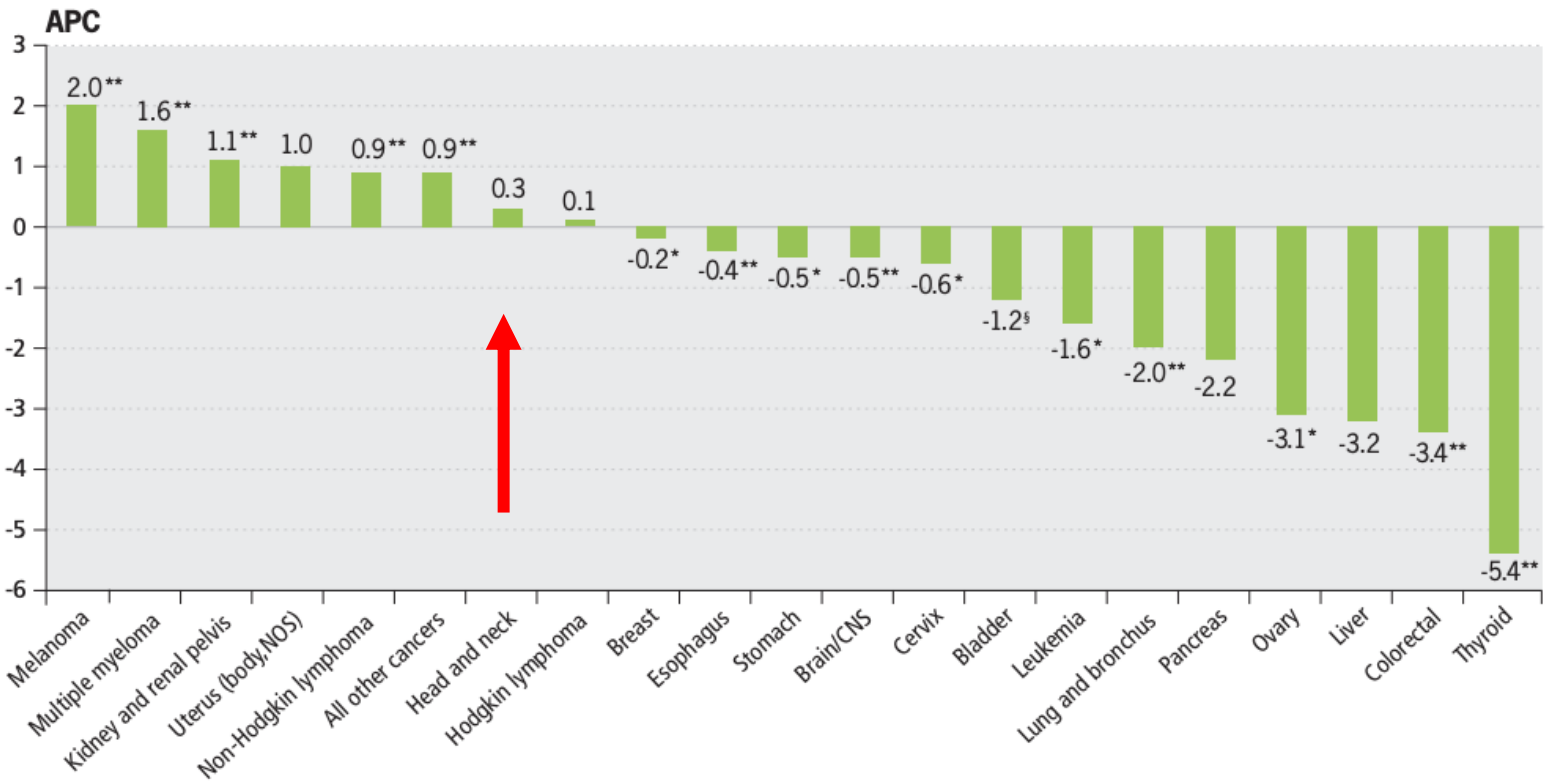


FIGURE 1.7 Most recent annual percent change (APC)† in age-standardized incidence rates (ASIR), by sex, Canada (excluding Quebec‡), 1984–2017




APC
3
2
1
0
-1
-2
-3
-4
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-6
2.0**
1.6**
1.1**
1.0
0.9**
0.9**
0.3
0.1
-0.2*
-0.4**
-0.5*
-0.5**
-0.6*
-1.2§
-1.6*
-2.0**
-2.2
-3.1*
-3.2
-3.4**
-5.4**
Melanoma
Multiple myeloma
Kidney and renal pelvis
Uterus (body,NOS)
Non-Hodgkin lymphoma
All other cancers
Head and neck
Hodgkin lymphoma
Breast
Esophagus
Stomach
Brain/CNS
Cervix
Bladder
Leukemia
Lung and bronchus
Pancreas
Ovary
Liver
Colorectal
Thyroid

Females

TABLE 1.1 Lifetime probability of developing cancer, Canada (excluding Quebec*), 2017

	Lifetime probability of developing cancer					
	%			One in:		
	Both sexes	Males	Females	Both sexes	Males	Females
All cancers†	**43.4**	**44.3**	**42.6**	**2.3**	**2.3**	**2.4**
Lung and bronchus	6.7	6.8	6.6	15	15	15
Breast	6.1	0.1	12.1	16	934	8
Colorectal	5.7	6.1	5.3	18	16	19
Prostate	—	11.9	—	—	8	—
Bladder	3.0	4.6	1.4	34	22	73
Non-Hodgkin lymphoma	2.5	2.7	2.2	40	37	45
Melanoma	2.2	2.4	1.9	46	41	51
Uterus (body, NOS)	—	—	3.2	—	—	31
Kidney and renal pelvis	1.5	2.0	1.1	65	51	92
Head and neck	2	2	0.9	66	46	114
Pancreas	1.5	1.5	1.4	68	67	69
Leukemia	1.5	1.8	1.3	65	55	80
Thyroid	1.2	0.6	1.7	85	158	58
Stomach	1.0	1.3	0.7	104	80	146
Multiple myeloma	0.9	1.0	0.8	111	95	131
Liver	0.6	0.9	0.3	159	109	299
Brain/CNS	1	1	0.6	155	137	178
Ovary	—	—	1.3	—	—	79
Esophagus	0.6	0.9	0.3	169	113	329
Cervix	—	—	0.6	—	—	161
Testis	—	0.4	—	—	237	—
Hodgkin lymphoma	0.2	0.3	0.2	448	392	525

TABLE 1.2 Projected new cases and age-standardized incidence rates (ASIR) for cancers, by sex, Canada,* 2021

	New cases (2021 estimates)			Cases per 100,000		
	Total†	Males	Females	Both sexes	Males	Females
All cancers‡	**229,200**	**118,200**	**110,900**	**515.2**	**556.3**	**484.9**
Lung and bronchus	29,600	14,800	14,800	59.5	62.0	57.9
Breast	28,000	260	27,700	66.5	1.2	126.8
Colorectal	24,800	13,700	11,100	54.9	64.1	46.6
Prostate	24,000	24,000	—	—	117.9	—
Bladder	12,500	9,500	3,000	25.0	41.4	11.3
Non-Hodgkin lymphoma	11,100	6,200	5,000	25.7	30.3	21.8
Melanoma	8,700	4,700	4,000	22.9	26.1	20.7
Uterus (body, NOS)	8,000	—	8,000	—	—	37.2
Kidney and renal pelvis	7,800	5,200	2,600	17.6	24.5	11.3
Head and neck	7,400	5,400	2,000	16.5	25.1	8.8
Pancreas	6,700	3,700	3,000	14.1	16.5	12.0
Leukemia	6,700	4,000	2,700	15.7	20.0	11.9
Thyroid	6,700	1,800	4,900	17.3	9.2	25.2
Stomach	4,000	2,600	1,400	8.7	12.3	5.7
Multiple myeloma	3,800	2,300	1,500	8.4	10.9	6.2
Liver	3,300	2,600	800	7.1	11.5	3.1
Brain/CNS	3,100	1,800	1,350	7.2	8.6	5.8
Ovary	3,000	—	3,000	—	—	13.5
Esophagus	2,400	1,900	560	5.6	9.2	2.4
Cervix	1,450	—	1,450	—	—	7.5
Testis	1,200	1,200	—	—	6.5	—
Hodgkin lymphoma	1,050	600	460	2.7	3.0	2.4
All other cancers	23,800	12,200	11,600	50.8	56.0	46.9

FIGURE 2.2 Percent distribution of projected cancer deaths, by sex, Canada, 2021

Males
44,600
Deaths

Lung and bronchus	24.2%
Colorectal	11.9%
Prostate	10.1%
Pancreas	6.5%
Bladder	4.3%
Leukemia	4.0%
Esophagus	3.9%
Non-Hodgkin lymphoma	3.7%
Head and neck	3.4%
Brain/CNS	3.1%
Liver*	2.9%
Kidney and renal pelvis	2.8%
Stomach	2.8%
Multiple myeloma	2.1%
Melanoma	1.8%
Thyroid	0.2%
Hodgkin lymphoma	0.1%
Breast	0.1%
Testis	0.1%
All other cancers	12.1%

Females
40,000
Deaths

Lung and bronchus	25.8%
Breast	13.5%
Colorectal	10.8%
Pancreas	6.8%
Ovary	4.9%
Uterus (body, NOS)	3.5%
Leukemia	3.3%
Non-Hodgkin lymphoma	3.1%
Brain/CNS	2.6%
Stomach	1.9%
Bladder	1.8%
Multiple myeloma	1.7%
Kidney and renal pelvis	1.7%
Head and neck	1.4%
Esophagus	1.3%
Melanoma	1.1%
Cervix	1.0%
Liver*	0.8%
Thyroid	0.3%
Hodgkin lymphoma	0.1%
All other cancers	12.8%

Summary of cancer statistics from *Canadian Cancer Statistics 2017*

TABLE A1 Incidence, mortality and survival statistics for selected cancers, both sexes combined, Canada

	Projected incidence			Projected mortality			5-year net survival
Both sexes combined	**Rank**	**Cases**	**ASIR***	**Rank**	**Deaths**	**ASMR***	**%**
All cancers	**—**	**206,200**	**515.9**	**—**	**80,800**	**198.1**	**60**
Lung and bronchus	1	28,600	69.9	1	21,100	51.4	17
Colorectal	2	26,800	66.3	2	9,400	23.1	64
Breast	3	26,500	68.1	3	5,000	12.6	87
Prostate	4	21,300	110.4	5	4,100	23.8	95
Bladder	5	8,900	21.8	8	2,400	5.7	73
Non-Hodgkin lymphoma	6	8,300	20.8	7	2,700	6.7	66
Uterus (body, NOS)	7	7,300	35.7	18	1,150	5.3	84
Melanoma	8	7,200	18.5	15	1,250	3.1	88
Thyroid	9	7,100	19.0	21	220	0.5	98
Kidney and renal pelvis	10	6,600	16.5	12	1,900	4.6	67
Leukemia	11	6,200	15.5	6	2,900	7.2	58
Pancreas	12	5,500	13.5	4	4,800	11.9	8
Oral	13	4,700	11.9	16	1,250	3.1	63
Stomach	14	3,500	8.6	11	2,100	5.1	25
Brain/CNS	15	3,000	7.8	9	2,400	6.0	24
Multiple myeloma	16	2,900	7.1	14	1,450	3.5	42
Ovary	17	2,800	13.7	13	1,800	8.2	44
Liver	18	2,500	6.1	17	1,200	3.0	19
Esophagus	19	2,300	5.7	10	2,200	5.3	14
Cervix	20	1,550	8.3	20	400	2.0	73
Larynx	21	1,150	2.8	19	440	1.1	63
Testis	22	1,100	6.1	23	45	0.2	96
Hodgkin lymphoma	23	990	2.7	7	140	0.4	85
All other cancers	—	19,500	48.5	—	10,400	25.5	—

Source: *Canadian Cancer Statistics 2017*

ASIR=age-standardized incidence rate
ASMR=age-standardized mortality rate
CNS=central nervous system
NOS=not otherwise specified

* Rates are age-standardized to the 2011 Canadian population and are per 100,000 males and females

— Not applicable

Transmission of oral HPV

- Transmission modes:
  - Linked to sexual habit
  - Feto-maternelle

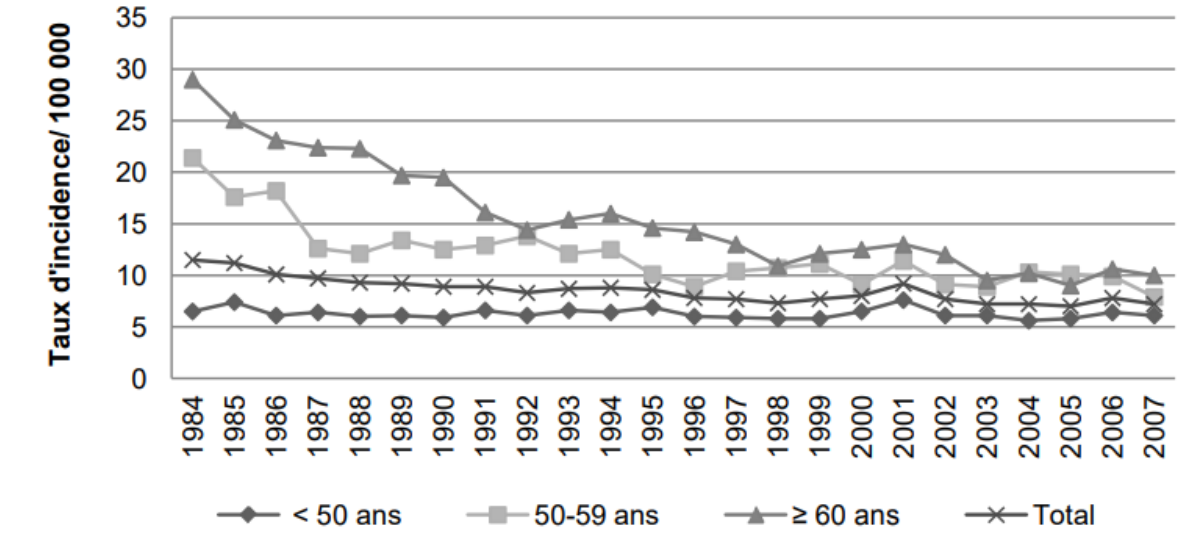
- Epidemic of oropharynx cancer
  - North America: 75-90% of OPC
    - Increase over 20 years
  - Western Europe: 25to 40% of OPC
    - Increase in the last 10 years

Tableau 4 Prévalence globale du VPH et prévalence spécifique des principaux génotypes à haut risque, par siège de cancer en Amérique du Nord

		Prévalence globale, %	Prévalence spécifique,%				
			VPH 16	VPH 18	VPH 31	VPH 33	VPH 45
Siège du cancer	**Référence**						
Col utérin	Li *et al.*, 2011[2]	~100	60	19	4	4	5
Vulve	De Vuyst *et al.*, 2009[5]	66	52	4	1	8	2
Vagin	De Vuyst *et al.*, 2009[5]	70	60	10	0	0	0
Anus*	De Vuyst *et al.*, 2009[5]	83	71	7	3	4	0
Pénis*	Backes *et al.*,2009[4]	49	45	2	2	1	1
Oropharynx£	Mehanna *et al.*, 2012[109]	70	-	-	-	-	-
Oropharynx*	Kreimer *et al.*, 2005[6]	47	42	1	0	2	0
Cavité orale*	Kreimer *et al.*, 2005[6]	16	10	3	0	1	0
Larynx*	Kreimer *et al.*, 2005[6]	14	10	3	2	0	0

* Pour ces sièges de cancer, seuls les carcinomes épidermoïdes ont été retenus dans les méta-analyses spécifiques. Pour les cancers de la vulve et du vagin, tous les carcinomes ont été retenus (la grande majorité des cas étaient des épidermoïdes).

£ Dans la plus récente méta-analyse, seule la prévalence globale du VPH dans le cancer de l'oropharynx a été rapportée. Aucune information sur la prévalence spécifique des génotypes à haut risque oncogène n'est présentée.



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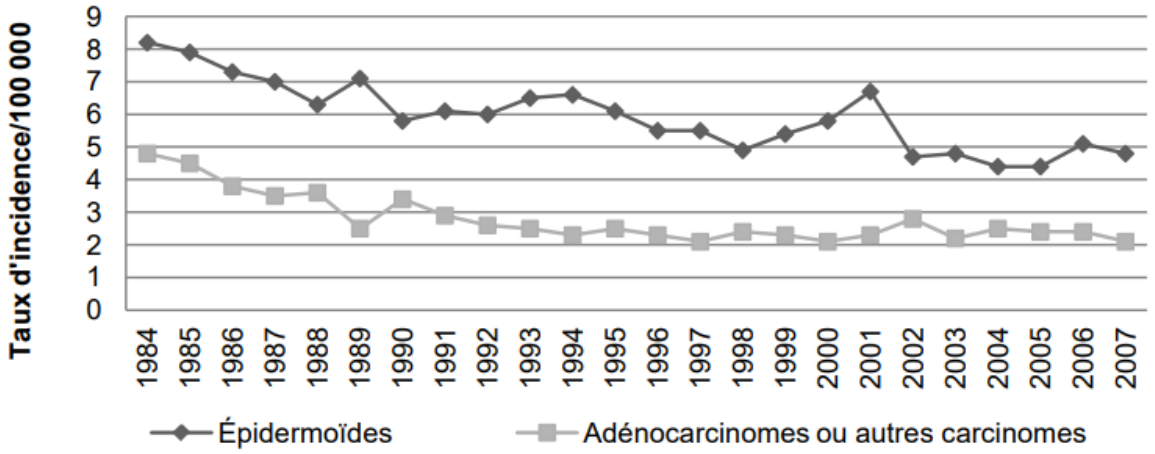


Figure 3 **Évolution dans le temps des taux standardisés d'incidence du cancer du col utérin selon (a) le groupe d'âge et (b) la morphologie, Québec, 1984-2007**

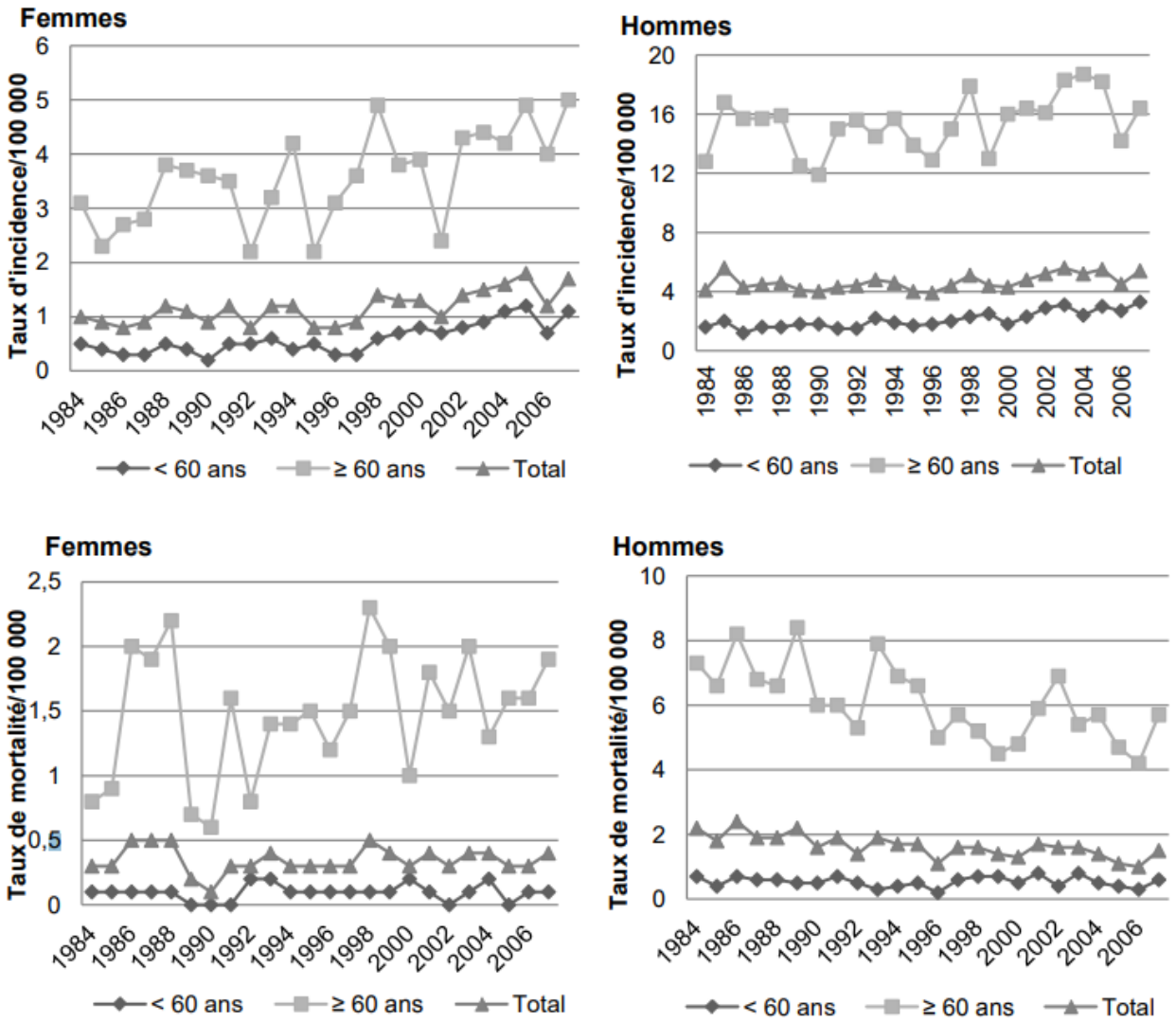


Figure 10 **Évolution dans le temps des taux standardisés d'incidence (morphologie épidermoïde) et de mortalité (toutes morphologies) par cancer de l'oropharynx, Québec, 1984-2007**

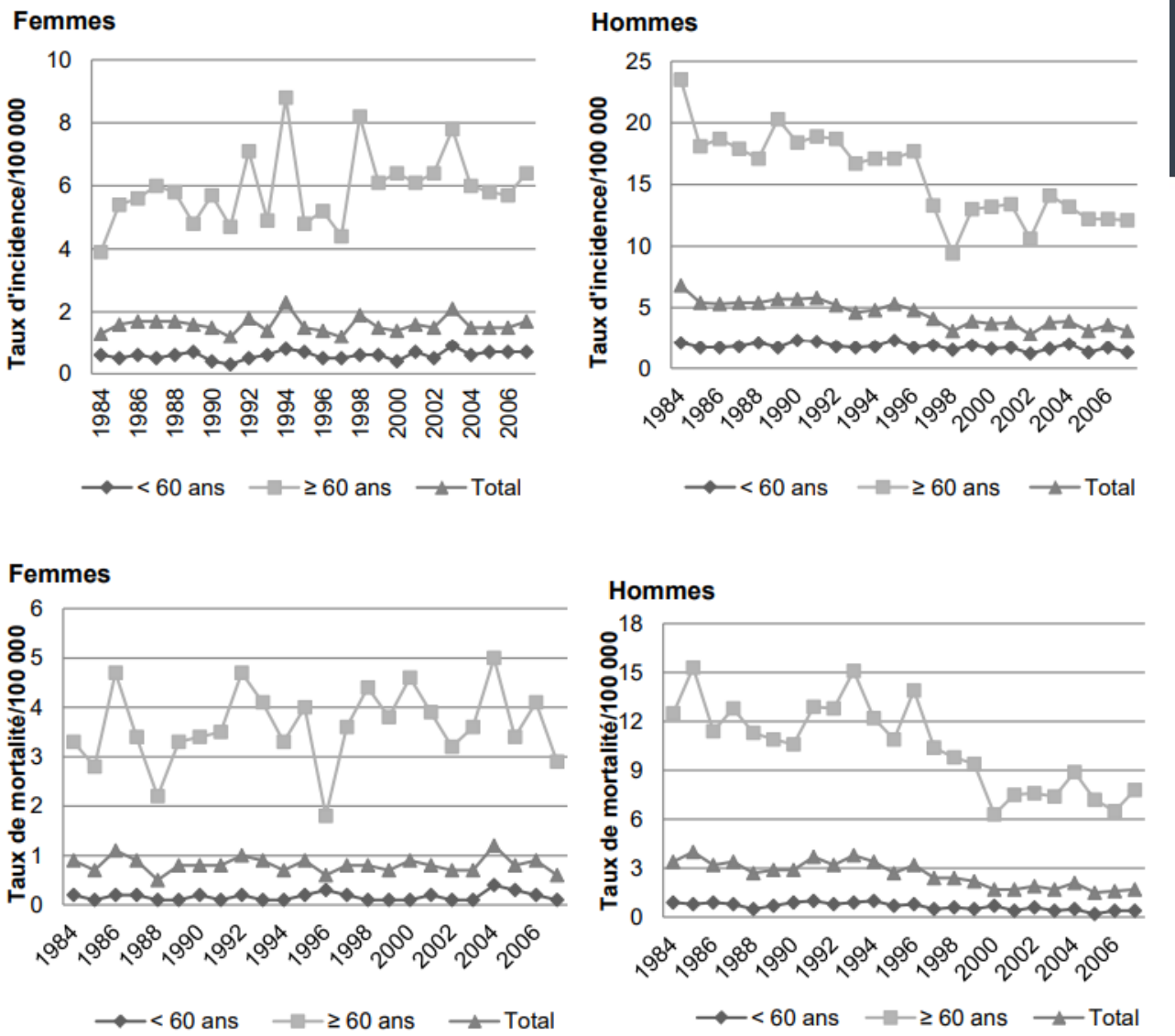


Figure 12 **Évolution dans le temps des taux standardisés d'incidence (morphologie épidermoïde) et de mortalité (toutes morphologies) par cancer de la cavité orale, Québec, 1984-2007**

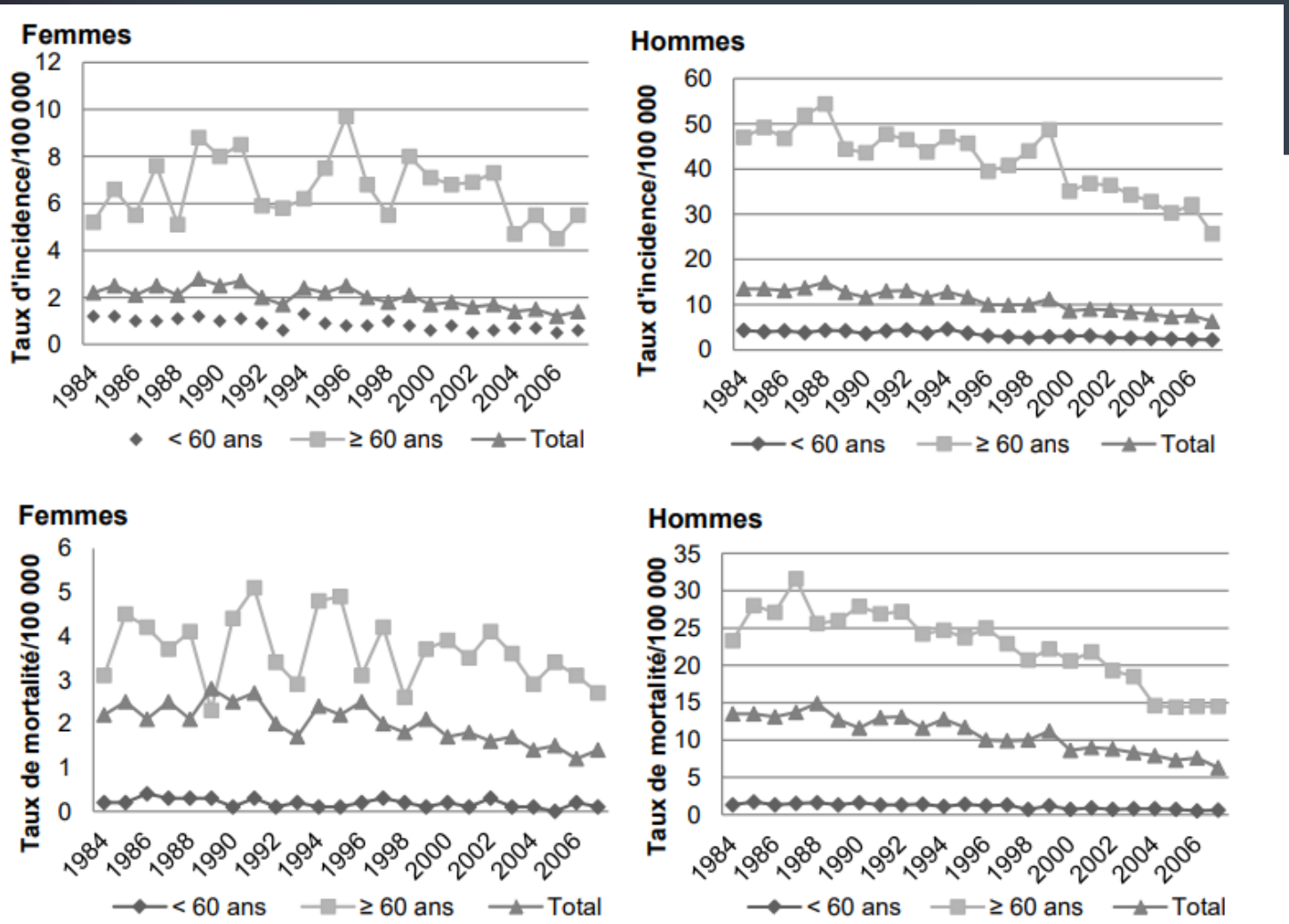


Figure 14 **Évolution dans le temps des taux standardisés d'incidence (morphologie épidermoïde) et de mortalité par cancer du larynx, Québec, 1984-2007**

Tableau 2 : Incidence du cancer de l'oropharynx lié au virus du papillome humain au Canada chez les hommes

Année	Nombre de cas par 100 000	
	Canada	États-Unis
1997	4,1	s.o.
2012	6,4	s.o.
2013–2017	s.o.	8,7
2017	s.o.	8,9

Abréviation : s.o., sans objet

Statistiques Canada

Table 5. Joint effect of smoking and HPV infection on the risk of OPCs, HeNCe Life study, Canadian site

	HPV negative		LR-HPV		HPV 18, 31, 33, 35, 39, 51		HPV 16		Combined effects			
Smoking pack-years	n_{ca}	n_{co}	n_{ca}	n_{co}	n_{ca}	n_{co}	n_{ca}	n_{co}	HPV negative OR (95% CI)	LR-HPV OR (95% CI)	HPV 18, 31, 33, 35, 39, 51 OR (95% CI)	HPV 16 OR (95% CI)
Assuming independance												
Non-to moderate smokers (≤37 pack-years)	44	283	6	25	11	9	61	6	1.00 (referent)	1.86 (0.91–3.82)	4.82 (2.16–10.73)	52.77 (25.47–109.33)
Heavy smokers (>37 pack-years)	25	85	7	9	4	6	30	4	1.48 (0.91–2.42)	2.76 (1.15–6.59)	7.14 (2.73–18.70)	78.24 (31.98–191.41)
Assuming joint effects[a]												
Non- to moderate smokers (≤37 pack-years)	44	283	6	25	11	9	61	6	1.00 (referent)	1.44 (0.55–3.78)	7.21 (2.71–19.17)	70.39 (28.12–176.17)
Heavy smokers (>37 pack-years)	25	85	7	9	4	6	30	4	1.71 (0.95–3.05)	4.50 (1.50–13.49)	3.69 (0.94–14.48)	48.76 (15.83–150.17)

$P_{interaction} = 0.228$

Both models adjusted for age, sex, education years (continuous) and ethanol (L) (none to moderate vs. heavy).

n_{ca}, number of cases; n_{co}, number of controls.

[a]Entering cross-product terms for smoking pack-years (none to moderate vs. heavy) and HPV variable.

Table 6. Joint effect of alcohol drinking and HPV infection on the risk of OPCs, HeNCe Life study, Canadian site

	HPV negative		LR-HPV		HPV 18, 31, 33, 35, 39, 51		HPV 16		Combined effects			
Ethanol (L)[a]	n_{ca}	n_{co}	n_{ca}	n_{co}	n_{ca}	n_{co}	n_{ca}	n_{co}	HPV negative OR (95% CI)	LR-HPV OR (95% CI)	HPV 18, 31, 33, 35, 39, 51 OR (95% CI)	HPV 16 OR (95% CI)
Non- to moderate drinkers (≤369 L)	42	286	7	17	8	11	66	6	1.00	1.86 (0.91–3.82)	4.82 (2.16–10.73)	52.77 (25.47–109.33)
Heavy drinkers (>369 L)	27	82	6	17	7	4	25	4	1.95 (1.17–3.25)	3.62 (1.56–8.40)	9.39 (3.59–24.55)	102.80 (39.73–265.98)
Non- to moderate drinkers (≤369 L)	42	286	7	17	8	11	66	6	1.00	3.37 (1.28–8.92)	4.86 (1.76–13.40)	85.14 (33.63–215.59)
Heavy drinkers (>369 L)	27	82	6	17	7	4	25	4	2.73 (1.48–5.05)	2.73 (0.97–7.69)	13.47 (3.56–50.95)	50.60 (15.96–160.40)

Both models adjusted for age, sex, education years (continuous) and smoking pack-years (none to moderate vs. heavy).

n_{ca}, number of cases; n_{co}, number of controls.

[a]Entering a joint effect term for ethanol (none to moderate vs. heavy) and HPV variable.

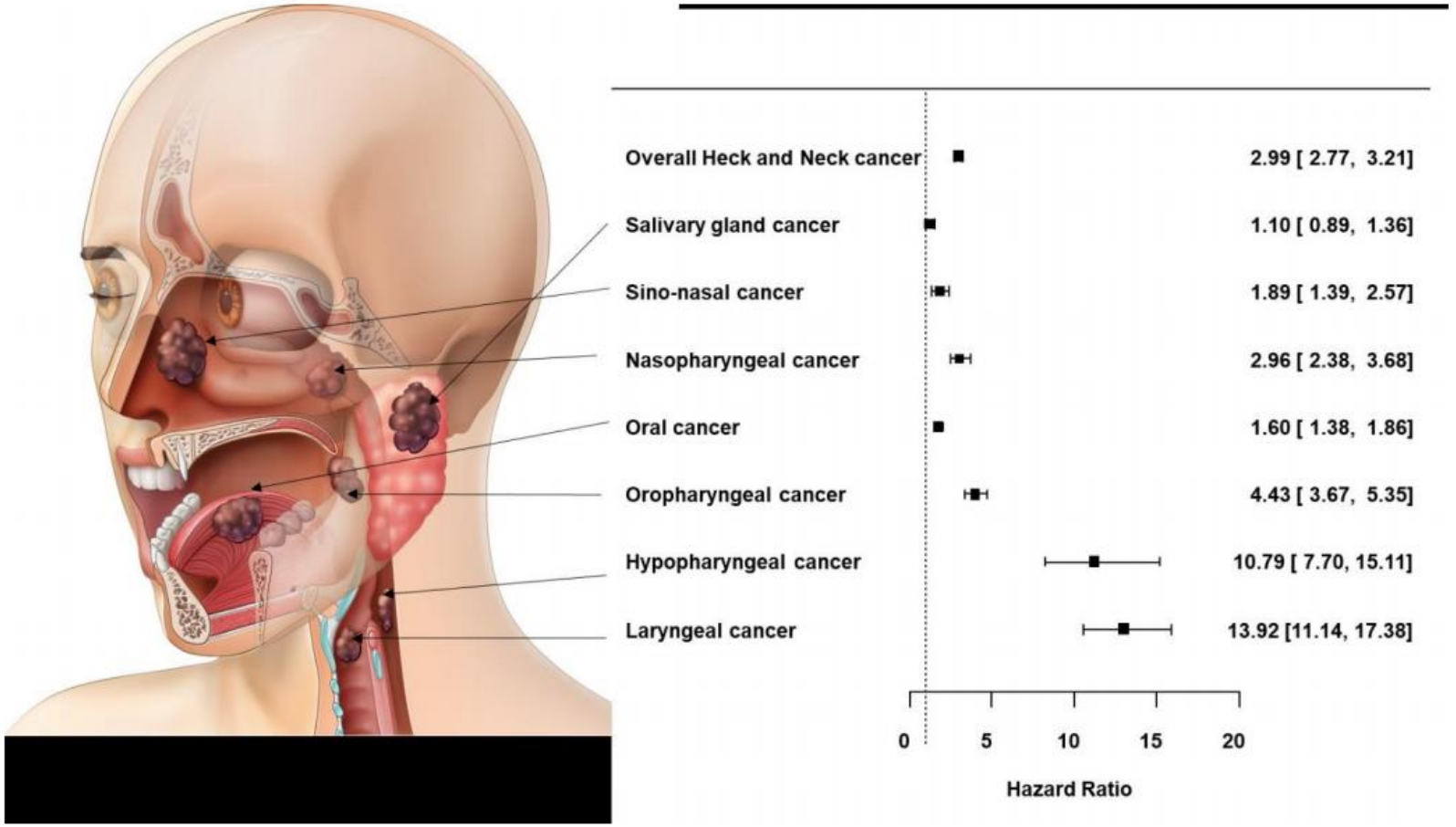
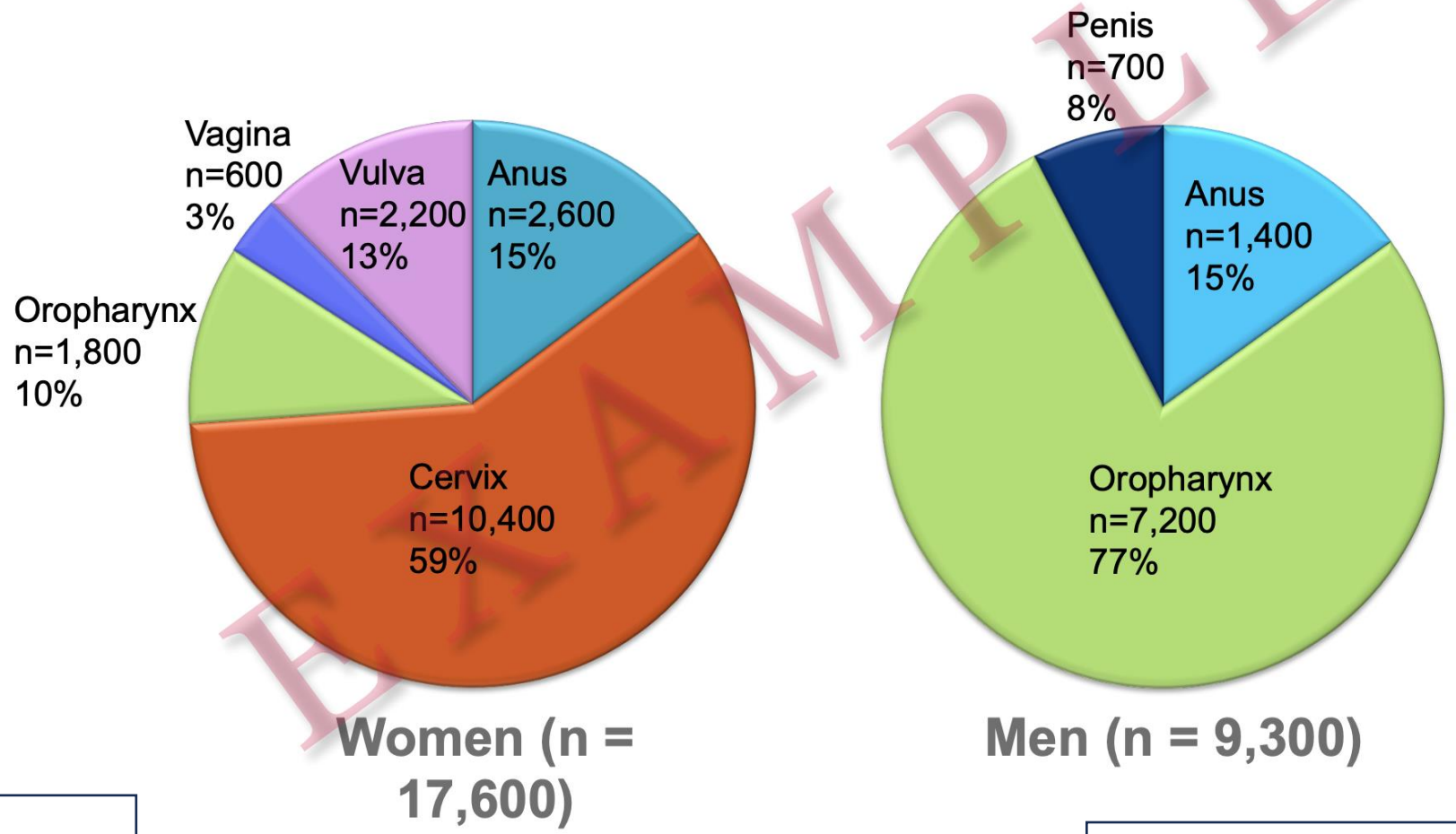


Figure 4. Forest plot of the hazard ratios for all subsites of head-and-neck cancers in males compared to females (never-smokers and never-drinkers only). A multivariate Cox's proportional hazard model adjusted for age, body mass index, low income, regular exercise, and diabetes mellitus and hypertension status, was employed.

Cancers 2022

Average number of new cancers probably caused by HPV, by sex, United States 2006-2010

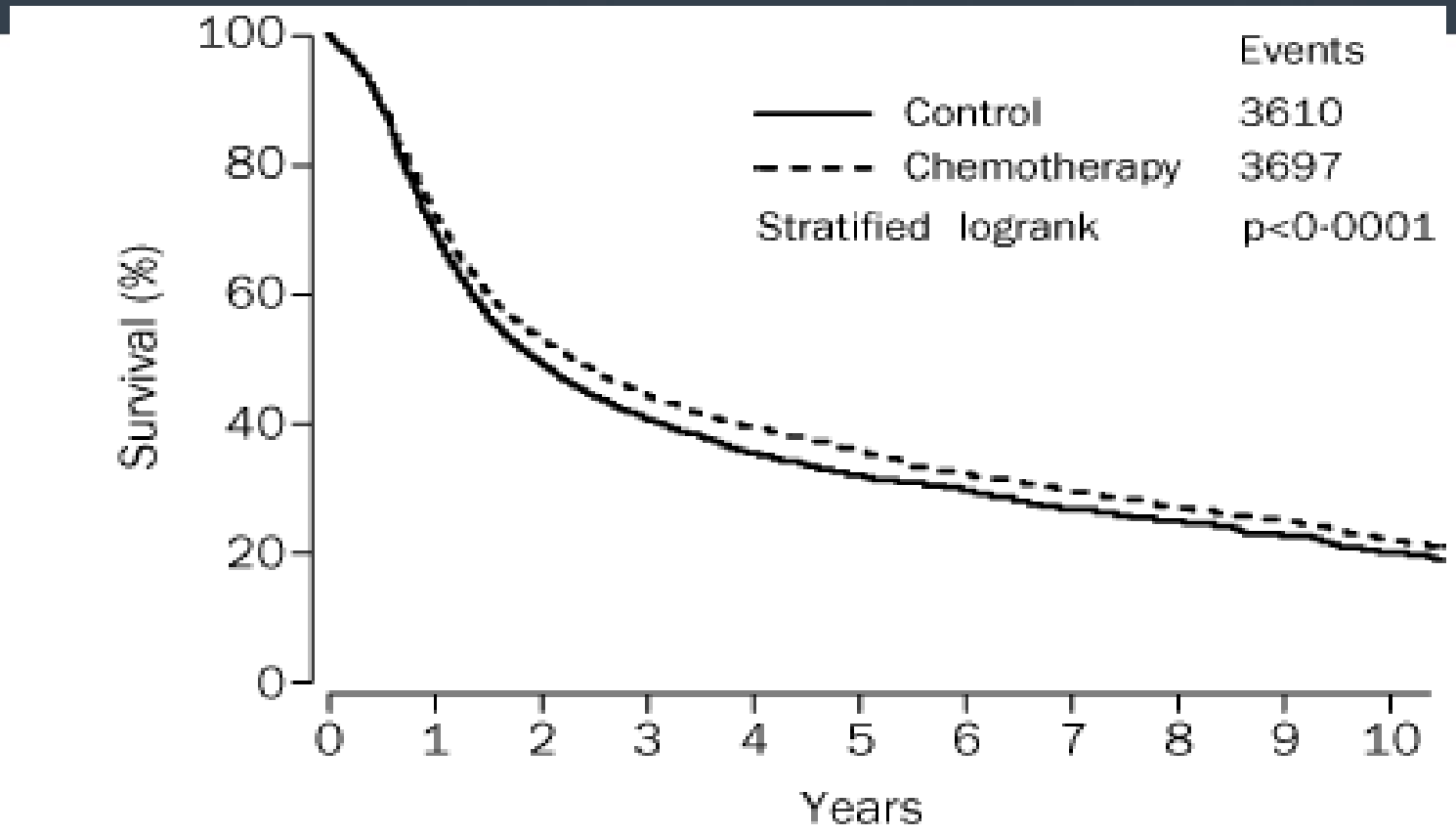


CDC, United States Cancer Statistics (USCS), 2006-2010

META-ANALYSE CIMIOTHÉRAPIE
Cancer ORL, *Pignon*

- Randomised phase III trials between 1965 and 1993
- Initial therapy for non metastatic H&N (excluding NP)
- 26 studies included
- Some chemotherapy used without single agent proof of activity

Pignon et al.



Number of patients

Control	5272	3530	2403	1793	1345	1005	740	553	412	308	23
Chemotherapy	5578	3913	2706	2106	1634	1218	881	649	470	367	27

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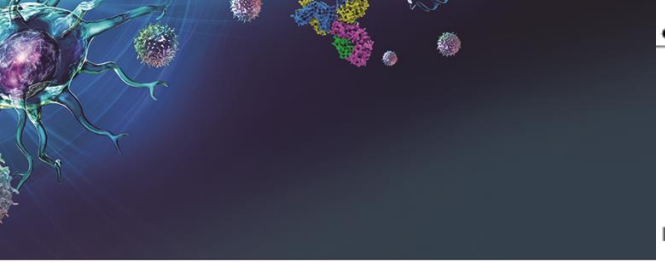
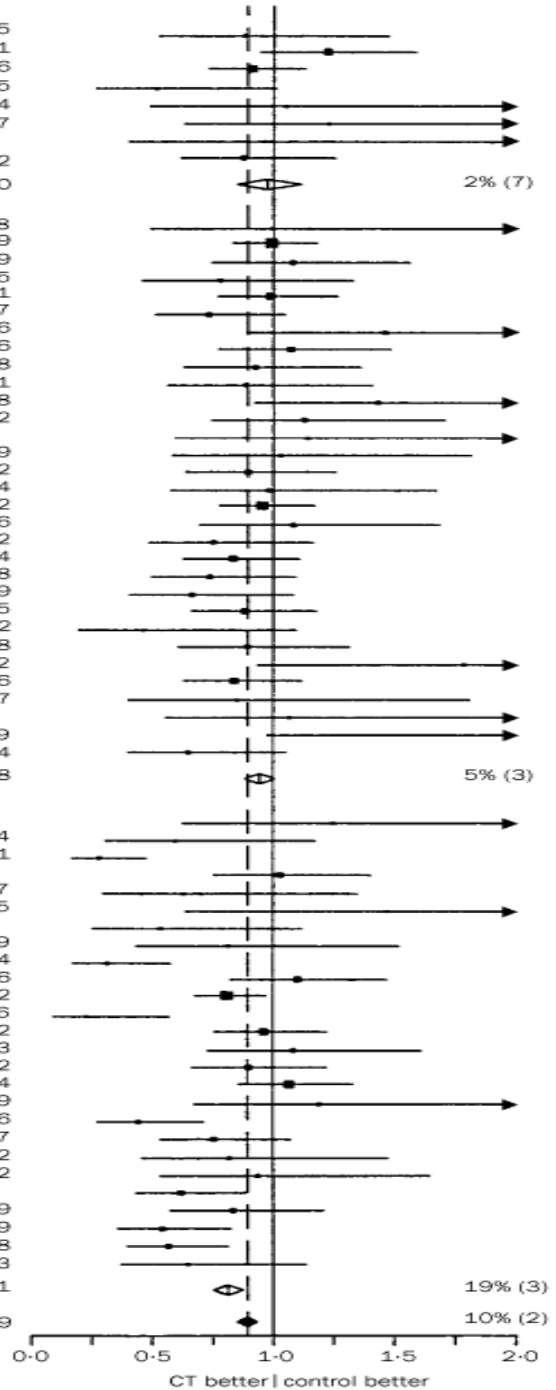


Category/trial	Events/patients CT	Control	O–E	Variance	Hazard ratio (CT:control)	Risk reduction (SD)
(a) Adjuvant						
Pitié–74	31/48	31/48	−1·8	14·5		
GETTECadj	120/143	110/143	11·8	57·1		
Int 0034	161/251	163/248	−7·4	80·6		
JHCFUS	12/96	22/95	−5·6	8·5		
TMH R–4	13/65	13/70	0·4	6·4		
KKD–86	18/56	17/56	1·8	8·7		
HNU–87a	10/58	10/53	−0·2	5		
HNU–87b	58/213	63/211	−3·9	30·2		
Subtotal (a)	423/930	429/924	−4·8	211·0		2% (7)
(b) Neoadjuvant						
IGR–65	20/20	16/16	0	7·8		
RTOG 6801	248/340	258/340	−0·8	125·9		
EORTC 24771	53/108	60/123	2·2	27·9		
DENVER–77	29/31	28/28	−3·3	13·5		
HNCP	179/302	98/160	−0·6	63·1		
EORTC 78–OCP	55/113	65/112	−9·2	29·7		
MCW–1	38/43	29/40	6·3	16·6		
SWOG 8006	75/87	73/80	2·6	36·6		
Pitié–81	53/56	51/56	−2	25·8		
Buenos Aires	55/82	29/38	−2·1	18·1		
Créteil–82	44/58	37/64	7·2	19·8		
HNCGICO2	44/48	46/52	2·7	22·2		
MCW–2	16/30	22/33	1·2	9		
AC CAMARGO	25/30	24/30	0·4	11·9		
SECOG II	68/84	66/79	−3·6	33·2		
EORTC 24844	32/74	24/65	−0·3	13·4		
SHNG 85	186/233	184/228	−4·2	92·2		
HNCGICO3	41/55	38/53	1·6	19·6		
Créteil–86	37/79	44/77	−5·7	20·2		
GSTTC–86	91/118	100/119	−8·5	47·4		
GETTECneo1	46/86	55/88	−7·5	24·8		
GETTECneo2	27/71	37/73	−6·5	15·9		
AHNTG	92/140	95/140	−5·7	46·5		
Las Palmas	11/19	12/17	−4	5·2		
Rennes–87	50/66	54/67	−2·9	25·8		
Parma	24/38	13/31	5·4	9·2		
CFHNS	90/161	97/163	−8·1	46·6		
Cologne	13/50	14/47	−1·1	6·7		
Songkla	21/30	16/24	0·6	9		
HNAP–02	15/25	9/25	4·6	5·9		
BNH 003	31/63	36/61	−7·1	16·4		
Subtotal (b)	1809/2740	1730/2529	−48·4	865·8		5% (3)
(c) Concomitant						
MDA–70	24/24	12/12	1·8	8		
WIA–OC5a	22/25	19/25	−4·3	8·4		
WIA–OC5b	27/38	40/41	−17·9	14·1		
EORTC 73–OC	89/107	76/92	1·2	40		
Bergen	15/16	14/16	−3·1	6·7		
RT–BLM–73	13/23	9/23	2·1	5·5		
WIA–OC5c	15/21	16/19	−4·4	7		
Turku	20/23	20/23	−2	9·9		
UW–77	30/30	28/28	−12	10·4		
NRH–78	94/111	90/111	4·5	45·6		
Barcelona	248/297	245/276	−25·3	121·2		
UW–79	13/13	14/14	−6·8	4·6		
Manchester	136/156	130/157	−2·4	66·2		
Yale 80	51/59	47/61	2	24·3		
PMHCGS	83/106	84/106	−4·3	41·2		
ECOG 2382	162/186	157/185	5·4	79·4		
AC CAMARGO	25/30	24/30	2·1	11·9		
Toulouse	32/45	42/45	−13·5	16·6		
SECOG II	63/76	66/79	−8·7	31·7		
CH–7401	21/30	24/32	−2·2	11·2		
Yale 86	23/39	26/44	−0·8	12·2		
INRC HN–8	59/80	67/77	−14·3	30		
Ontario	56/88	58/87	−5·1	28·9		
Kragujevac	72/106	43/53	−13·3	21·9		
Bavaria 89	49/147	72/151	−16·8	29·8		
LOHNG 91	23/32	28/32	−5·3	12·3		
Subtotal (c)	1465/1908	1451/1819	−143·3	698·1		19% (3)
Total (a, b, c)	3697/5578	3610/5272	−196·6	1774·9		10% (2)



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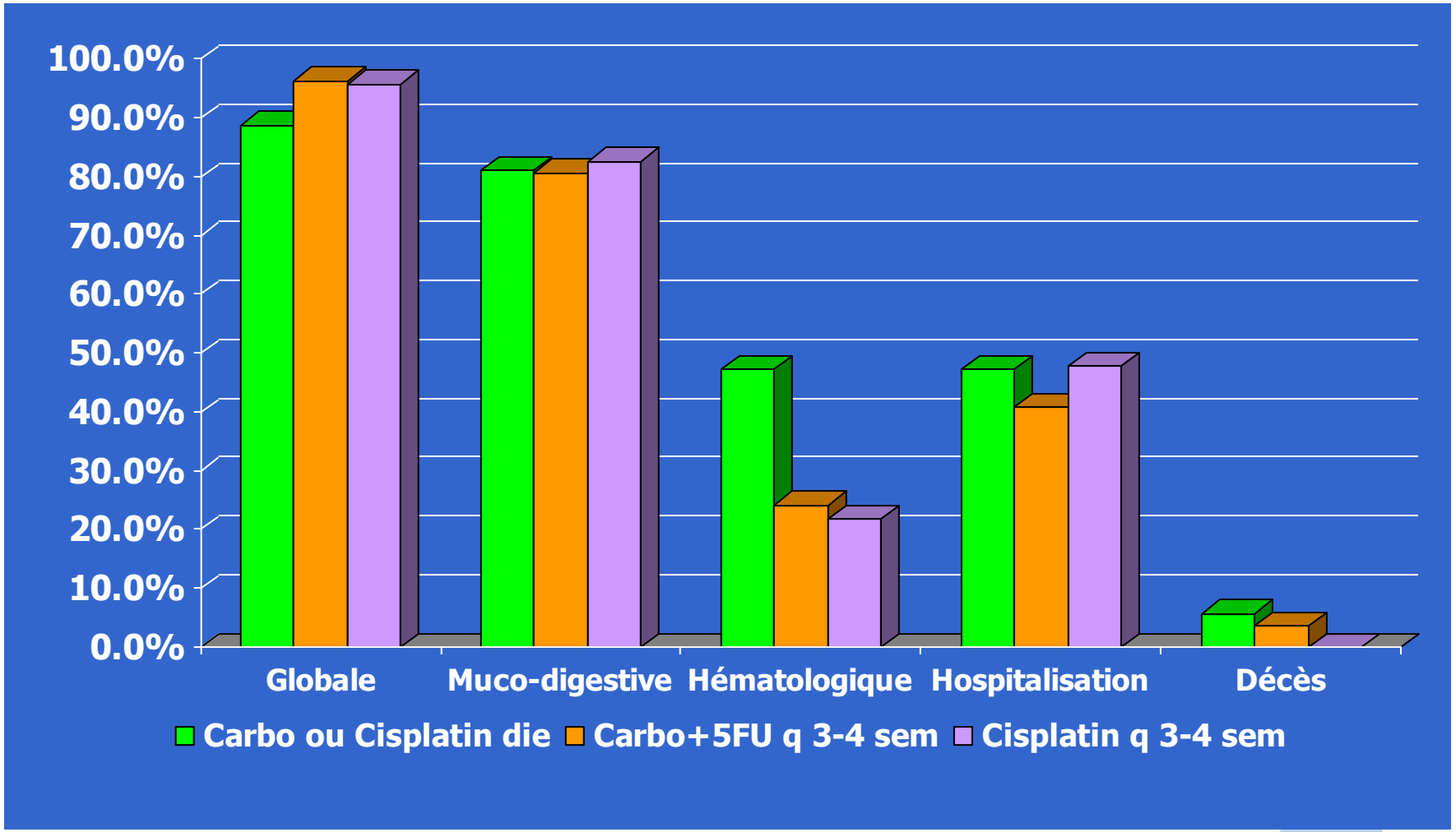
Acute toxicities:



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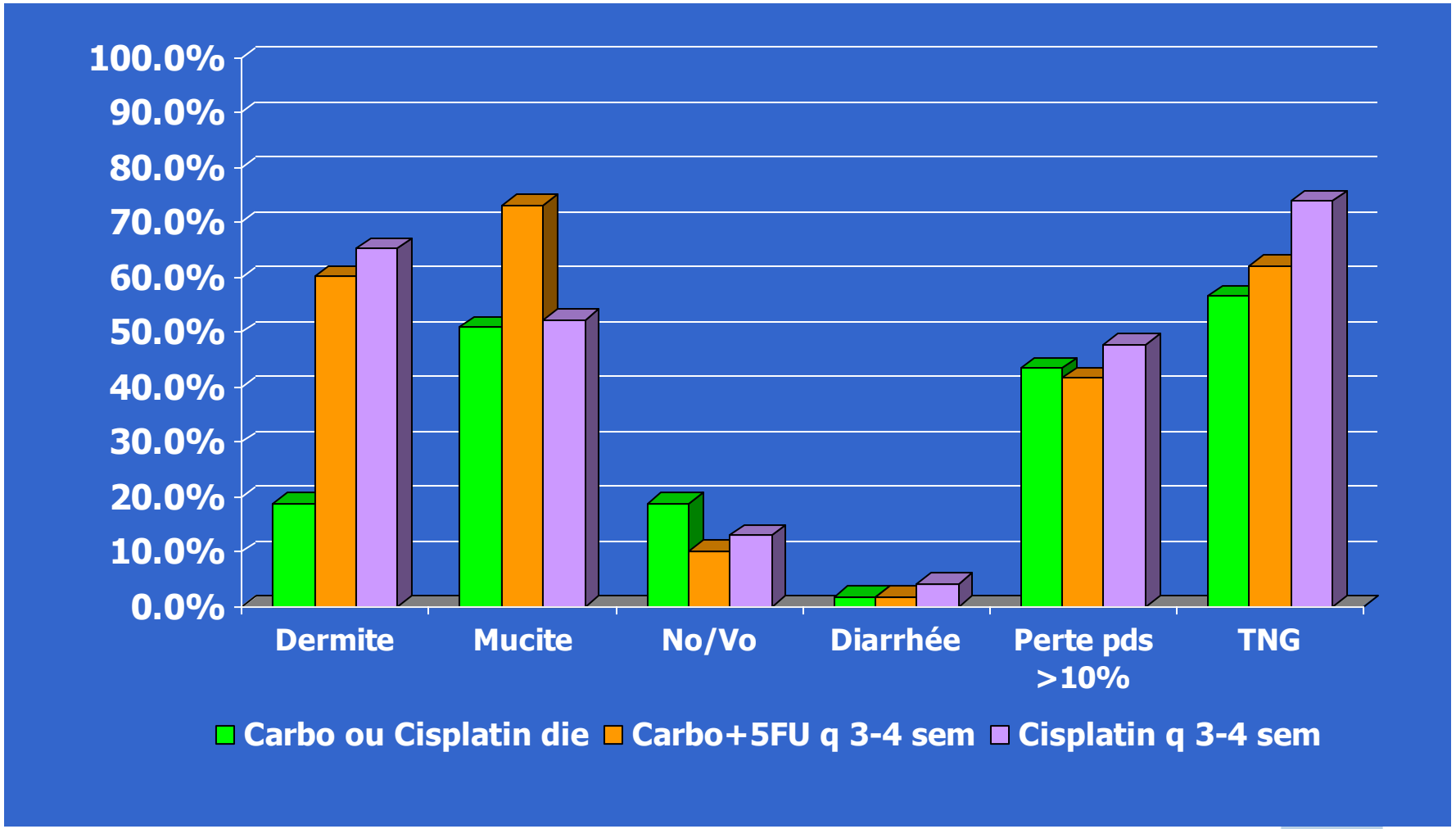
Muco-digestive toxicities:



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Comparison to reported results

Studies on concommittant chemoradiation

Étude	# patients	chimiothérapie	Fréquence RT	Contrôle LCR 3 ans	Survie globale 3 ans
Brizel (1998)	56	Cisplatin+5FU	BID	70%	55%
Calais (1999)	111	Carboplatin+5FU	QD	66%	51%
Jeremic (2000)	65	Cisplatin	BID	75%	46%
Wendt (1998)	130	Cisplatin+5FU	BID	36%	48%
Notre-Dame (2005)	318	Cisplatin / Carbo+5FU	QD	85%	63%

Comparison to reported studies

Surgical series

Étude	# patients	Contrôle LCR 3 ans	Survie globale 3 ans
Cooper (2004)	231	70%	45%
Kramer (1987)	141	66%	45%
Mirimanoff (1998)	47	63%	53%
Peters (1993)	240	73%	48%
Tupchong (1991)	116	70%	45%
Notre-Dame (2005)	318	85%	63%

Données du CHUM sur le HPV

Patient Characteristic		Number	%
HPV	+	175	68.63
	-	80	31.37
Age (years)	Median	57.00	
	Range	25.25 - 78.72	
TNM Stage	I	0	0
	II	2	0.78
	III	35	13.73
	IVa	166	65.10
	IVb	44	17.25
	Recurrence	8	3.74
KPS	60	1	0.47
	70	4	1.89
	80	41	19.34
	90	148	69.81
	100	18	8.49
Chemotherapy	Daily carboplatin or cisplatin	27	10.63
	Daily Carboplatin + 5FU	146	57.48
	Cisplatin q 1 week or q 3 weeks	81	31.89
Radiotherapy	Conventional	221	86.66
	IMRT	34	13.33

Table 1. Patient characteristics

Primary	HPV+	HPV-	Total
Oropharynx	137	32	169
Larynx	14	18	32
Oral Cavity	9	16	25
Hypopharynx	6	9	15
Nasopharynx	6	2	8
Paranasal Sinuses	2	1	3
Nose	1	1	2
Unknown	0	1	1
Total	175	80	255

Table 2. Primary sites

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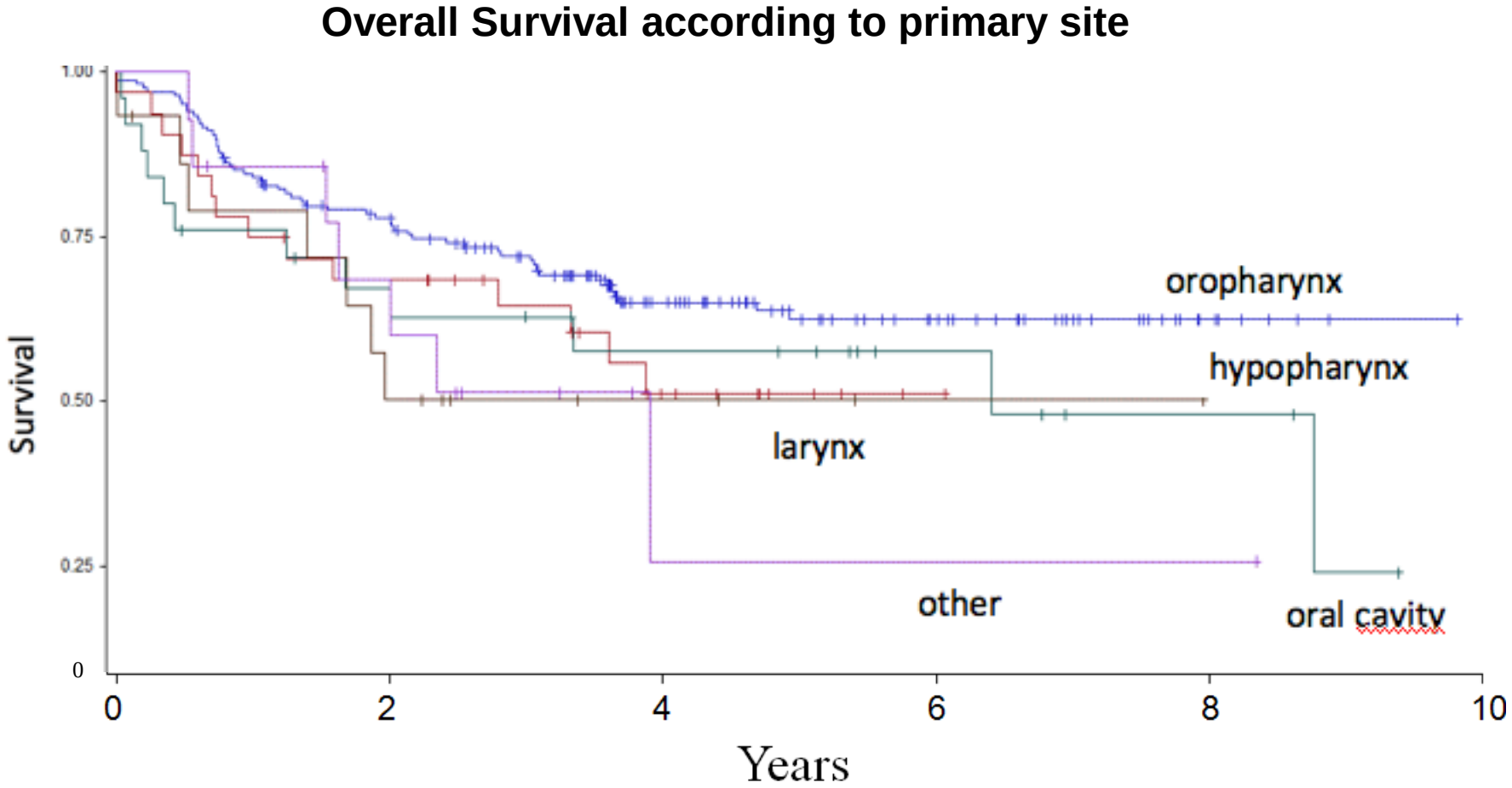
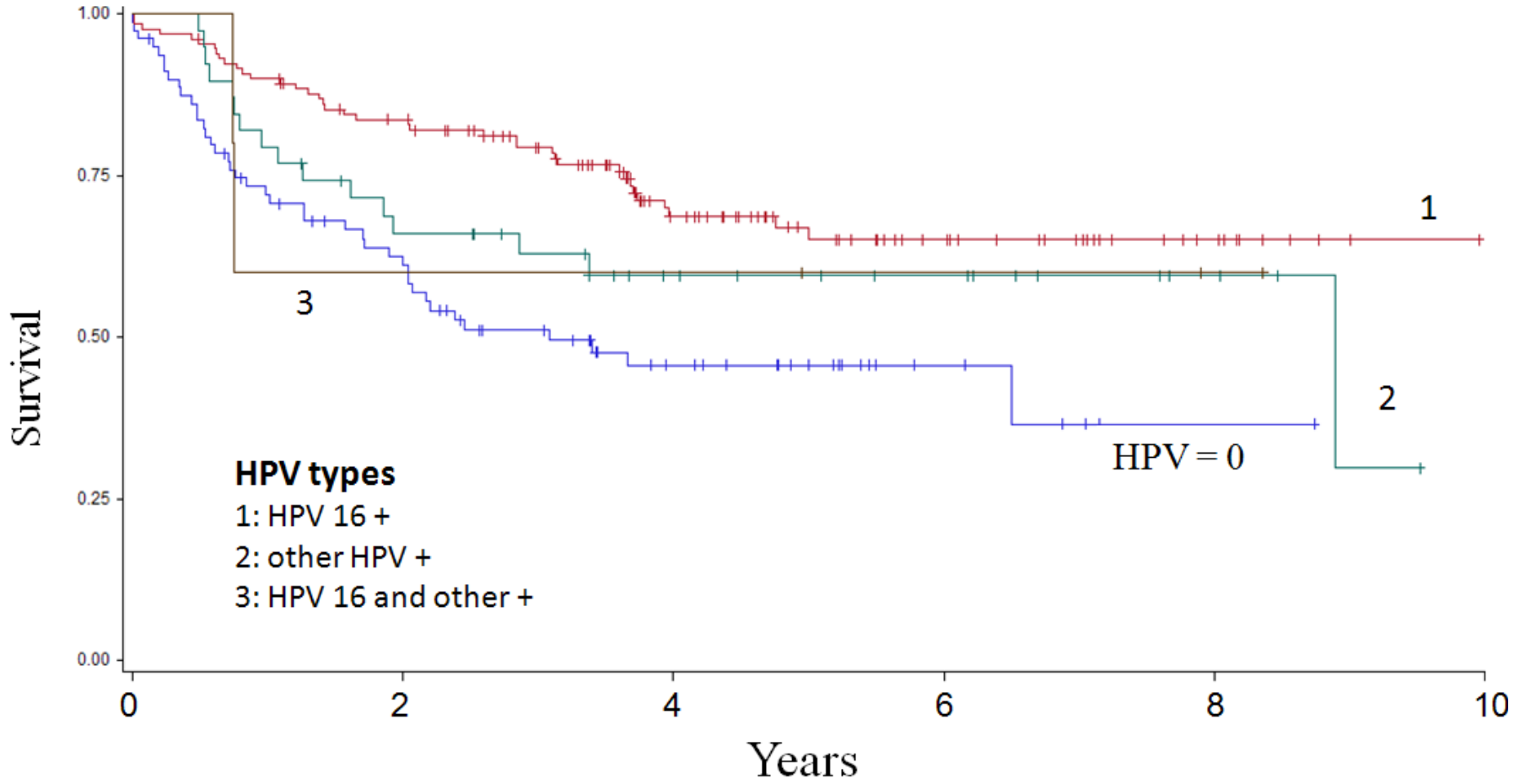
Survival according to TNM and primary site

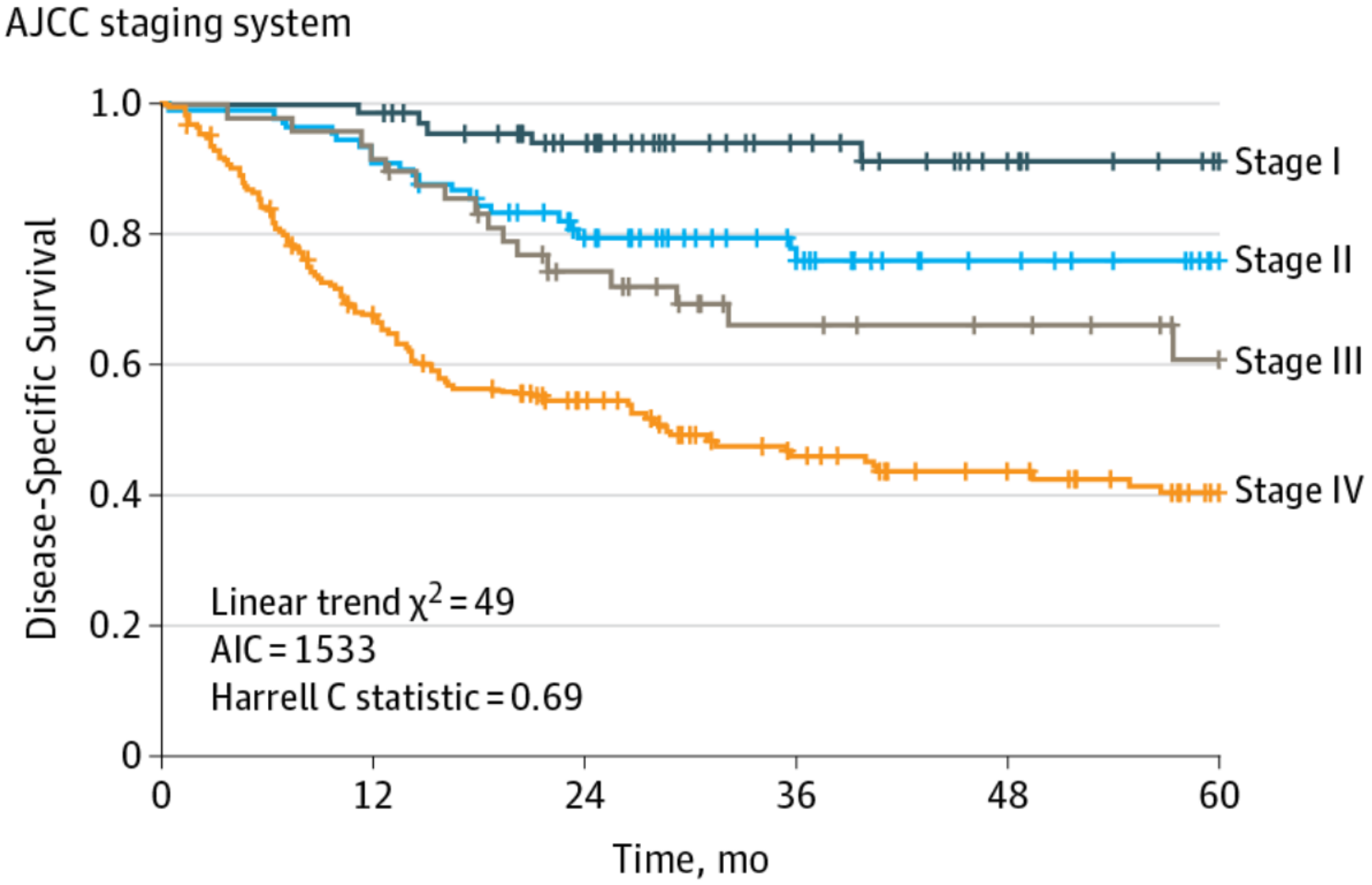


Survie globale selon le statut HPV



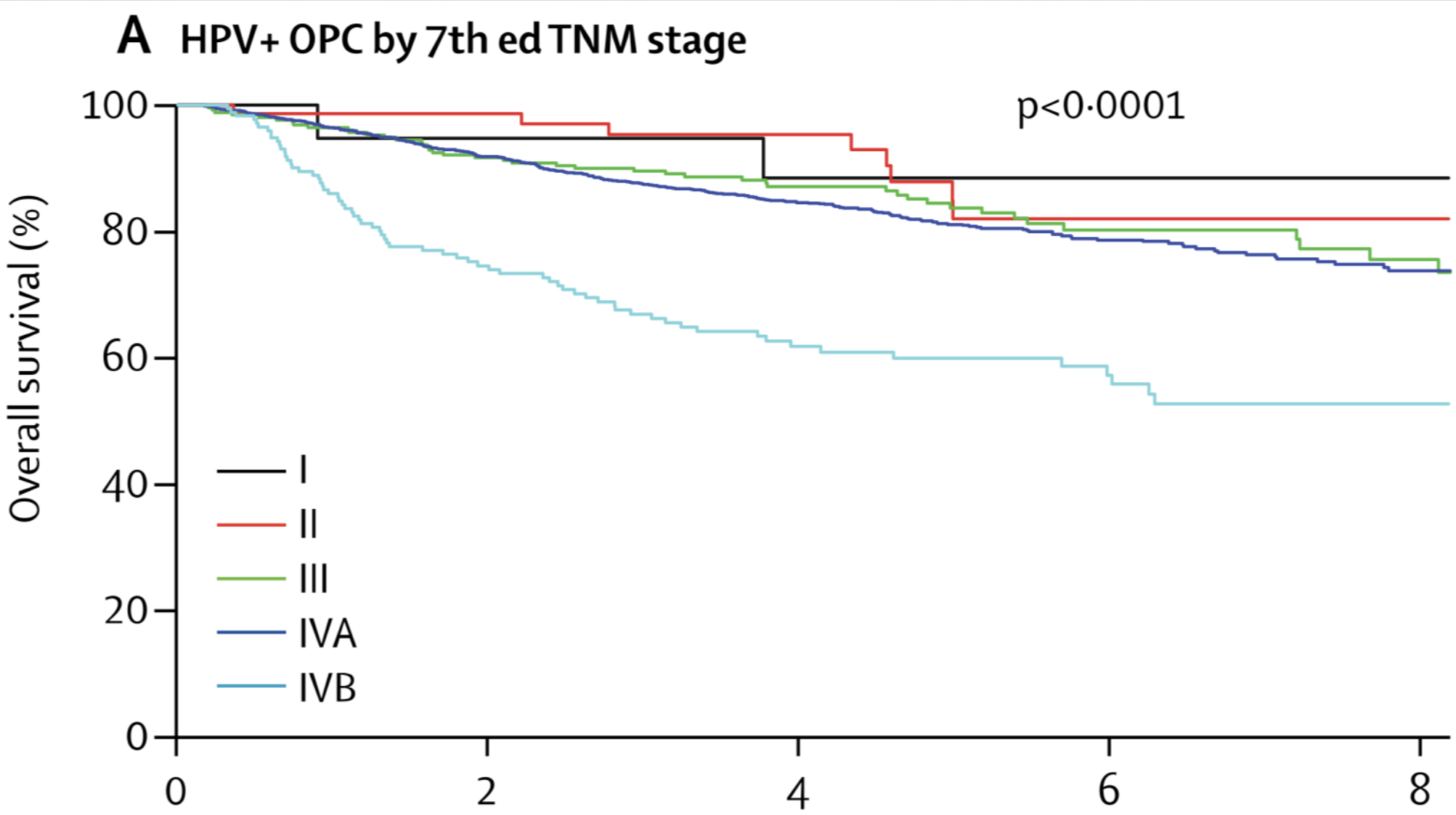
CHUM

Classification AJCC version 7



https://pre

Pronostic pour COP et HPV+



Research

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation | FROM THE AMERICAN HEAD AND NECK SOCIETY

Performance of Liquid Biopsy for Diagnosis and Surveillance of Human Papillomavirus–Associated Oropharyngeal Cancer

Rocco M. Ferrandino, MD, MSCR; Sida Chen, MD; Catharine Kappauf, MD; Joshua Barlow, BA; Brandon S. Gold, MD; Michael H. Berger, MD; William H. Westra, MD; Marita S. Teng, MD; Mohemmed N. Khan, MD; Marshall R. Posner, MD; Krzysztof J. Misiukiewicz, MD; Richard L. Bakst, MD; Kunal K. Sindhu, MD; Eric M. Genden, MD; Raymond L. Chai, MD; Scott A. Roof, MD

Table 2. Per-Test Performance Metrics for the Diagnosis and Surveillance Cohorts

	Diagnosis cohort (n = 163)		Surveillance cohort (n = 591)		
TTMV-HPV DNA test result	HPV-associated OPSCC	HPV-negative OPSCC	Recurrence	Disease free	Predictive value (95% CI), %
Positive, No.	139	0	38	0	100 (90.7-100)[a]
Negative, No.	13	11	5	548	99.1 (97.9-99.7)[b]
Sensitivity (95% CI), %	91.5 (85.8-95.4)	NA	88.4 (74.9-96.1)	NA	NA
Specificity (95% CI), %	NA	100 (71.5-100)	NA	100 (99.3-100)	NA

Abbreviations: NA, not applicable; HPV, human papillomavirus; OPSCC, oropharyngeal squamous cell carcinoma; TTMV-HPV DNA, tumor tissue–modified human papillomavirus DNA.

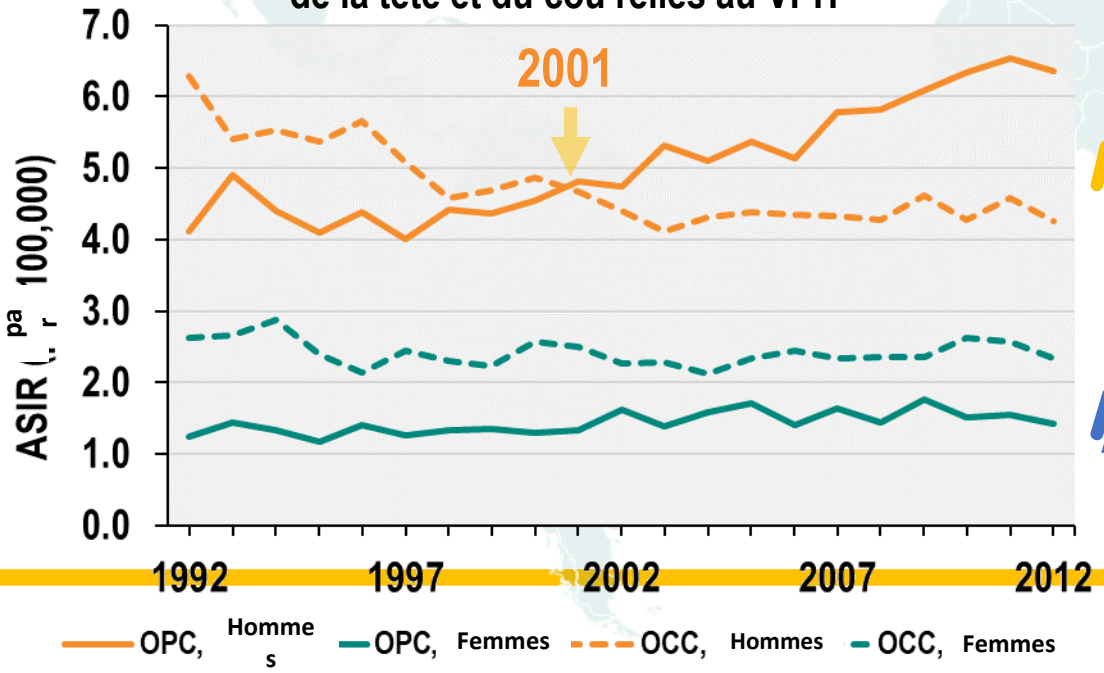
[a] Positive predictive value.

[b] Negative predictive value.

Incidence dans le temps des cancers de la tête et du cou au CANADA

VPH est associé au cancer de la tête et du cou (HNSCC), particulièrement le cancer oropharyngé (OPC)[1,2]

Taux d'incidence standardisé par age (ASIR) pour les cancers de la tête et du cou reliés au VPH



Chez les **HOMMES**, l'incidence des cancers **Oropharyngés (OPC)** dépasse l'incidence des cancers de la **Cavité Orale** en 2001.

Chez les **FEMMES**, l'incidence des cancers de la **Cavité Orale (OCC)** est relativement stable et est supérieure à l'incidence des **Cancers Oropharyngés (OPC)**.

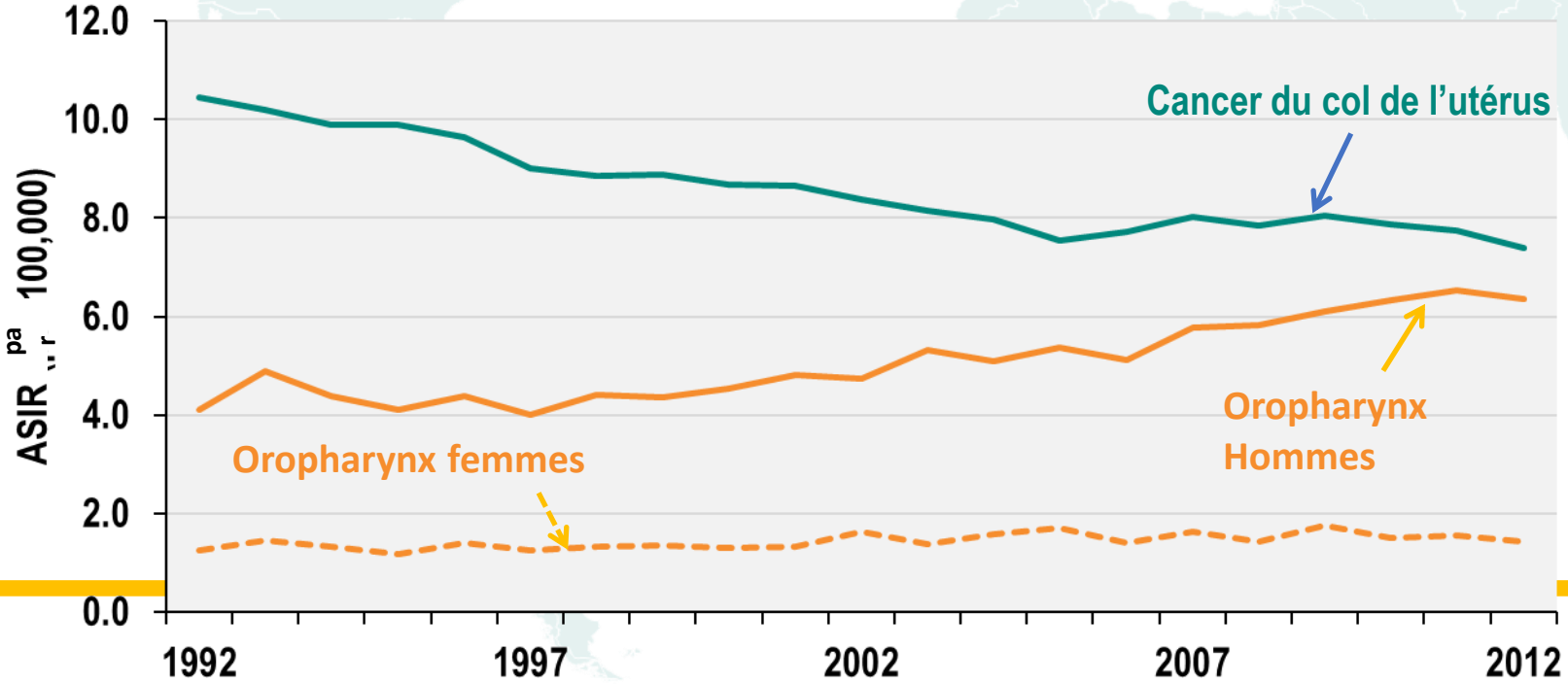
ASIR: age-standardized incidence rate; OPC=oropharyngeal cancer; OCC=oral cavity cancer

1. Syrjänen KJ et al. Br J Oral Surg. 1983 Jun; 21(2):147-53.; **2.** IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. IARC Monogr Eval Carcinog Risks Hum. 2007; 90:1-636.; **3.** Canadian Cancer Statistics 2016.

Tendance des cancers reliés au VPH AU CANADA[1]

- Le taux de **Cancer du col** à diminué entre 1992 et 2005, et demeuré relativement stable par la suite.
- Le taux de cancer de L'**Oropharynx** a augmenté significativement

Taux d'incidence standardisé des cancers reliés au VPH



Cas de Cancers selon le sexe, Canada, 2012§

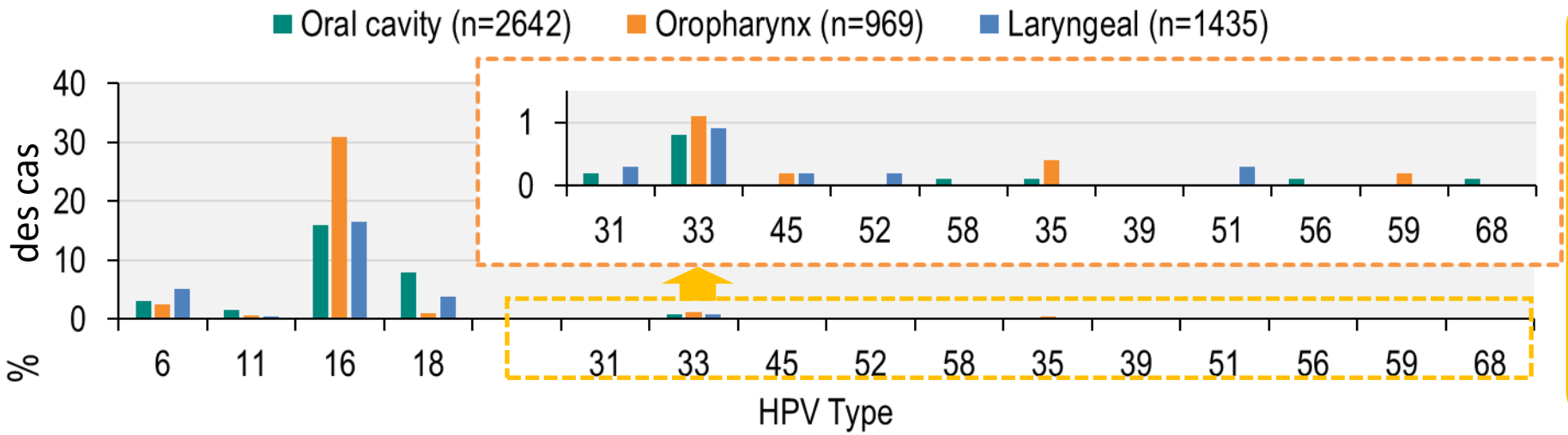
Cas de Cancers	Col Utérus	Oropharynx
Les deux sexes*	NA	**1335**
Hommes	NA	1070
Femmes	**1300**	260

Les types de cancers reliés au VPH les plus courants au Canada en 2012 sont les cancers oropharyngés et le cancer du col de l'utérus.

1. Canadian Cancer Statistics 2016. § Quebec data are to 2010; Note: Rates are age-standardized to the 2011 Canadian population; Analysis by: Health Statistics Division, Statistics Canada

Types de VPH RELIÉS AU INFECTIONS ORALES ET AUX CANCERS DE LA TÊTE ET DU COU

Distribution des types de VPH dans les cancers (Données Internationales, 2005)[1]



Les VPH 16 et 18, sont les types **oncogènes à Haut Risque** les plus communs

Les VPH 6 et 11, sont les types **à bas risque oncogène** les plus communs

Prévalence des types de VPH dans les infections orales (NHANES 2011 à 2014)[2]

4493 hommes et 4641 femmes **agés de 18 à 69 ans** selon NHANES (National Health and Nutrition Examination Survey), 2011- 2014, au EU.

Prévalence des infections orales au VPH

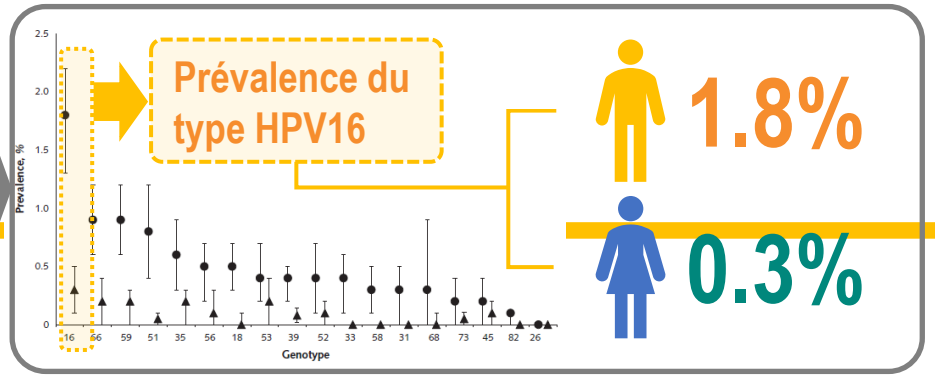
11.5%

3.2%

Prévalence des infections à Haut Risque

7.3%

1.4%

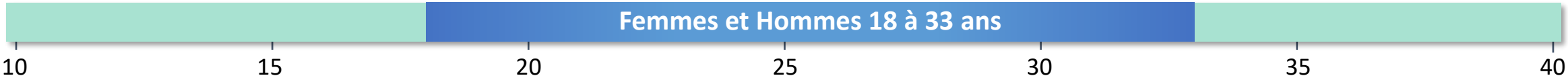


1.8%

0.3%

1. Kreimer et al. Cancer Epidemiol Biomarkers Prev. 2005 Feb;14(2):467-75.; **2.** Sonawane et al. Ann Intern Med. 2017 Nov 21;167(10):714-724.

Impact de la vaccination sur les infection VPH orales chez les jeunes adultes aux États Unis.

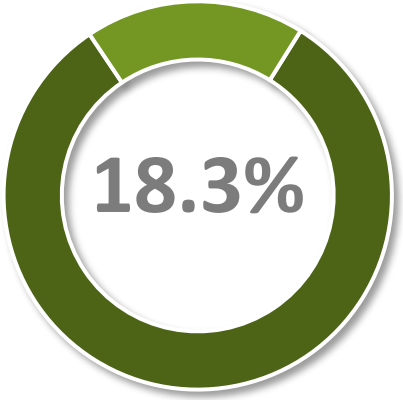


L'effet de la vaccination prophylactique contre le VPH au niveau de la population sur le fardeau de l'infection orale au VPH aux États-Unis a été étudié dans une étude transversale. Les données de 2627 hommes et femmes de 18 à 33 ans de l'étude NHANES (2011-2014) ont été utilisées comme échantillon représentatif de la population américaine. Les échantillons de rinçage et de gargarisme oraux ont été évalués pour la présence d'ADN de VPH. L'infection orale au VPH pour les types 6, 11, 16 ou 18 a été comparée en fonction du statut vaccinal.

Entre 2011 et 2014,

18.3% de la population de 18 à 33 ans

déclarait avoir reçu au moins une dose du vaccin 4-valent contre le VPH avant l'âge de 26 ans



Dans cette étude,

La vaccination contre le VPH était associée à une réduction estimée à 88%

De la prévalence des types de VPH 6, 11, 16, ou 18 chez les jeunes adultes vaccinés comparativement au non-vaccinés

Cependant, l'effet au niveau de la population était globalement modeste et particulièrement faible chez les hommes. Cela a été attribué au faible taux de vaccination dans la population

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

Conclusion

- HPV associated OPC is on the rise, mainly in men: epidemic proportions
- Treatment causes severe side effects/long term sequelaes
- No reliable test to screen for HPV associated OPC
- Vaccination should be the main means of stopping this epidemic
  - No age restriction
    - Transmission is caused by people of any age
    - Prevalence of oral HPV > 10% calls for a large vaccination effort to stop transmission and possible development of disease

Presenter

Dr. John-Peter Bradford BA, MA, ABD, PhD

- Head and Neck Cancer Thriver & Advocate
- Co-founder, LSTN (Life-Saving Therapies Network)

Who Am I and Why Am I Here?

- ✓ Today, I'm here as a person who has survived HPV-related Head and Neck Cancer (HNC)
  - I had excellent medical care. But I also drew on all my skills and gifts. These include being a psychotherapist, a mediator, businessman, management advisor, scientist/academic, author, hack musician
- ✓ As you listen, please remember that we're all different. Your skills and gifts are what you can draw on to deal with HNC
- ✓ I'm going to tell you about what it's like to have HNC and suggest some ways to deal with it

jp@lifesavingtherapies.com

An HNC Survivors Toolkit

- ✓ **Be courageous and kind**
  - It can be a very nasty and difficult ride – your attitude matters a lot
  - Do not wallow in fear
  - Accept love and be loving
  - Side effects don't determine who you are
- ✓ **Support Network**
  - It is very important to have competent and caring helpers… in all aspects of your journey (more later)
  - It should supplement and add to your skills and gifts
- ✓ **Learn continuously**
  - About your disease, yourself, treatments, nutrition
- ✓ **Advocacy**
  - Advocate for yourself; surround yourself with competence

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Life-Saving Therapies Network
Better Therapies, Faster Access

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Diagnosis

- ✓Do it yourself – I found my cancer
- ✓Do not tolerate delays
- ✓HNC can be in the throat, mouth, tongue and nasal cavity
- ✓75% are HPV-related
- ✓Understand the stage – size and spread – and what it means
- ✓Be realistic

jp@lifesavingtherapies.com

Treatment

- ✓Understand the options
  - Standard of care may not be the best for you
- ✓Chemo
- ✓Immunotherapy
- ✓Radiation
- ✓Surgery
- ✓Precision targeted
- ✓A combo

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Dealing With Treatment Side Effects

- ✓ **Nasty side-effects – short and long term – do not define you**
  - Mind numbing fatigue and brain fog
  - Blistering and painful sunburnt throat and neck/face
  - Loss of saliva
  - Loss of taste and/or tolerance for spicey foods
  - Disfigurement
  - Hearing loss
  - Not caring – be compassionate and kind; stop feeling sorry for yourself

jp@lifesavingtherapies.com

Physical and Mental Support

- ✓ **Diet, nutrition and reasonable exercise are important**
  - Feeding tubes can be the enemy
  - Keep your weight
  - Do more than lie around but don't overdo
- ✓ **Your support network is very important**
  - Key caregiver or caregivers – love, support and gate keeping
  - Someone level-headed and smart who can go to medical appointments with you – to take notes, ask questions, synthesize information
  - People who call, write, visit – emotional support, fun, thoughtful, relief for your primary caregiver(s)
  - Shoppers and food makers
  - Drivers
  - People who complement your gifts and skills

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And….

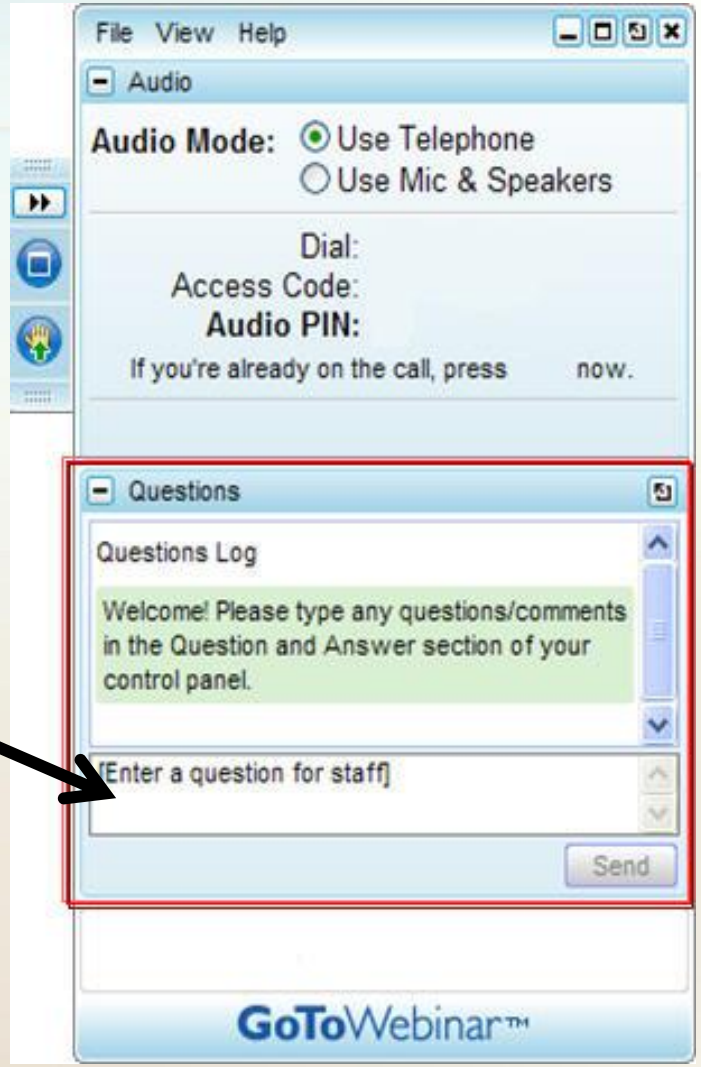
- ✓ **Encourage others to get vaccinated**
  - I have received a broad-spectrum vaccine post-treatment
- ✓ **Remember, your support people gave to you. GIVE BACK to them and others**
  - Be grateful, be kind, be knowledgeable, share unreservedly
  - Help others navigate the system
  - Use your gifts to help people in treatment and to change policy to get faster access to better treatments for people
  - ***Be a rainbow in someone's cloud***

jp@lifesavingtherapies.com

Question & Answer Period

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

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



The rate of HPV head & neck cancers is rapidly rising:
what more can be done in prevention?

Evaluation: https://forms.gle/FYPTFDRYnPsN6CKk9

Slide Set, Video recording, HPV documents at:
hpvglobalaction.org & www.CIDCgroup.org

Join CIDC's next free webinar on Wednesday, September 13, 2023 at 12:00pm ET, entitled:
"**Low-Risk HPV is NOT No-Risk HPV: Anogenital Warts and Respiratory Papillomatosis in Males**"
Register: *https://attendee.gotowebinar.com/register/6983761841795743584*

Thank you for participating!

This educational program is made possible through the support of **Merck Canada**