

HNC: epidemiology and prevention

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Conflict of interest

1. Appointment

Medical School Hannover

2. Consultant

BMS, MSD, Roche, Ipsen, Novartis, Roche

3. Stocks

Astra Zeneca, BMS, MSD

4. Patent

none

5. Honoraria

Astra Zeneca, BMS, MSD, Merck Serono, Eisai, Roche, Ipsen, Novartis

6. Financial research support

Pfizer (Wyeth), BMS, MSD

7. Other financial support

MSD, BMS, Merck Serono

Head & Neck Cancers (HNC): mainly squamous cell carcinomas

- HNC: involves lip, oral cavity, pharynx, larynx, paranasal sinuses, or salivary glands^{1,a}
- Major occurrence: lip/oral cavity, nasopharynx, oropharynx, hypopharynx, and larynx²
- 90% of HNCs are squamous cell carcinomas (SCCHN)²

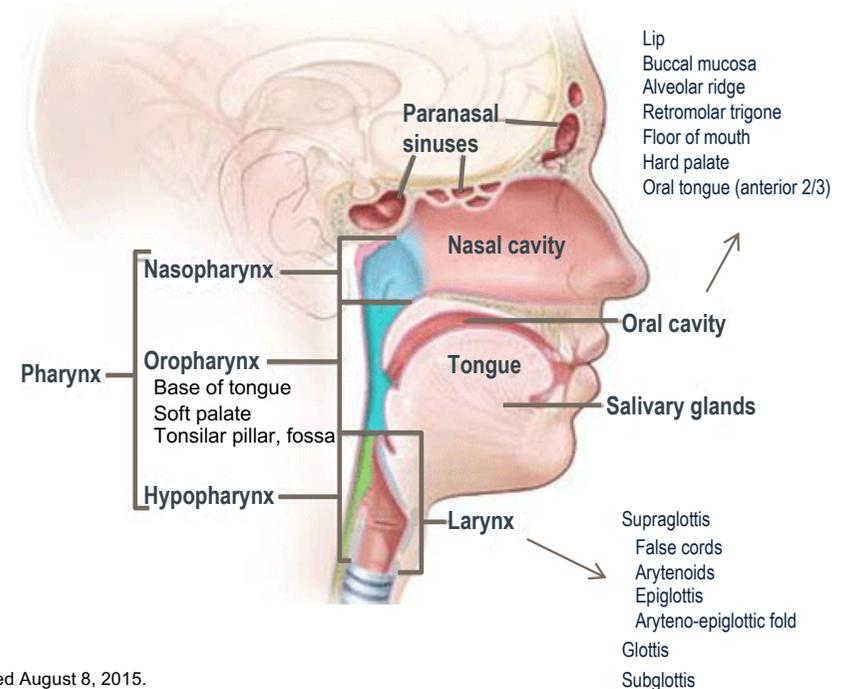


Image from National Cancer Institute. Head and neck cancers. <http://www.cancer.gov/cancertopics/factsheet/Sites-Types/head-and-neck>. Accessed August 8, 2015.

^a Salivary gland treatment included in National Comprehensive Cancer Network (NCCN) guidelines for head and neck cancer.³

1. National Cancer Institute. Head and neck cancers. <http://www.cancer.gov/cancertopics/factsheet/Sites-Types/head-and-neck>. Accessed July 9, 2015.

2. Burtneß B. *InPractice*. Medical Management of Head and Neck Cancer. https://www.inpractice.com/Textbooks/Oncology/Head_and_Neck_Cancer/ch26a_HN_MedicalMgmt.aspx. Accessed July 6, 2015.

3. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines. Head and Neck Cancers*. Version 1.2016. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed July 12, 2016.

Cancer statistics 2018

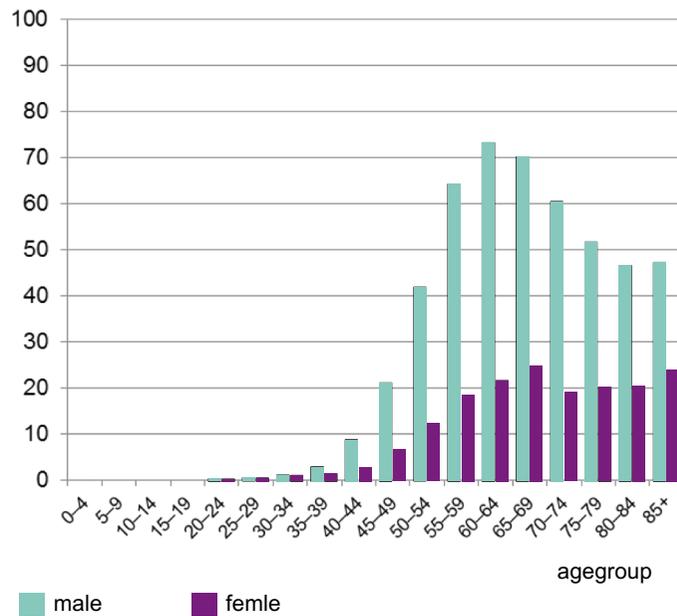
Estimated New Cases

			Males	Females			
Prostate	164,690	19%			Breast	266,120	30%
Lung & bronchus	121,680	14%			Lung & bronchus	112,350	13%
Colon & rectum	75,610	9%			Colon & rectum	64,640	7%
Urinary bladder	62,380	7%			Uterine corpus	63,230	7%
Melanoma of the skin	55,150	6%			Thyroid	40,900	5%
Kidney & renal pelvis	42,680	5%			Melanoma of the skin	36,120	4%
Non-Hodgkin lymphoma	41,730	5%			Non-Hodgkin lymphoma	32,950	4%
Oral cavity & pharynx	37,160	4%			Pancreas	26,240	3%
Leukemia	35,030	4%			Leukemia	25,270	3%
Liver & intrahepatic bile duct	30,610	4%			Kidney & renal pelvis	22,660	3%
All Sites	856,370	100%	All Sites	878,980	100%		

SCCHN: age-specific distribution

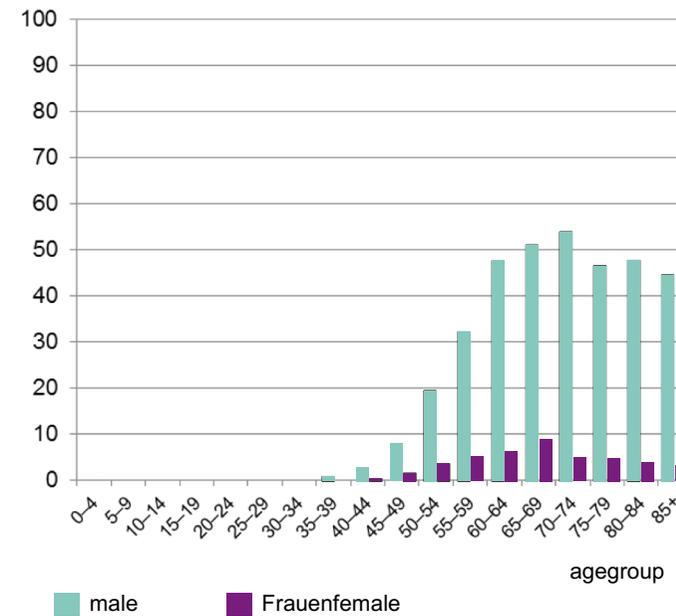
SCCHN: pharynx and oral cavity

Age-specific incidence according to gender,
ICD-10 C00 – C14, Germany 2011 – 2012 per 100.000



SCCHN: larynx

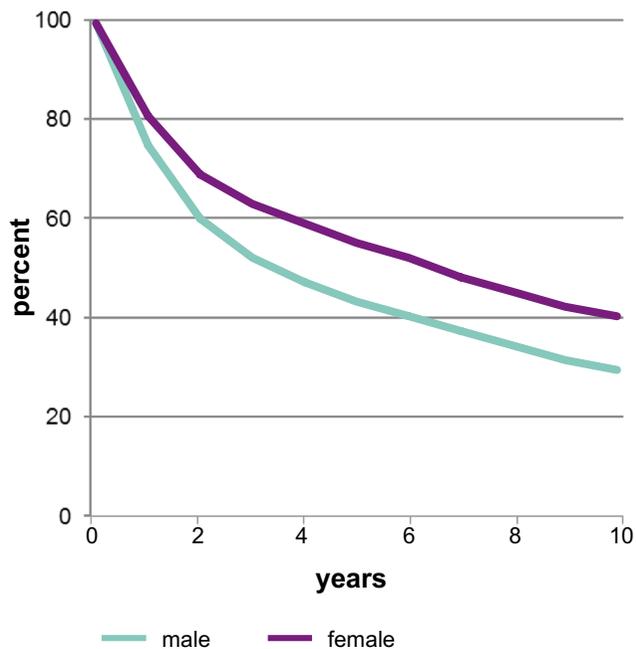
Age-specific incidence according to gender,
ICD-10 C32, Germany 2011 – 2012 per 100.000



SCCHN: outcome gender-dependent

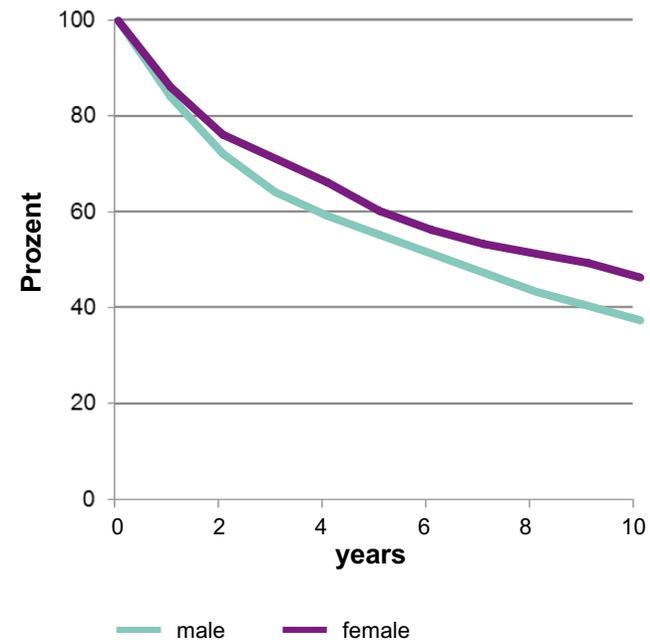
SCCHN: pharynx and oral cavity

OS since diagnosis according to gender, ICD-10 C00 – C14, Germany 2011 – 2012

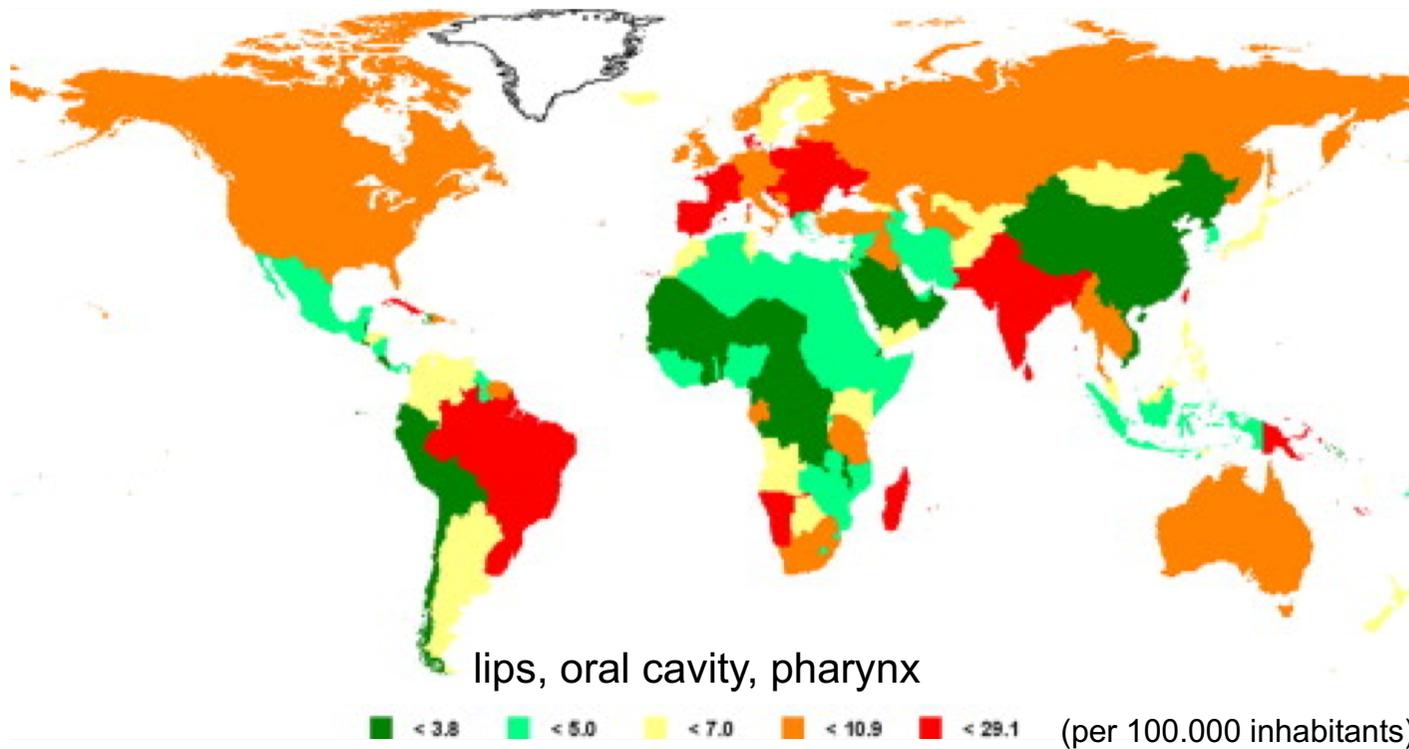


SCCHN: larynx

OS since diagnosis according to gender, according to gender, ICD-10 C32, Germany 2011 – 2012



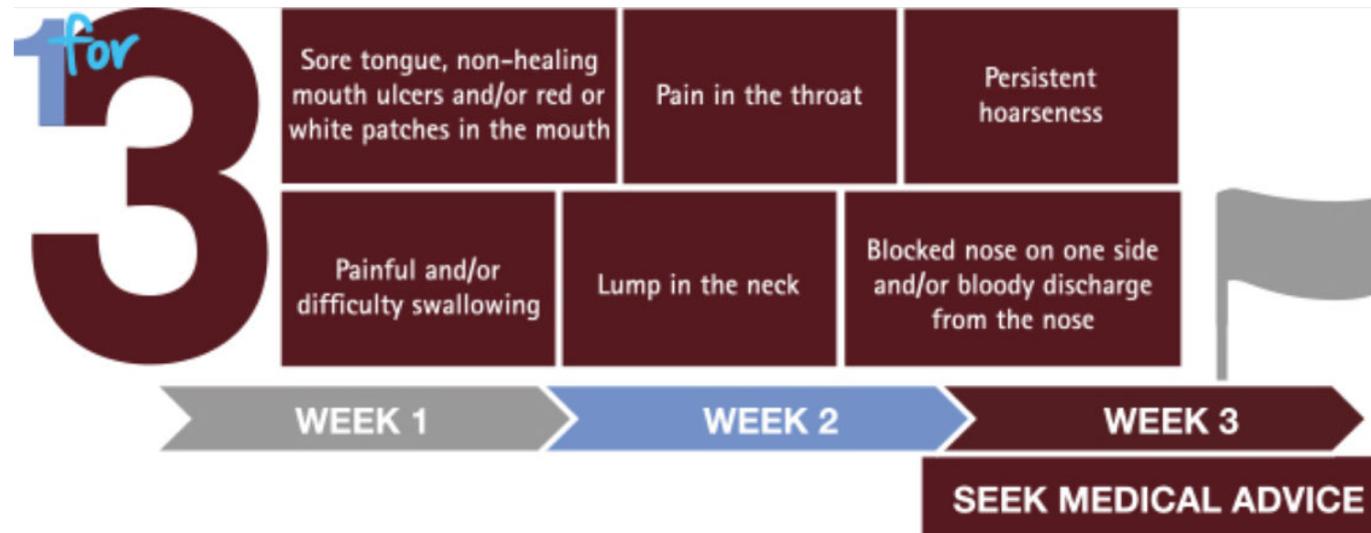
Geographic incidence varies for SCCHN



Awareness campaigns – key ingredient for early detection



- Risk Factors**
-  Smoking
 -  Alcohol
 -  Human papilloma virus (HPV)



Access to specialized care is associated with early stage

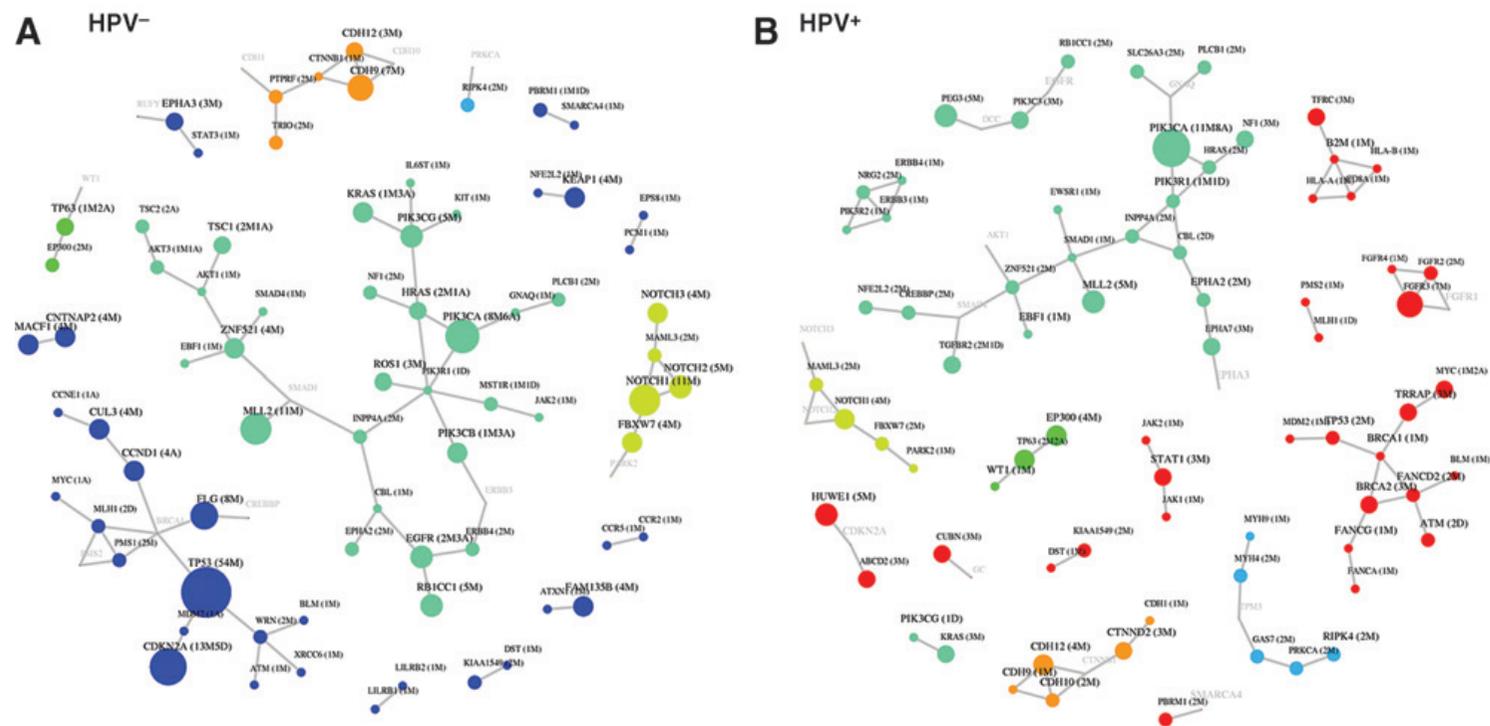
Factors associated with early-stage diagnosis were:

- previous consultation to a specialist physician (OR = 0.5 [0.4–0.8])
- ease of access to this specialist (OR = 0.6 [0.4–0.9])
- having a health professional in close contact (OR = 0.6 [0.4–0.8]).

What are known risk factors?

	Preventive measure
Tobacco	✓
Alcohol	✓
HPV	✓
UV-exposure (lips)	✓
Poor oral/dental hygiene	✓
Occupational hazards	✓
Gastroesophageal reflux disease	✓
Genetic syndrome (i.e. Fanconi)	-

Molecular drivers vary in SCCHN



Seiwert et al. (2015). *Clinical Cancer Research*, 21(3), 632–641.
<http://doi.org/10.1158/1078-0432.CCR-13-3310>

HPV-associated cancers

Table 1. Number of cancer cases attributable to HPV and corresponding attributable fraction (AF) by cancer site, sex and age; World, 2012

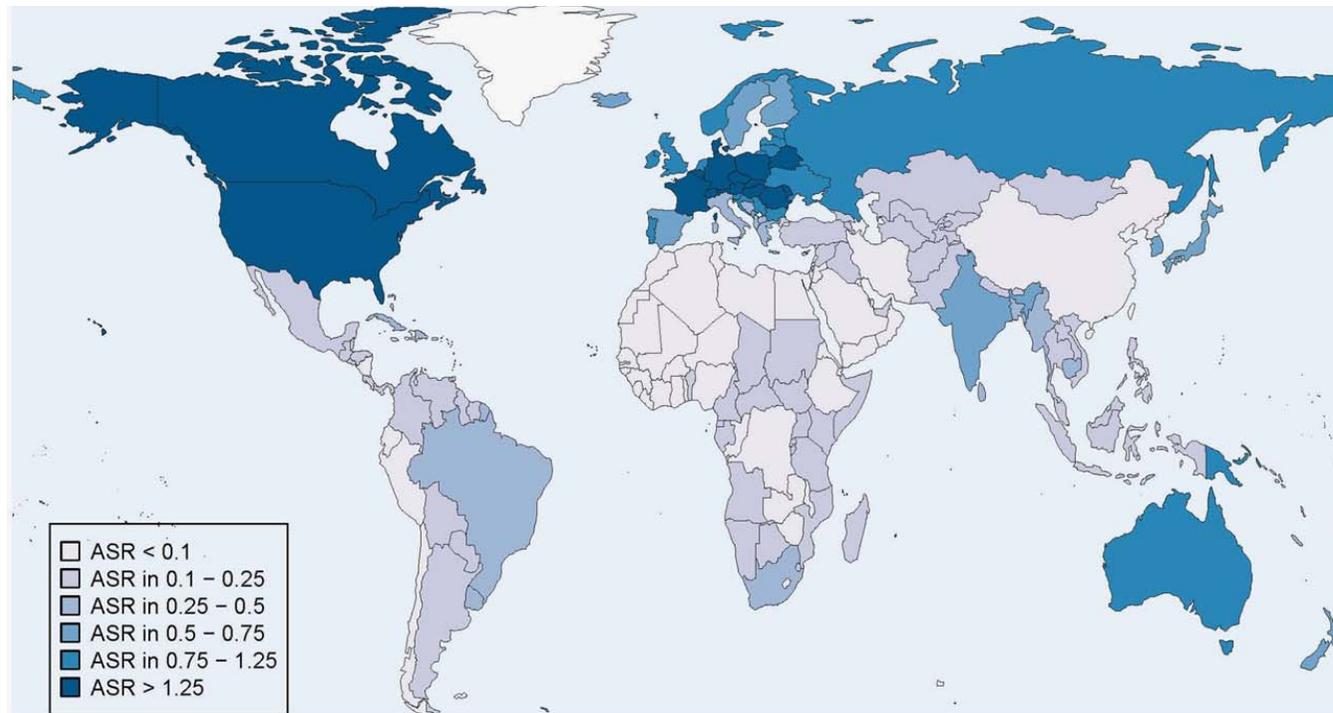
HPV-related cancer site (ICD-10 code)	Number of incident cases ^{1,2}	Number attributable to HPV	AF (%)	Number attributable to HPV by gender		Number attributable to HPV by age group		
				Males	Females	<50 years	50–69 years	70+ years
Cervix uteri (C53)	530,000	530,000	100.0	0	530,000	250,000	220,000	58,000
Anus ³ (C21)	40,000	35,000	88.0	17,000	18,000	6,600	17,000	12,000
Vulva ³ (C51)	34,000	8,500	24.9	0	8,500	2,600	3,400	2,500
Vagina ³ (C52)	15,000	12,000	78.0	0	12,000	2,500	5,200	3,900
Penis ³ (C60)	26,000	13,000	50.0	13,000	0	2,700	5,800	4,400
Oropharynx ³ (C01, C09–10)	96,000	29,000	30.8	24,000	5,500	5,400	18,000	6,000
Oral cavity ³ (C02–06)	200,000	4,400	2.2	2,900	1,500	890	2,300	1,200
Larynx (C32)	160,000	3,800	2.4	3,300	460	420	2,200	1,200
Other pharynx ³ (C12–C14)	78,000	0	0	–	–	–	–	–
Total HPV-related sites	1,200,000	630,000	54.0	60,000	570,000	270,000	270,000	88,000

¹Source: Globocan 2012.

²Numbers are rounded to two significant digits.

³These cancer sites were not directly available in GLOBOCAN 2012; therefore, data from the Cancer Incidence in Five Continents (CI5-X) database were used to estimate the corresponding number of cases.

Adjusted incidence of HPV+ SCCHN per 100,000

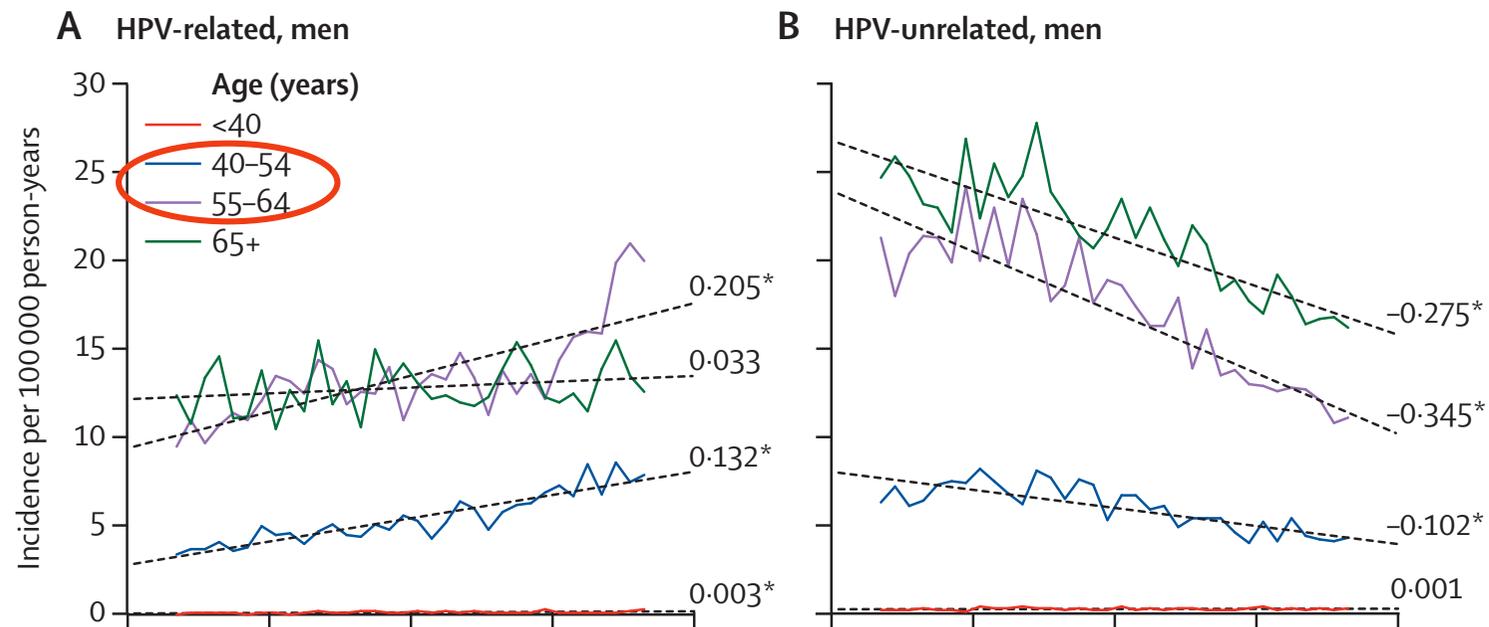


Martel et al. (2017). International Journal of Cancer Journal International Du Cancer, 141(4), 664–670. <http://doi.org/10.1002/ijc.30716>

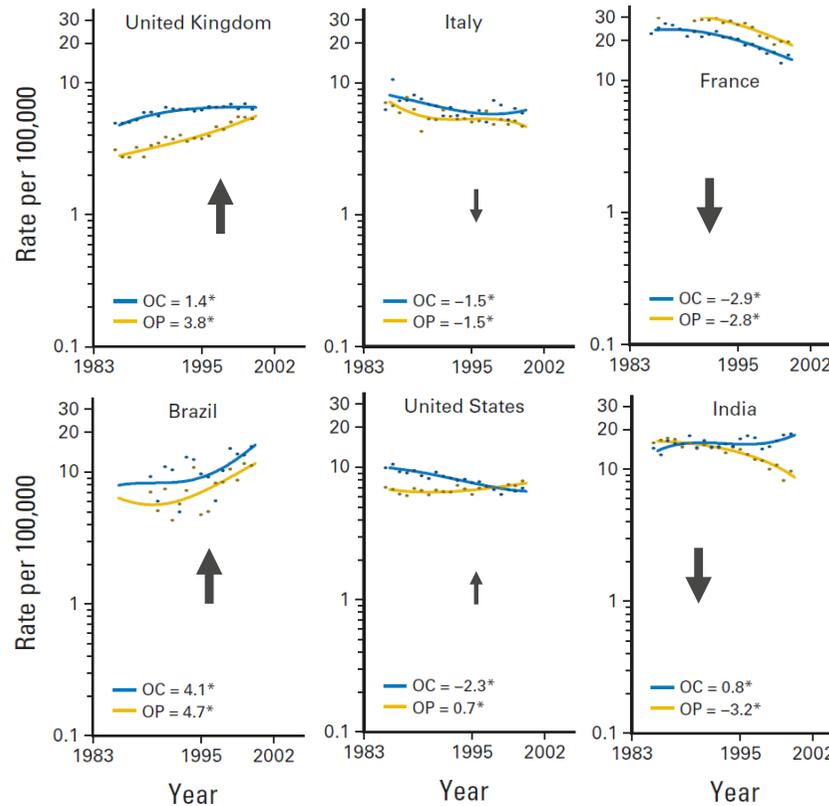
M_HH

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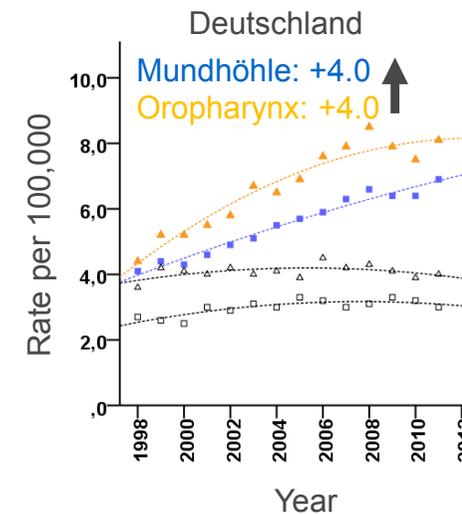
SCCHN: male increase of HPV-tumors



Incidence rates vary geographically



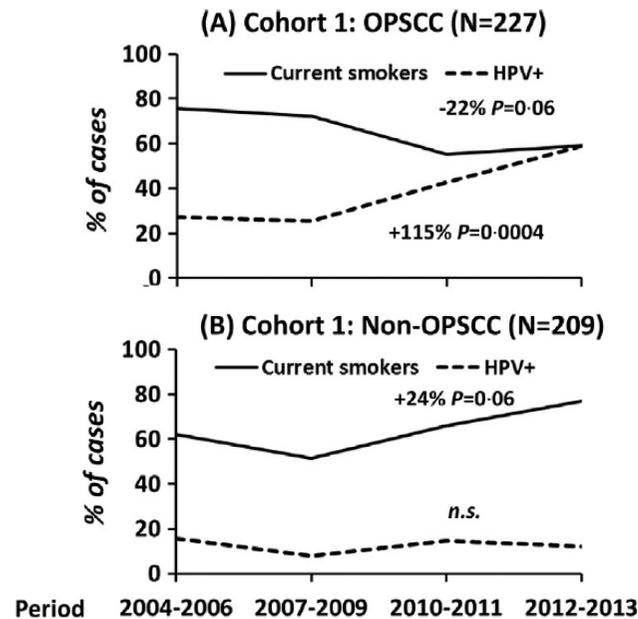
Chaturvedi et al., *J Clin Oncol.* 2013 Dec 20; 31(36): 4550–4559



Tinhofer et al., *Eur J Cancer.* 2015 Mar;51(4):514-21

HPV and tobacco have different impact across the world

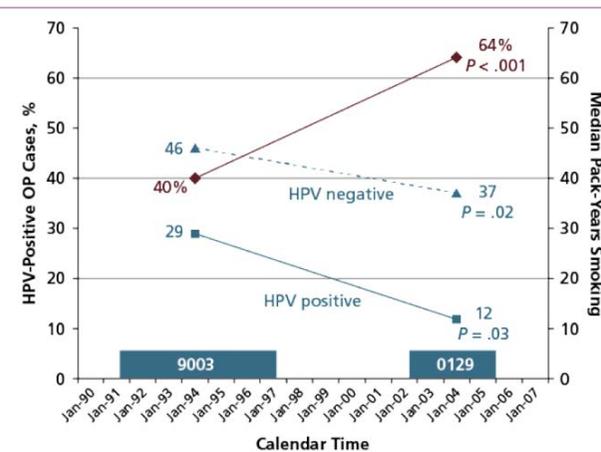
Germany



Tinhofer et al., *Eur J Cancer*.
2015 Mar;51(4):514-21

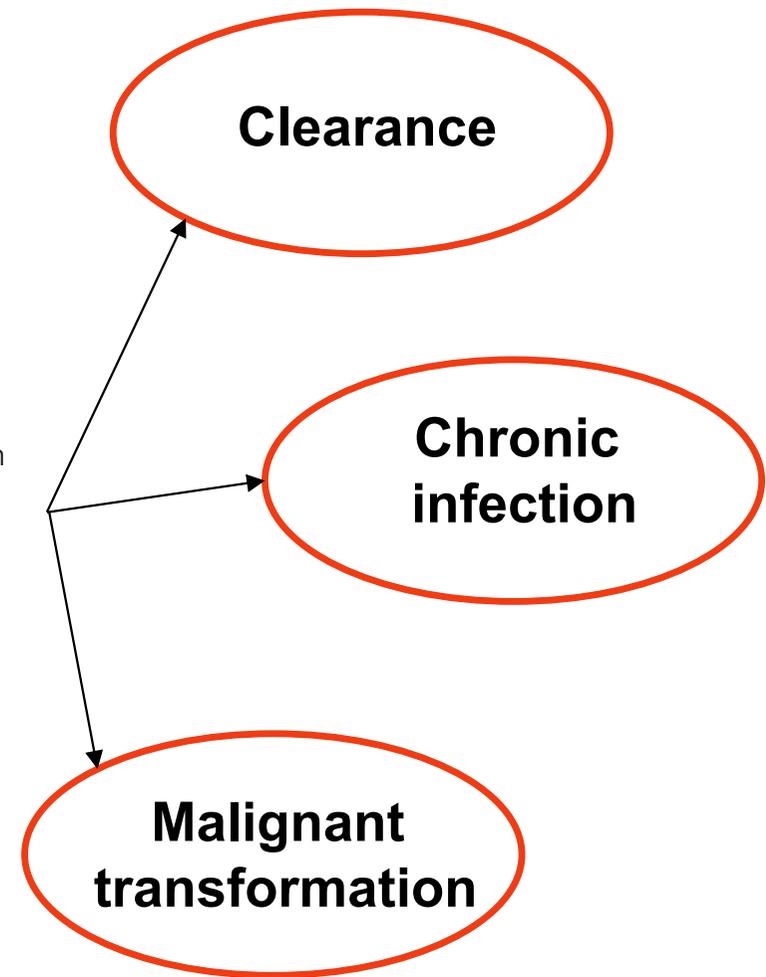
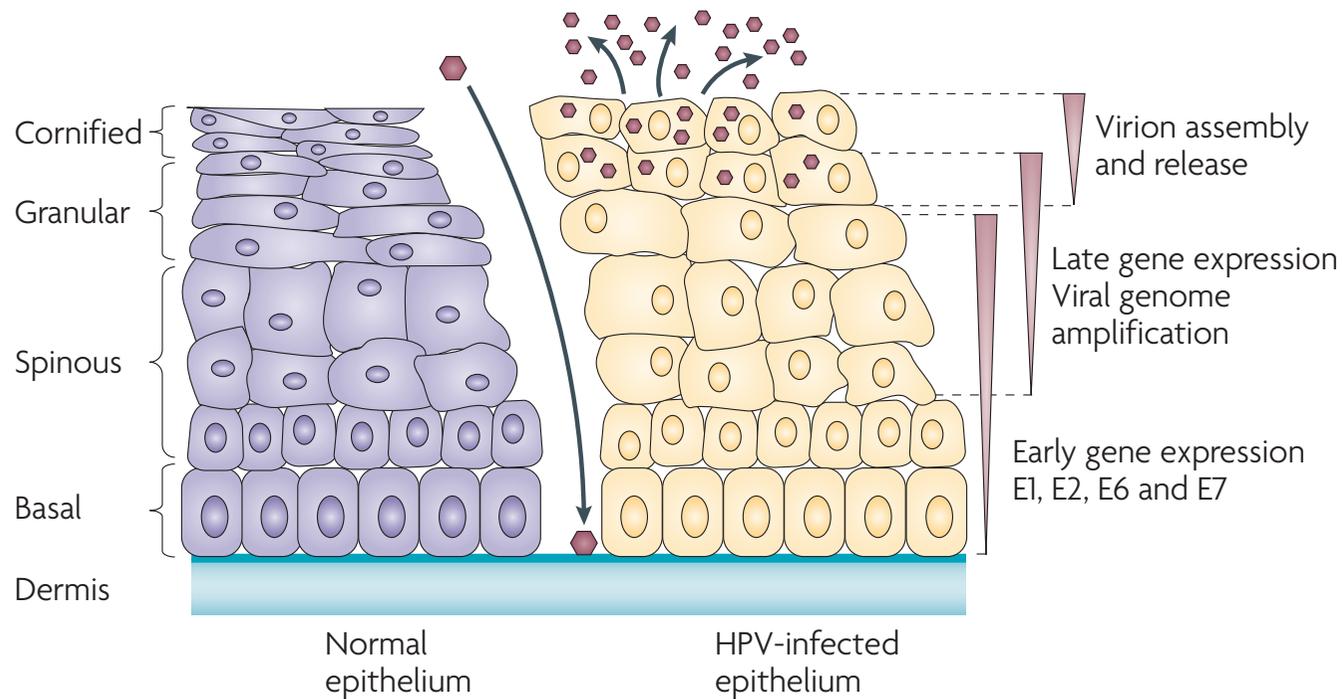
USA

HPV Status and Tobacco Use: RTOG 9003 vs 0129



Gillison M et al., *ASCO 2010, Abstr 5510*

HPV-infection

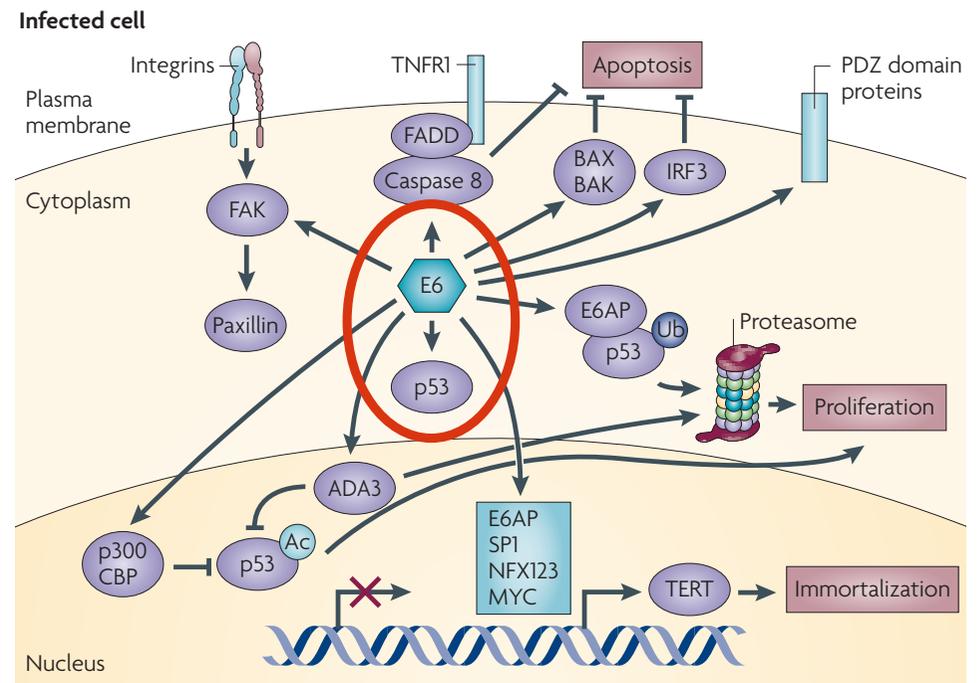
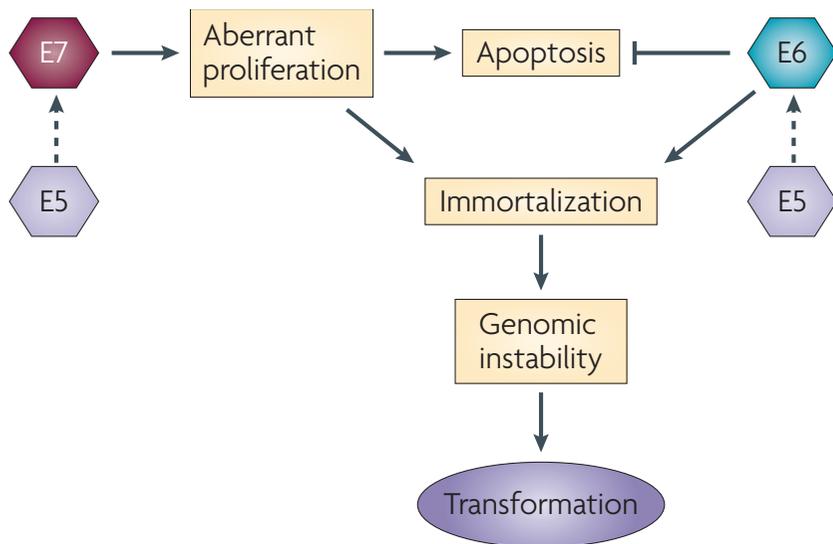


Oral HPV infections are rare in asymptomatic men

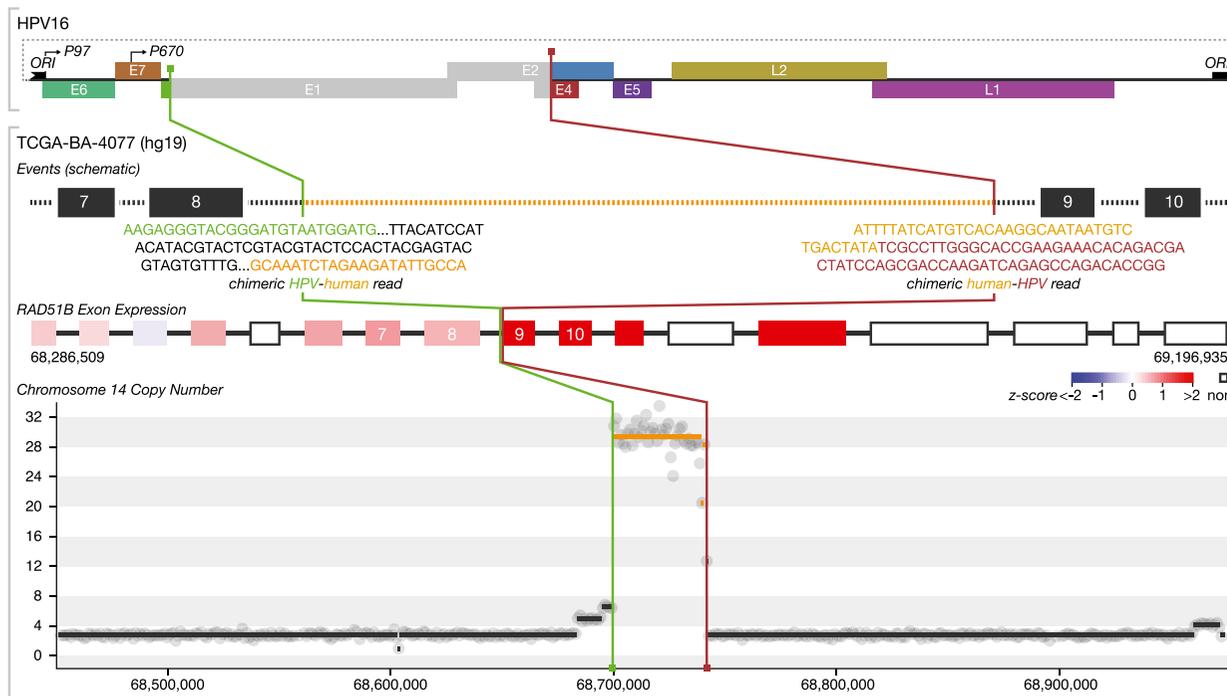
N=1626	Incidental infection	Oncogenic infection	HPV16
n (%)	115 (4.4%)	53 (1.7%)	18 (0.6%)
Clearance;	n 45	18	5
	mo. 6.9 mo.	6.3 mo.	7.3 mo.

Incidence is stable across age groups
Median FU: 12.7 months (IQR 12.1–14.7)

Expression of viral oncoproteins (E6, E7) during carcinogenesis



Type of DNA-integration is a key component in viral carcinogenesis



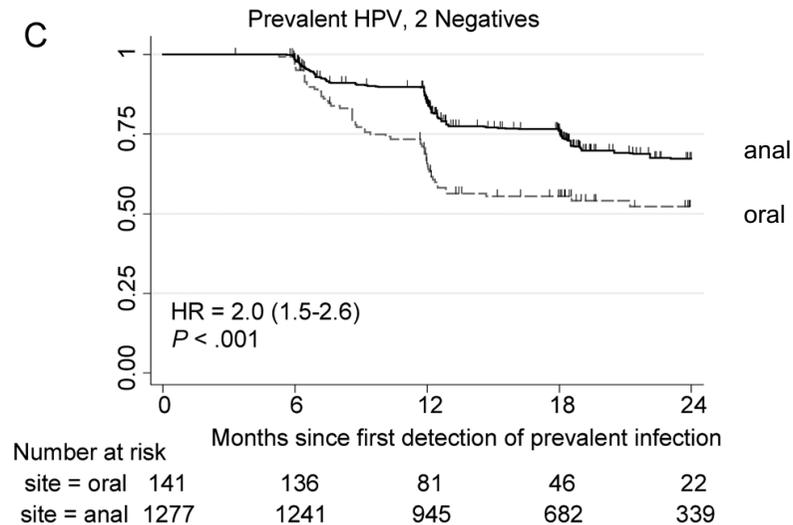
HPV integration alters:

- Amplification
- Disruption
- Rearrangement

Natural History of Anal vs Oral HPV Infection in HIV-Infected Men and Women

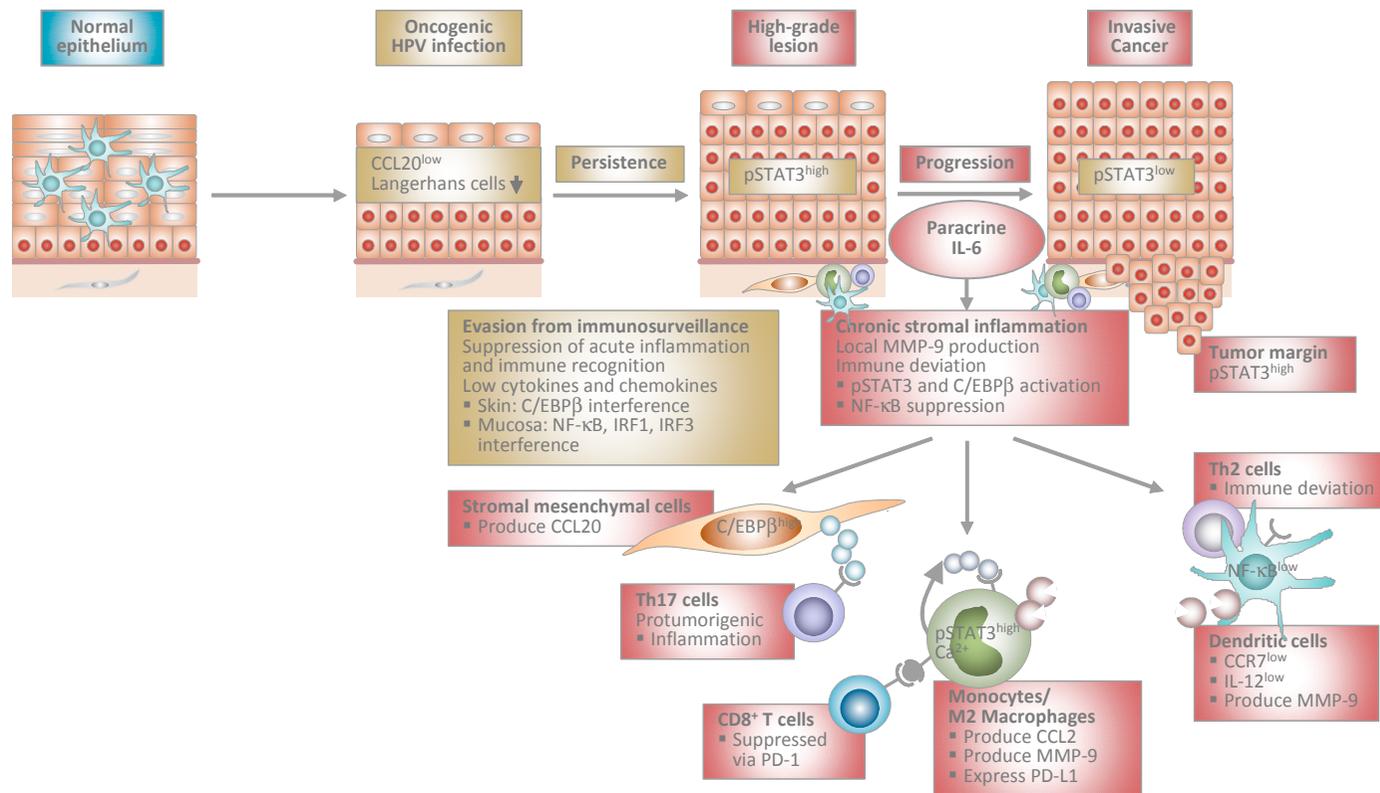
Daniel C. Beachler,¹ Gypsyamber D'Souza,¹ Elizabeth A. Sugar,^{1,2} Wiehong Xiao,³ and Maura L. Gillison³

¹Department of Epidemiology, and ²Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; and ³Viral Oncology Program, Ohio State University Comprehensive Cancer Center, Columbus

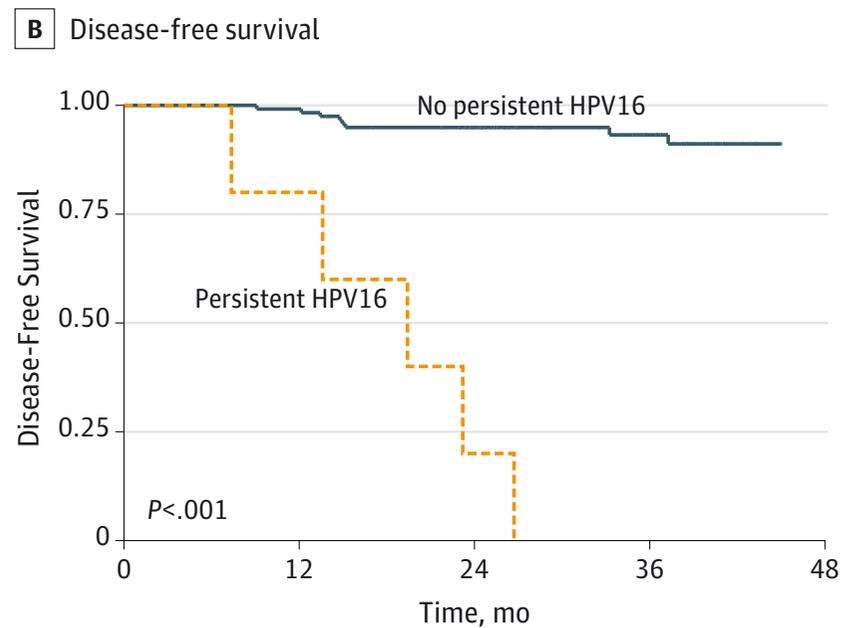


Late HPV-Clearance increases the risk for malignant transformation

HPV+ SCCHN is immunogenic



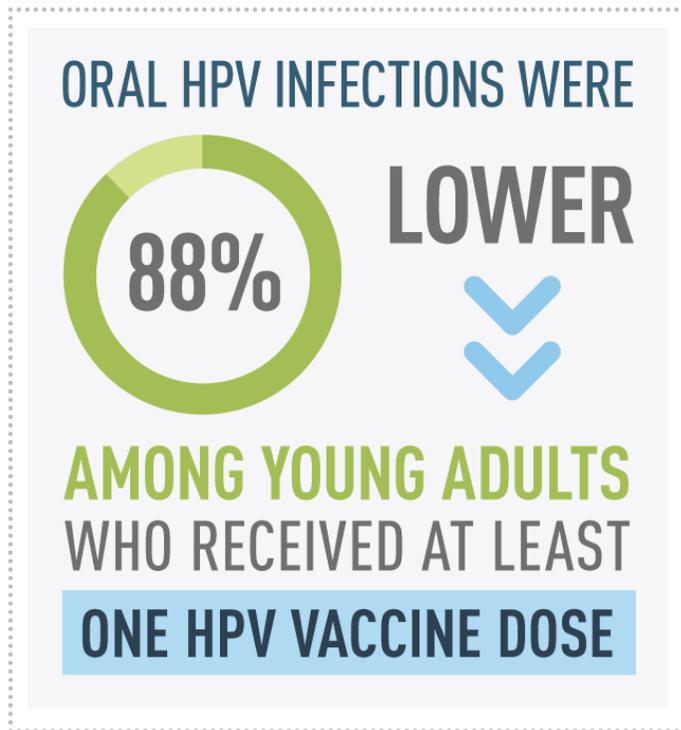
HPV16 persistence after definite treatment is associated with poor outcome



DNA analyses in oral rinses	No. at risk				
	No persistent HPV16	Persistent HPV16			
	119	5	118	4	99
					1
					49
					0
					7
					0

Rettig, E. M., Wentz, A., Posner, M. R., Gross, N. D., Haddad, R. I., Gillison, et al. (2015). *JAMA Oncology*, 1(7), 907. <http://doi.org/10.1001/jamaoncol.2015.2524>

HPV-vaccination programs should be expanded



Source: Gillison ML, et al. 2017 ASCO Annual Meeting, Abstract #6003.

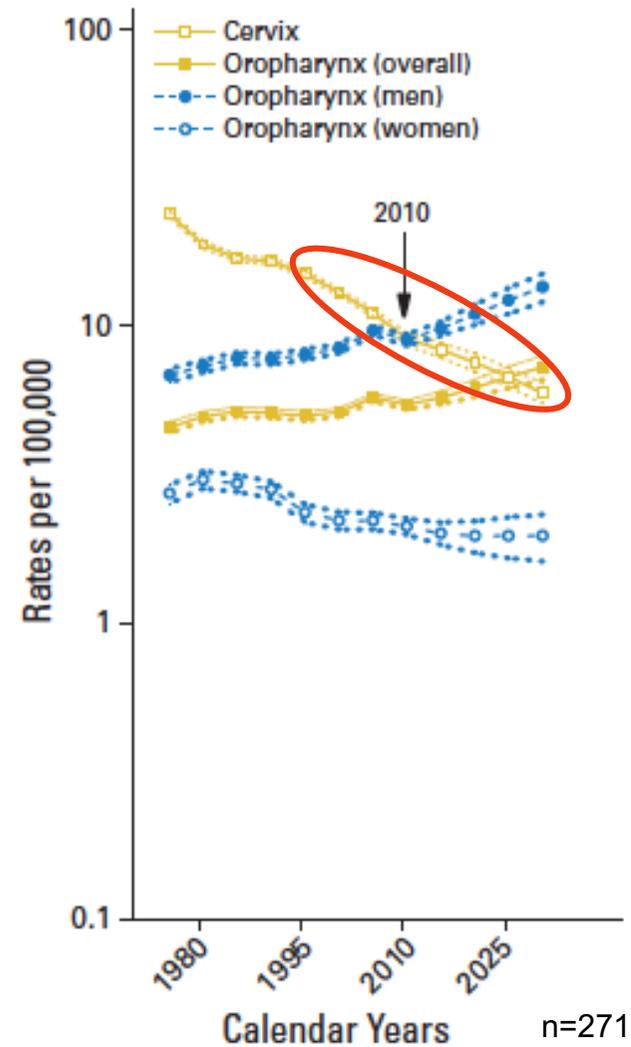
cancer.gov

Caveat:

1. Not all subjects are heterosexual
2. Uptake of vaccination is too low so far (29.2% female; 6.9% male)

HPV-prevention: vaccination

- HPV quadrivalent vaccine (Type 6, 11, 16, 18) in cervix Ca since 2006/7
- Decrease in CIN/condyloma
- Impact on SCCHN is also likely

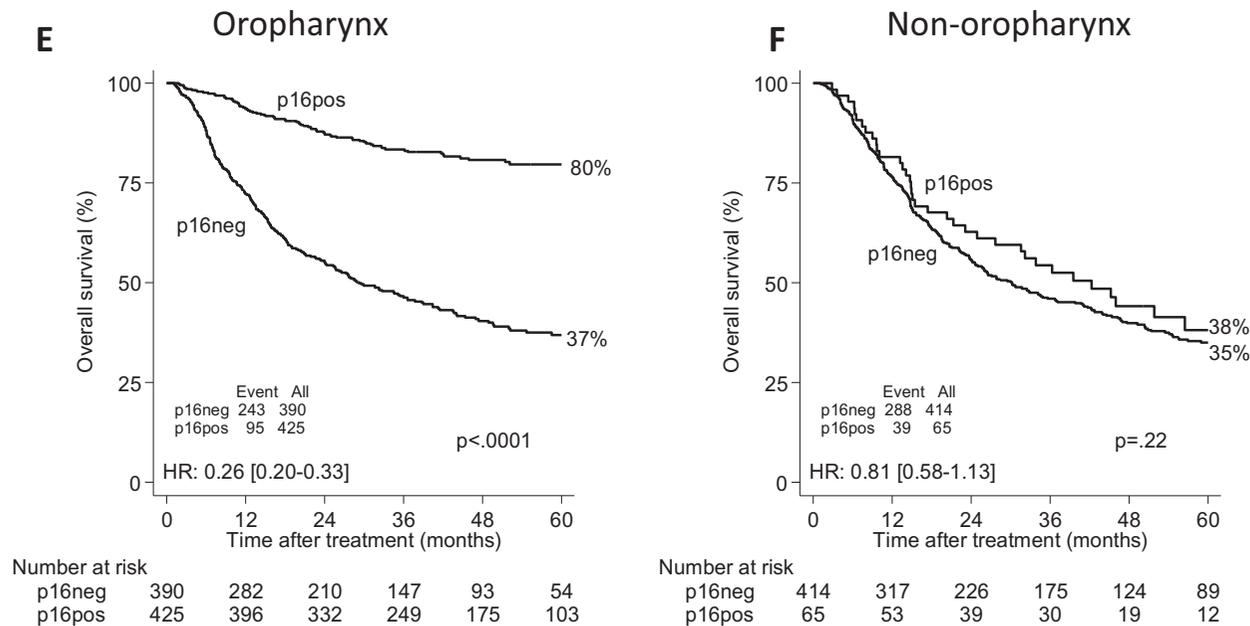


No cumulation of HPV infections in families with HPV+ SCCHN

Table 2. Oral HPV DNA Prevalence in Patients With HPV-OPC and Their Partners Compared With General US Population of Similar Age (NHANES)

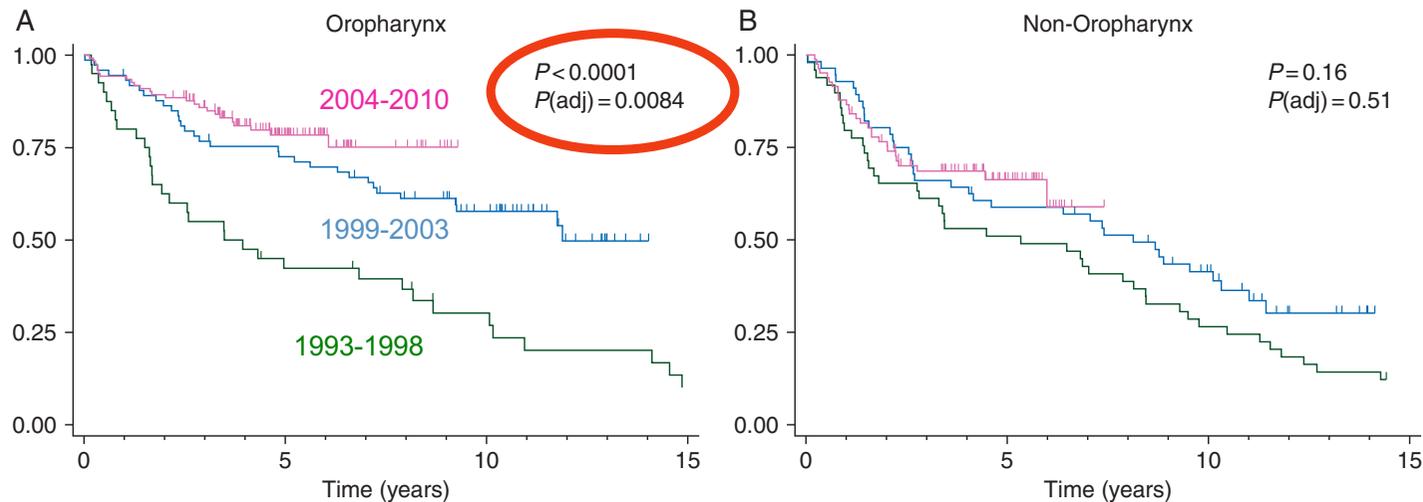
	NHANES Population (%)*	Partners		Patients	
		No.	%	No.	%
Baseline		(n = 93)		(n = 164)	
Any oral HPV	9.1	4†	4.3	106	64.6
Any oncogenic HPV	4.7	1†	1.1	100‡	61.0
HPV16	1.4	0	0.0	88	53.7
HPV16 qPCR ≥ 3§	—	0	0.0	71	45.5
HPV16 qPCR > 0§	—	2	2.3	83	53.2
Among women		(n = 87)		(n = 17)	
Any oral HPV at baseline	4.3	2	2.3	11	64.7
Any oncogenic HPV	1.3	1	1.2	10	58.8
HPV16 at baseline	0.5	0	0.0	9	52.9
Among men		(n = 6)		(n = 147)	
Any oral HPV at baseline	14.0	2	33.3	95	64.3
Any oncogenic HPV	8.2	0	0.0	90	61.2
HPV16 at baseline	2.4	0	0.0	79	53.7

HPV prognostication is bound to oropharynx carcinoma

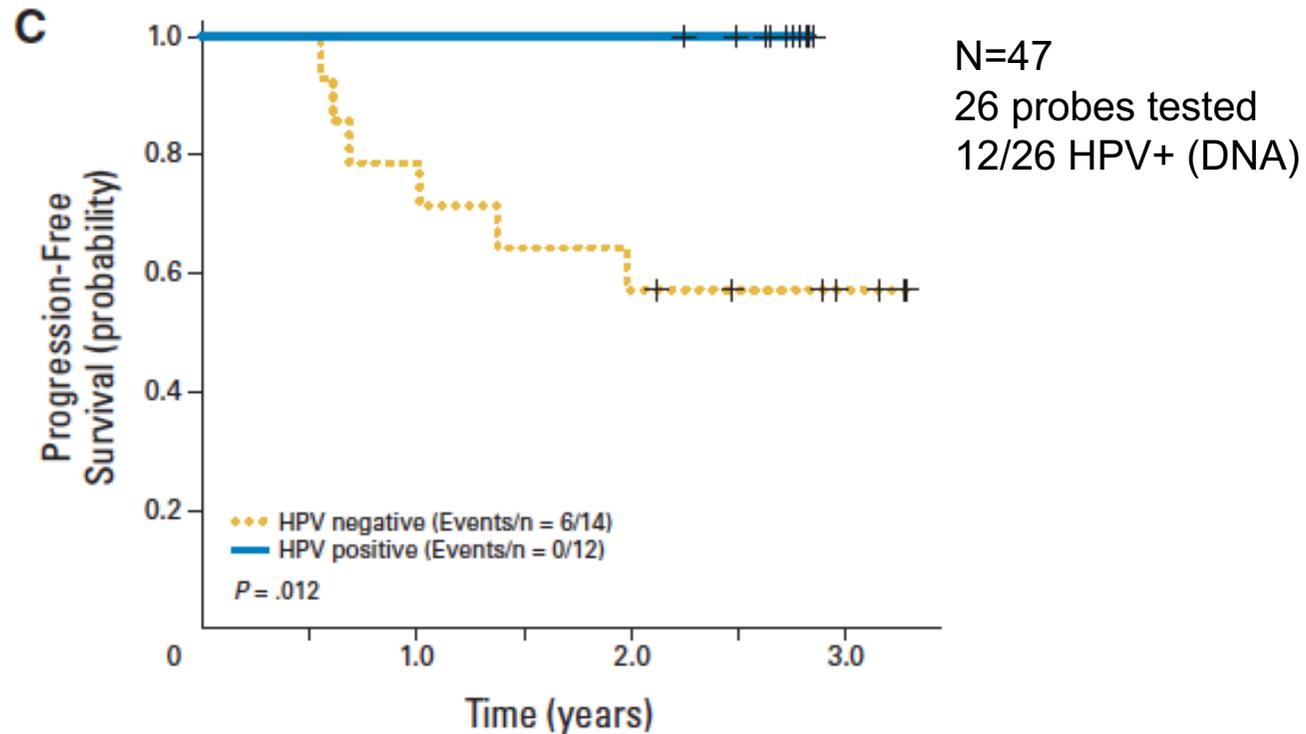


Advanced SCCHN with RCT treatment

OS improvement only in oropharynx carcinoma (USA)

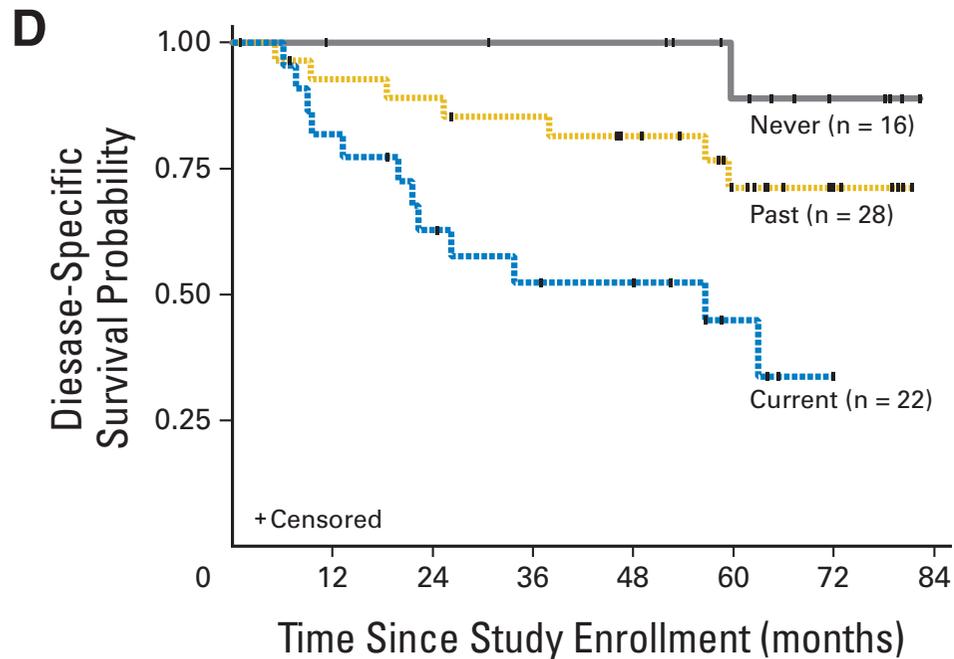


HPV+ SCCHN are explicitly chemosensitive



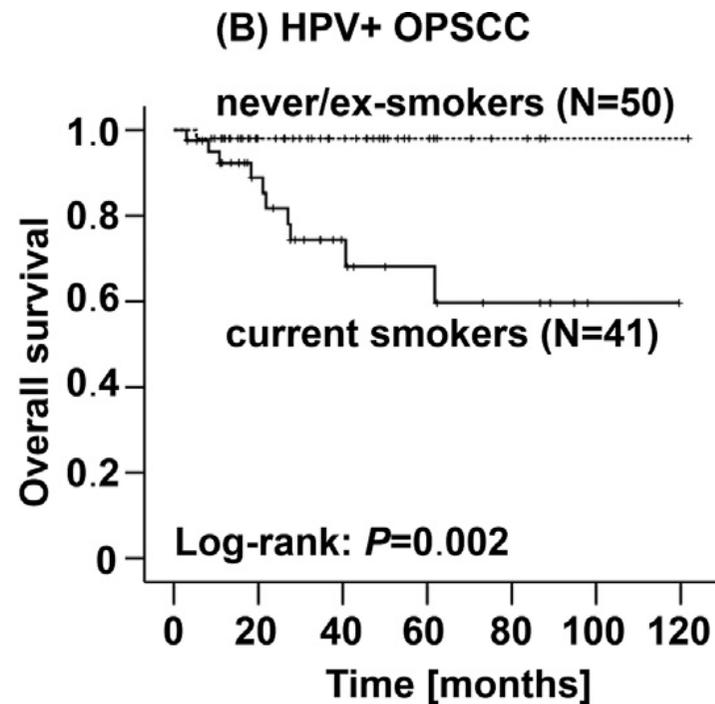
ICT: CET/Pacl/Carbo → RT or RCT or surgery

Smokers have a poor prognosis (IC+RCT)

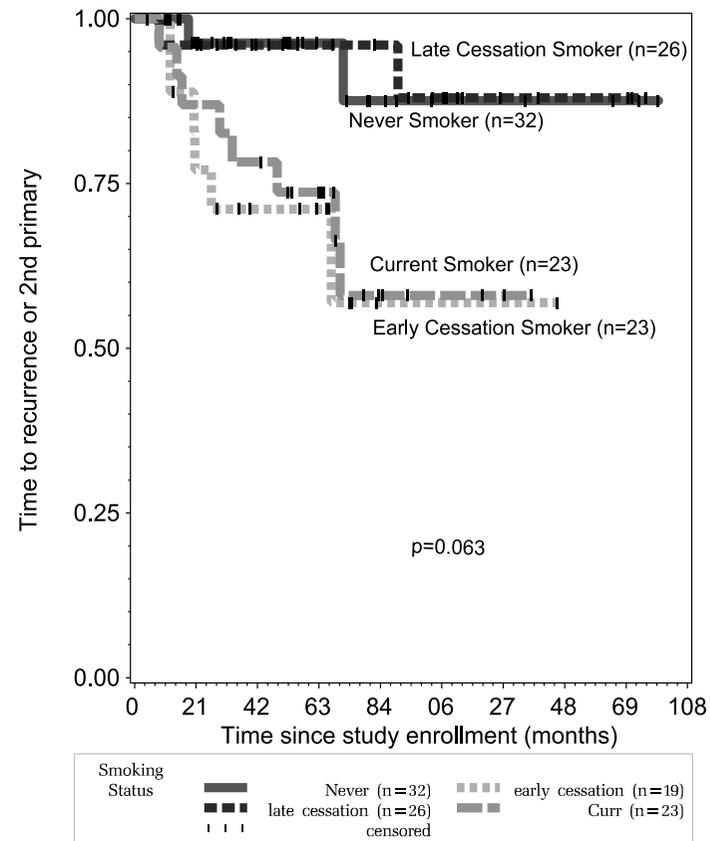


Worden et al. Journal of Clinical Oncology 2008;26:3138–46.

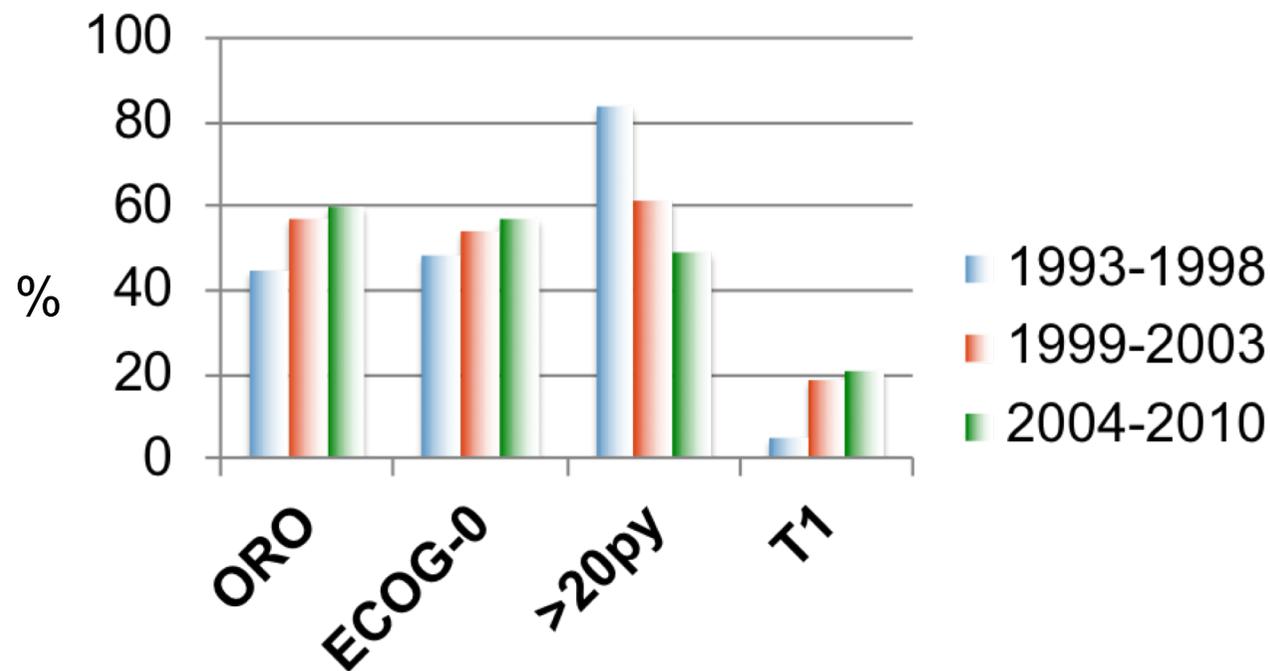
1 factor is too simple - smoking compromises outcome in HPV+ SCCHN



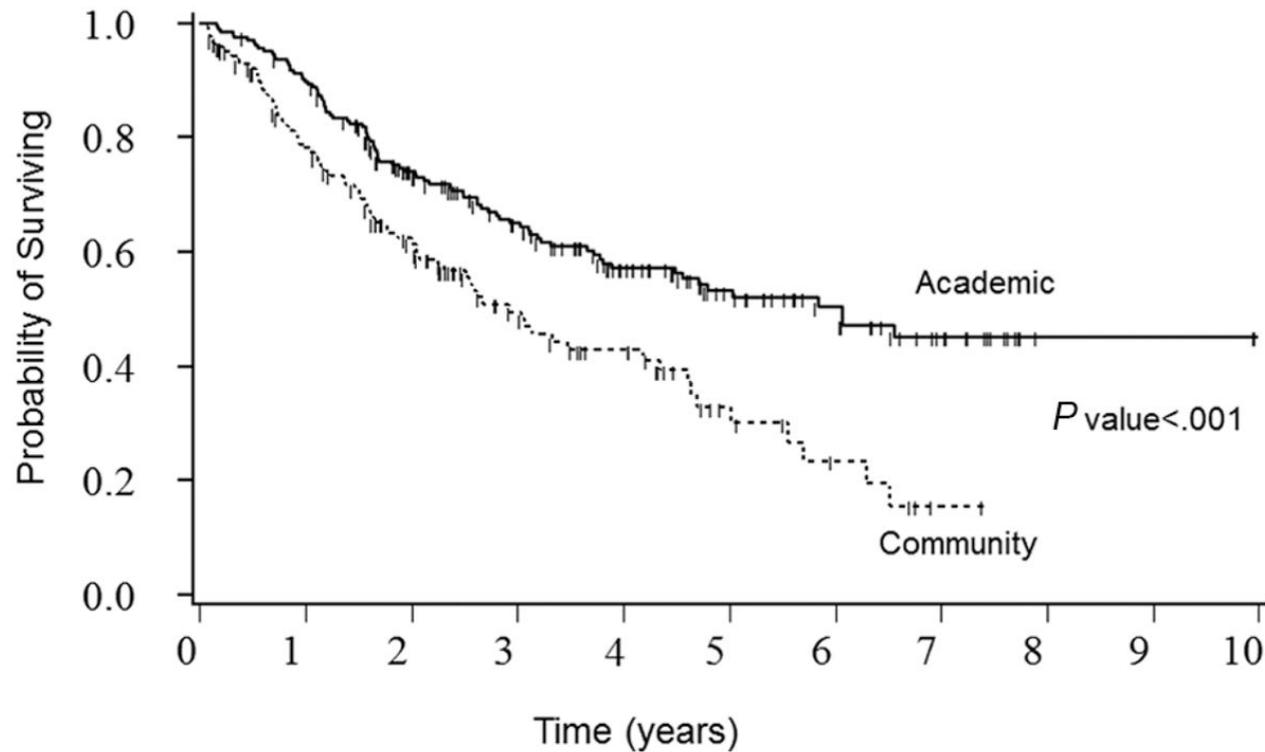
Tobacco cessation impacts HPV+ SCCHN



Early diagnosis & decline of tobacco (USA)



Academic centers do better



MDT have influence on Rx-decision

Type of change resulting from the Tumor Board presentation	All patients (N=120) n/N (%)
No change in either diagnosis or treatment	79/120 (66)
Change in either diagnosis or treatment	32/120 (27)
Change in treatment plan without a change in diagnosis	19/120 (16)
Change in diagnosis without a change in treatment plan	10/120 (8)
Change in both diagnosis and treatment	3/120 (3)
Other*	9/120 (7)

*Patients were categorized as “other” if they required further diagnostic workup (e.g. new imaging or biopsies) before a decision could be made

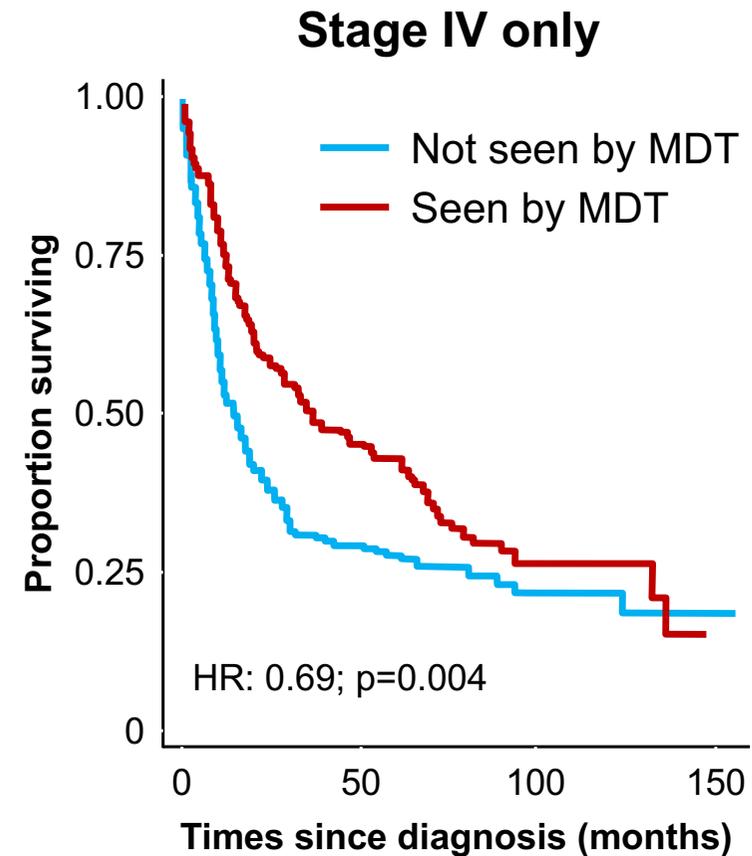
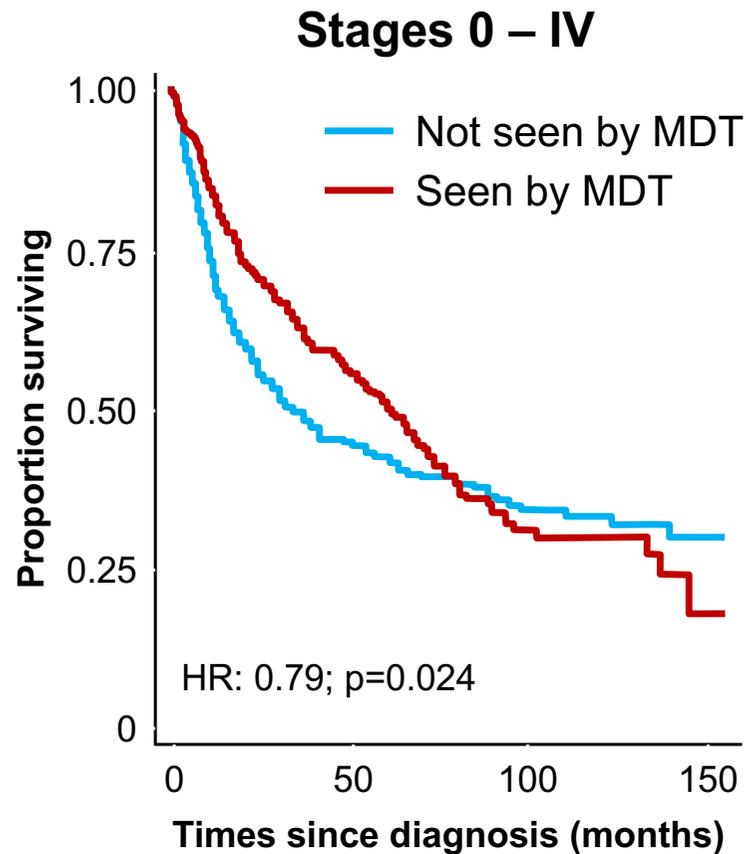
Changes in tumor diagnosis, staging, or treatment plan: 27%

Trend towards implementation of Multi disciplinary teams (MDT)

Country ¹	Legally mandatory	Recommended in guidelines
Australia		✓
Belgium	✓	
Canada		✓
France	✓	
Netherlands	✓	
UK		✓

1. State Government Victoria DoH. Multidisciplinary cancer care. 2012. Available at: www.gha.net.au/UploadLibrary/411214604MultidisciplinaryCancerCareLitReview/FINAL.pdf.

Better 5-y OS with MDTs



Conclusions

- HNC is a common disease on a global scale
- Alcohol, tobacco and HPV are key driver
- Non-smoking campaigns and vaccinations are important preventive strategies
- Survival improved in HPV+ oropharynx carcinoma only
- Biggest medical need for SCCHN with conventional hazards
- Multidisciplinary teams are a key ingredient in SCCHN treatments