

Head and Neck Cancer: Epidemiology

Professor Kevin Harrington

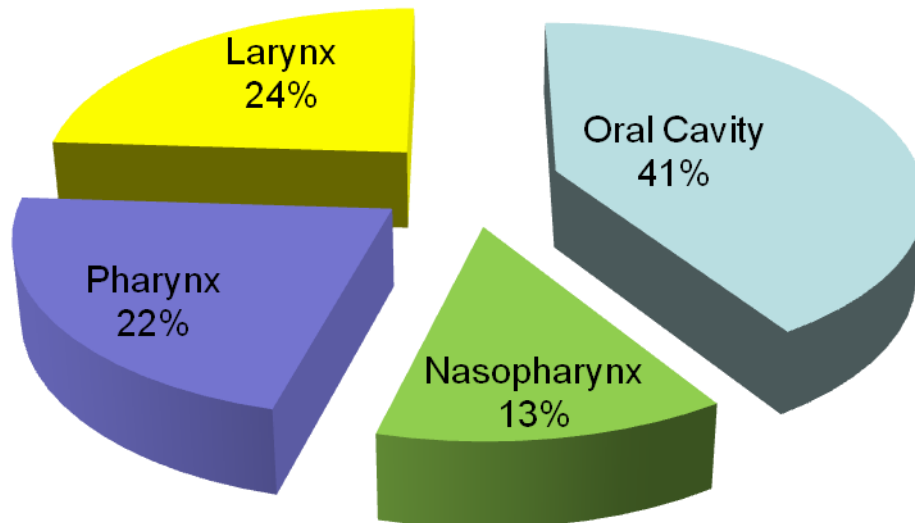
Joint Head of Division of Radiotherapy and Imaging

The Institute of Cancer Research/The Royal Marsden NIHR Biomedical
Research Centre Radiotherapy Theme Lead Team Leader, Targeted
Therapy Team



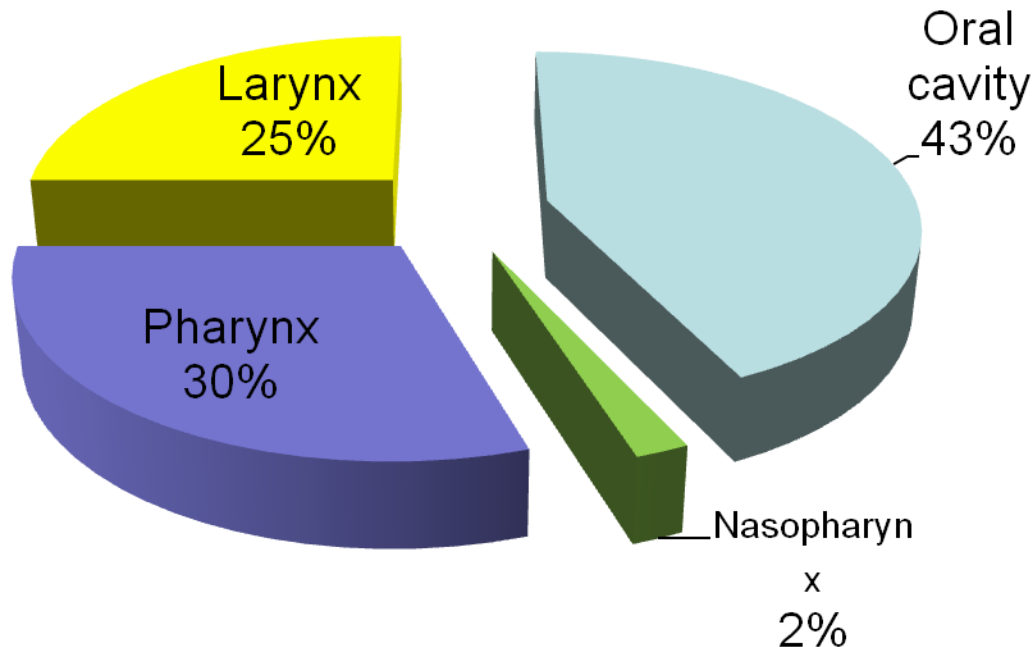
Head and Neck Cancer: Worldwide

- 640,000 cases/year
- 356,000 deaths per annum (55% mortality)
- 5% incidence of all cancers (excl. skin)
- 5% mortality of all cancers



Head and Neck Cancer: UK

- 8600 cases/year
- 2900 deaths per annum (33% mortality)
- 4% incidence of all cancers (excl. skin)
- 2% mortality of all cancers



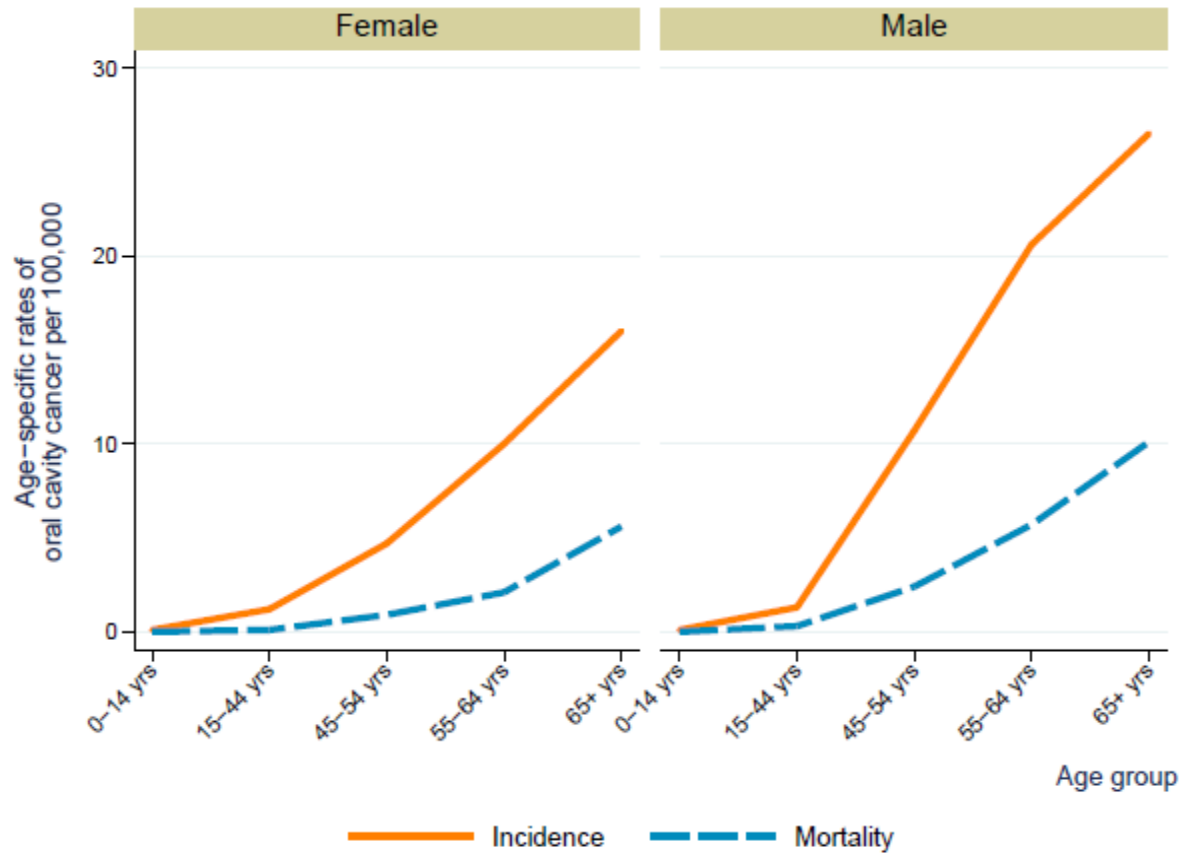
Head and Neck Cancer: Epidemiology

Geographical distribution - wide variations

- France (supraglottic, oral cancers)
- Hong Kong (nasopharyngeal cancers)
- India (oral cancers)



Head and Neck Cancer: Epidemiology



Data sources:

IARC, Globocan 2008. Age-specific data from GLOBOCAN 2008 were obtained from IARC, personal communication. For specific estimation methodology refer to http://globocan.iarc.fr/DataSource_and_methods.asp.



Head and Neck Cancer: Aetiology

- >75% overall risk related to tobacco and alcohol
- Betel quid (tobacco, betel leaf, slaked lime, areca nut)
- Mate (**yerba mate** , *Ilex paraguarensis*)
- Dental hygiene - questionable
- Occupational exposure - wood dusts (RR-2.4), organic chemicals (RR-1.9), coal products (RR-1.7-2.3), nickel, formaldehyde (RR-1.6), chromium
- Viruses - HPV (25-75%) , EBV (WHO III NPC), HIV (5%).



Head and Neck Cancer: Aetiology

International Head and Neck Cancer Epidemiology Consortium (INHANCE) dataset

- Diet : Fruit (RR 0.52), Vegetables (RR 0.66), Red meat (RR 1.4)
- Coffee: (RR 0.6 > 4 cups/day) , Tea –no effect
- Exercise: low (RR 0.78), moderate (RR 0.67) and high (RR 0.53).



Head and Neck Cancer: Aetiology

BRITISH MEDICAL JOURNAL

LONDON SATURDAY JUNE 26 1954

THE MORTALITY OF DOCTORS IN RELATION TO THEIR SMOKING HABITS

A PRELIMINARY REPORT

BY

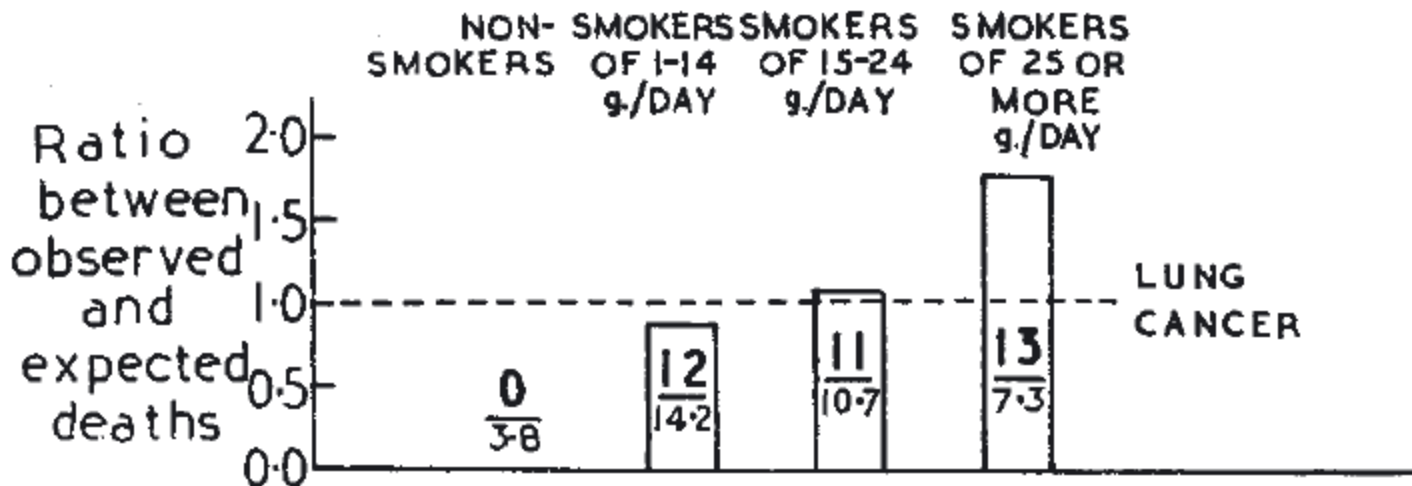
RICHARD DOLL, M.D., M.R.C.P.

Member of the Statistical Research Unit of the Medical Research Council

AND

A. BRADFORD HILL, C.B.E., F.R.S.

Professor of Medical Statistics, London School of Hygiene and Tropical Medicine; Honorary Director of the Statistical Research Unit of the Medical Research Council



Head and Neck Cancer: Aetiology

Tobacco

- 30 known carcinogens (polycyclic aromatic HCs, nitrosoamines)
- Tar content directly correlates with oral cancer risk
- Unfiltered > filtered cigarettes
- Inhalation > no inhalation
- RR laryngeal cancer = 15.5:1 men, 12.4:1 women
- After stopping smoking, RR reaches control at 15 yrs
- Passive smoking RR 1.6.



Head and Neck Cancer: Aetiology

Tobacco

- Black (air-cured) vs blond (flue-cured)
- Increased alkalinity of air-cured causes more irritation
- Black tobacco associated more with UADT lesions
- Blond tobacco associated more with LADT lesions
- Smokeless tobacco (paan, snuff).



Head and Neck Cancer: Aetiology

Smoking : Issues

- Increased co-morbidity
- Poor treatment tolerance
- Increased mortality

Hazard ratios for mortality from head and neck cancer

Smoker	
Never smoked	1.00*
Current smoker	1.66 (1.32, 2.09)
Previous smoker	1.22 (0.94, 1.58)



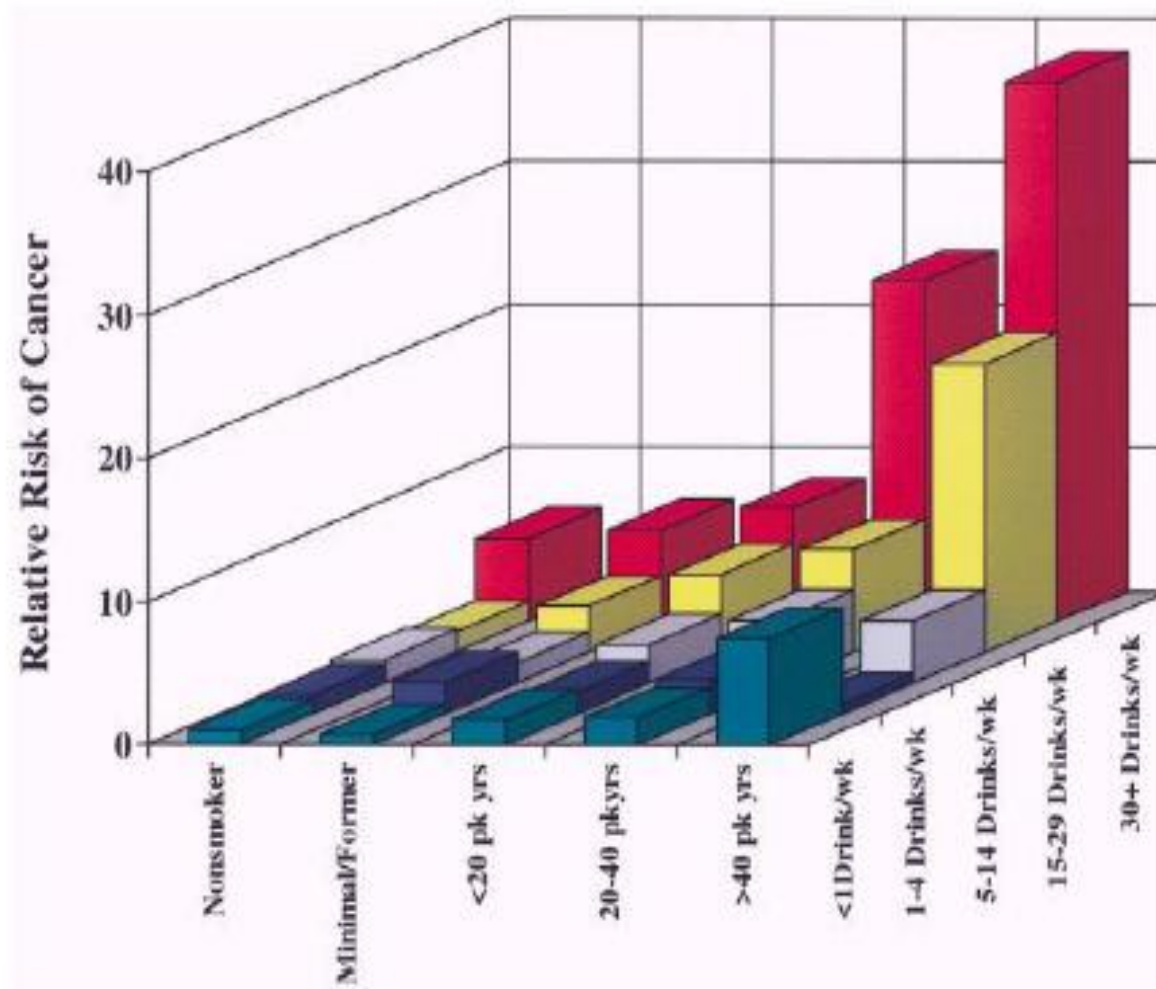
Head and Neck Cancer: Aetiology

Alcohol

- Independent activity
- Glottic vs. supraglottic cancers more likely in non-drinkers
- Effect compounded by tobacco consumption
- Synergistic effect
 - ? local solvent
 - cytochrome P450 activation
 - decrease activity of DNA repair enzymes.



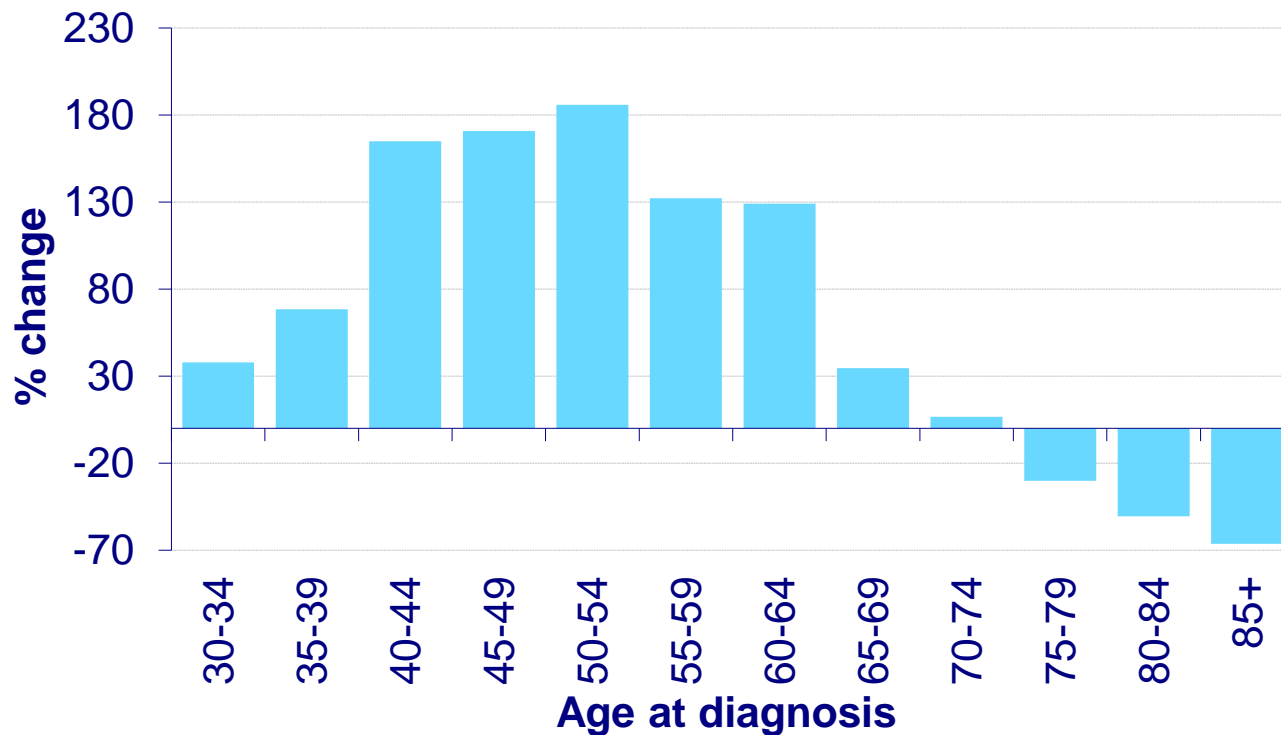
Interaction between tobacco and smoking



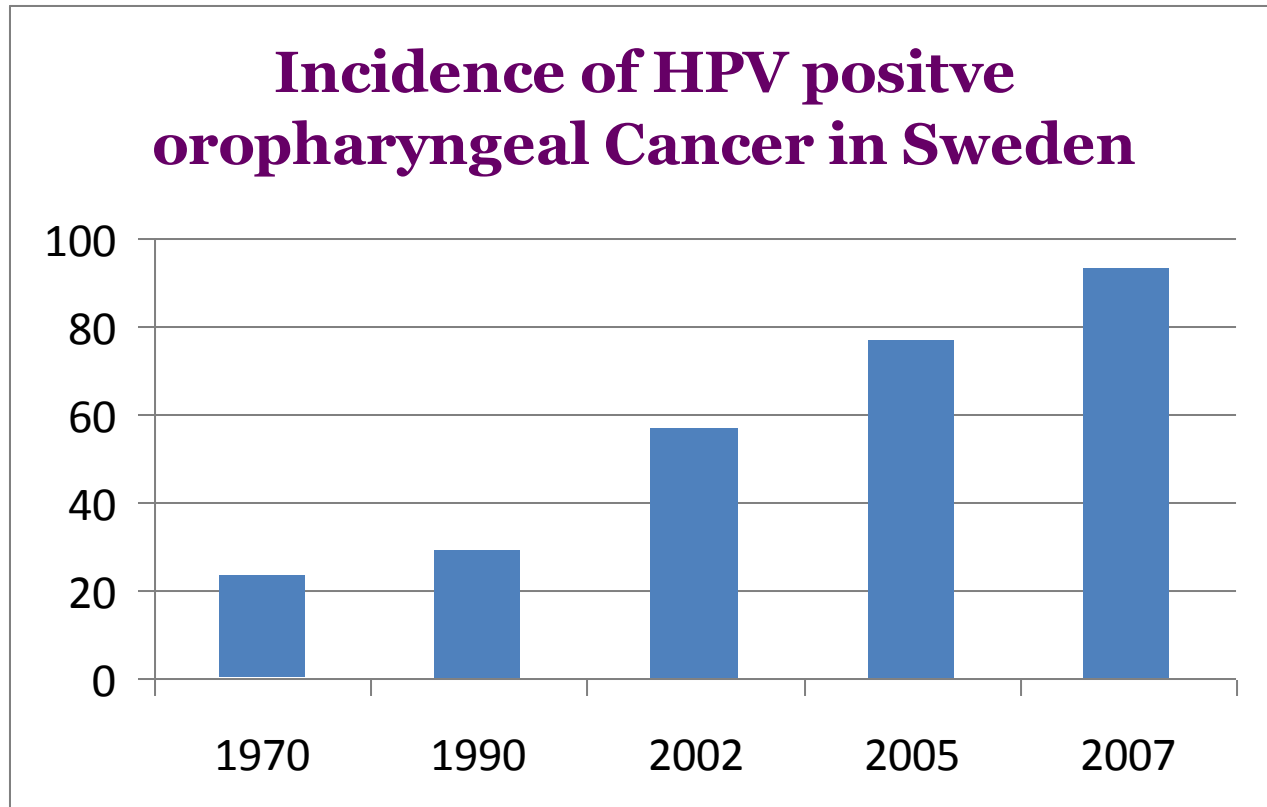
HPV and Head and Neck Cancer

Incidence of tonsillar cancer increased from 28 in 1997 to 703 in 2007

Percentage change in incidence rates for oral cancer



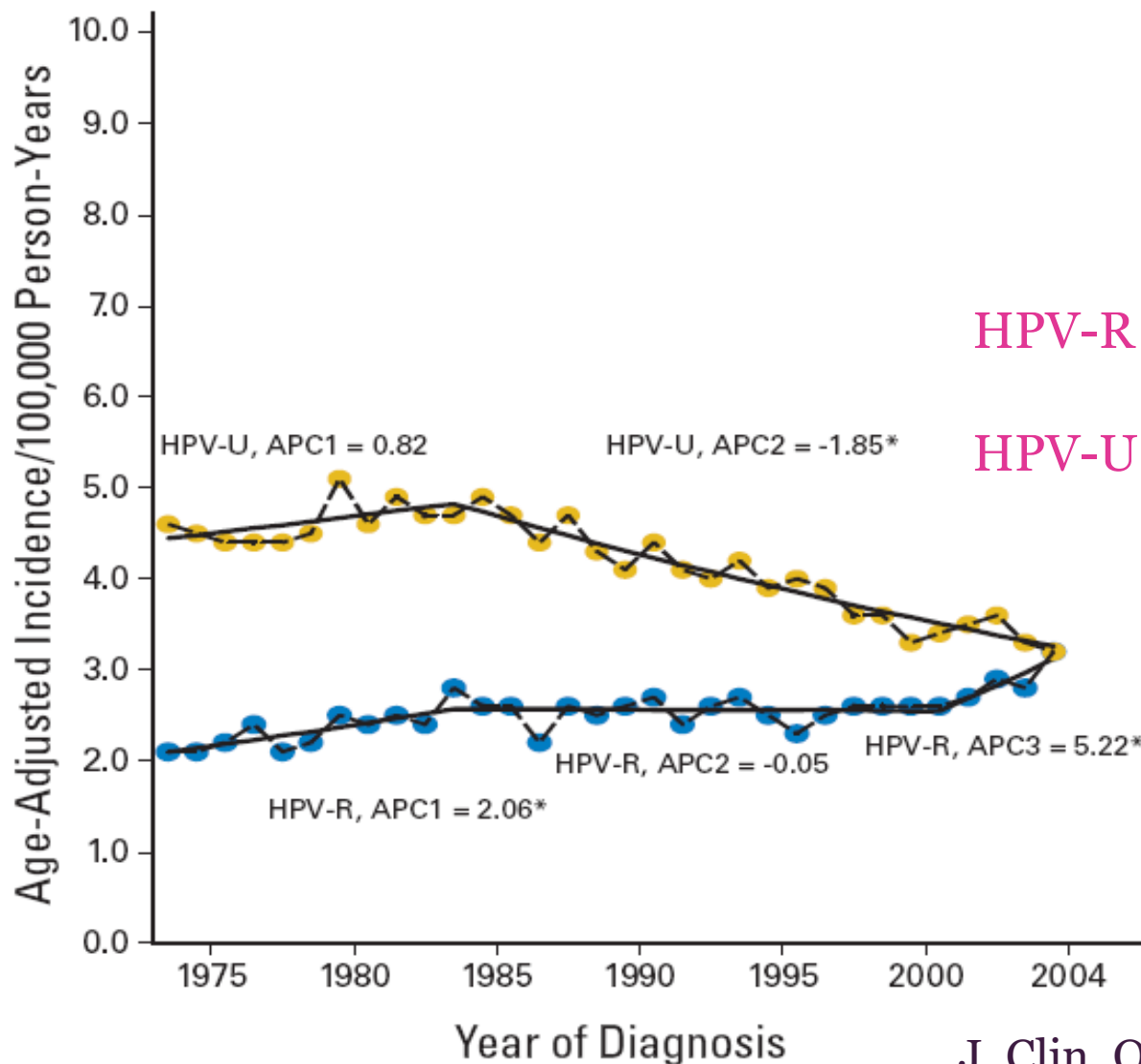
Incidence of HPV positive oropharyngeal Cancer in Sweden



Int J Cancer. 2009 Jul 15;125(2):362-6.

Int J Cancer. 2009 Jul 15;125(2):362-6.

Age-adjusted Incidence by Calendar Year of Diagnosis for HPV induced cancers



HPV-R tumours increasing

HPV-U tumours decreasing



HPV and Head and Neck Cancer

- 40-60% of oropharyngeal cancers HPV+ve
- Sexually Transmitted through oral sex
- Prevalence in UK women with normal cytology 8.9%
- HPV has been detected in the genital tract of 72% of Men in UK
- Patients tend to be younger at diagnosis
- Usually non-smokers.



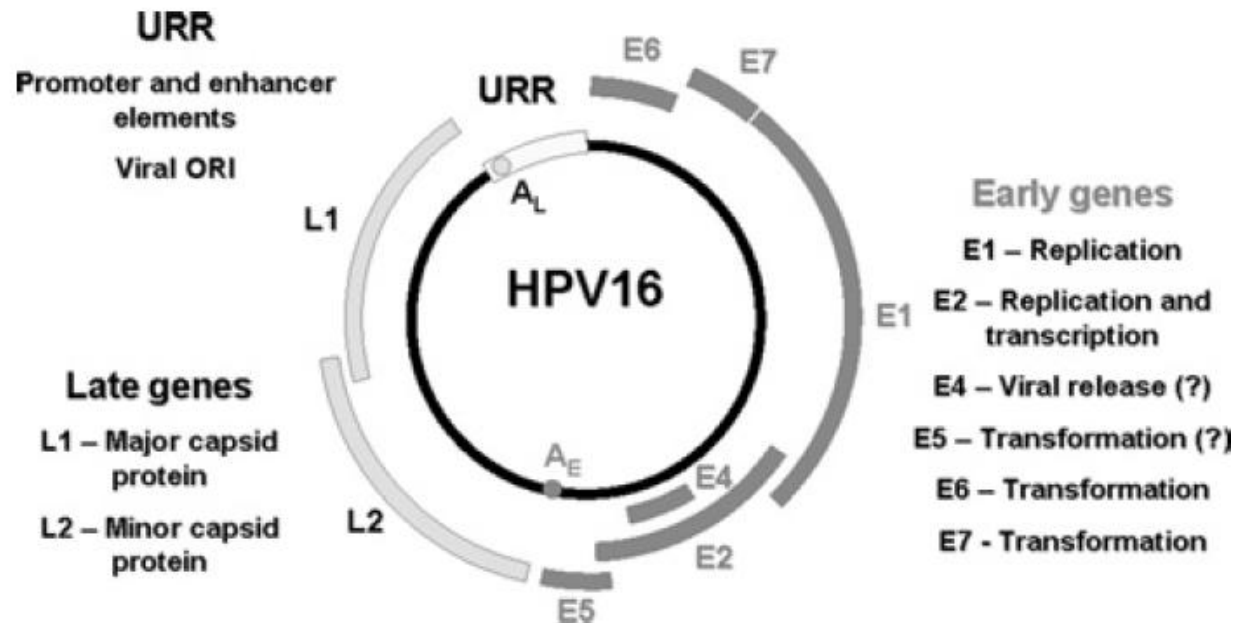
Risk Factors for HPV-Induced Cancers

- Lifetime partners >5 – OR = 3.0
- Coitarche < 19 yrs – OR = 2.4
- Oral sex before 21 yrs – OR = 2.3
- No condom with oral sex – OR = 3.7
- Infreq condom use – OR = 2.4
- HPV16 L1 sero+ve – OR = 32
- Oral HPV16 – OR = 15

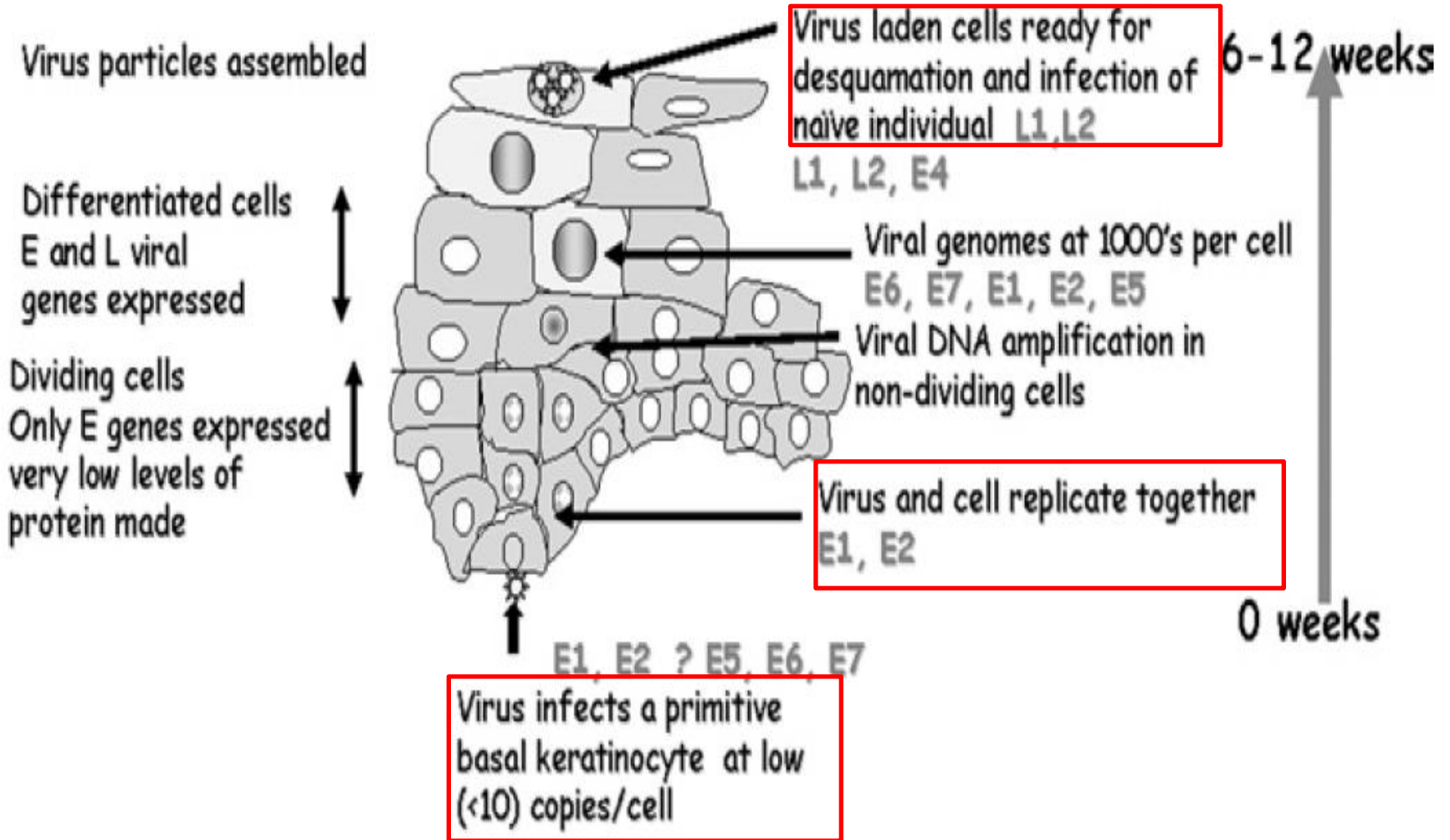


HPV Genome

- Small double-stranded DNA viruses
- Absolute species specificity
- Cutaneous or mucosal predilection
- Low- and high-risk types.



HPV Life Cycle



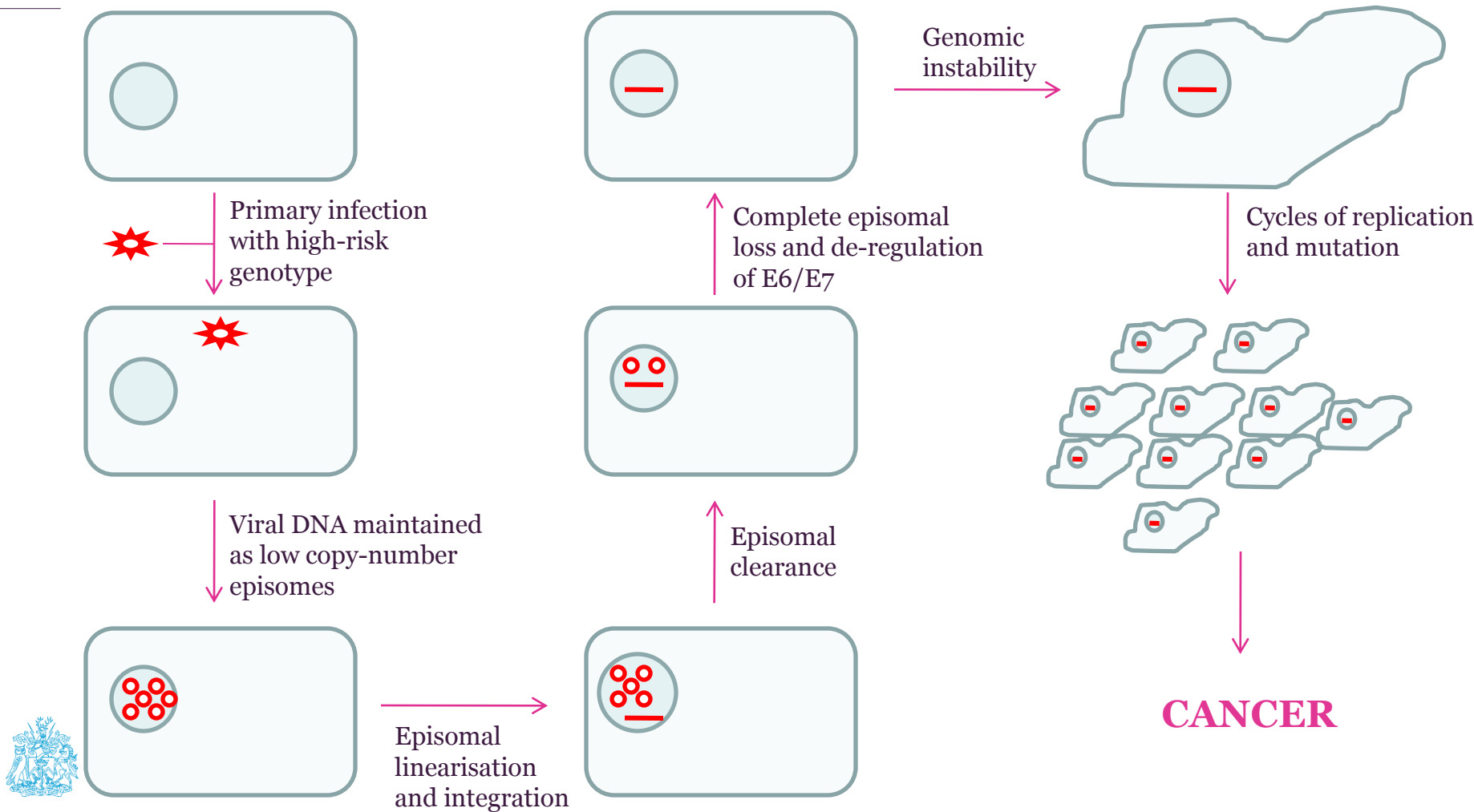
No viraemia, no cytolysis or death, long infectious cycle

Natural History of HPV Infection

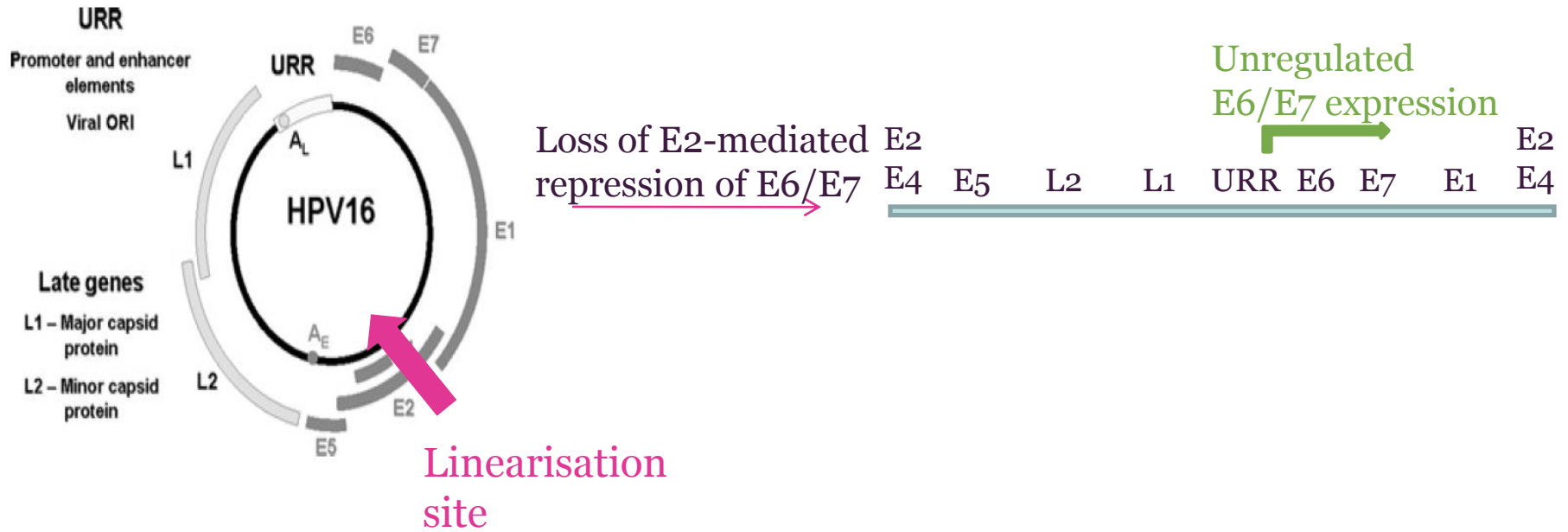
- Oropharyngeal mucosa most prone
- Said to infect tonsillar crypt.
- Relatively immune silent
- Immune response against L1 protein
- Sero-positivity indicates previous infection.



Events Leading to Selection of Aggressive Clones



Molecular Effects of Integration (1)

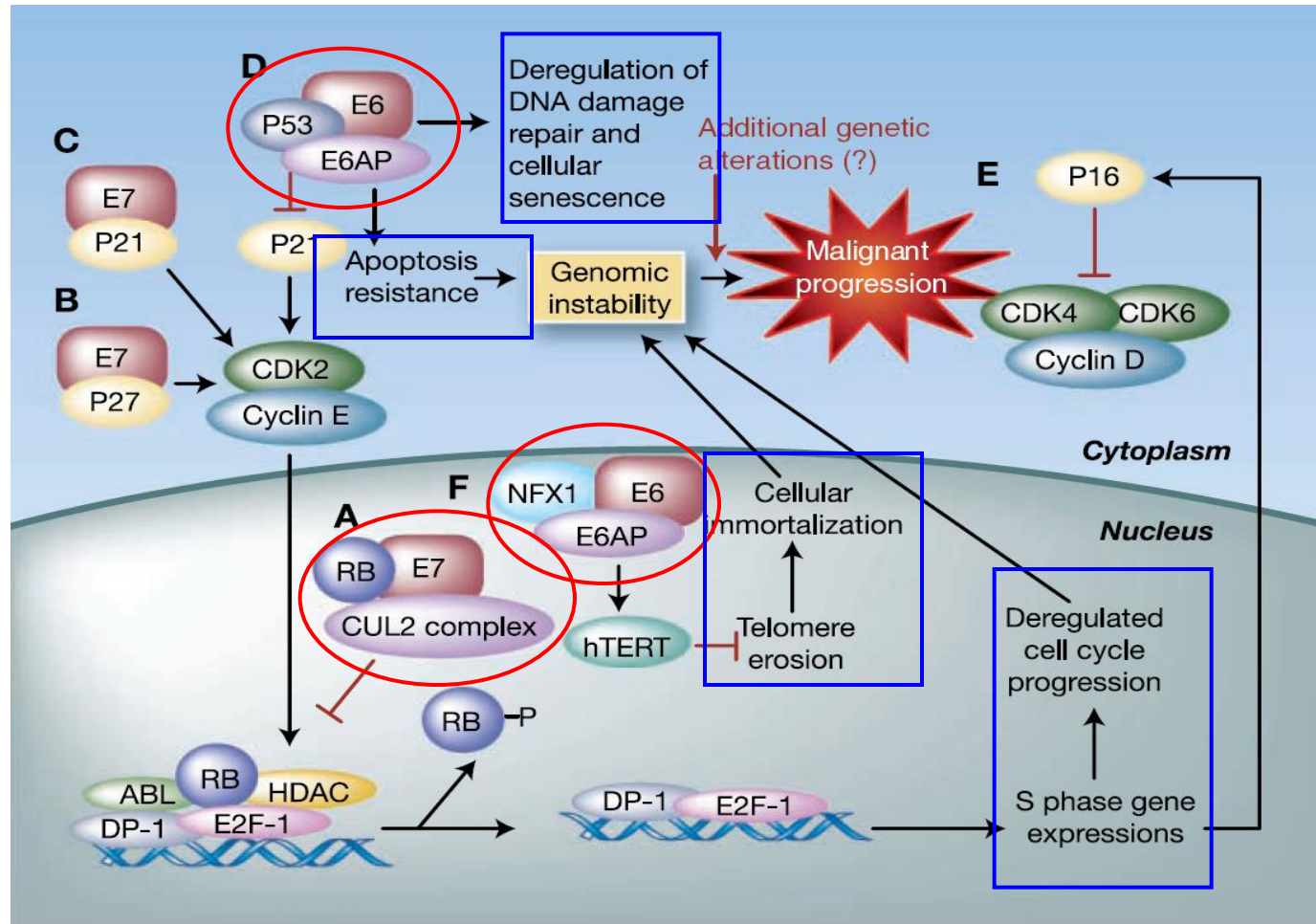


De-repressed E6/E7 drive cell division, genomic instability and abrogation of apoptosis



Human Papillomavirus in Head and Neck Cancer: Its Role in Pathogenesis and Clinical Implications

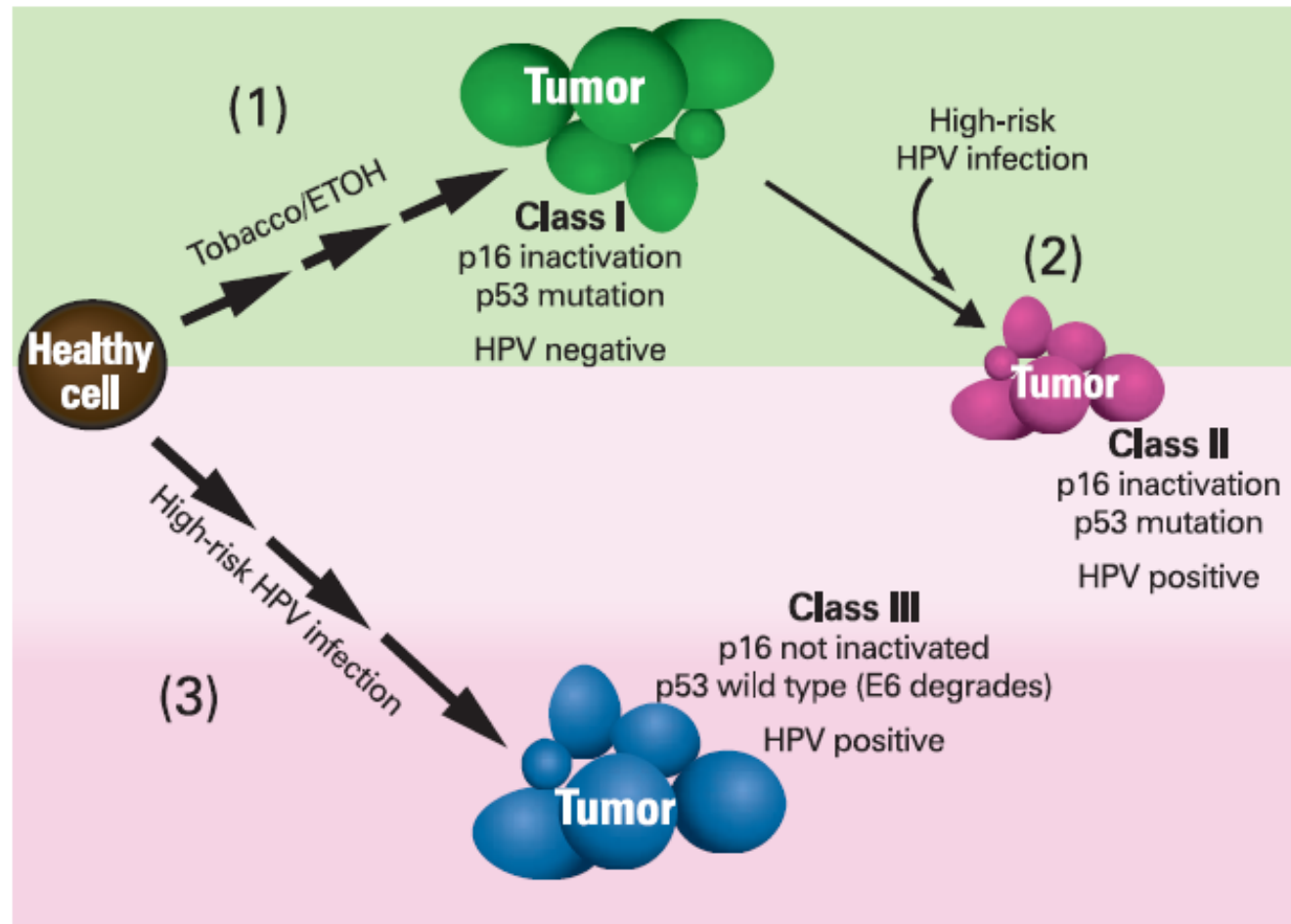
Christine H. Chung^{1,2} and Maura L. Gillison³



Molecular Classification Identifies a Subset of Human Papillomavirus–Associated Oropharyngeal Cancers With Favorable Prognosis

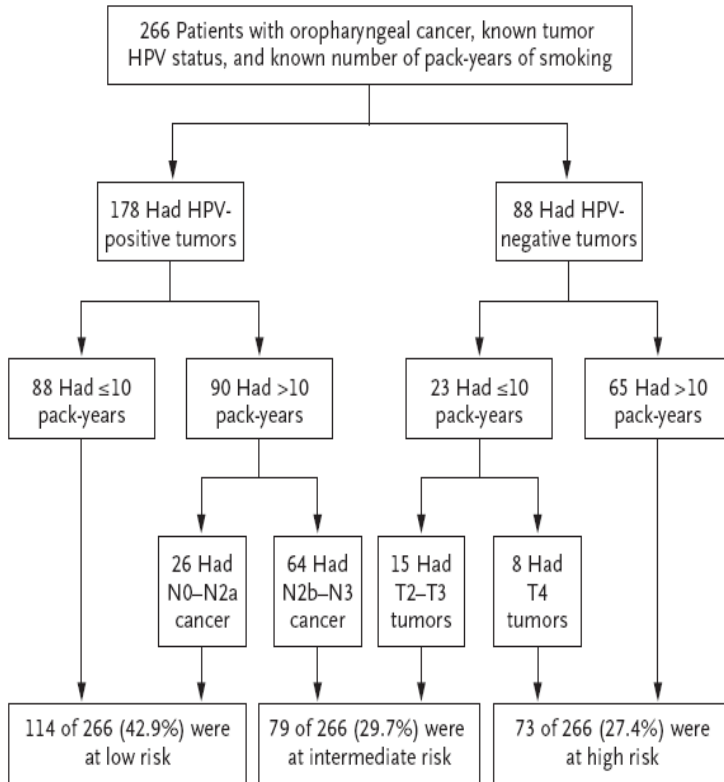
Paul M. Weinberger, Ziwei Yu, Bruce G. Haffty, Diane Kowalski, Malini Harigopal, Janet Brandsma, Clarence Sasaki, John Joe, Robert L. Camp, David L. Rimm, and Amanda Psyrri

J Clin Oncol 24:736-747. © 2006 by American Society of Clinical Oncology

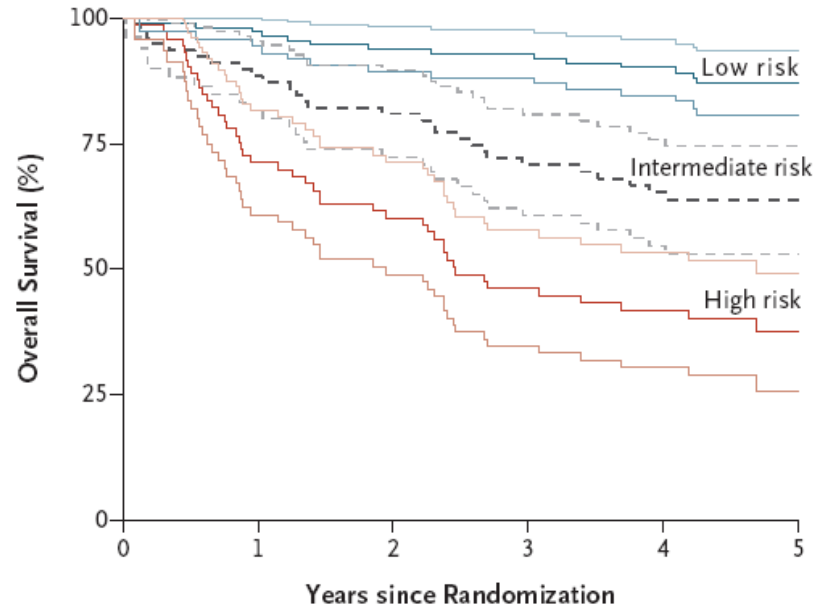


Delineation of Prognostic Groups

A



B



No. at Risk

	0	1	2	3	4	5
Low risk	114	111	106	102	95	46
Intermediate risk	79	70	64	54	44	24
High risk	73	52	43	33	28	8



Conclusion

- HNC curable in more than 50%
- Change in the disease paradigm.
- Epidemic of oropharyngeal cancers (HPV related)
- Focus on smoking and alcohol cessation should continue as these are relatively simple targets for primary prevention
- A three pronged strategy of smoking and alcohol cessation and vaccination against HPV will dramatically reduce the incidence of this cancer.

