

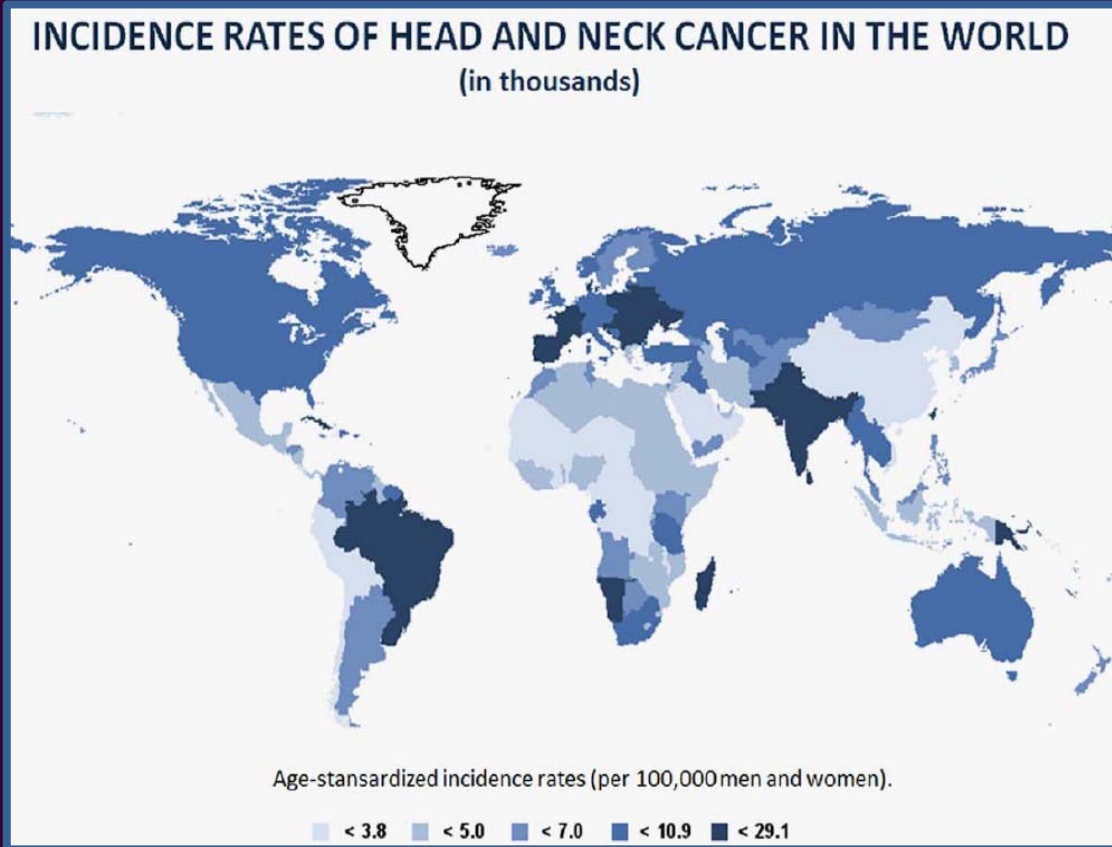
Update of the role of Human Papillomavirus in Head and Neck Cancer

2013 International & 12th National Head and Neck Tumour Conference
Shanghai, 11-13 Oct 2013

Prof. Paul KS Chan

Department of Microbiology

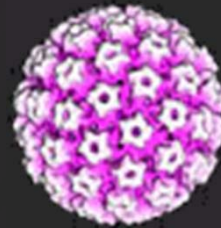
IARC GOBALCAN 2008



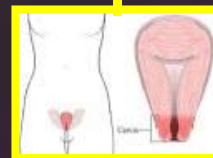
550,300 head & neck cancer / yr

Head & neck cancer ranks:
7th in men
13th in women

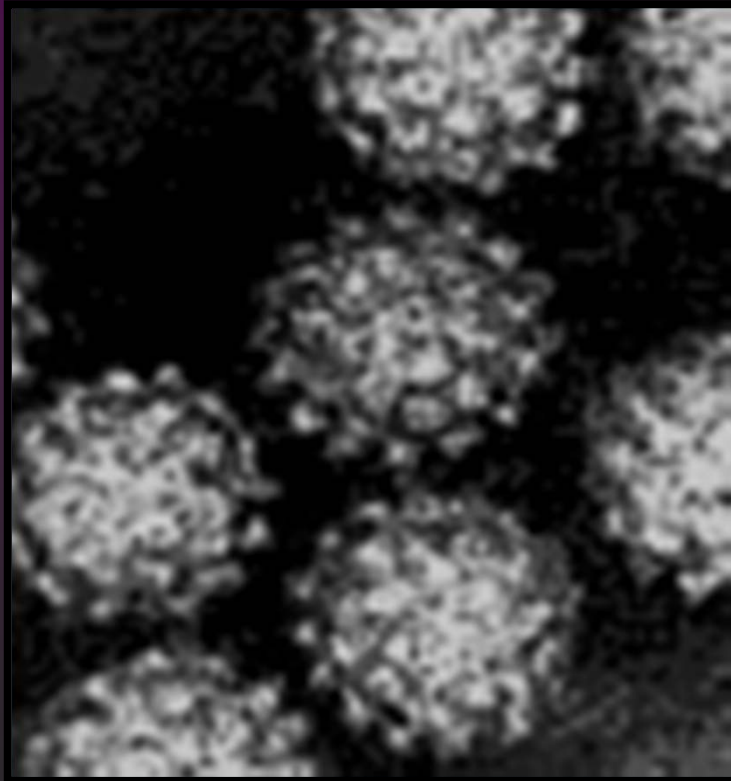
Human Papillomaviruses HPV



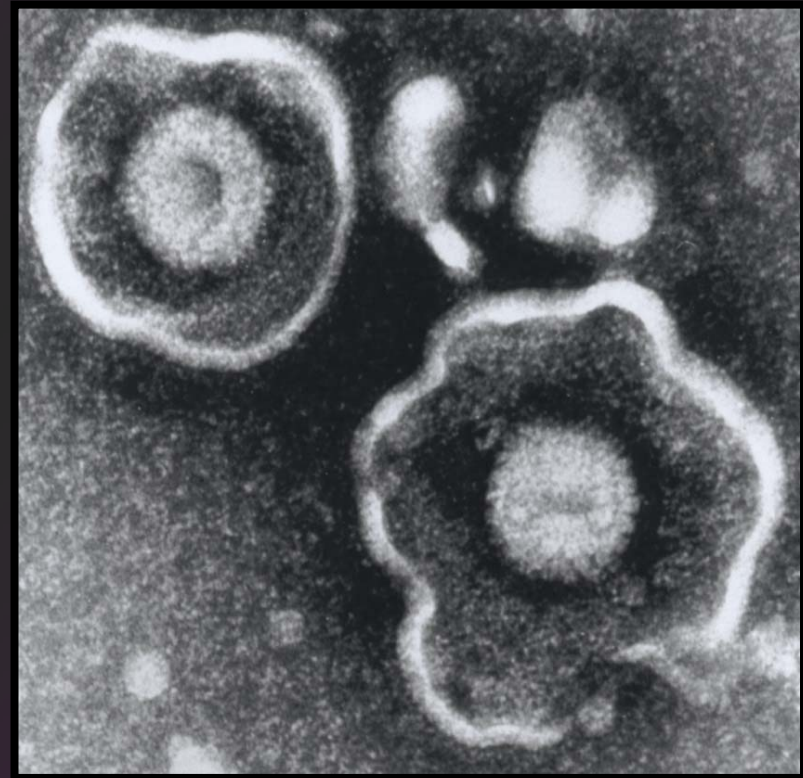
Oropharyngeal cancer



Vaginal cancer
Vulval cancer
Anal cancer
Penile cancer



Non-enveloped
Papillomavirus



Enveloped
Herpesvirus

Transmission

Cutaneous HPV:

- Direct skin contact
 - Fomite / environment
- 

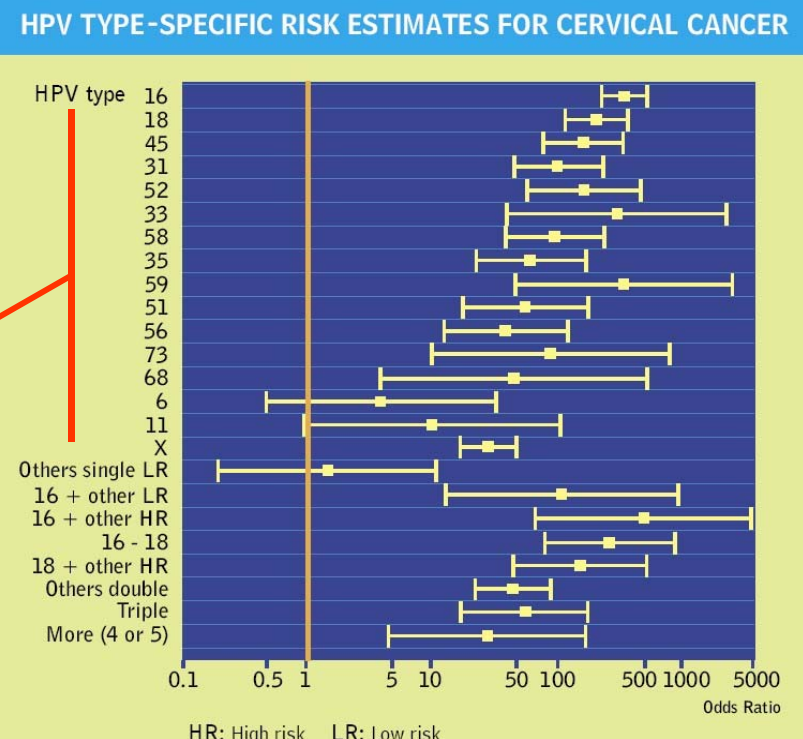
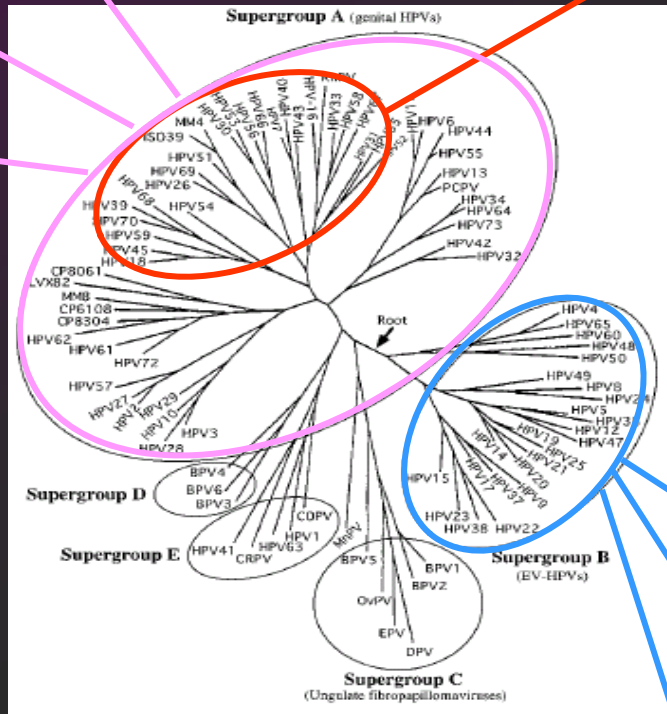
Mucosal (Anogenital / oral) HPV:

Sexual:

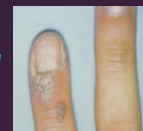
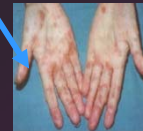
- Through sexual intercourse
- Genital–genital, manual–genital, oral–genital
- Condom use reduce the risk, but it is not fully protective

Nonsexual:

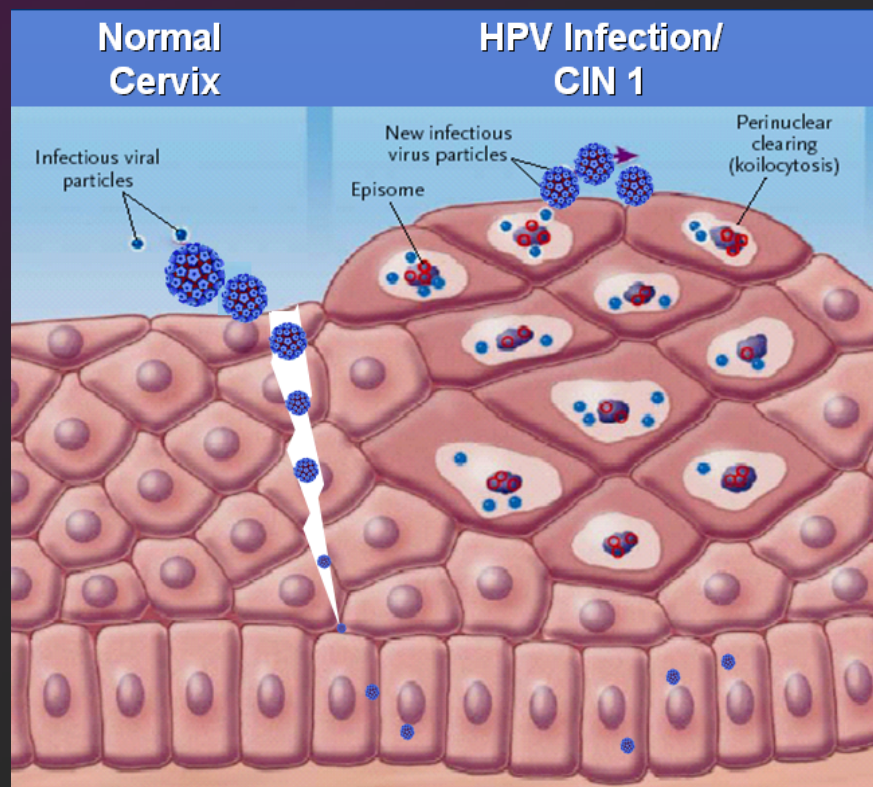
- Mother to newborn (vertical transmission)
 - Fomites / environment
- 



N Engl J Med 2003; 248:518-27



Previous HPV infection
does not result in long-term protection

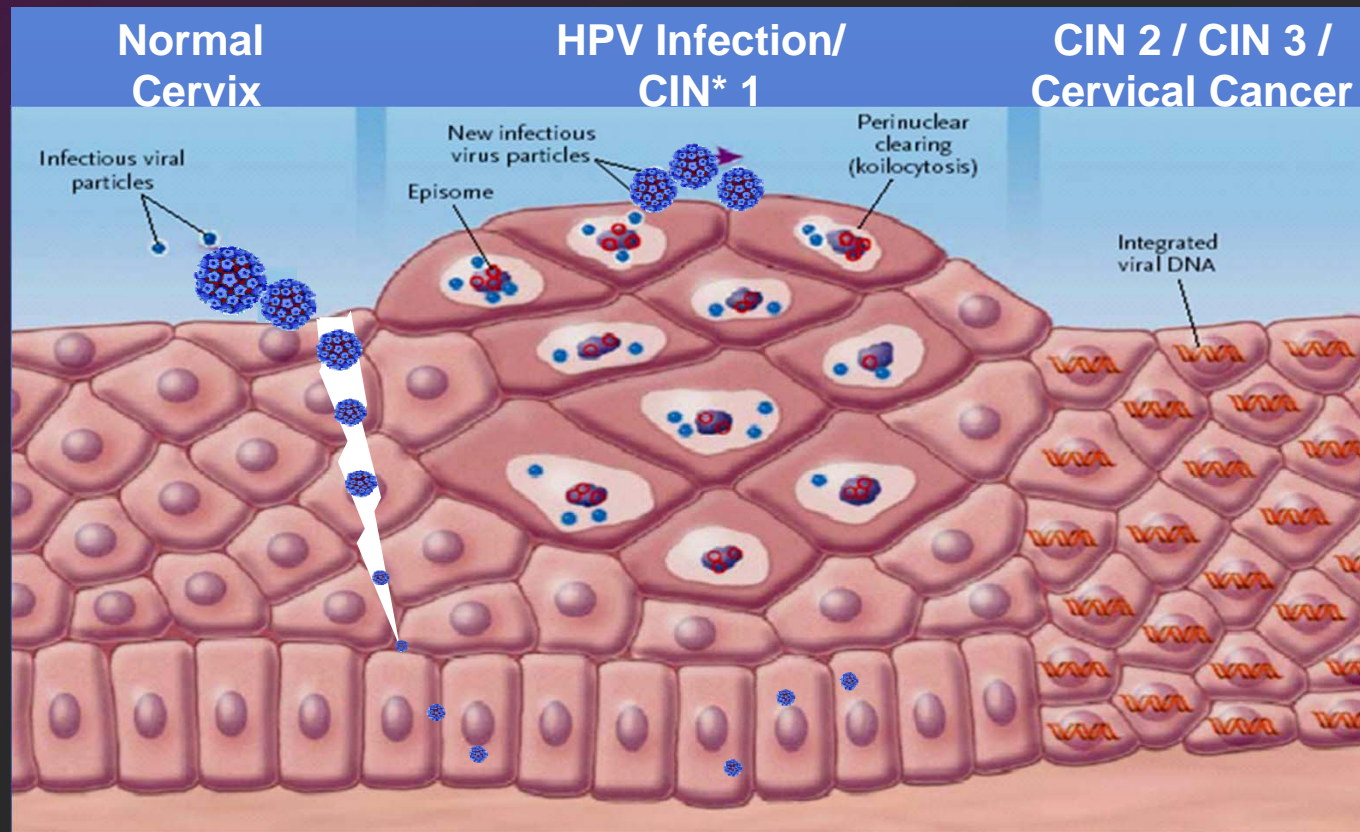


- Poor immune stimulator
- Only ~60% seroconvert
- Low level of serum antibody

Productive
infection

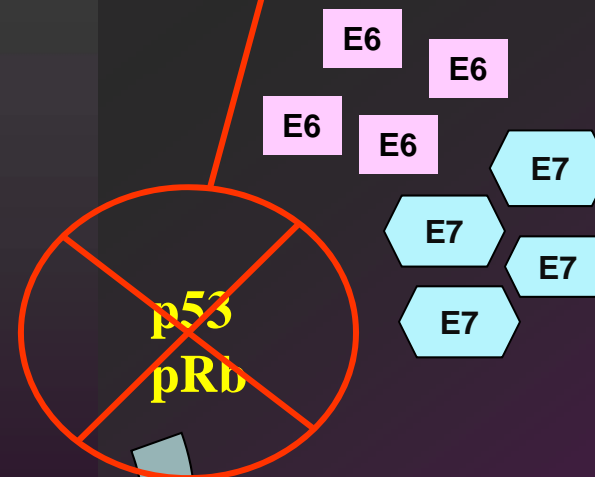
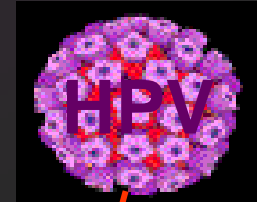
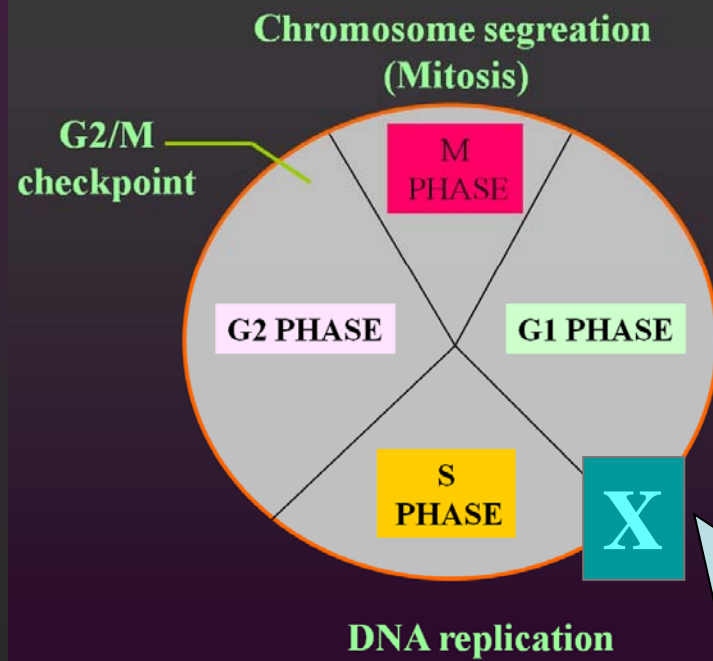


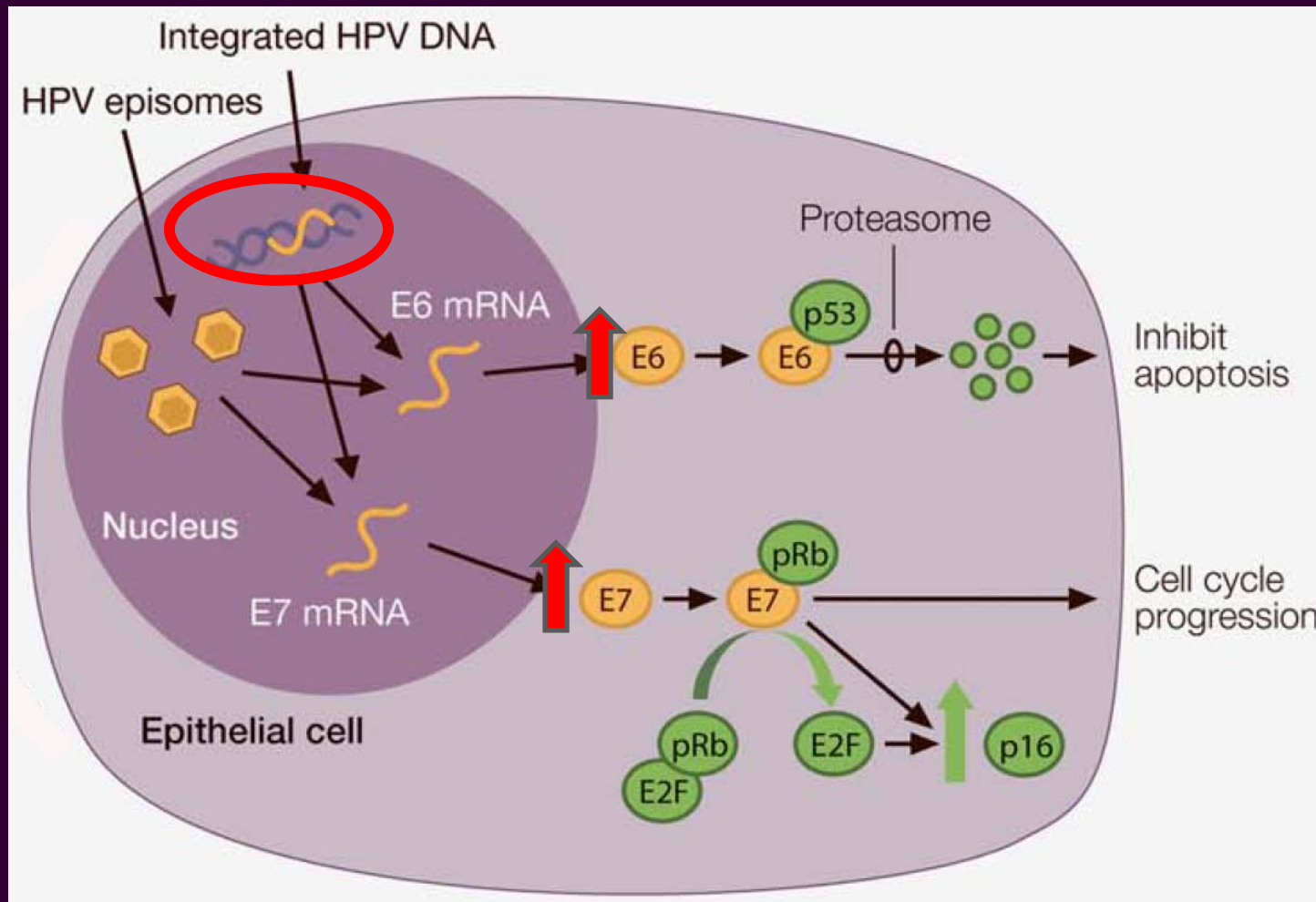
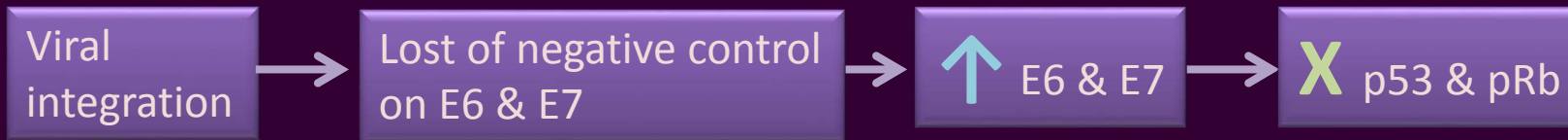
Transforming
infection



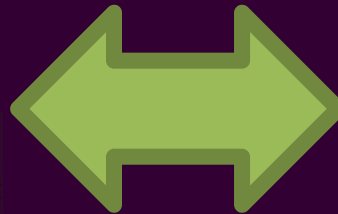
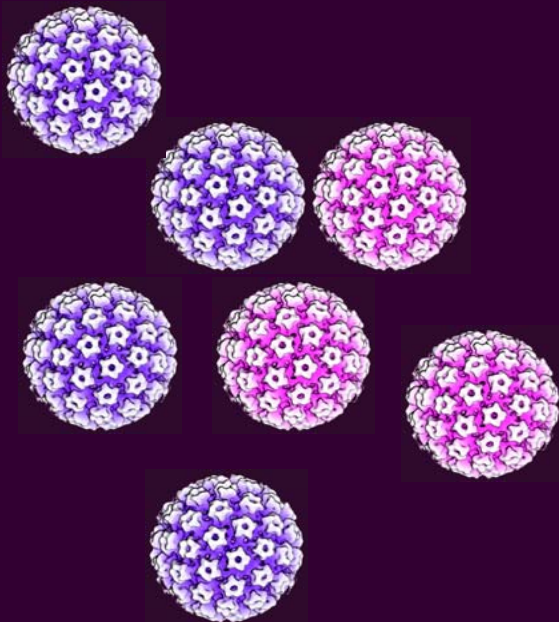
*CIN = cervical intraepithelial neoplasia
Adapted from Goodman A, Wilbur DC. *N Engl J Med.* 2003;349:1555–1564.

Normal Cell Cycle Control

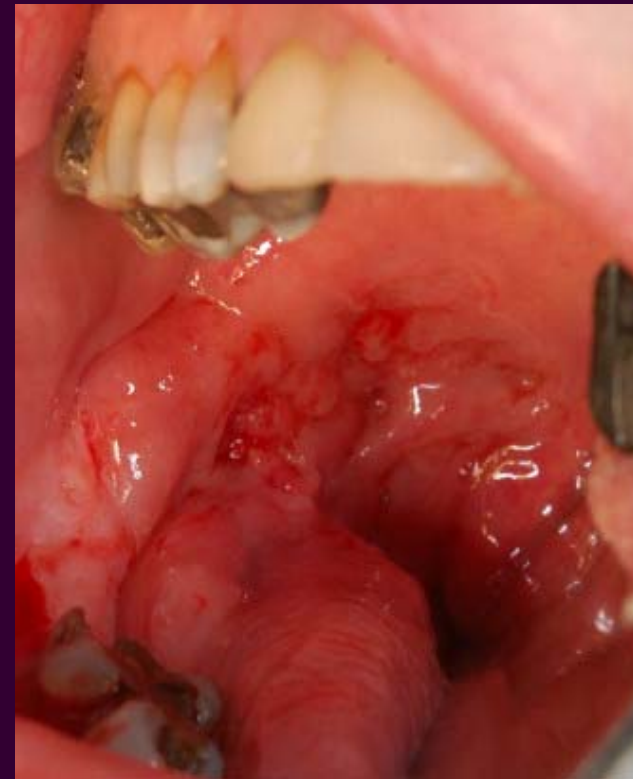




Human papillomavirus



Oropharyngeal cancer



How common is oral HPV infection ?

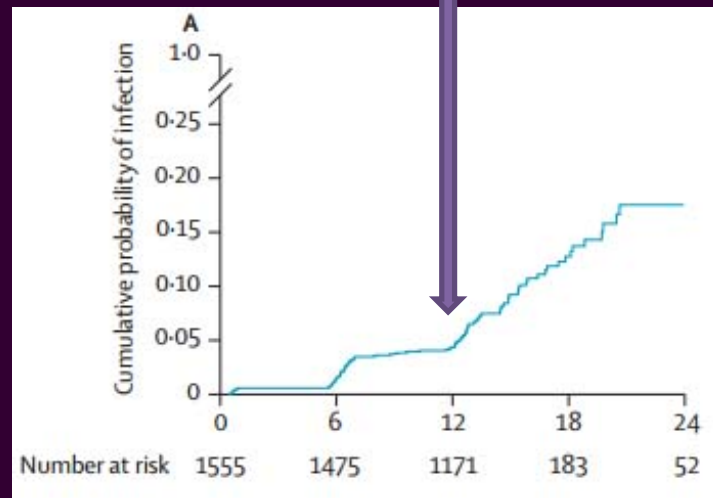
HPV Infection in Men (HIM) study

Brazil, Mexico, USA

1626 men, age 18-73 yr, healthy, HIV-negative

HPV test every 6 month

4.4% acquired oral HPV (all types)
1.7% acquired oral **oncogenic** HPV



Acquisition rate of oncogenic HPV / 1000 person-months

Oral: 2.5

Genital : 22.2

Anal : 3.7



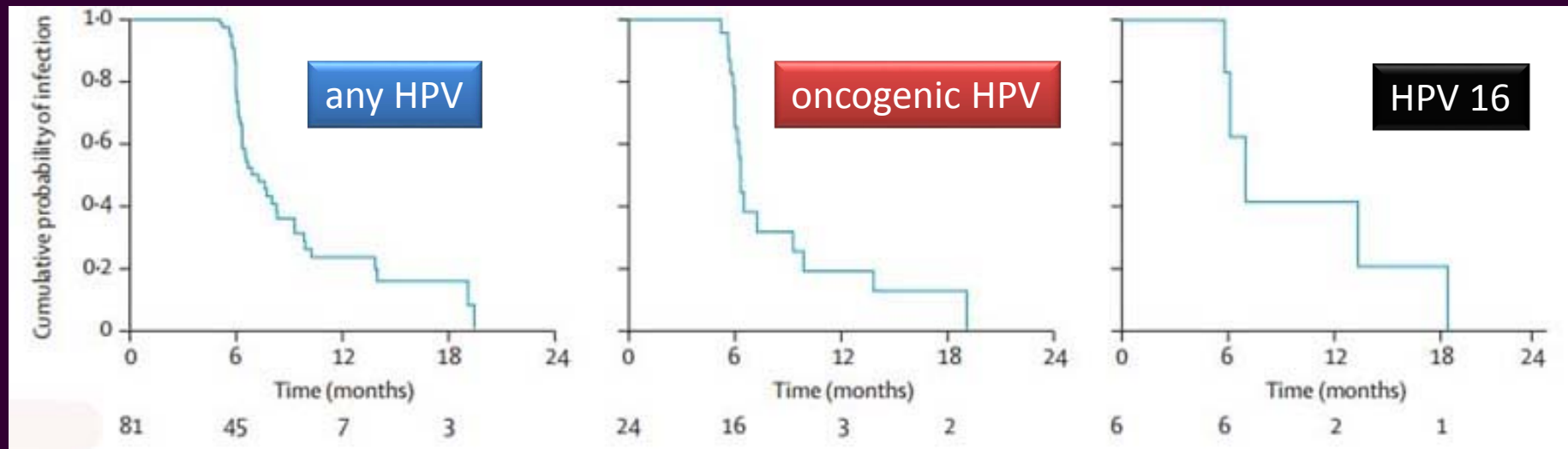
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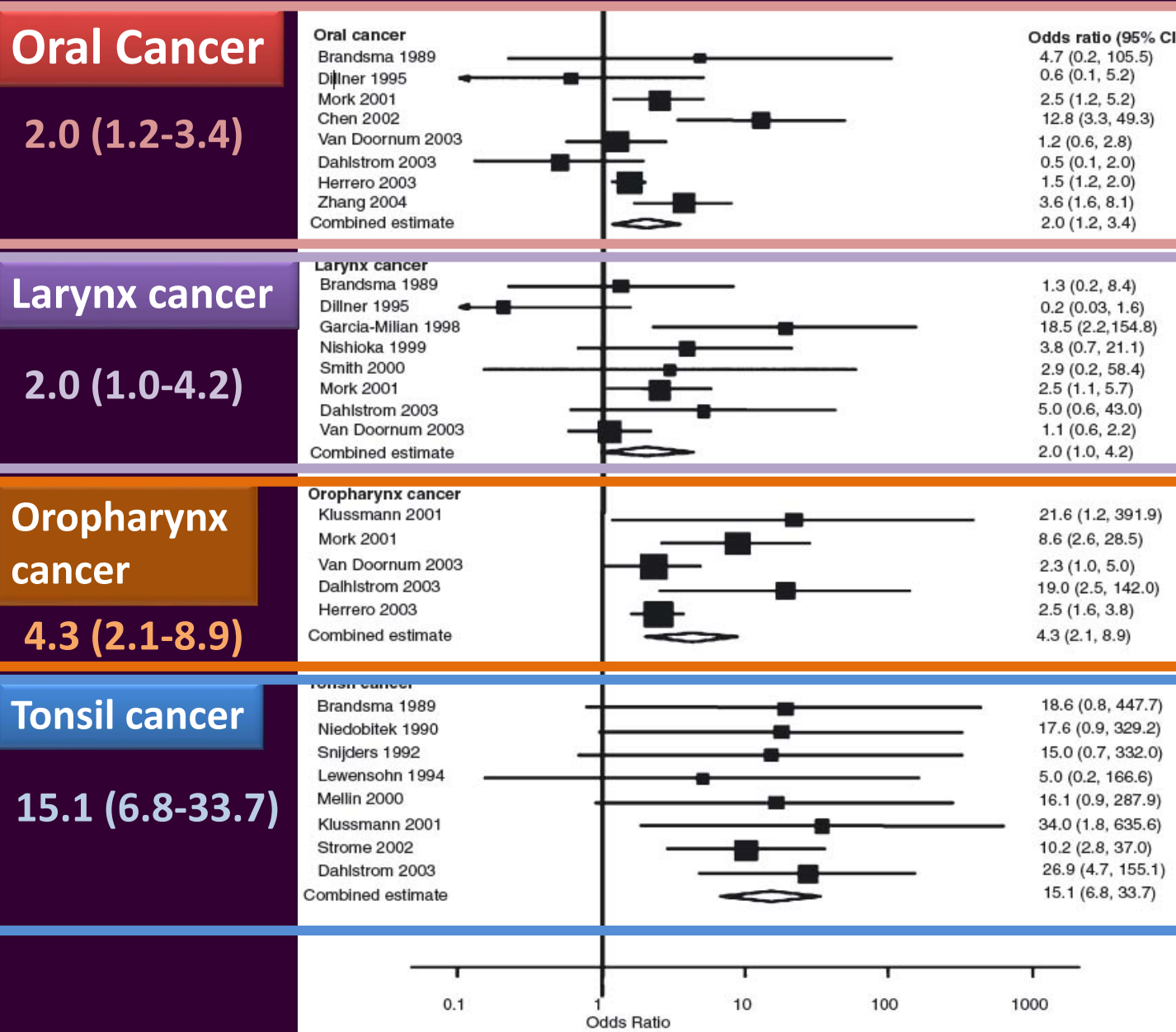
HPV test every 6 months

Clearance :
 Most cleared < 1 yr
 Similar across HPV groups

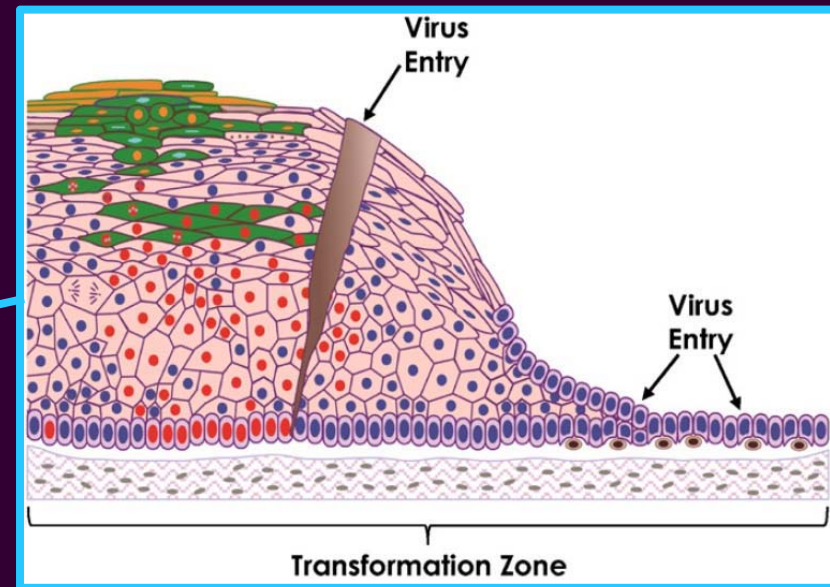
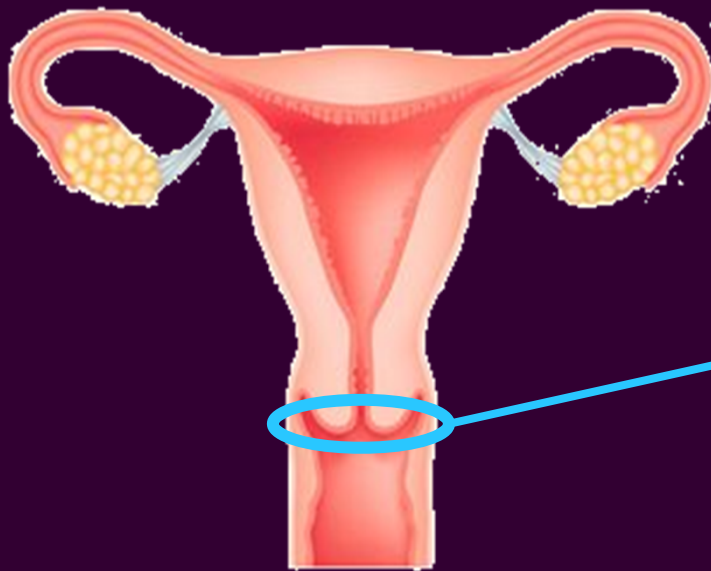


Any preferred anatomical sites within H & N region?

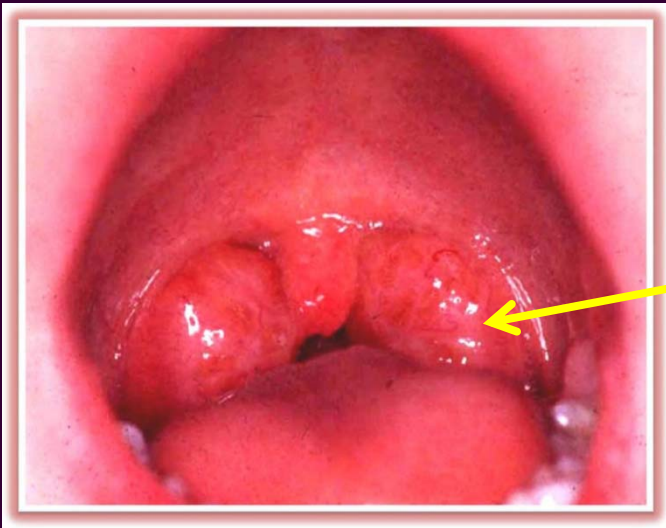
Association of head & neck squamous cell cancer with HPV16



Cervical cancer develops from transformation zone



Tonsillar cancer develops from crypts



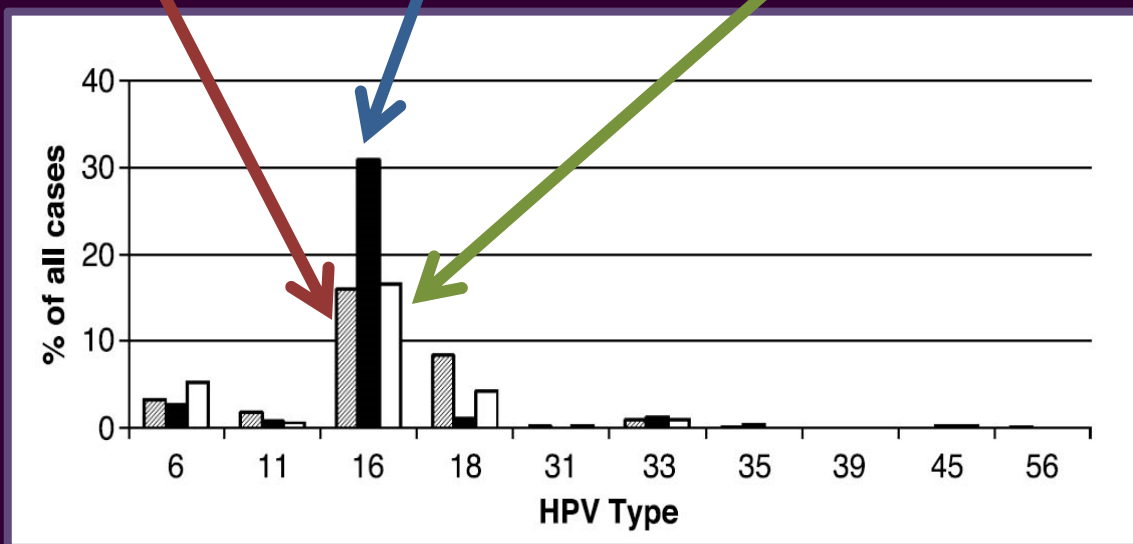
Which HPV type ?

HPV type distribution in head and neck cancer

Oral cavity SCC
2642 cases

Oropharyngeal SCC
969 cases

Laryngeal SCC
1435 cases



HPV16 among HPV-positive SCC

Oropharyngeal : 86.7%

Oral cavity: 68.2%

Laryngeal: 69.2%

HPV18 among HPV-positive SCC

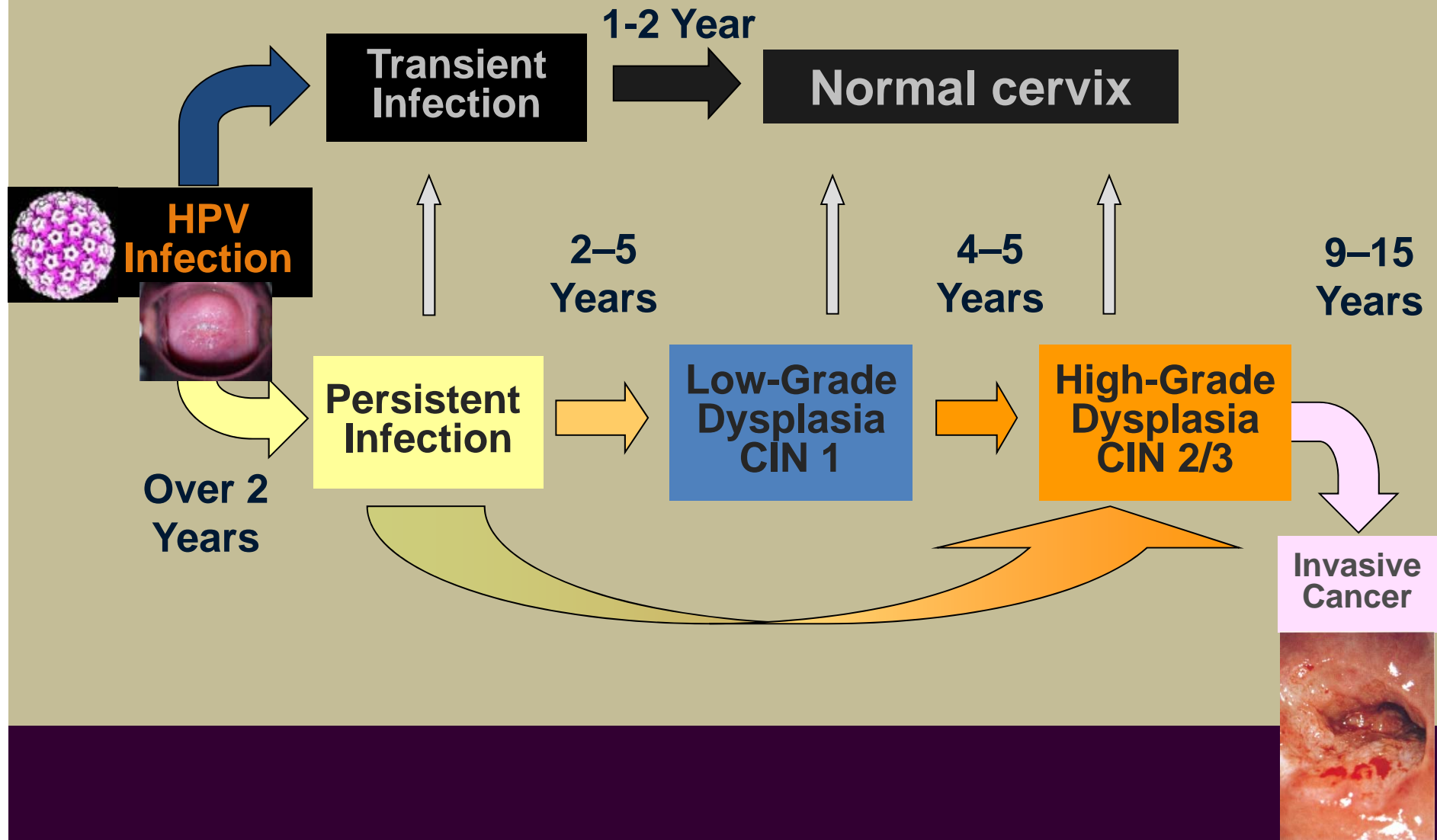
Oropharyngeal : 1.0%

Oral cavity: 8.0%

Laryngeal: 3.9%

Role of HPV in oral precancerous lesions ?

Natural History of cervical HPV Infection



HPV prevalence in oral potentially malignant disorder (OPMD)







Leukoplakia

Erythroplakia

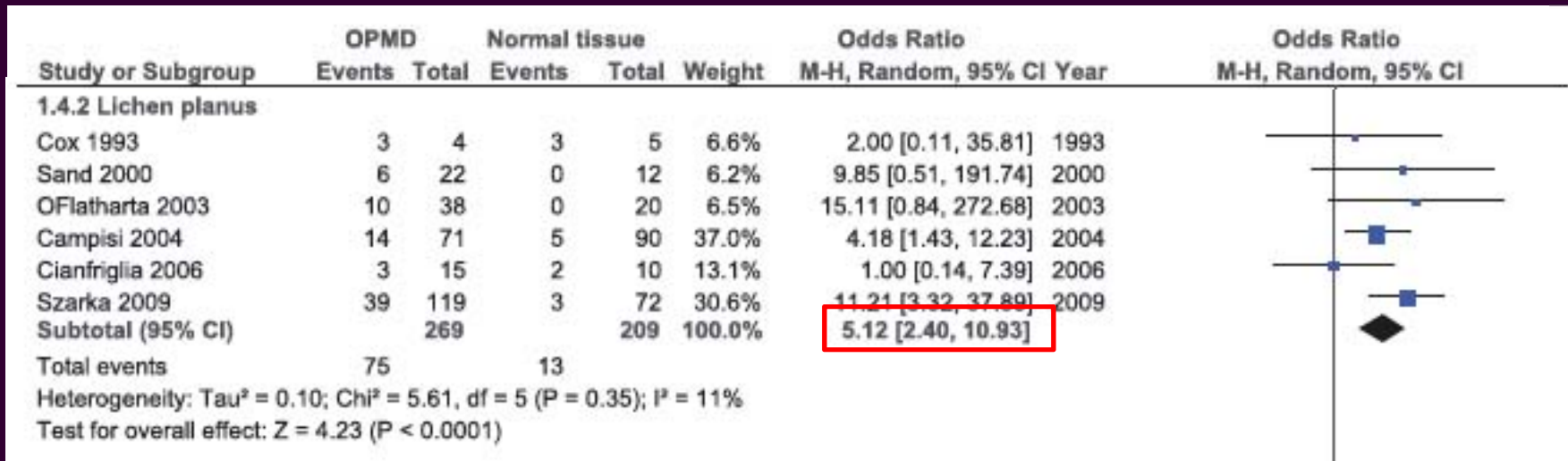
Oral proliferative verrucous leukoplakia

Lichen planus

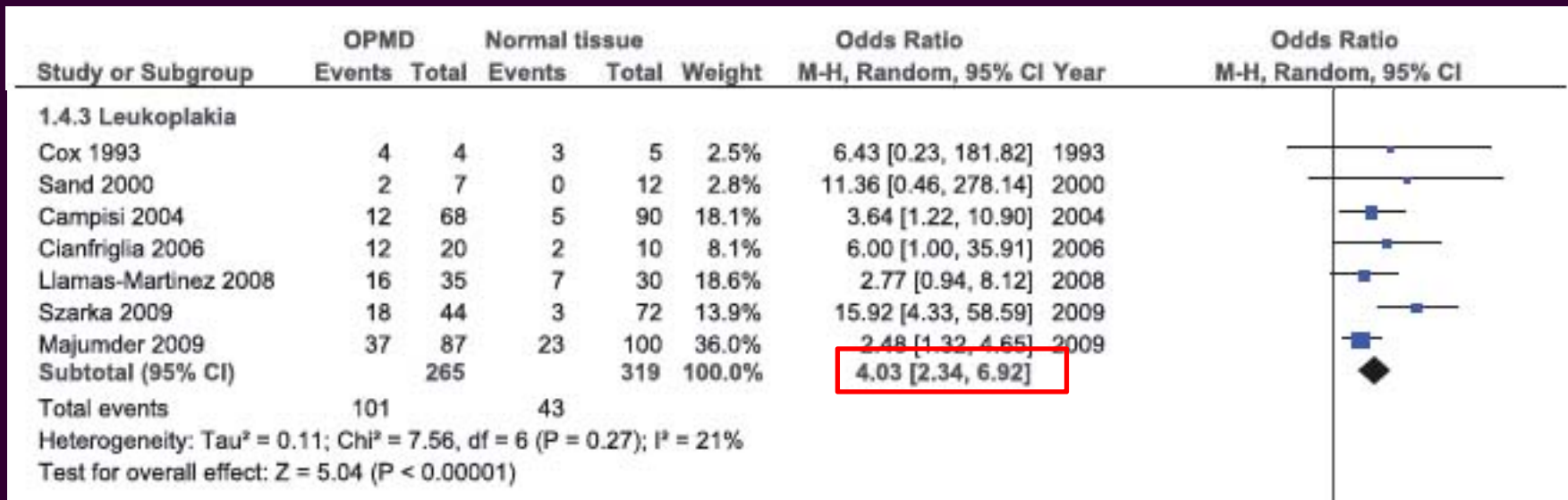
Submucous fibrosis

Study or Subgroup	OPMD		Normal tissue		Weight	Odds Ratio		Year	Odds Ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI			
1.4.1 OPMD not specified										
Maitland 1987	16	21	5	12	11.7%	4.48	[0.97, 20.59]	1987		
Nielsen 1996	17	49	0	20	3.3%	22.08	[1.26, 387.42]	1996		
Giovannelli 2002	16	59	5	90	23.8%	6.33	[2.17, 18.42]	2002		
Luo 2007	14	46	12	90	35.6%	2.84	[1.19, 6.81]	2007		
Debanth 2009	41	92	5	35	25.5%	4.82	[1.72, 13.54]	2009		
Subtotal (95% CI)		267		247	100.0%	4.44	[2.64, 7.49]			
Total events	104		27							
Heterogeneity: Tau ² = 0.00; Chi ² = 2.76, df = 4 (P = 0.60); I ² = 0%										
Test for overall effect: Z = 5.60 (P < 0.00001)										

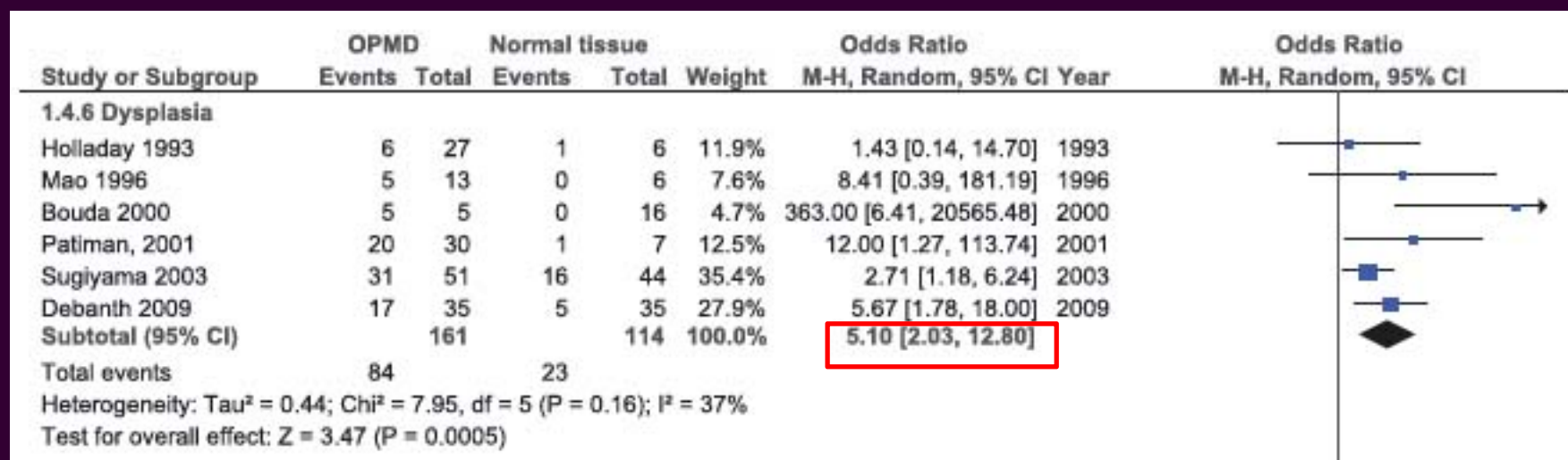
Lichen planus



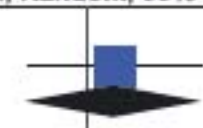
Leukoplakia



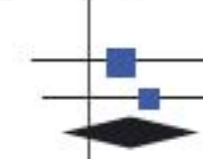
Dysplasia



Oral proliferative verrucous leukoplakia

Study or Subgroup	OPMD		Normal tissue		Weight	Odds Ratio		Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		M-H, Random, 95% CI	Year	
1.4.4 OVPL								
Gopalakrishnan 1997	2	10	1	10	100.0%	2.25 [0.17, 29.77]	1997	
Subtotal (95% CI)		10		10	100.0%	2.25 [0.17, 29.77]		
Total events	2		1					
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.62 (P = 0.54)								

Carcinoma in-situ

Study or Subgroup	OPMD		Normal tissue		Weight	Odds Ratio		Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		M-H, Random, 95% CI	Year	
1.4.7 Carcinoma in situ								
Holladay 1993	3	9	1	6	60.2%	2.50 [0.19, 32.19]	1993	
Mao 1996	3	10	0	6	39.8%	6.07 [0.26, 140.70]	1996	
Subtotal (95% CI)		19		12	100.0%	3.56 [0.49, 25.84]		
Total events	6		1					
Heterogeneity: Tau ² = 0.00; Chi ² = 0.19, df = 1 (P = 0.67); I ² = 0%								
Test for overall effect: Z = 1.25 (P = 0.21)								

A distinct entity ?

Unique characteristics of HPV-positive oropharyngeal cancer



Demographic & risk factors:

- Male
- White
- Younger
- Non-smoker
- Non-drinker
- Higher socioeconomic status
- Sexual behavior

Clinical characteristics:

- Early T stage, advanced nodal stage
- Better response to treatment

Pathological features:

- Arise from tonsillar crypts
- Without significant keratinization
- Basaloid morphology
- Lymphocyte infiltration
- ↑ p16
- Wild type p53

Trend of disease burden ?

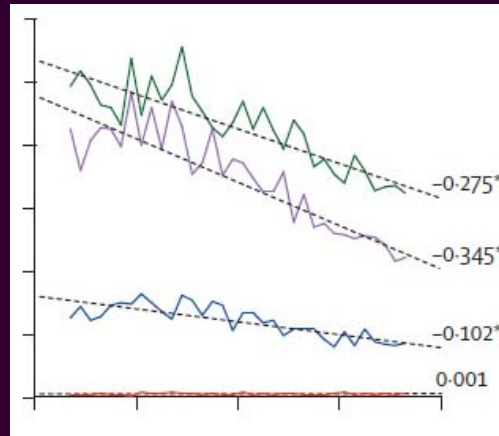
Changes in incidence of head & neck cancer 1973-2006, USA



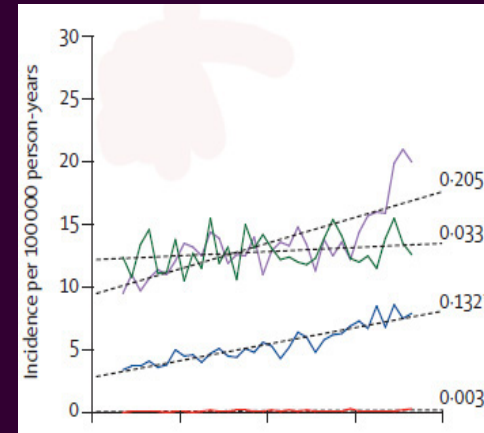
NOT HPV-related sites, men

Age (years)

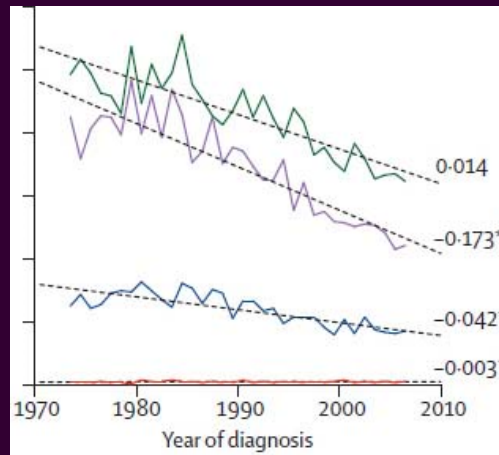
- <40
- 40-54
- 55-64
- 65+



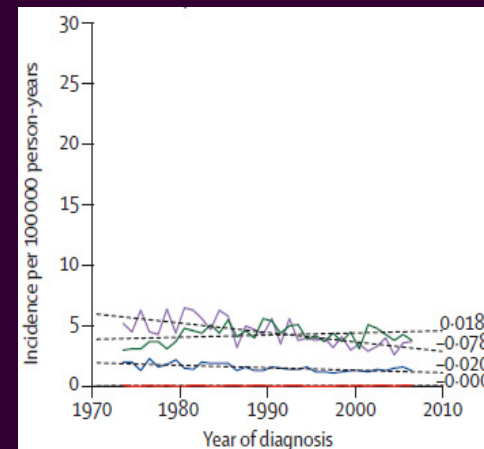
HPV-related sites, Men



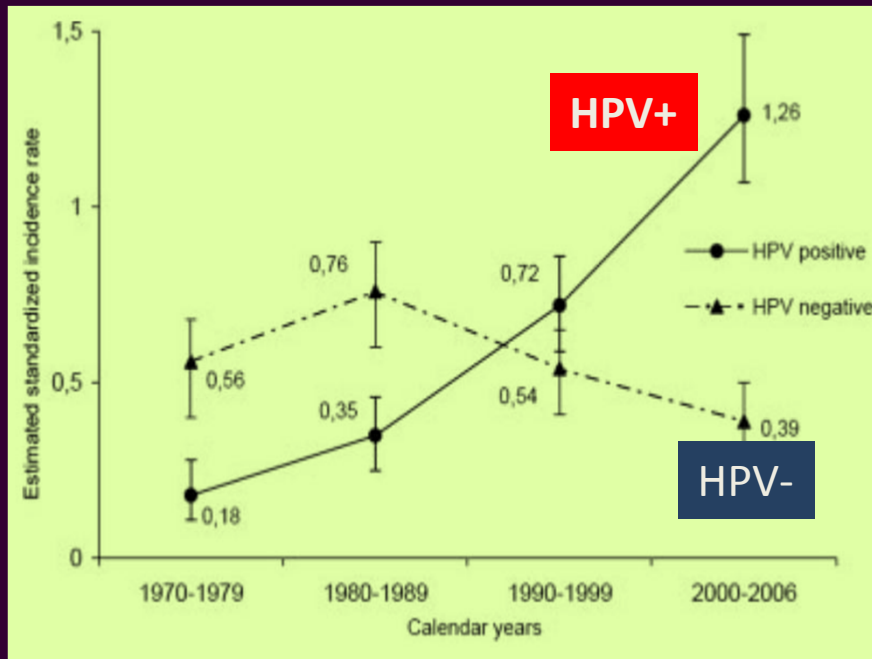
NOT HPV-related sites, women



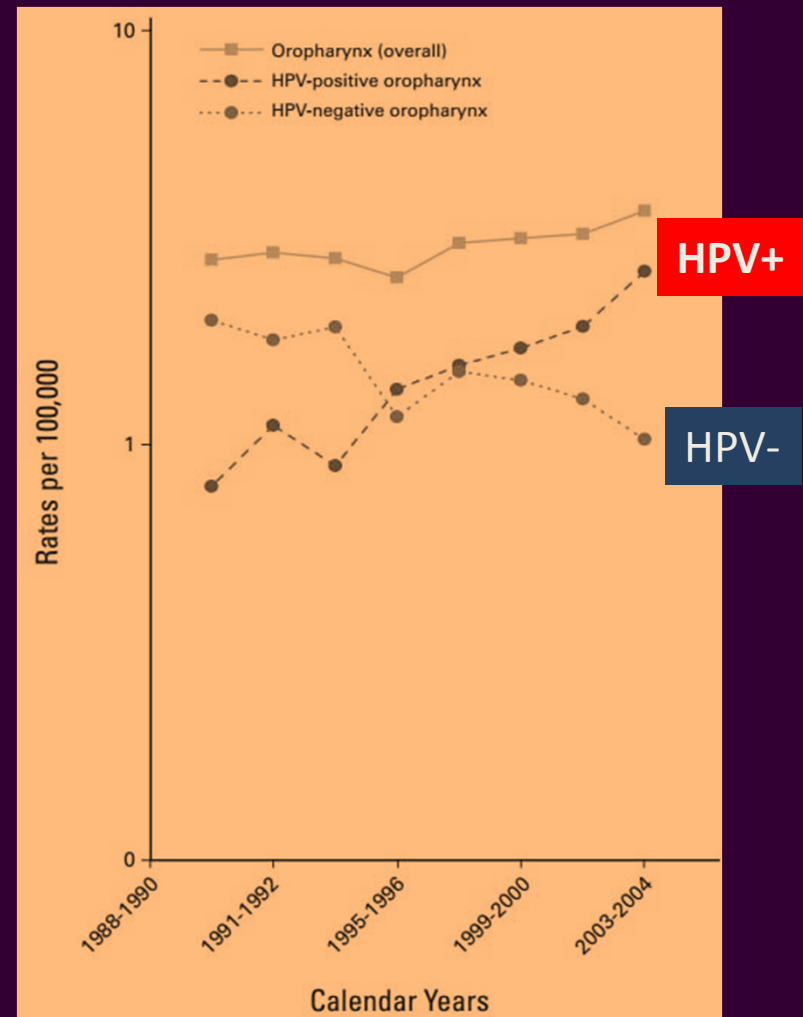
HPV-related sites, Women



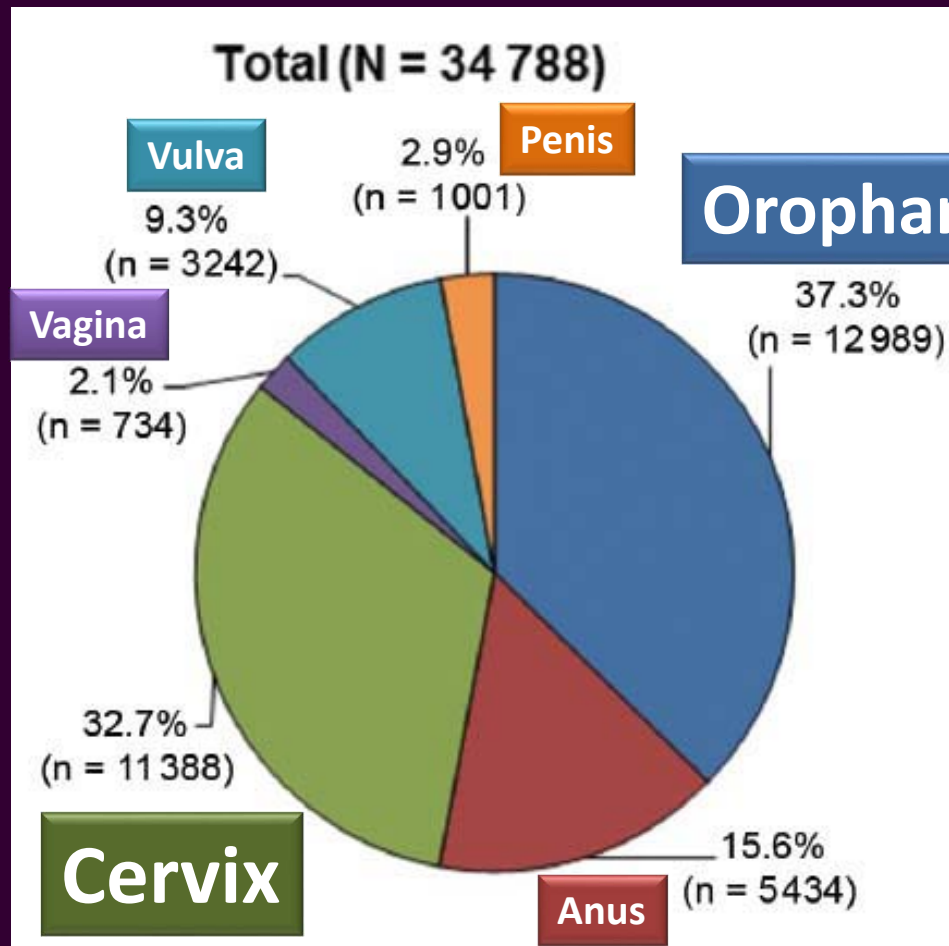
Tonsillar SCC Stockholm 1970-2006,



Oropharyngeal SCC Hawaii, Iowa, Los Angeles 1988-2004



No. of new cancers at anatomical sites and cellular types
in which HPV is frequently found
USA, 2009

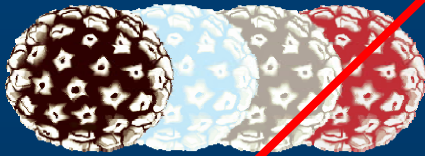


Estimated contribution of HPV:

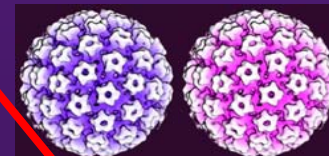
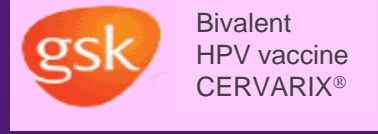
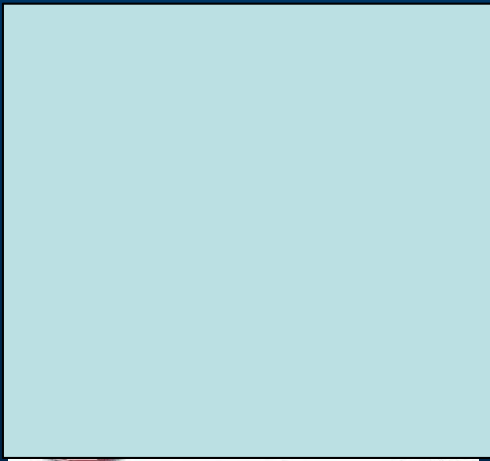
- Cervical cancer: ~100%
- Anal cancer: 90%
- Oropharyngeal cancer: >60%
- Vagina, vulva, penile ~40%

Prevent by screening & vaccination ?

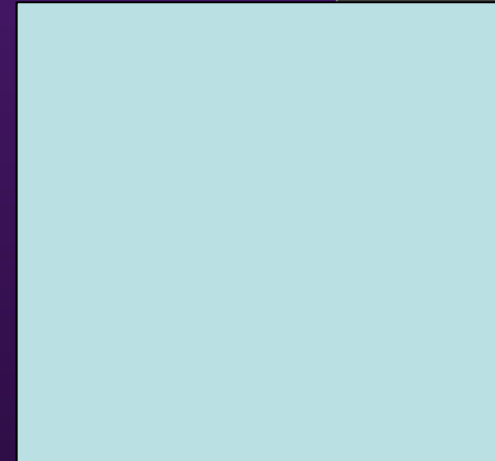
High-risk
HPVs



HPV 6,11, 16,18 + Aluminium



HPV 16,18 + Al + AS04



We are just at the beginning of a cancer epidemic !

