

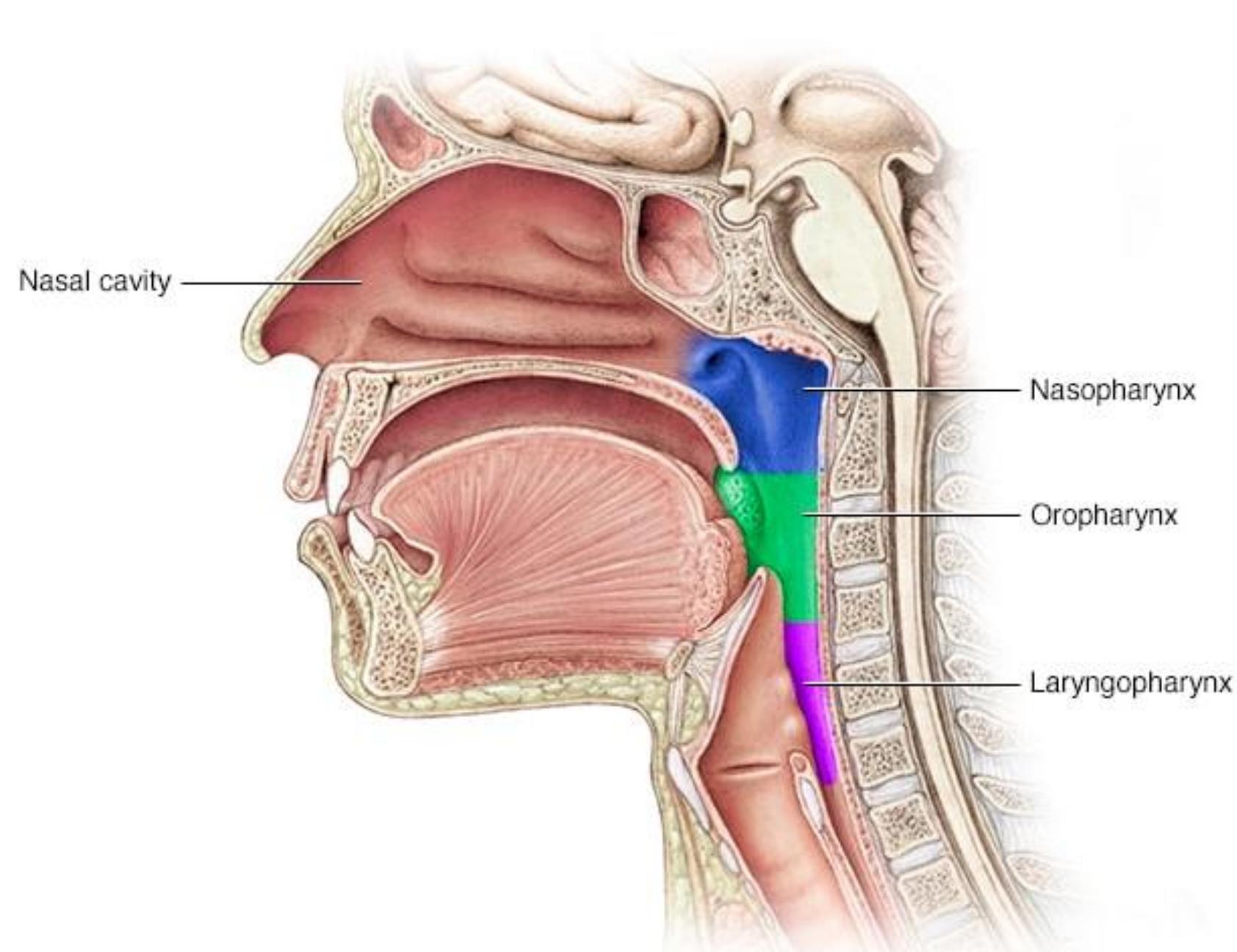
# HPV associated oropharyngeal cancer

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Head and Neck Tumor Group  
Mayo Clinic

# Objectives

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- Review basic facts about human papillomavirus and HPV-related cancers
- Discuss epidemiology, risk factors, and clinical features of HPV-associated oropharyngeal cancer
- Overview treatment for HPV oropharyngeal cancers
- Discuss importance of HPV vaccination for cancer prevention



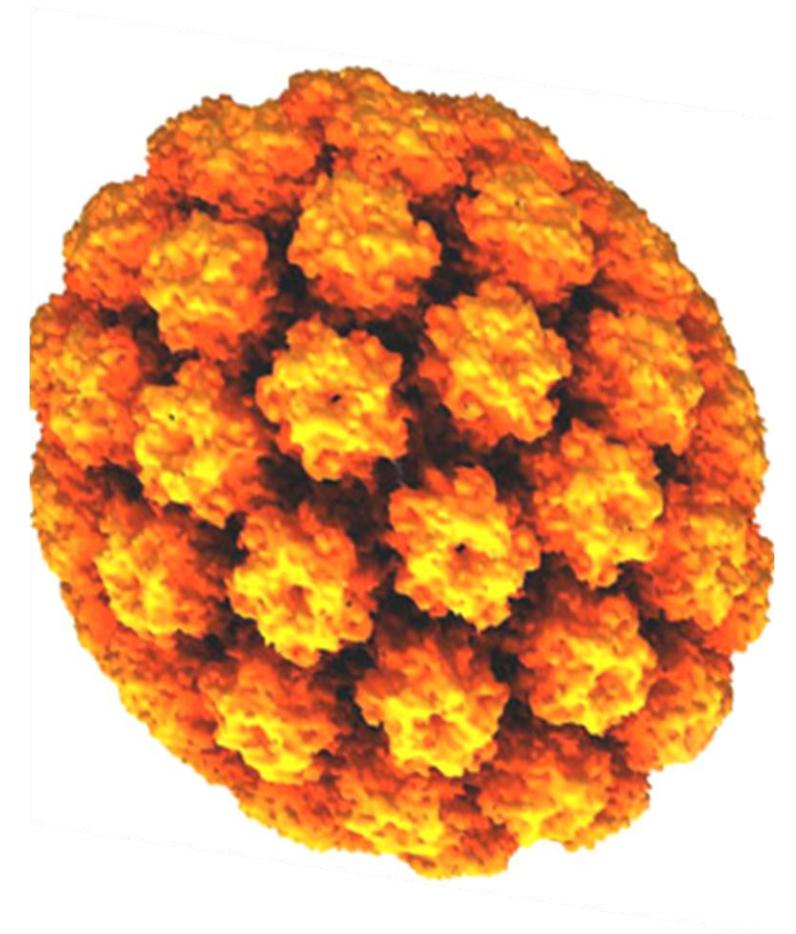
# What is the oropharynx?

- Palatine tonsil
- & lingual tonsil (base of tongue) most common

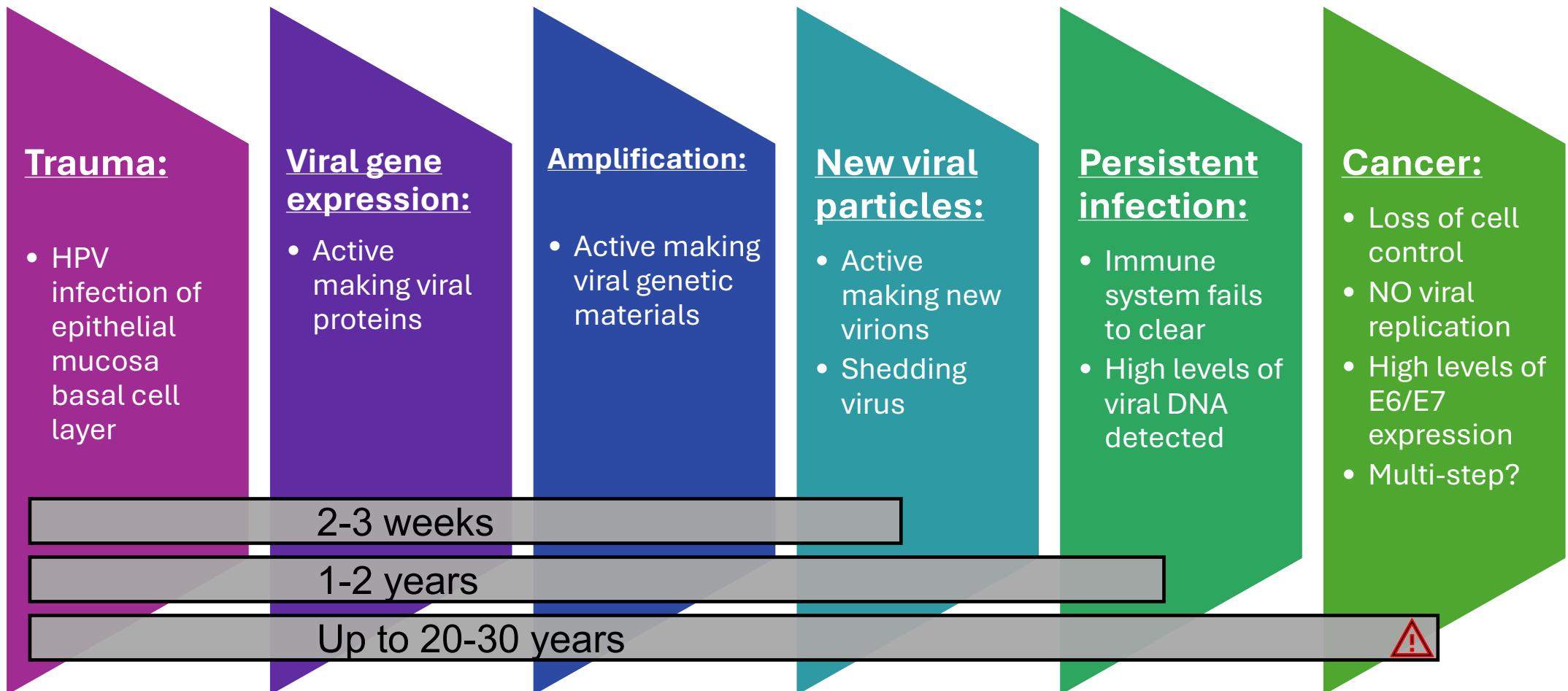
# HPV facts

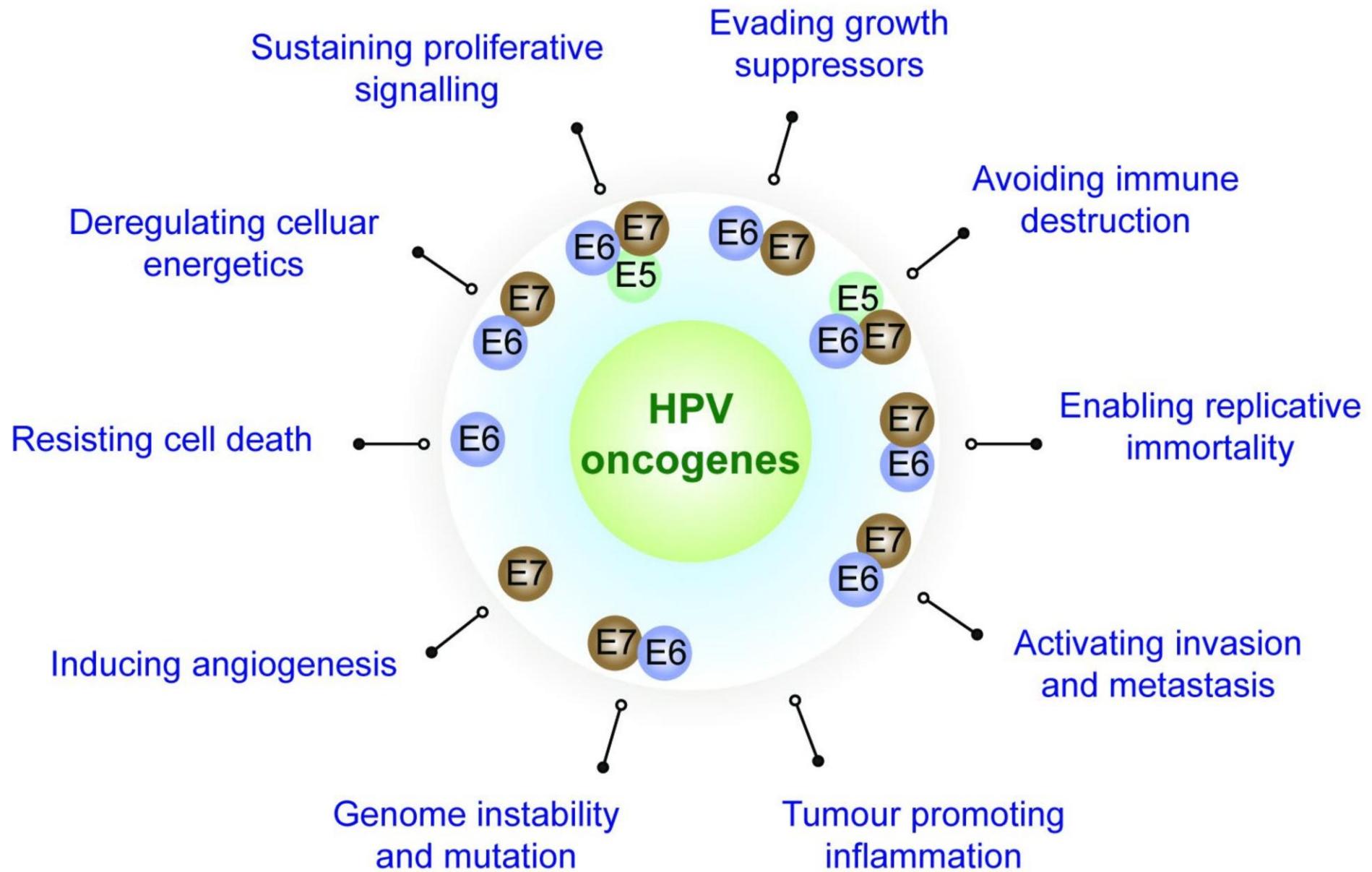
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- Human Papillomavirus: DNA-based virus with over 150 types
- 15 are classified as high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82)
- 6 million new infections yearly
- Predominantly (but not exclusively) sexually transmitted
- 80-90% adults infected
- Majority of infections asymptomatic
- ≈90% cleared in 2 years
- >90% of HPV-HNSCC due to HPV 16
- Expression of early viral proteins E6 and E7 lead to inactivation of tumor suppressor genes

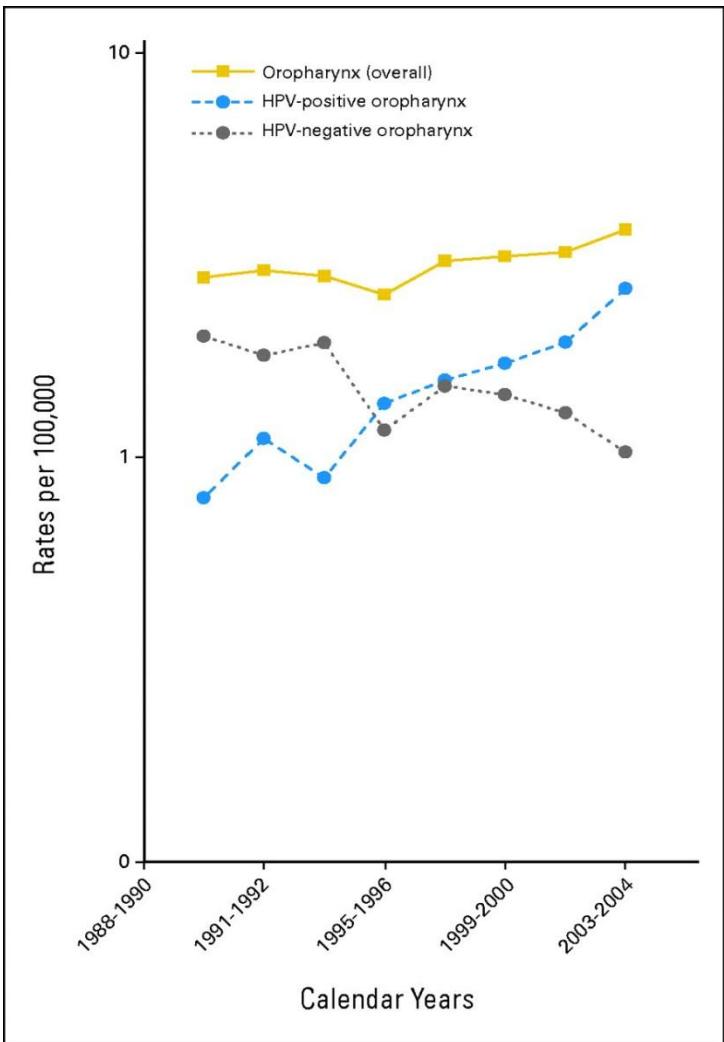


# HPV INFECTION & ONCOGENESIS



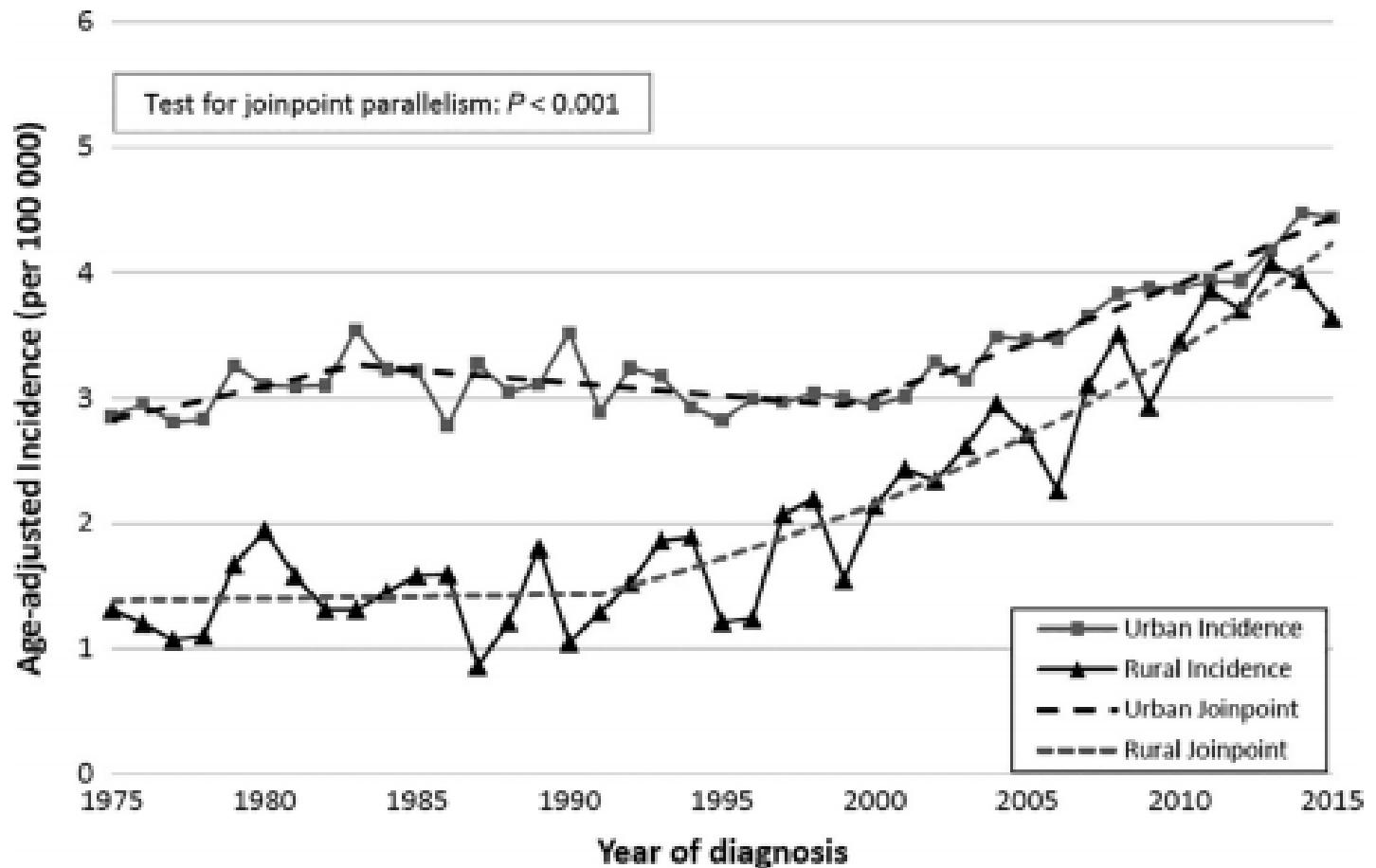


# Rising incidence of HPV+ oropharynx cancer



HPV(+)OPSCC:  
**225% ↑ from  
1988 to 2004**

# Incidence rates of oropharynx cancer in rural areas rising sharply compared with urban



$P$ -value  $<0.05$  on the parallelism test indicates that the trend between urban and rural incidence is significantly different.

# Oropharynx Cancer: Risk Factors

## HPV-negative

- Smoking
- Heavy alcohol use
- Poor oral hygiene
- Chewing tobacco



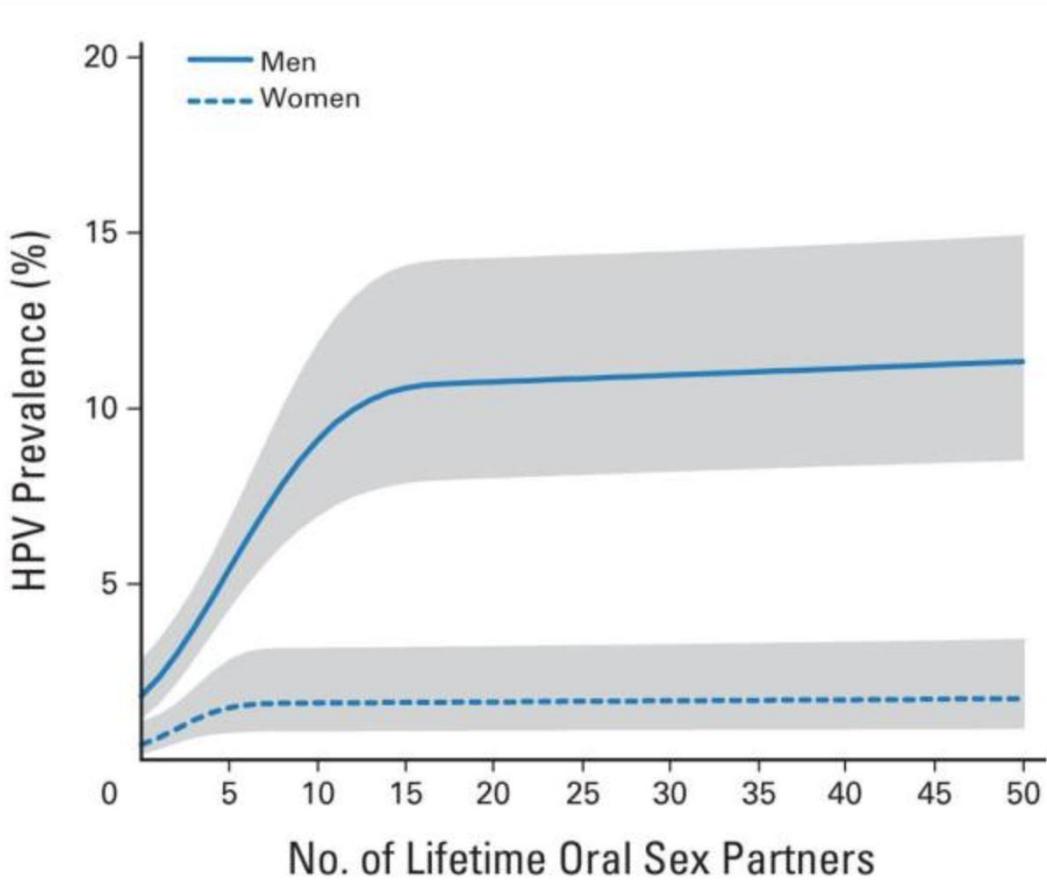
## HPV-positive

- # Lifetime sexual partners
- Oral sex
- Deep mouth kissing
- Current smoking
- Marijuana use



# HPV Prevalence

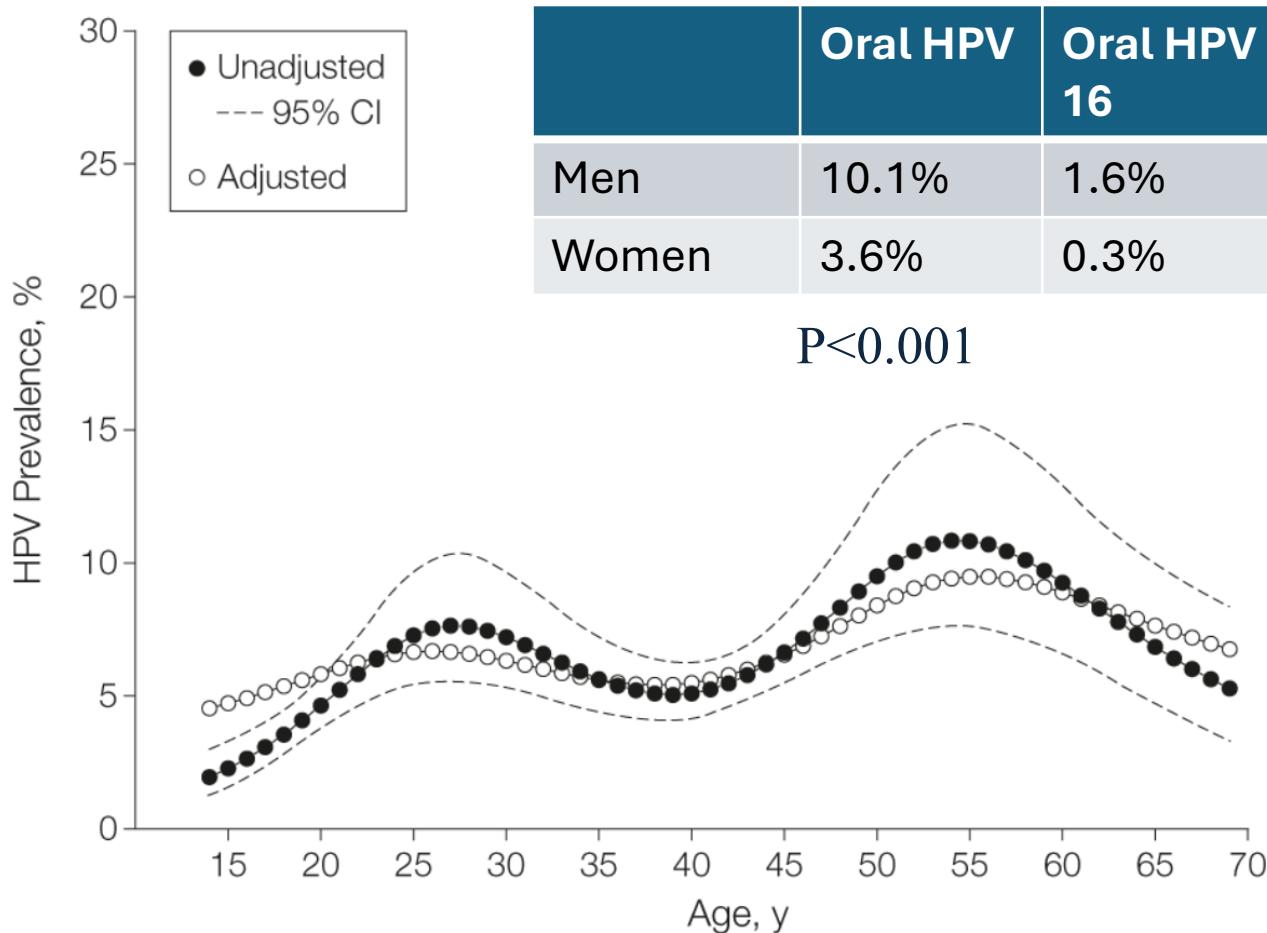
## Effect of partner number



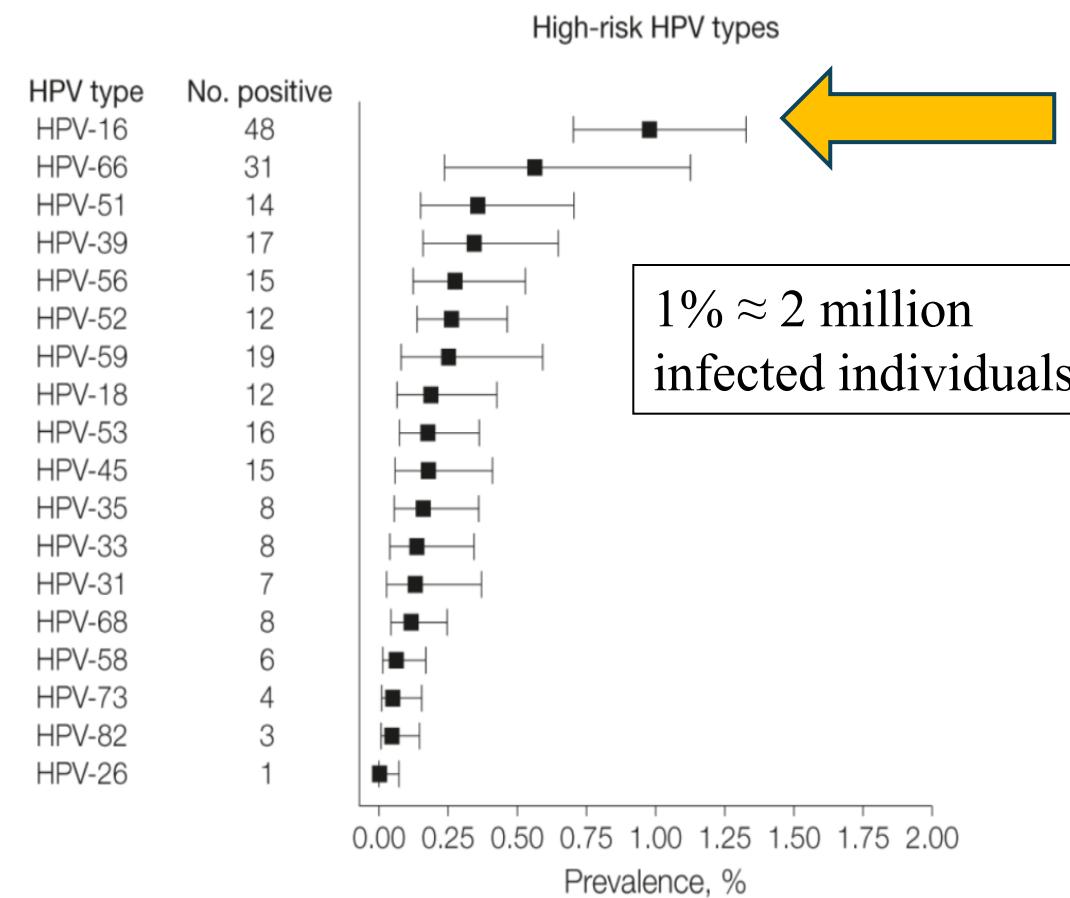
- Risk of HPV exposure/infection with increasing # sexual partners
- Unequal effect size for males vs females

# Oral HPV Prevalence

Overall modeled prevalence, any HPV



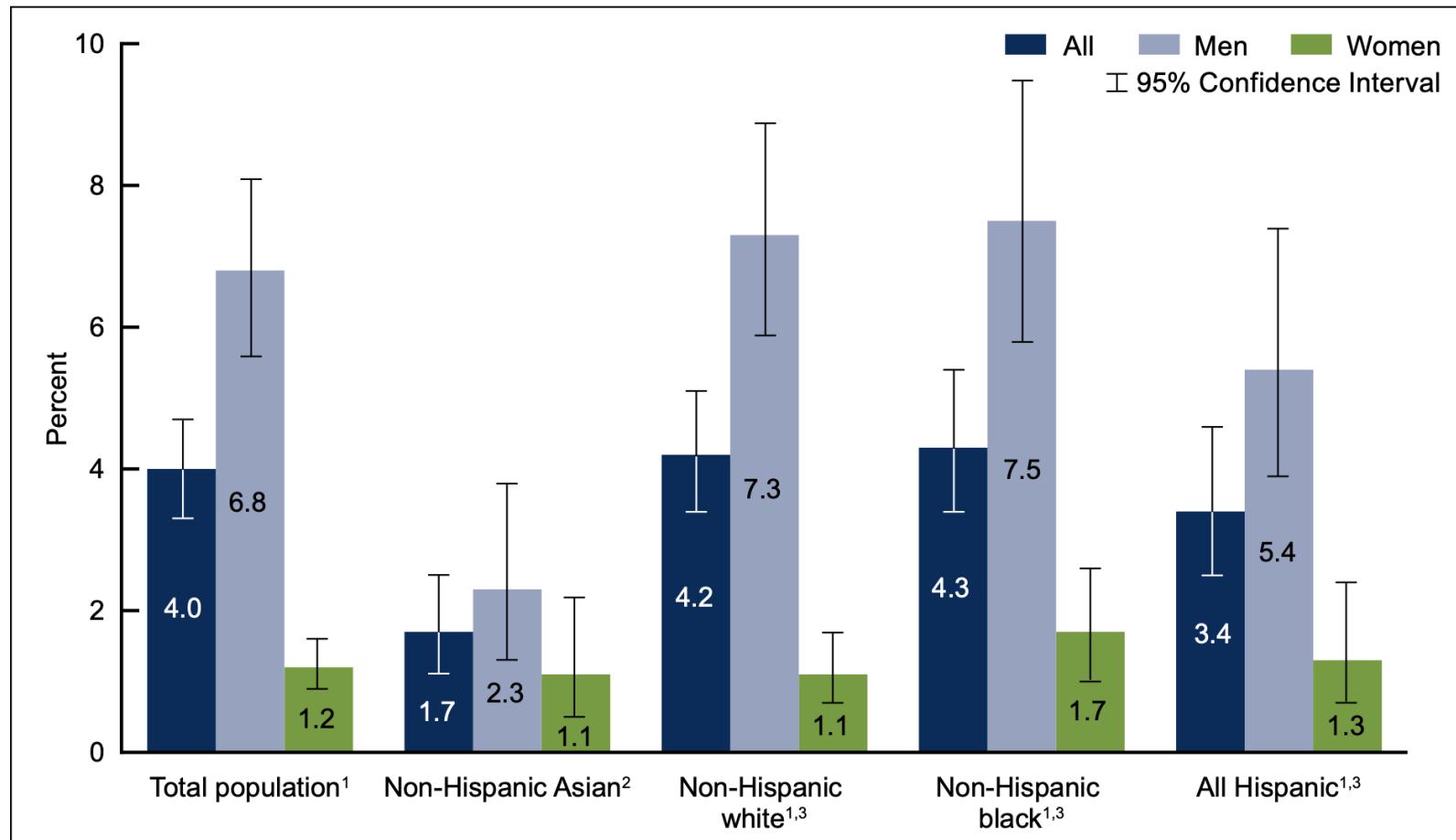
↑50x risk for HPV-OPC



# Oral HPV Prevalence

## High risk Oral HPV rate, 2011-2014 in adults

Figure 2. Prevalence of high-risk oral HPV among adults aged 18–69, by race and Hispanic origin and sex: United States, 2011–2014



- Overall rate for high risk HPV subtypes: 4.0%
  - 7.3% for low risk
- Higher rates in men

# Oropharynx cancer 8<sup>th</sup> most common cancer in men

## Estimated New Cases

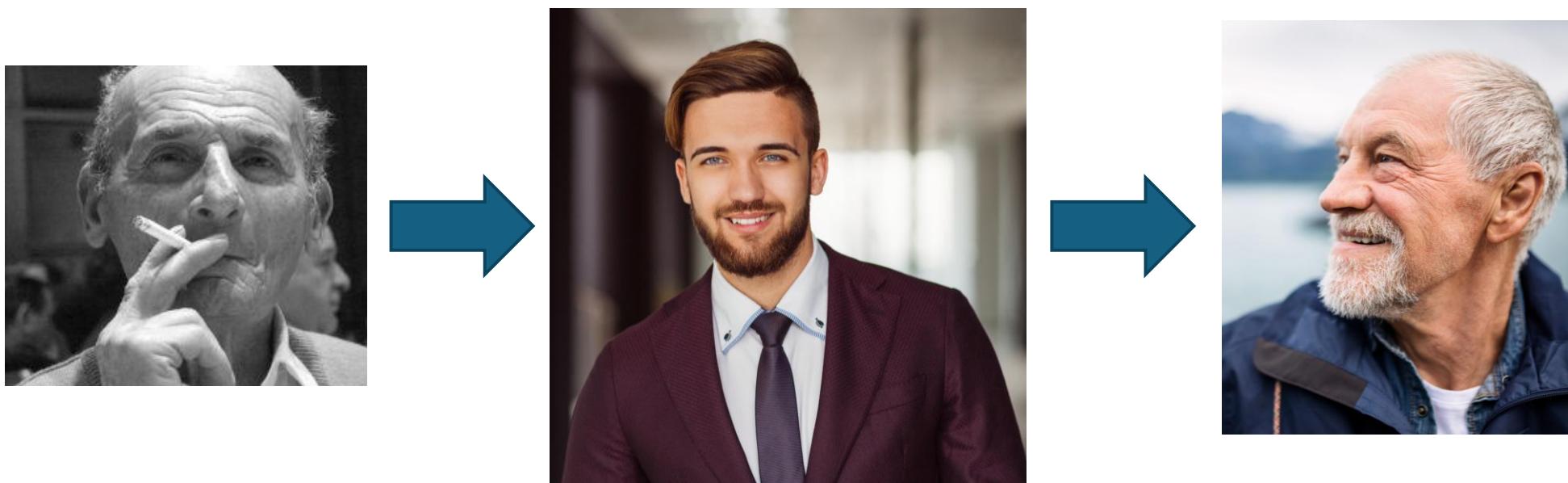
			Males	Females		
	Prostate	248,530	26%		Breast	281,550
	Lung & bronchus	119,100	12%		Lung & bronchus	116,660
	Colon & rectum	79,520	8%		Colon & rectum	69,980
	Urinary bladder	64,280	7%		Uterine corpus	66,570
	Melanoma of the skin	62,260	6%		Melanoma of the skin	43,850
	Kidney & renal pelvis	48,780	5%		Non-Hodgkin lymphoma	35,930
	Non-Hodgkin lymphoma	45,630	5%		Thyroid	32,130
→	Oral cavity & pharynx	38,800	4%		Pancreas	28,480
	Leukemia	35,530	4%		Kidney & renal pelvis	27,300
	Pancreas	31,950	3%		Leukemia	25,560
	All Sites	970,250	100%		All Sites	927,910
						100%



# HPV+ Oropharynx Cancer: Population

- Younger – median age 55 years
- Male predominant (7-8x higher in men)
- >70% male (vs 62%)
- No tobacco or ETOH
- Better prognosis

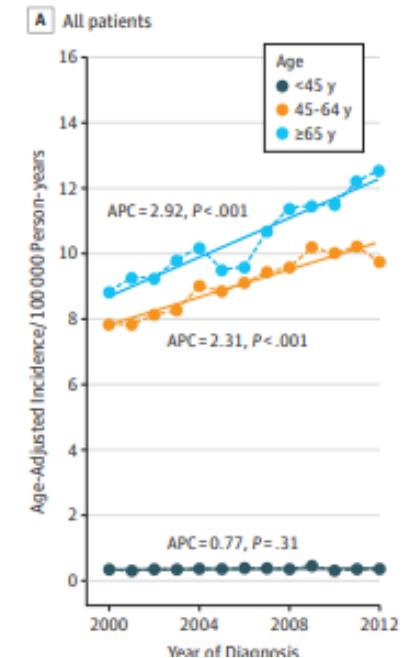
# The current and future face of oropharynx cancer



HPV oropharynx cancer  
8<sup>th</sup> most common cancer in  
men

HPV oropharynx cancer rising in  
patients > 65 years

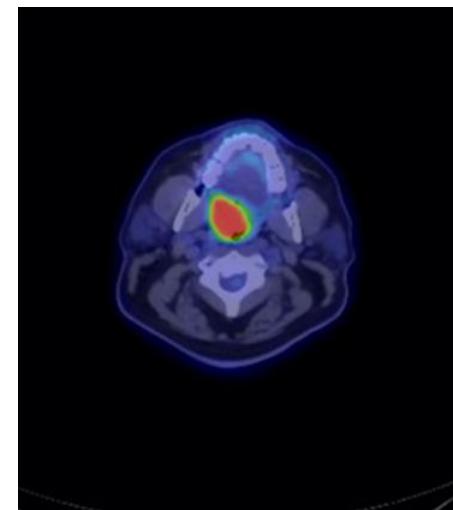
Zumsteg et al., JAMA Oncol, 2016;2(12):1617-1623





## Typical case presentation

A 55-year-old man, never smoker, notices a painless left-sided neck mass while shaving. He has no other symptoms. He sees his primary care provider and is treated with a course of antibiotics for two weeks. The mass persists. CT scan of the neck is obtained showing cystic lymphadenopathy and a tonsil mass. Fine needle aspiration of the cervical lymph node reveals HPV-associated squamous cell carcinoma.



- Cystic lymphadenopathy is highly suspicious and is cancer until proven otherwise
- Non-diagnostic FNA requires further evaluation

# Presenting Symptoms and Examination

- Common:
  - Neck mass (80%)
  - Sore throat (40%)
  - Otalgia (28%)
- Rare ( $\leq 10\%$ ):
  - Weight loss
  - Hemoptysis
  - Trismus
- Persistent pain, globus sensation, trismus suspicious for a more advanced tongue base cancer



Most patients are asymptomatic

# Clinical Pearl

Maintain a **HIGH** index of suspicion for cancer in patients with a neck mass and...

NO systemic symptoms

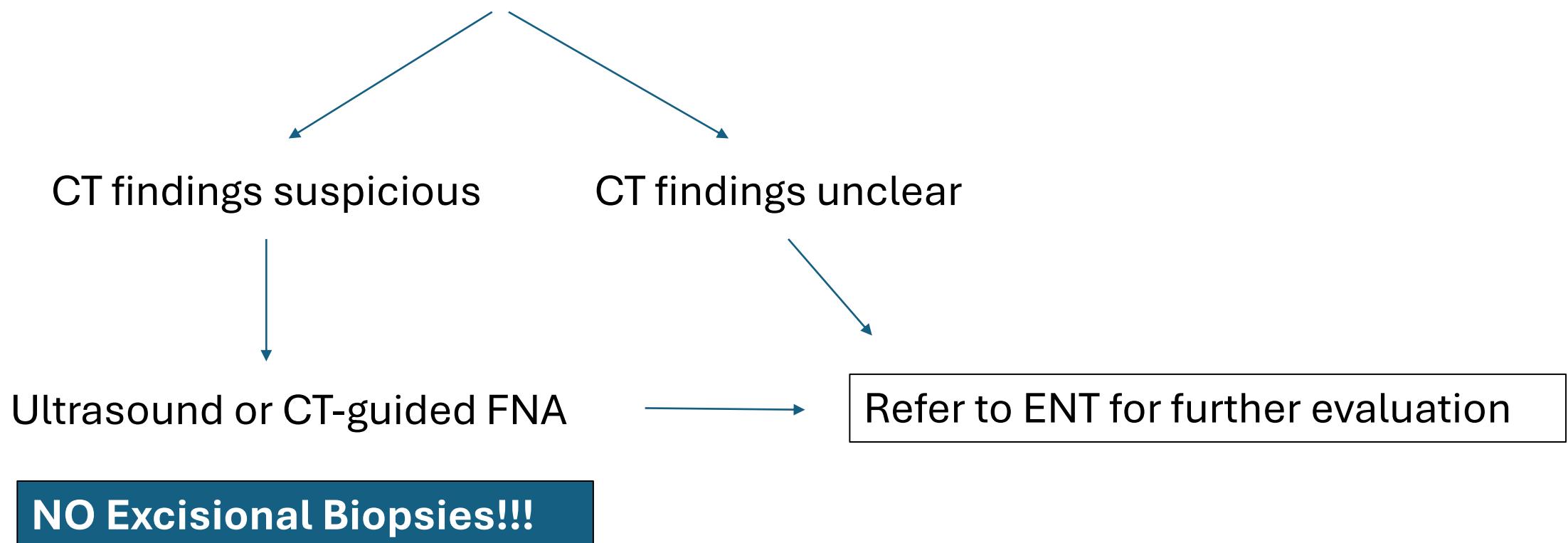
NO traditional risk factors

*It's cancer until proven otherwise!*

# If you see a patient with a neck mass...

Option 1: Refer immediately to ENT

Option 2: Examination & CT neck with contrast



# **Initial evaluation for patient with oropharynx cancer**

History and physical examination

Cross-sectional imaging (CT or MRI)

Tissue diagnosis (FNA)

PET/CT for staging

# Treatment for patients with HPV head and neck cancer

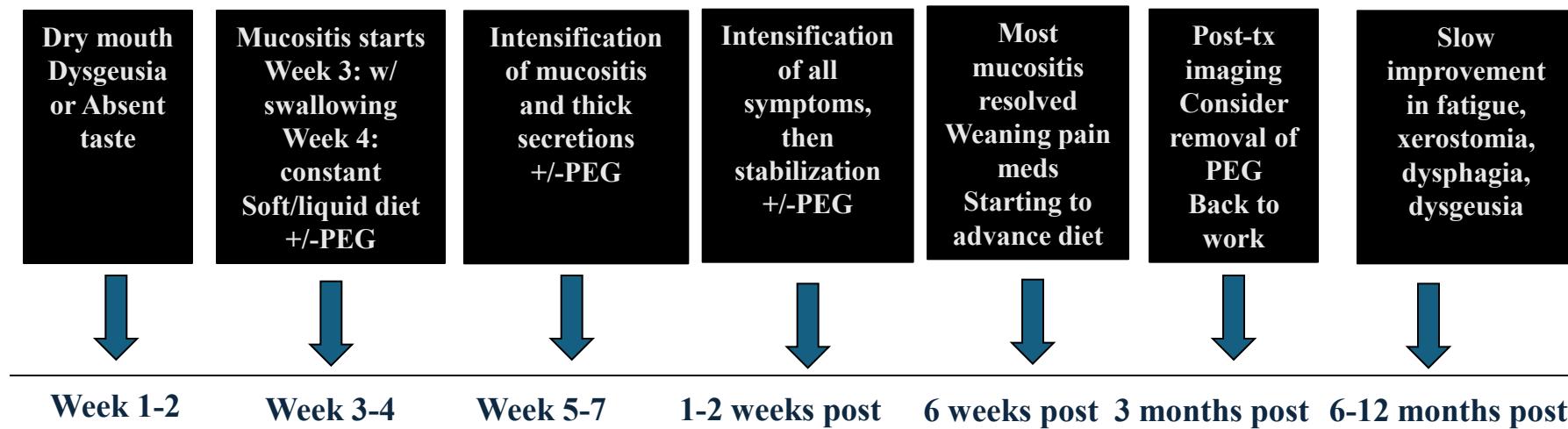
## **Early stage or locally-advanced**

- Treatment is curative
- Early stage treated with surgery or radiotherapy alone
- Locally advanced treated with combination therapy
  - Surgery → radiation +/- chemo
  - Radiation + chemotherapy
  - Chemotherapy → surgery or RT
  - De-escalation strategies under study

## **Recurrent or metastatic**

- Treatment is palliative
- Immunotherapy based treatment backbone
  - Immunotherapy alone
  - Immunotherapy + chemotherapy
- New agents under study
  - Therapeutic vaccines
  - Bispecifics
  - Antibody-drug conjugates

# Timeline of symptoms in patients undergoing adjuvant or definitive head and neck radiation or chemoradiation\*



Standard adjuvant: 6 weeks, Standard definitive: 7 weeks

\*Does not include chemotherapy side effects

# General Chemotherapy Toxicities

- Fatigue/malaise
- Nausea ± vomiting
- Decreased blood counts → neutropenic fever\*
- Anorexia/dysgeusia
- “Chemo brain”
- Neuropathy
- Cisplatin-specific toxicities: Acute renal failure, hearing loss/tinnitus, hypomagnesemia

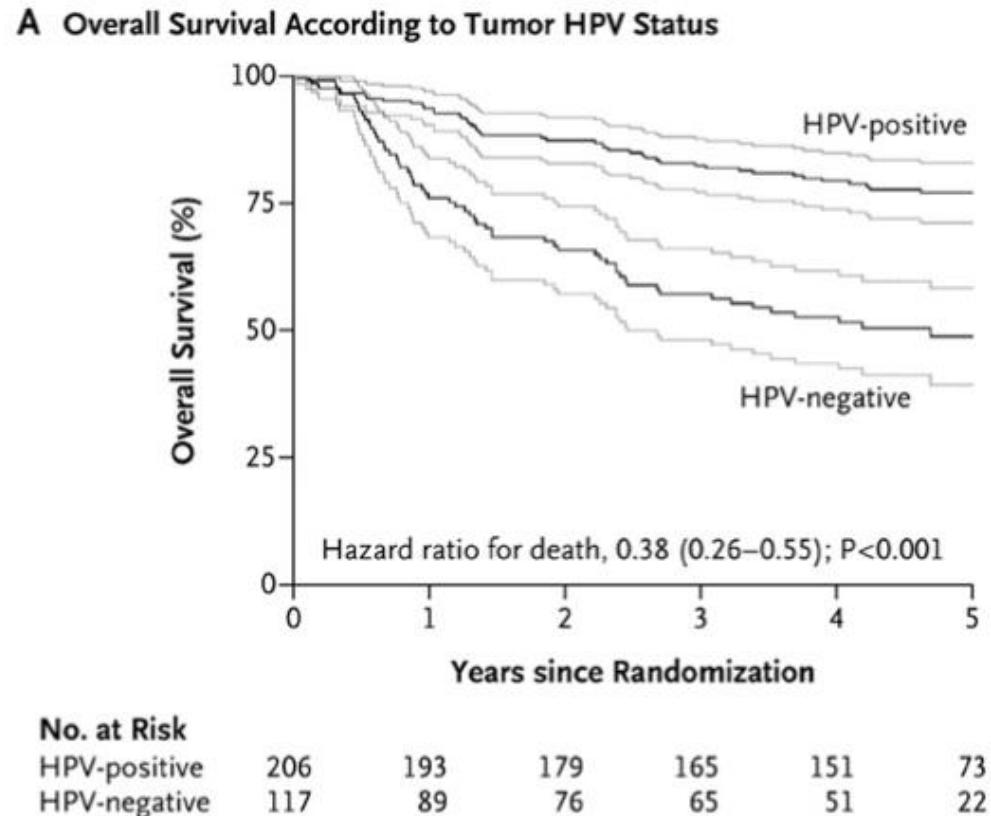
\*Most common cause of chemotherapy-related death



# Late toxicities of head and neck cancer treatment

- Xerostomia
- Dysphagia
- Hypothyroidism
- Pain
- Depression/anxiety
- Fatigue
- Lymphedema
- Fibrosis
- Dental issues
- Trismus
- Cervical stricture
- Osteoradionecrosis
- Blood pressure lability
- Carotid artery disease
- Prolonged lymphopenia
- **Suicide (3x higher)**

# Cure rates for HPV oropharynx cancer

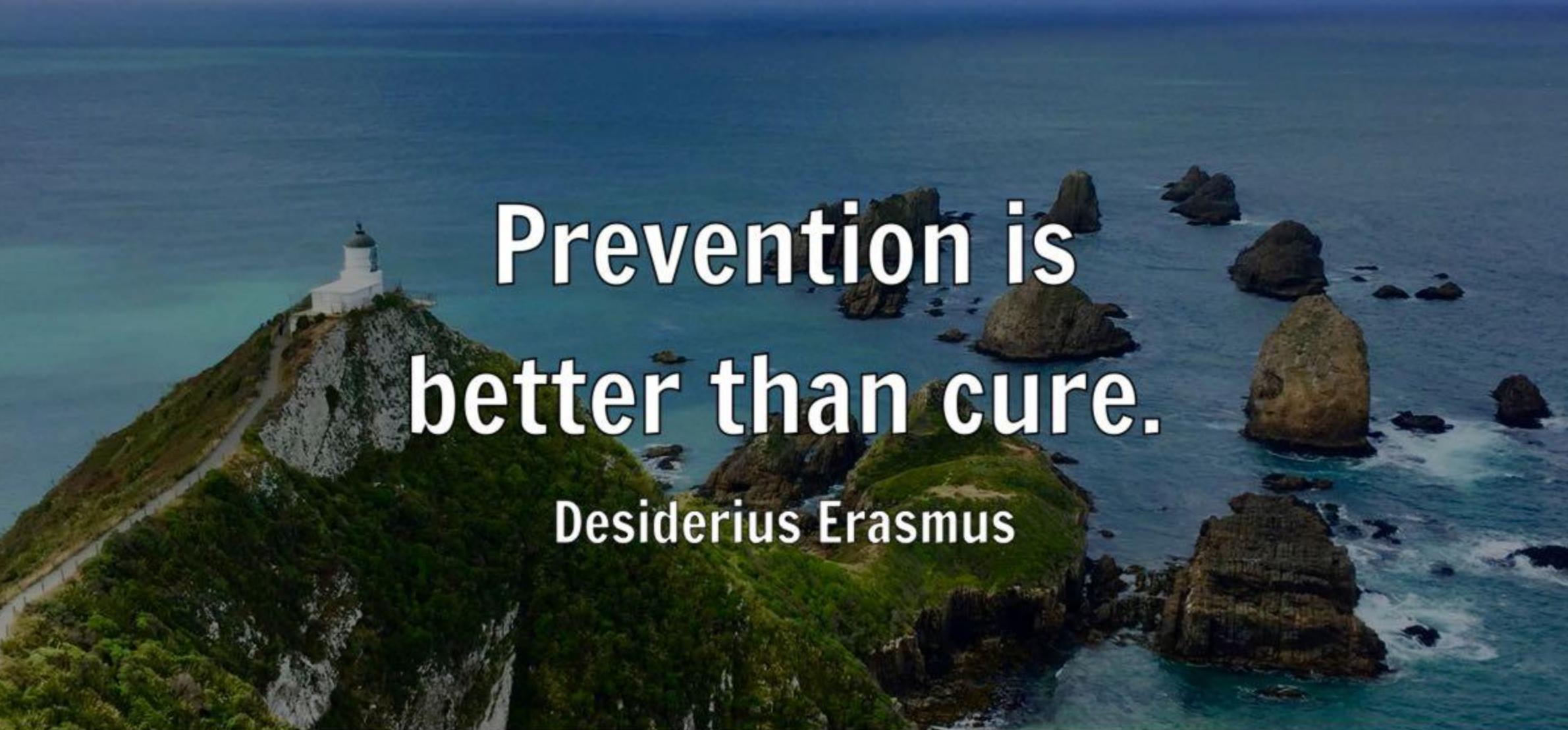


**5-year overall survival  
ranging from 79-81%**

Recurrence risk increases with increasing tumor size (T4) & increasing number of involved cervical lymph nodes

Ang et al, NEJM, 2010

20% recurrence  
≈ 4,000 patients  
annually

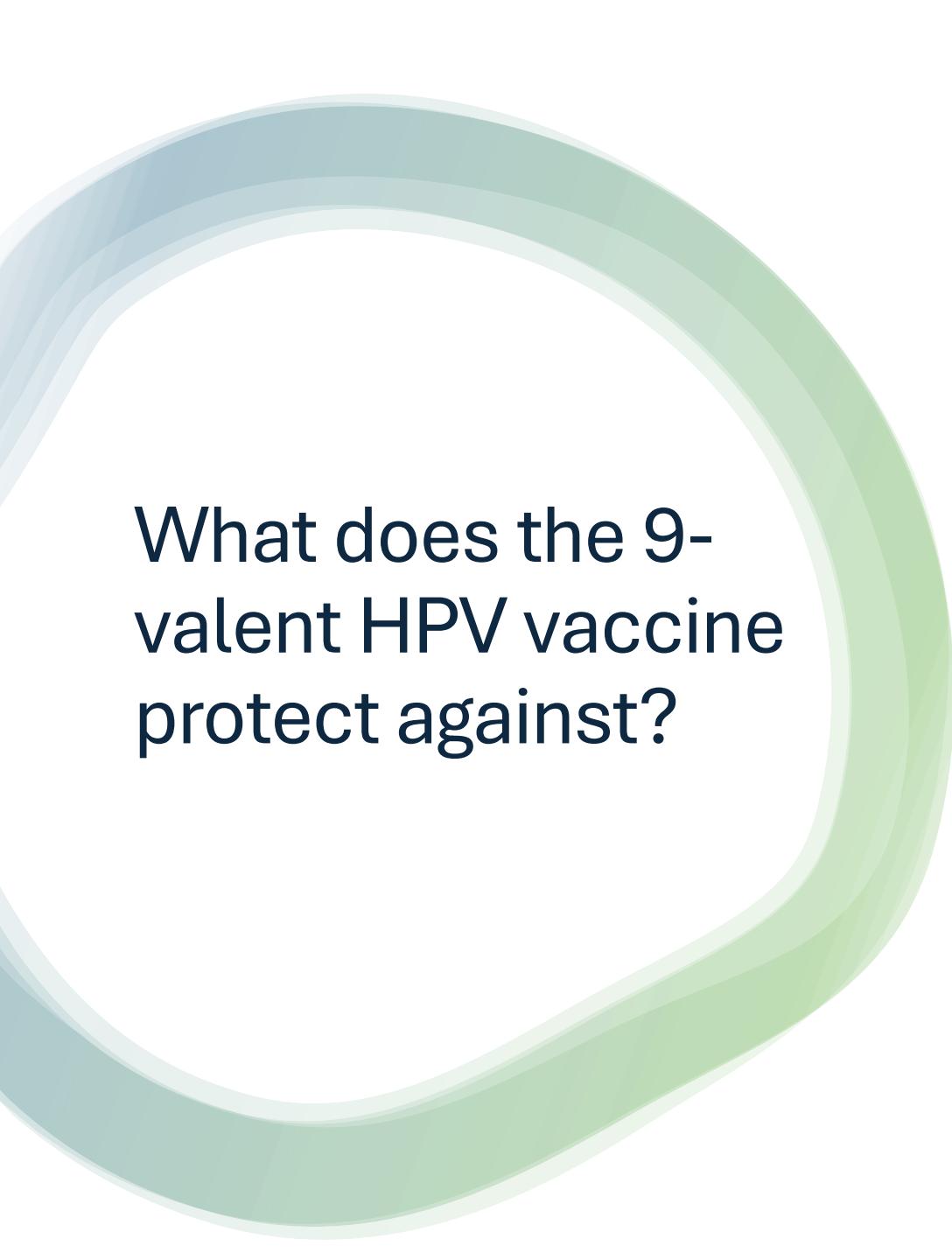


Prevention is  
better than cure.

Desiderius Erasmus

# HPV vaccination

Image used under license from Getty Images



## What does the 9-valent HPV vaccine protect against?

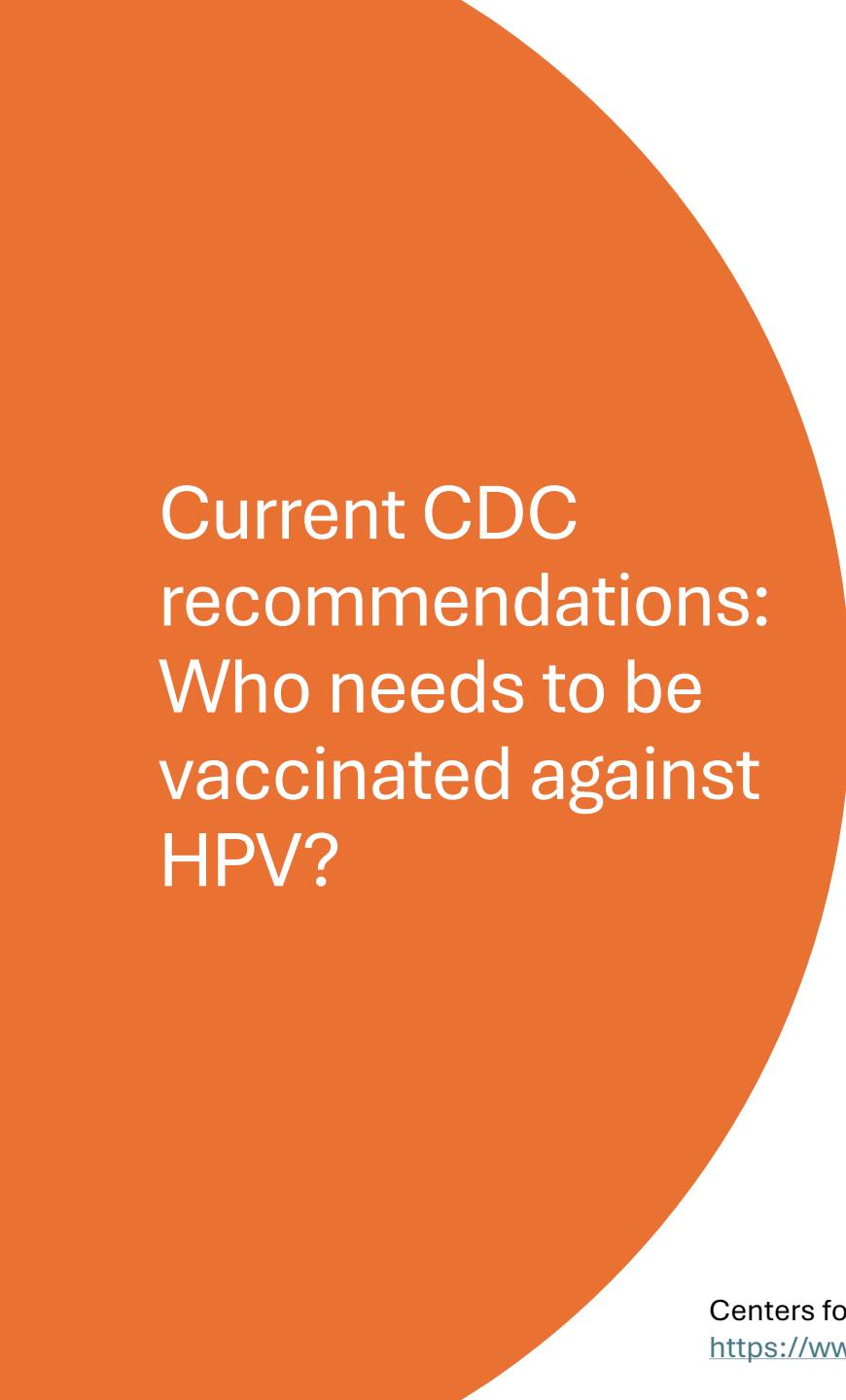
- Cervical cancer in females
- Vaginal cancer in females
- Vulvar cancers in females
- Penile cancers in males
- Anal cancer in both males and females
- Oropharyngeal cancers in both males and females
- Genital warts in both males and females
- Recurrent respiratory papillomatosis in both males and females

# Cancers Associated with and Attributed to Human Papillomavirus (HPV) Infection in the United States, 2015–2019

Cancer Site	No. of HPV-Associated Cancers	Percentage of Cancers Probably Caused by Any HPV Type	Estimated No. of Cancers Probably Caused by Any HPV Type <sup>t</sup>		
			Among Females	Among Males	Among Both Sexes
Cervix	12,293	91	11,100	0	11,100
Vagina	879	75	700	0	700
Vulva	4,282	69	2,900	0	2,900
Penis	1,375	63	0	900	900
Anus <sup>‡</sup>	7,531	91	4,700	2,200	6,900
Oropharynx	20,839	70	2,300	12,500	14,800
Total	47,199	79	21,700	15,600	37,300

\*

Adapted from data provided by the Centers for Disease Control and Prevention (CDC) (<https://www.cdc.gov/cancer/hpv/statistics/cases.htm>). Data were compiled from population-based cancer registries that participate in the CDC National Program of Cancer Registries and in the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute. The data met the criteria for high-quality data for all years in the 2015–2019 period, with coverage of 98% of the U.S. population.



## Current CDC recommendations: Who needs to be vaccinated against HPV?

- Recommended age for HPV vaccination is 11-26 years old
- HPV vaccination is recommended for all preteens (**including girls and boys**) at age 11-12 years.
  - Can start series at age 9
  - Ideal timing is before initiation of sexual activity
- FDA approval is through age 45
  - Individuals ages 27-45 may benefit from HPV vaccination based on risk
  - Benefit may be less in this patient cohort

# Types of HPV vaccines

- **9-valent HPV vaccine (Gardasil® 9, 9vHPV)**
  - 6, 11, 16, 18, 31, 33, 45, 52, 58
- Quadrivalent HPV vaccine (Gardasil®, 4vHPV)
  - 16, 18, 6, 11
- Bivalent HPV vaccine (Cervarix®, 2vHPV)
  - 16 & 18
- All three licensed by the U.S. Food and Drug Administration (FDA)
  - Only Gardasil® 9 currently distributed in the U.S.
- All three HPV vaccines protect against HPV types 16 and 18 that cause most HPV cancers
- Quadrivalent and 9-valent protect against HPV-related cancers and genital warts
  - Bivalent has no protection against warts



# CDC guidelines for HPV vaccination

## Routine vaccination schedule

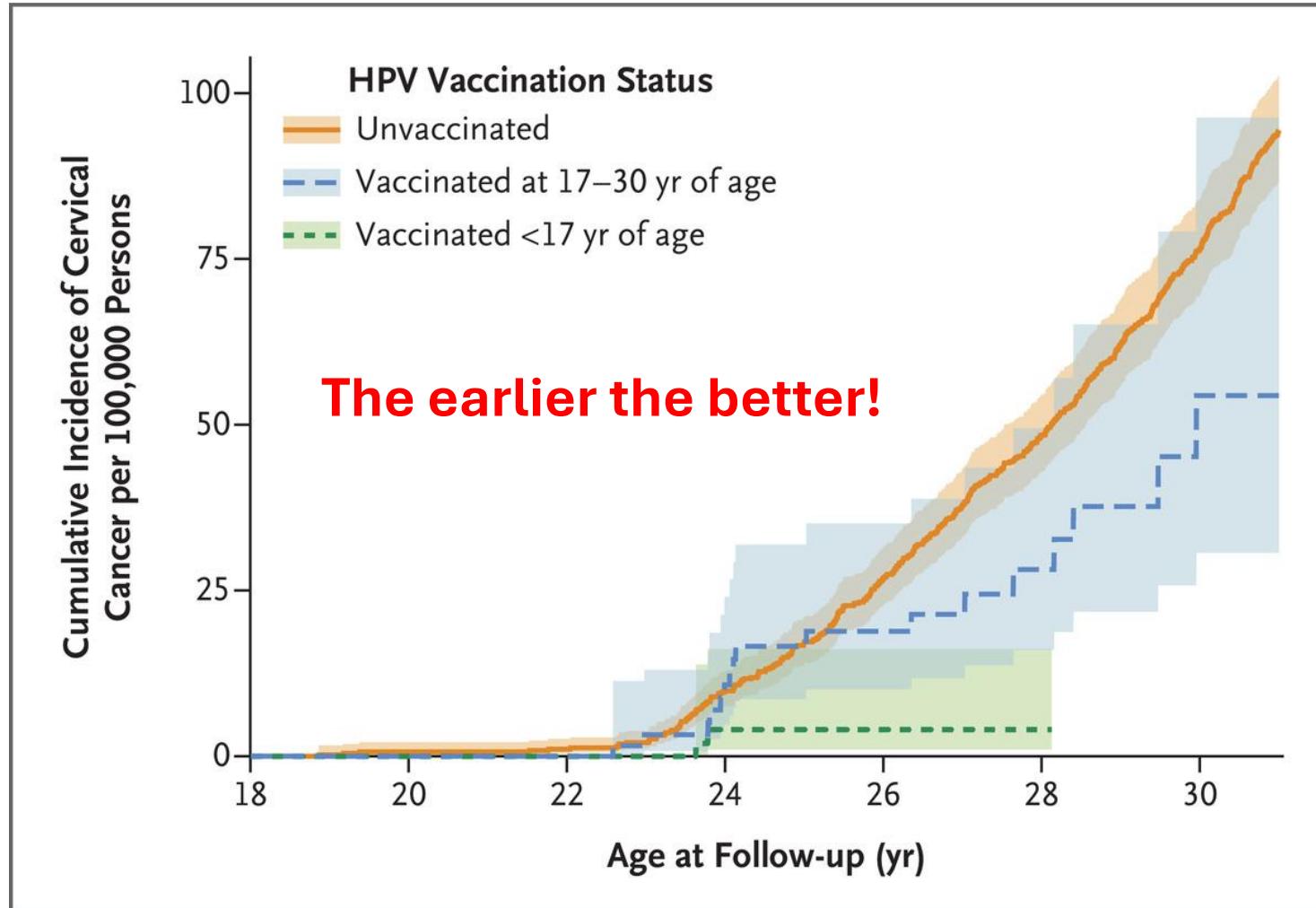
- Routinely recommended for **boys and girls at age 11-12 years**

	Age 9-10	Age 11-12	Age 13-14	Age 15+
# doses	2 doses	2 doses	2 doses	3 doses
Notes	Minimum age Rec. for hx of sexual assault, abuse	@ 0, 6-12 mo	@ 0, 6-12 mo	@ 0, 1-2 mo, 6 mo

- Special considerations

- Immunocompromise: 3 doses
- Pregnancy: not recommended until after pregnancy, though pregnancy test not needed

# Cumulative incidence of invasive cervical cancer according to HPV vaccination status and age of vaccination



# Safety of HPV vaccination: 9-valent vaccine

Through 2021, more than 135 million doses of HPV vaccine had been distributed in the United States

7 clinical trials with 15,000 individuals, at least 1 dose

Most common mild adverse effect: injection site reaction or allergic reaction

Syncope can occur → administer with patient sitting down

Large population-based evaluations of general safety, death, autoimmune conditions, and neurologic conditions have shown no safety concerns

# HPV vaccination decreases high-risk oral HPV infection & oral/oropharyngeal cancer

Analysis of National Health and Nutrition Examination Survey data (2011-2014) demonstrated that HPV vaccination was associated with a 94% reduction in vaccine-type oral HPV infection (0.1% in vaccinated vs. 1.6% in unvaccinated individuals;  $p=0.008$ ).<sup>1</sup>

A meta-analysis of six studies with 15,240 participants found that vaccinated individuals were 46% less likely to develop oral vaccine-type HPV infection overall, with an 80% reduction specifically for HPV16 infection.<sup>2</sup>

A U.S. hospital-based study reported that HPV vaccination was associated with a 99% reduced odds ratio for oral and oropharyngeal cancer (OR 0.008,  $p<0.0001$ ), with oropharyngeal sites showing particularly strong protection (OR 0.01).<sup>3</sup>

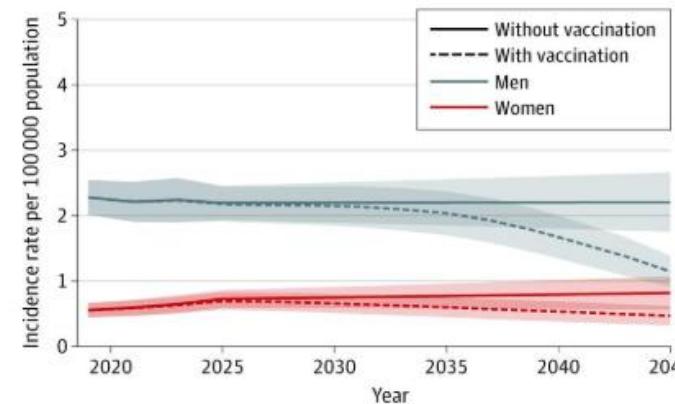
<sup>1</sup>Chaturvedi et al. J Clin Oncol. 2018 Jan 20;36(3):262-267. doi: 10.1200/JCO.2017.75.0141.

<sup>2</sup>Tsentemeidou et al. Sex Transm Dis. 2021 Sep 1;48(9):700-707. doi: 10.1097/OLQ.0000000000001405. PMID: 34110733.

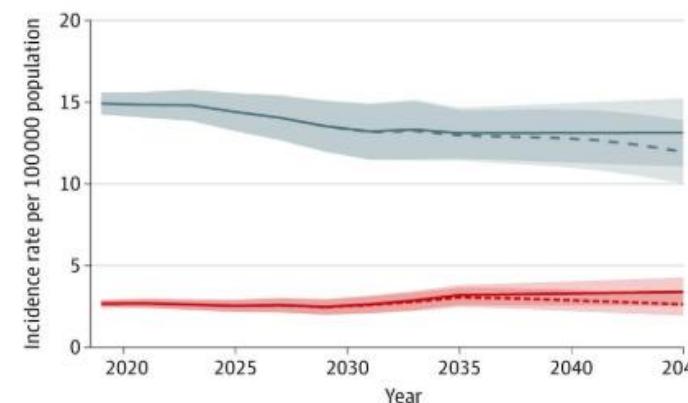
<sup>3</sup>Katz et al. J Oral Pathol Med. 2025 Oct;54(9):895-902. doi: 10.1111/jop.70016.

# Projected decreased incidence of HPV related oral and oropharynx cancer by gender and age through 2045

A] Age, 36-45 y



B] Age, 46-55 y

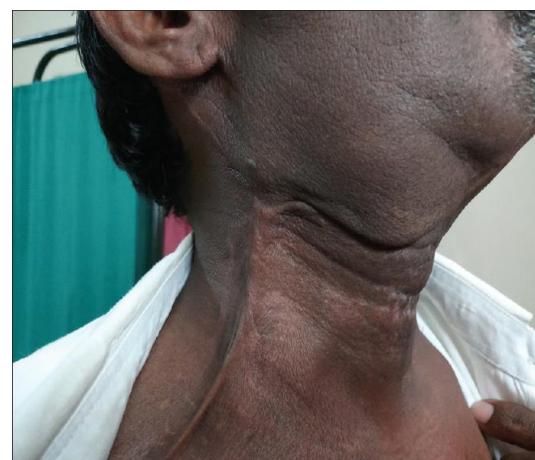
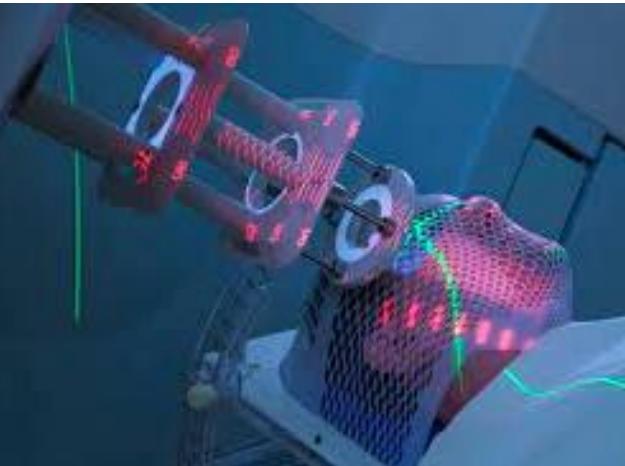


# Evidence-based communication recommendations for providers to increase HPV vaccination in clinical settings

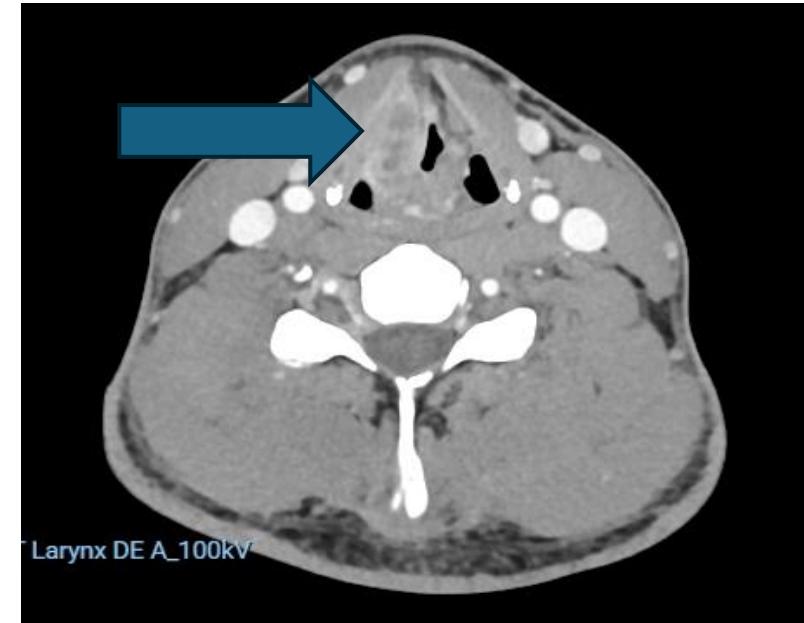
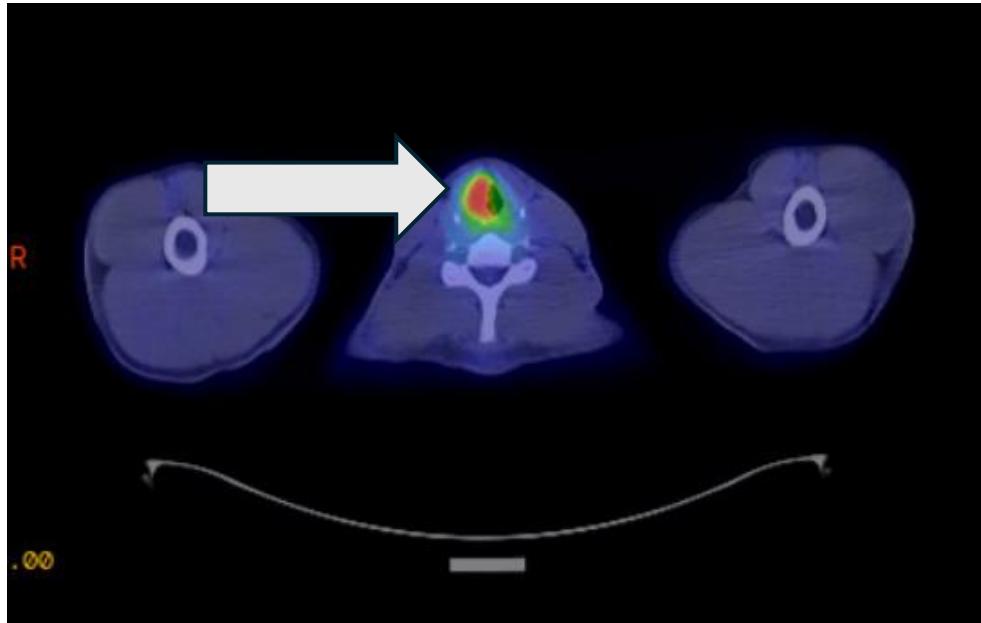
Quality	Communication practice
Strength of endorsement	Emphasize the importance of HPV vaccine
Urgency	Recommend same-day vaccination
Timeliness	Deliver recommendations by age 12
Consistency	Deliver recommendations to all adolescents, not just those perceived to be “at risk”
Prevention message	Emphasize cancer prevention
Concomitance	Recommend HPV vaccine at the same time and in the same way as other adolescent vaccines
Guideline-based rationale	Focus on the “routine” immunization schedule versus what is “required” for school entry
Type of language	Use presumptive not conversational language

# HPV vaccination: An oncologist's perspective

- 70-90% of the cancers I treat are preventable
- Treatment of HPV head and neck cancer includes surgery, radiation therapy, and chemotherapy
- Short- and long-term toxicity from head and neck cancer treatment is substantial
- Unnecessary suffering and loss of life
  - Both men and women
  - Young and old



22 year-old never smoker with larynx cancer



Laryngectomy performed January 28, 2025

# HPV vaccination University of Wisconsin-Lacrosse

- Pilot project
- Partnership between Mayo Clinic, UW-LaCrosse, Merck, and Scenic Bluffs (FQHC)
- 3 events per academic year
- Promoted by student team led by the university Wellness Coordinator

## HPV IMMUNIZATION CLINIC

Monday, March 31  
11:00Am - 5:00pm  
Cliffwood Bluff, 2120 Student Union

Vaccine available at no cost.  
Billed through insurance or paid for by Vaccines for Adults program.



### JOIN THE HERD

Build herd immunity to protect yourself and those around you from human papillomavirus (HPV) and long-term risk for cancer.

*Email [wellness@uwlax.edu](mailto:wellness@uwlax.edu) with questions.*

#### HPV Immunization Clinic Protect yourself and your peers

Join the herd! Safe and effective vaccination for human papillomavirus helps **build herd immunity to prevent genital warts and several cancers**. Wellness & Health Advocacy is partnering with Scenic Bluffs Community Health Centers, Mayo Clinic Health System, and the Wisconsin Cancer Collaborative to provide HPV immunizations at **no cost** for UWL students. Scenic Bluffs Community Health Centers will either bill insurance for the vaccine cost or provide it at no cost through the Vaccines for Adults program.

Students are encouraged to check their immunization records ([Wisconsin, Minnesota, Iowa, Illinois](#)) and attend the clinics to keep their immunizations current. Other vaccines (i.e., Tdap and COVID) will be available from Scenic Bluffs Community Health Centers.

*For every immunization received, students will earn tickets to enter our raffle!*

#### Related campus initiatives



#### When

- 11 a.m. to 5 p.m. Monday, March 31

#### Where

Cliffwood Bluff, 2120 Student Union

[UWL campus map](#) for building location and nearby parking lots.

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#### Contact

For questions about this event or to request disability accommodations [?](#), contact Issy Beach at [608.785.8977](tel:608.785.8977) or [wellness@uwlax.edu](mailto:wellness@uwlax.edu).

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#### Parking

Payment may be required. No permit? Use [Passport Parking](#).

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#### Additional parking info

[Website](#) | [Email](#) | [Call](#)



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Thank you for your attention

price.katharine@mayo.edu

A medical professional wearing a white coat and blue gloves is shown from the side, preparing to administer a vaccine to a patient's upper arm. The patient's arm is extended, and the medical professional's gloved hands are visible, holding a syringe and a small vial. The background is a clinical setting with medical equipment.

Please advocate for  
HPV vaccination to prevent  
cancer