

Protecting Our Children: 2015 Summit on HPV-Related Diseases

Epidemic of HPV Cancers in Men: What Can We Do Now?

June 18, 2015; Houston, Texas

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THE UNIVERSITY OF TEXAS

~~MD Anderson~~
Cancer Center

Making Cancer History®

No conflicts, disclosures, or off-label



Outline

- ❖ HPV in Men
- ❖ Cancer Epidemic
- ❖ Prevention
- ❖ Screening
- ❖ Plan of Action

2008 Nobel Prize in Physiology or Medicine



Harold zur Hausen, M.D.

**~40 HPV
Types**

**~ 80 HPV
Types**

**Mucosal
sites of infection**

**Cutaneous
sites of infection**

**High risk (oncogenic)
HPV 16, 18 most common**

**Low risk (non-oncogenic)
HPV 6, 11 most common**

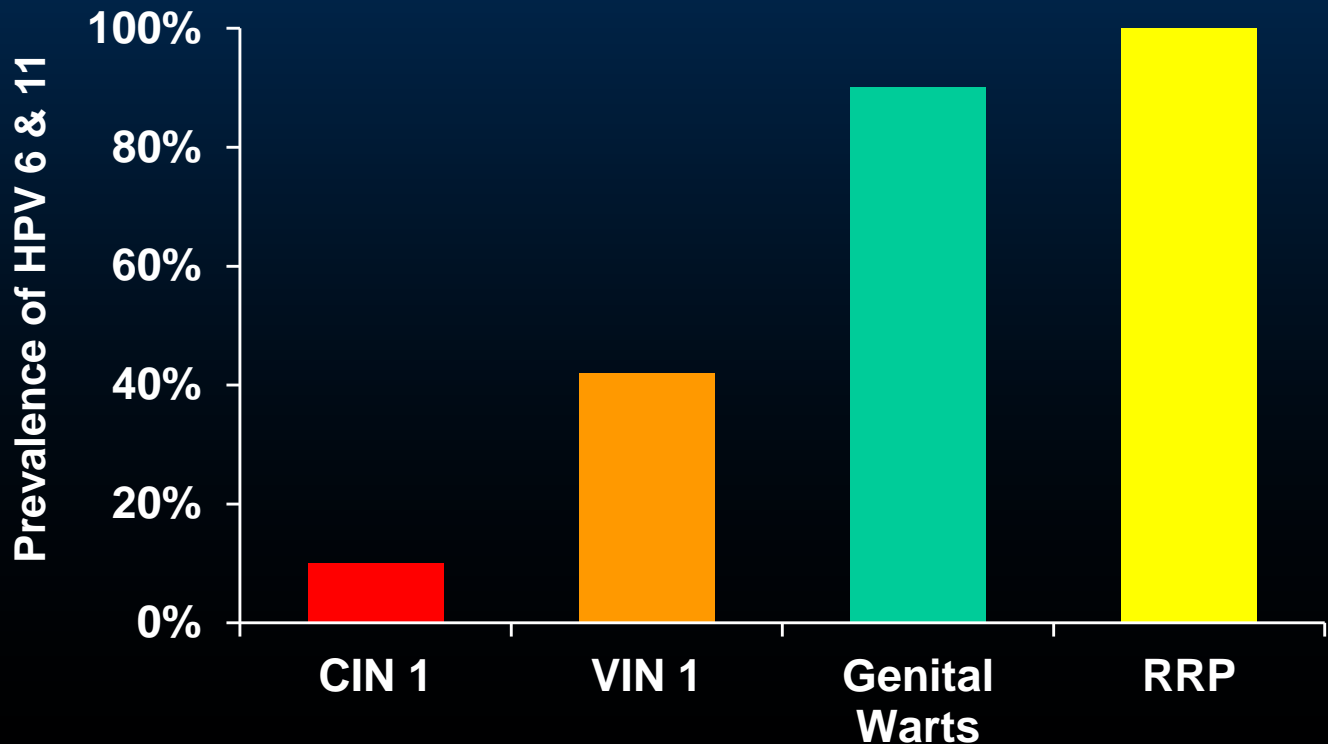
**Anogenital & Oropharyngeal Cancers
Cancer Precursors:
Anogenital High Grade Dysplasias**

**Genital Warts
Laryngeal Papillomas
Low Grade Cervical Disease**

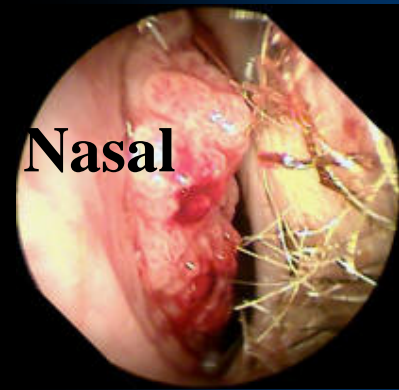
**“Common”
Cutaneous
Warts**

Benign Diseases Attributed to HPV

Each Year among Women in the U.S.:
1.4 million new cases of CIN 1
330,000 new cases of CIN 2-3
1 million new cases of genital warts



Nasal



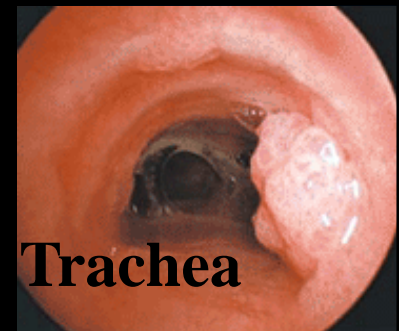
Palate



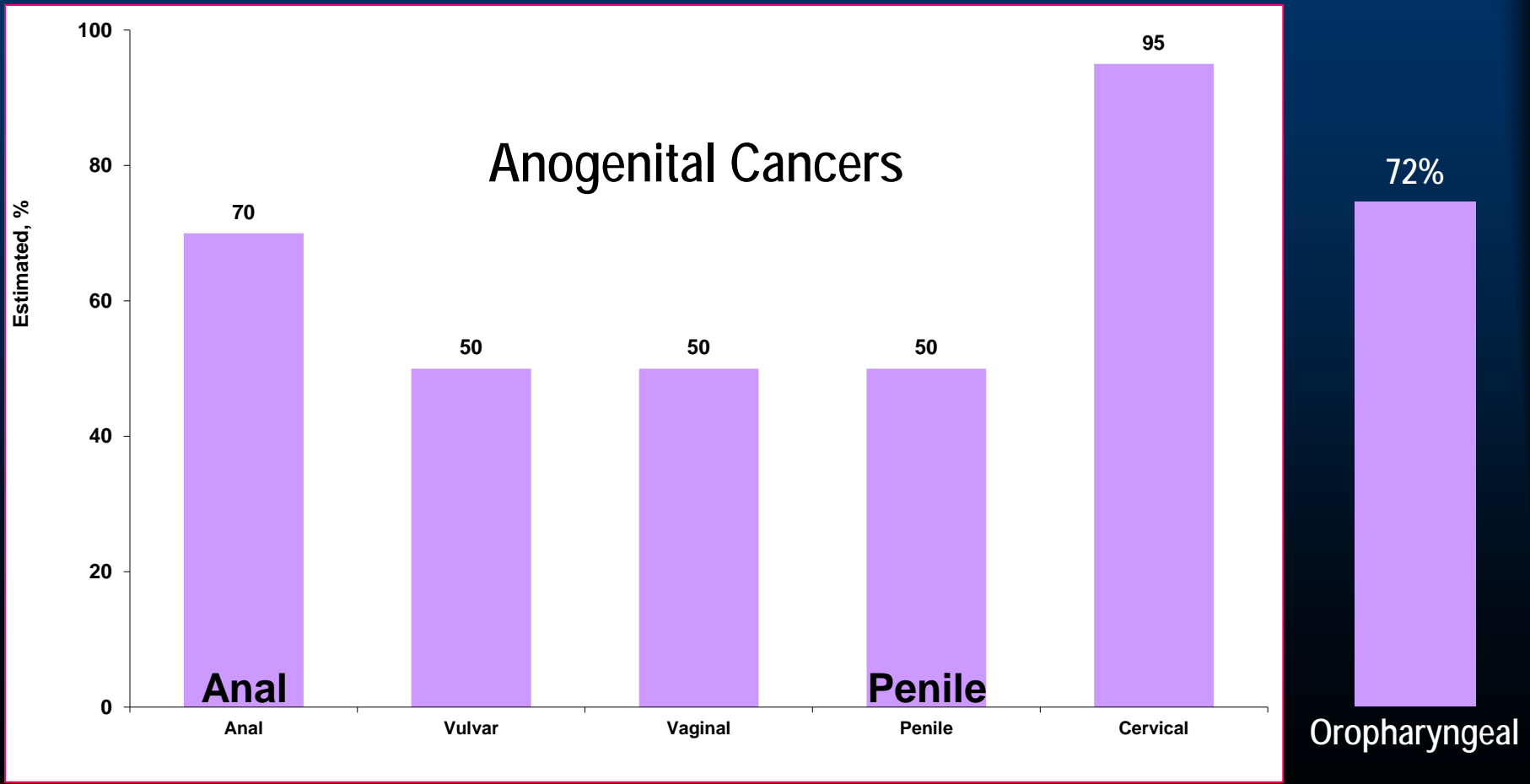
Larynx



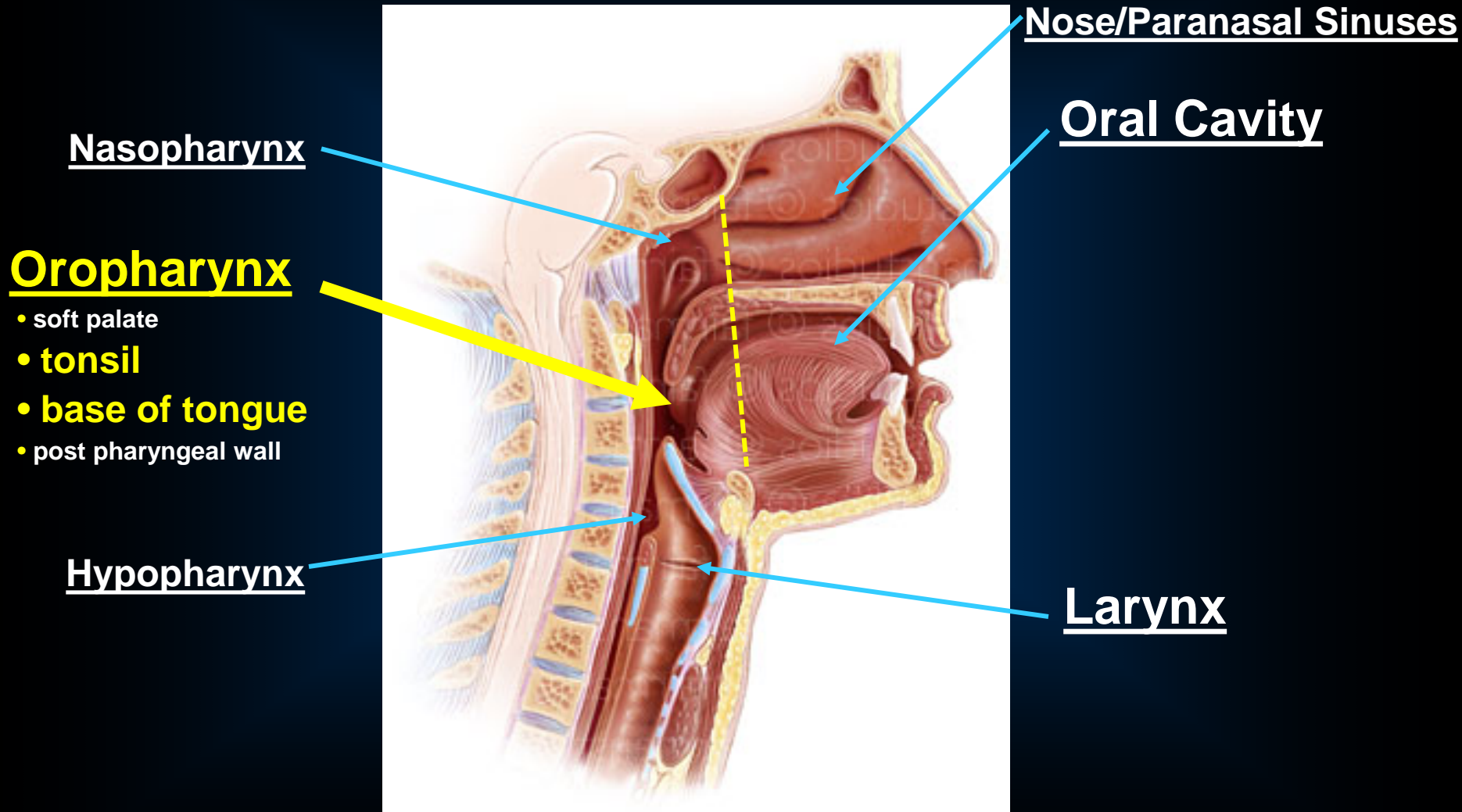
Trachea



Proportion of Cancers Attributed to HPV



H&N Squamous Cell Carcinomas



Genital HPV Infection

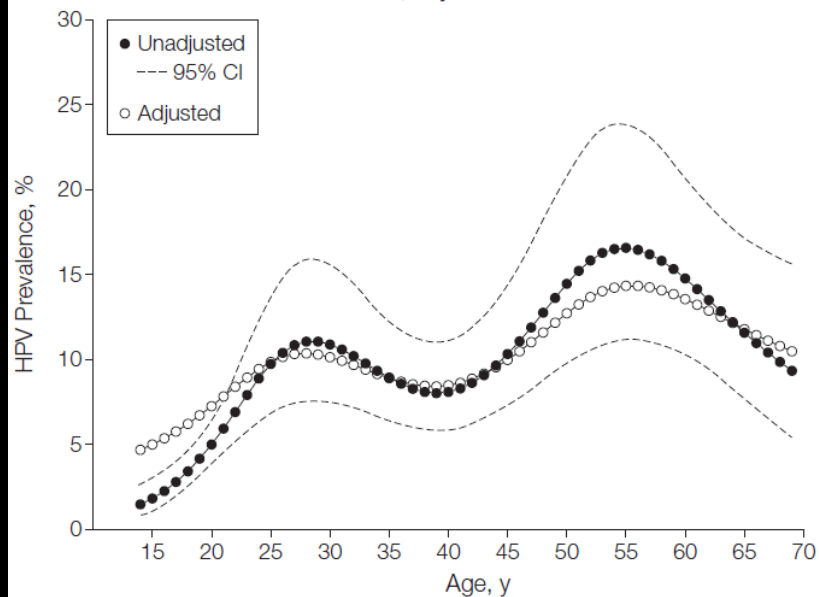
Most females & males will be infected with at least one HPV type at some point

- 80 million Americans currently infected
- 14 million new infections/year in the US
- the most common “STD”
- most are asymptomatic
- most common in teens & early 20s

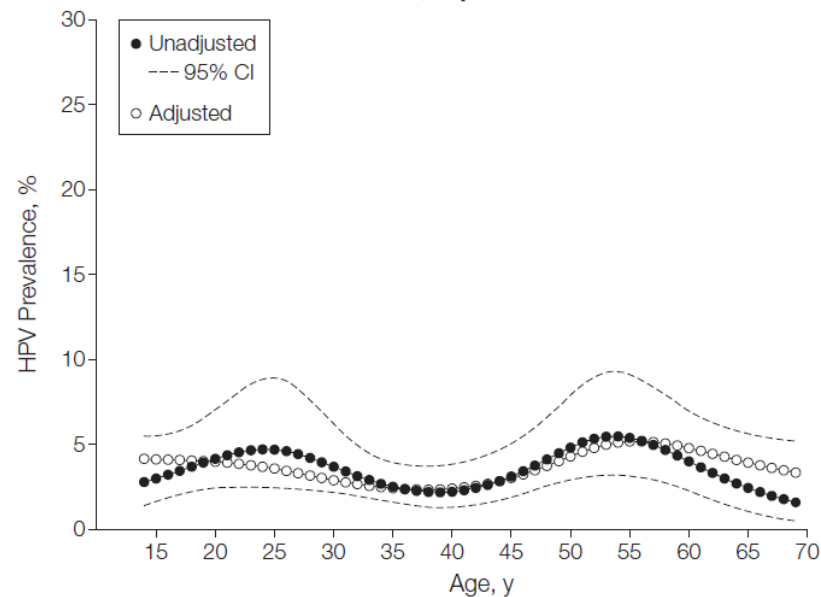
Oral HPV prevalence by age

JAMA. 2012;307(7):693-703

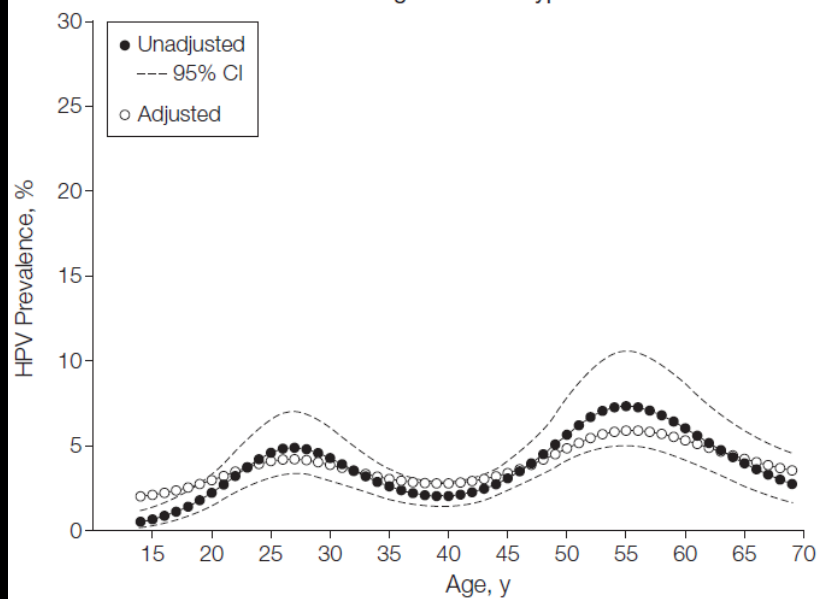
Men, any HPV infection



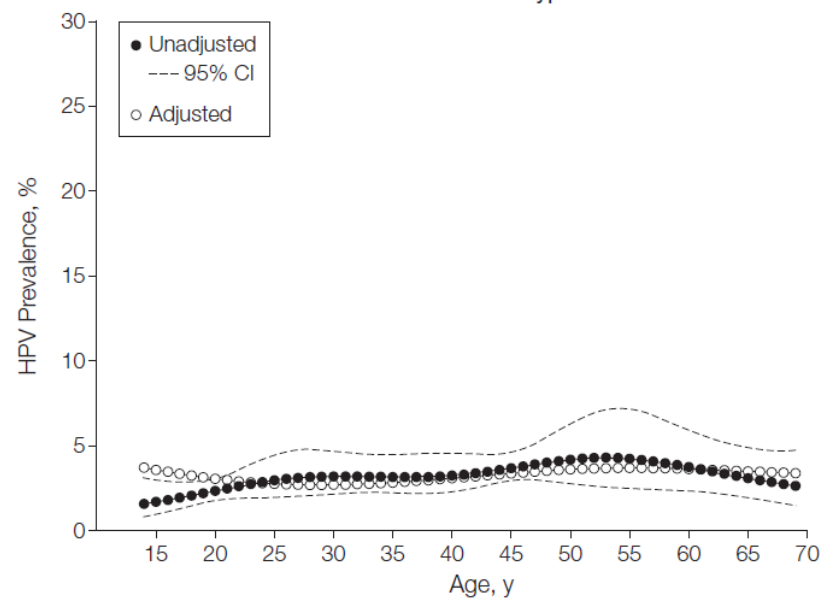
Women, any HPV infection



High-risk HPV types



Low-risk HPV types



Incidence and clearance of oral human papillomavirus infection in men: the HIM cohort study *Lancet 2013; 382: 877-87*

Aimée R Kreimer,* Christine M Pierce Campbell,* Hui-Yi Lin, William Fulp, Mary R Papenfuss, Martha Abrahamsen, Allan Hildesheim, Luisa L Villa, Jorge J Salmerón, Eduardo Lazcano-Ponce, Anna R Giuliano

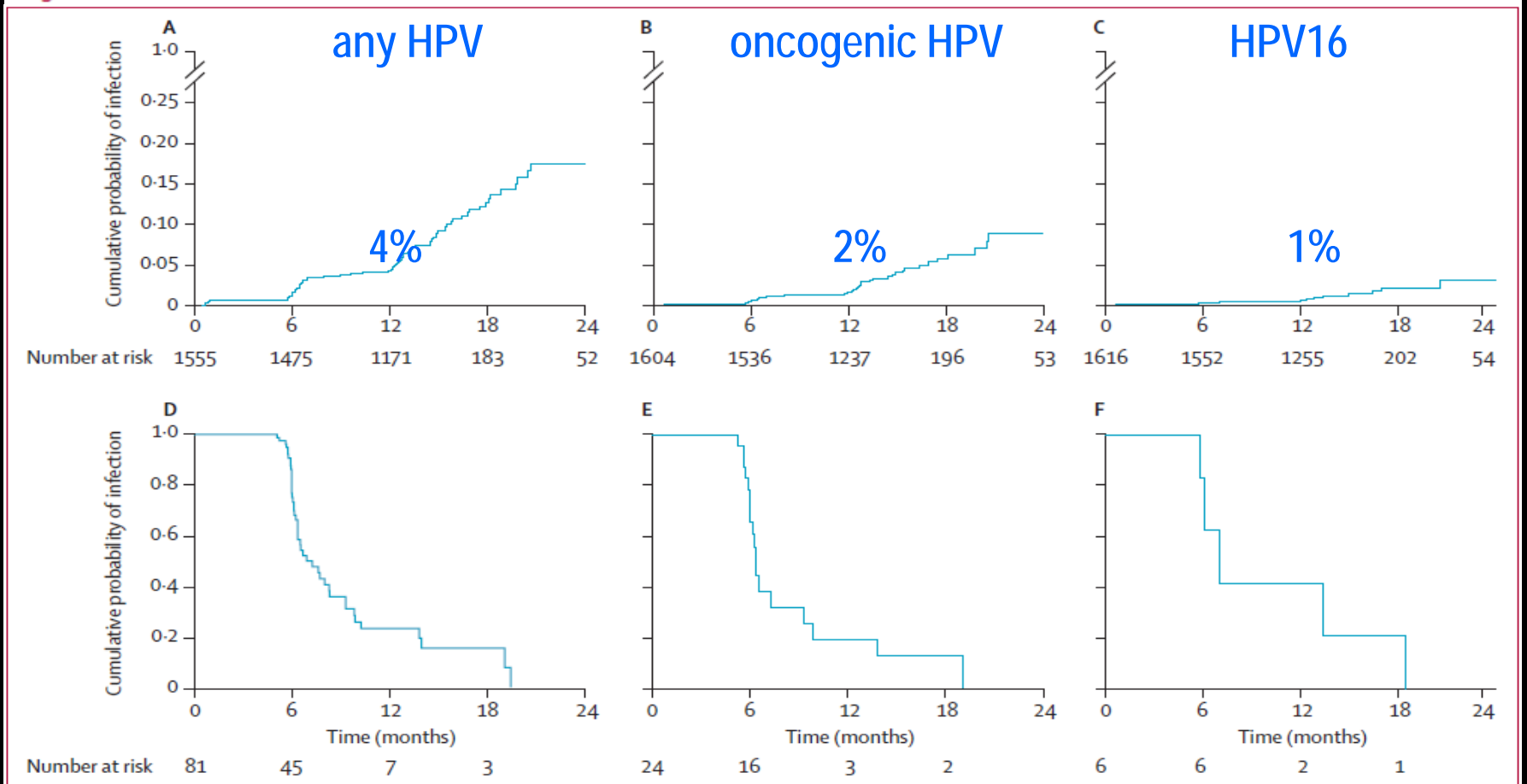


Figure 1: Kaplan-Meier estimates of the cumulative incidence and time to clearance of any, oncogenic, and type 16 oral human papillomavirus (HPV) infections (A) Incidence of any oral HPV. (B) Incidence of oncogenic oral HPV. (C) Incidence of oral HPV 16. (D) Clearance of any incident oral HPV. (E) Clearance of incident oncogenic oral HPV. (F) Clearance of incident oral HPV 16.

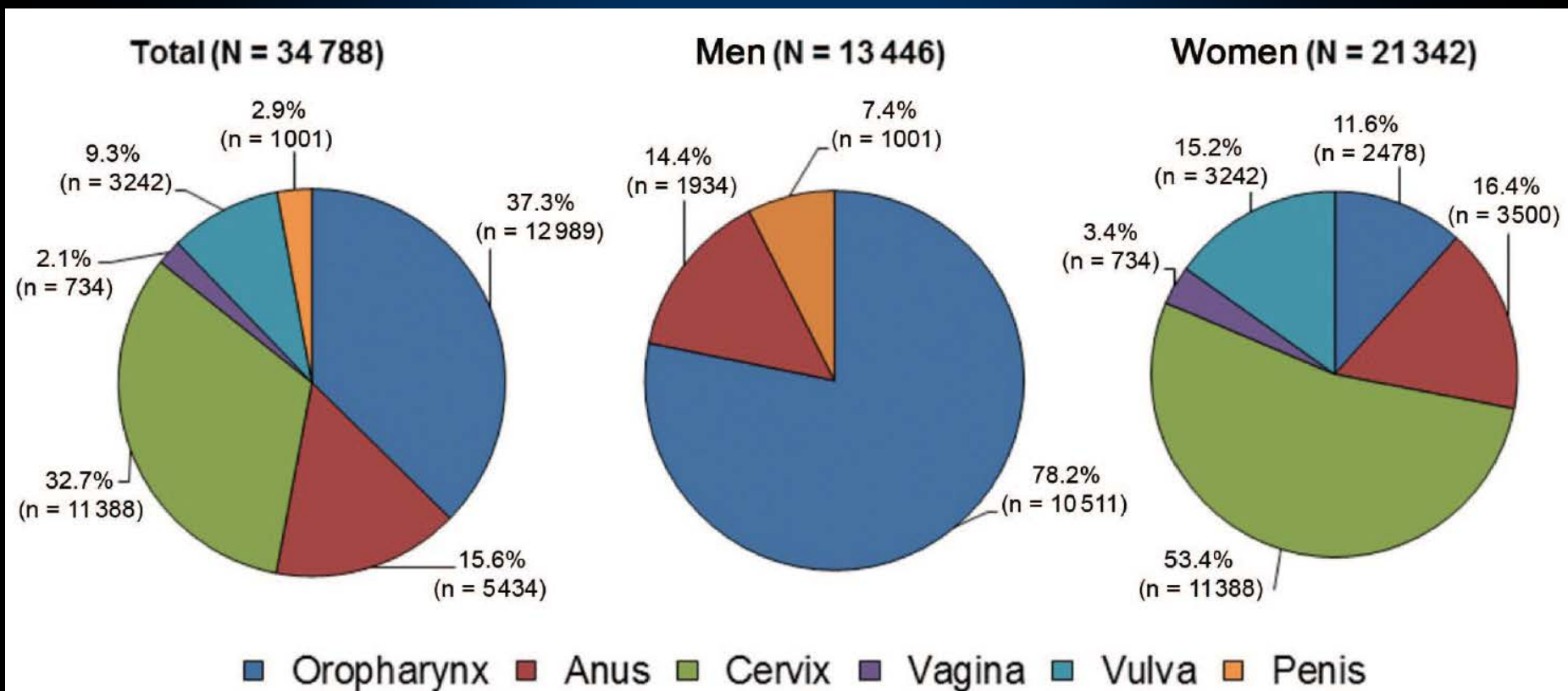
Outline

- ❖ HPV in Men
- ❖ Cancer Epidemic
- ❖ Prevention
- ❖ Screening
- ❖ Plan of Action

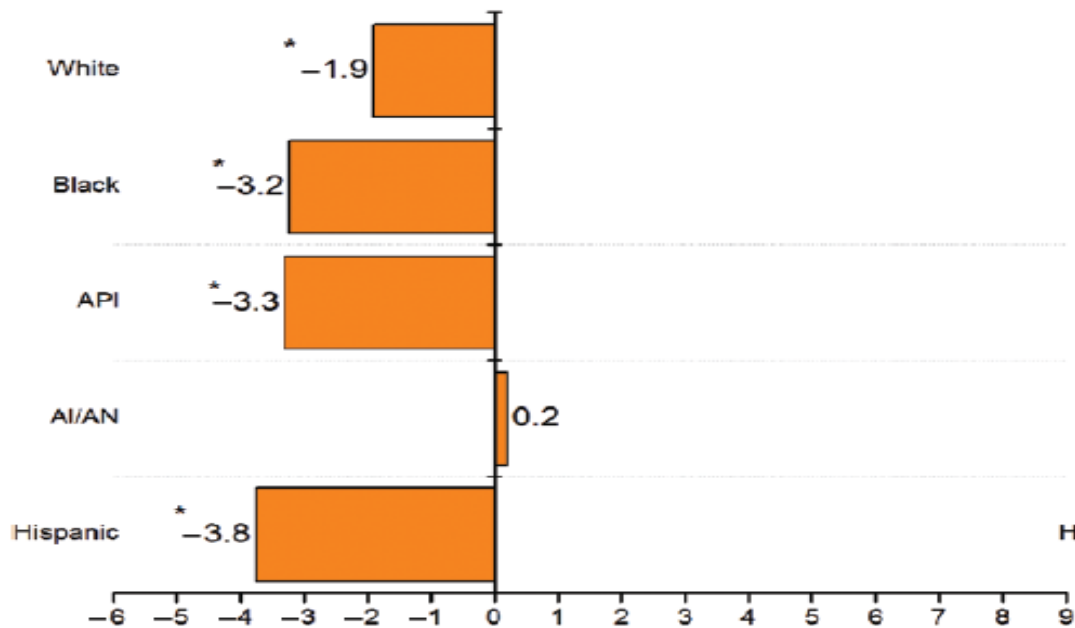
Annual Report to the Nation on the Status of Cancer, 1975–2009, Featuring the Burden and Trends in Human Papillomavirus (HPV)–Associated Cancers and HPV Vaccination Coverage Levels

Ahmedin Jemal, Edgar P. Simard, Christina Dorell, Anne-Michelle Noone, Lauri E. Markowitz, Betsy Kohler, Christie Ehemam, Mona Saraiya, Priti Bandi, Debbie Saslow, Kathleen A. Cronin, Meg Watson, Mark Schiffman, S. Jane Henley, Maria J. Schymura, Robert N. Anderson, David Yankey, Brenda K. Edwards

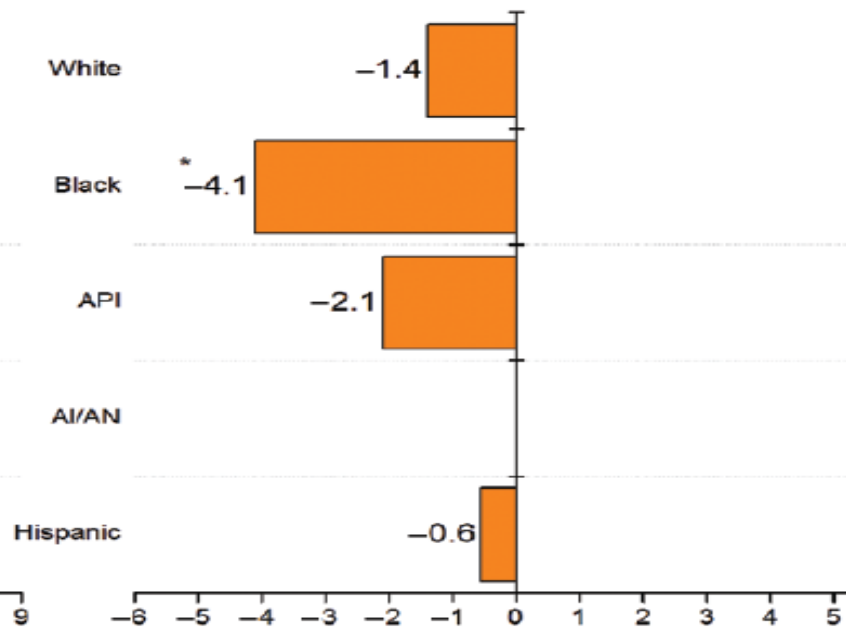
J Natl Cancer Inst 2013



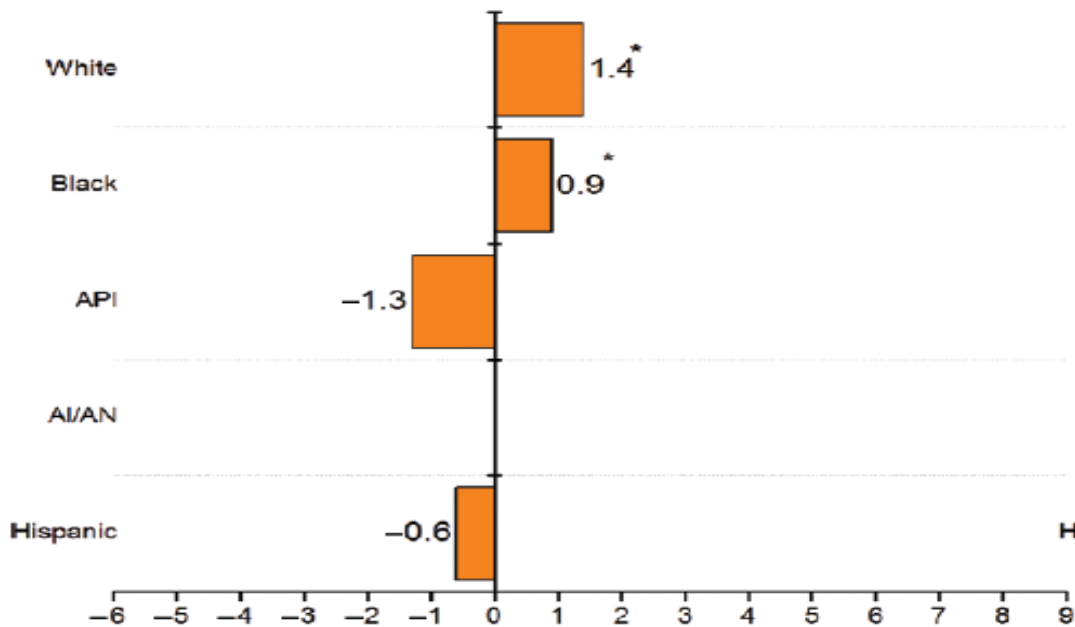
Cervix



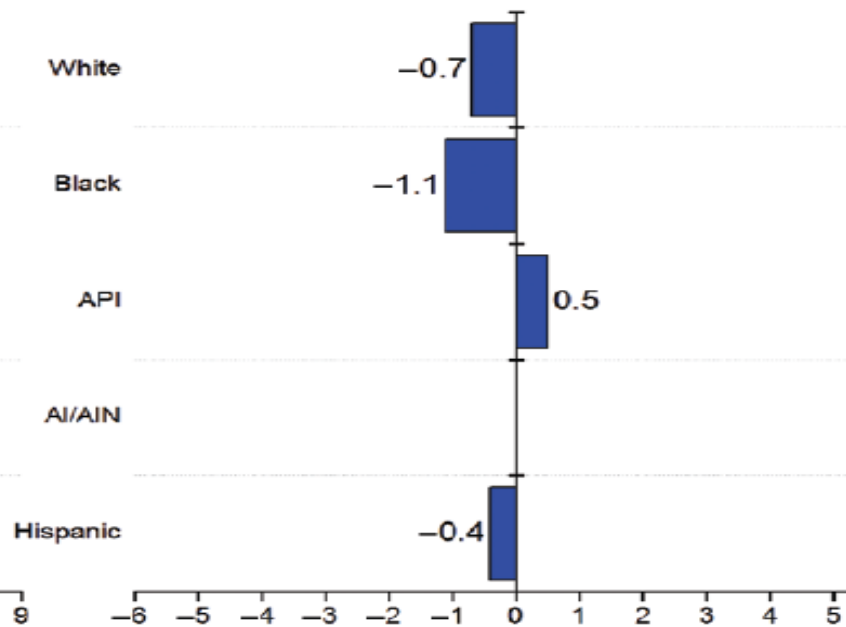
Vagina



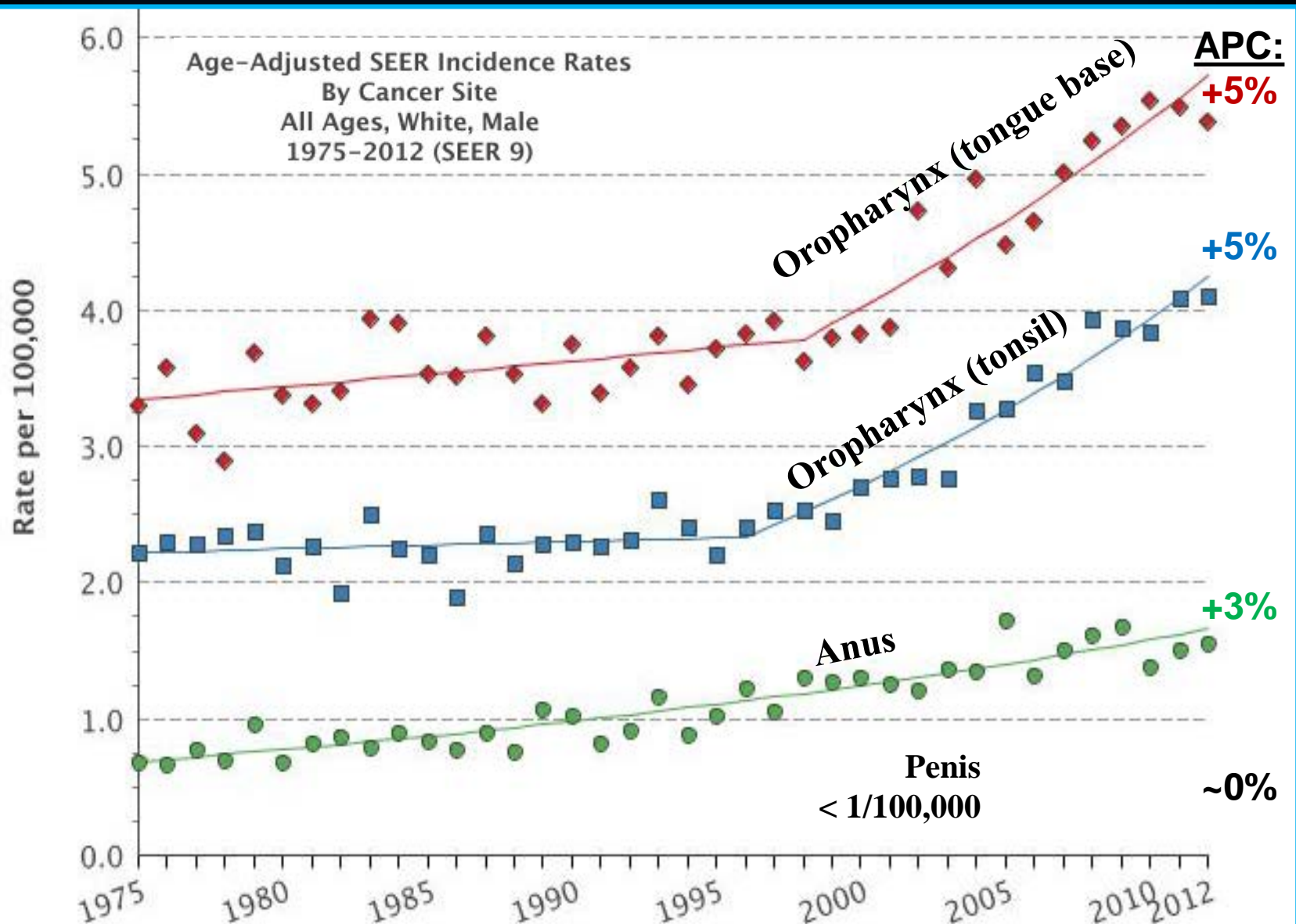
Vulva



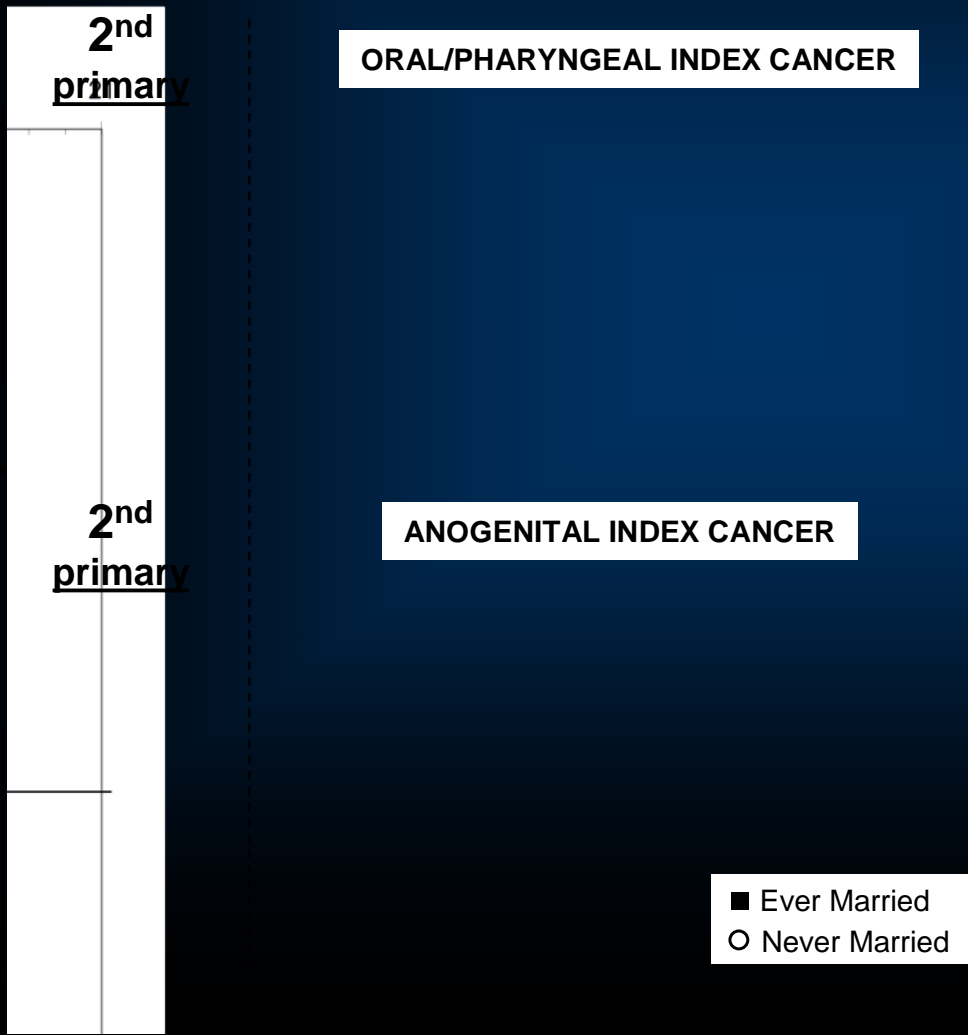
Penis



Epidemic of HPV Cancers in U.S. Men



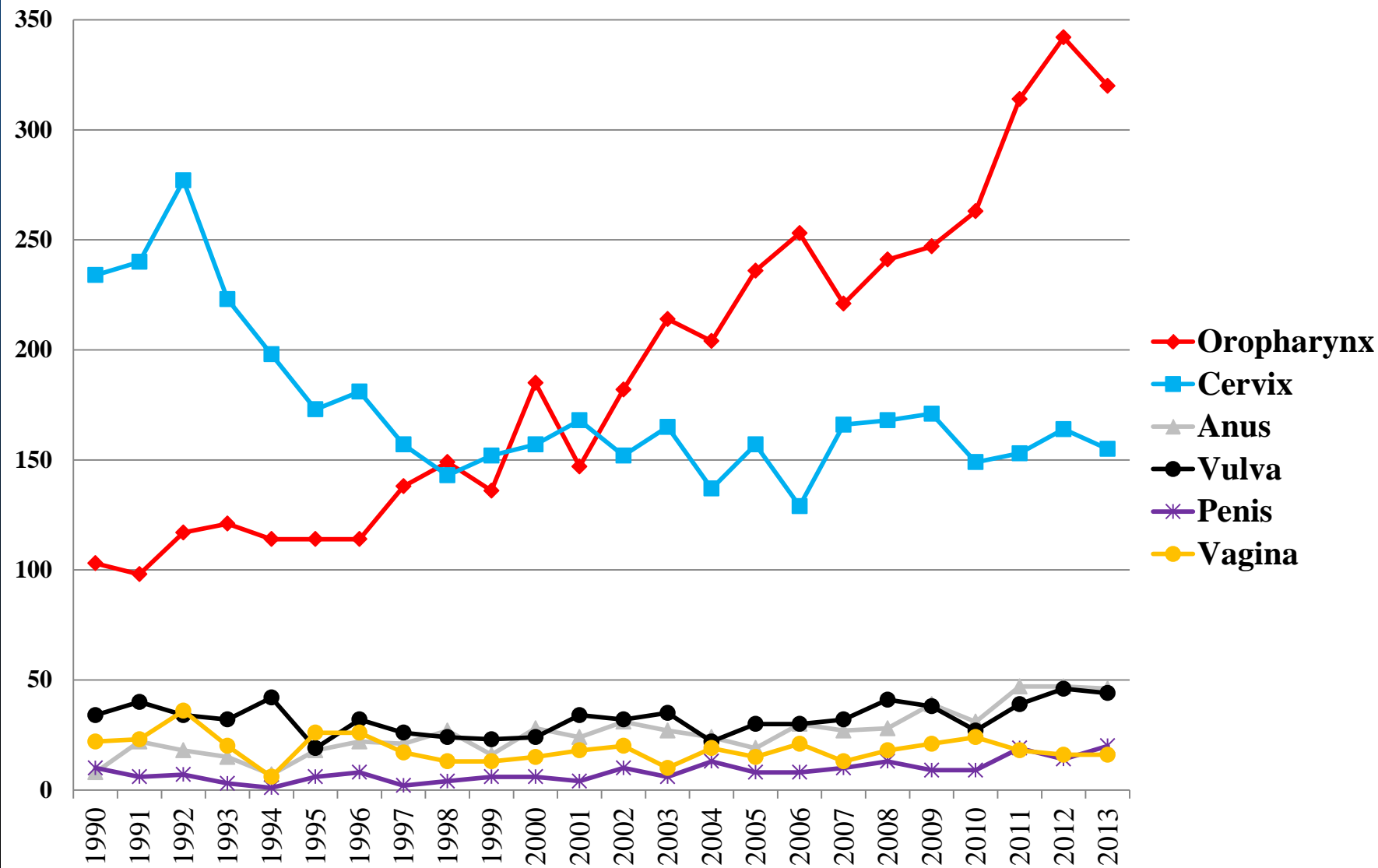
Second Primary Cancers in Men Segregated by Marital Status SEER Database



• Sikora, Morris, & Sturgis
Arch Oto-HNS, 2009

Newly Diagnosed-Untreated Cases Presenting to MD Anderson Each Year

Number of Cases



An Evolution in Demographics, Treatment, and Outcomes of Oropharyngeal Cancer at a Major Cancer Center

Kristina R. Dahlstrom, MS¹; Gabriel Calzada, MD¹; Jennifer D. Hanby, MD¹; Adam S. Garden, MD²; Bonnie S. Glisson, MD³; Guojun Li, MD, PhD^{1,4}; Dianna B. Roberts, PhD¹; Randal S. Weber, MD¹; and Erich M. Sturgis, MD, MPH^{1,4}

No. of Patients (%)

No. = 3,891

	1955-1964, n = 473	1965-1974, n = 666	1975-1984, n = 657	1985-1994, n = 850	1995-2004, n = 1245	P for Trend
Age, y						< .001
<46	23 (4.9)	42 (6.3)	52 (7.9)	91 (10.7)	174 (14)	
46-55	135 (28.5)	176 (26.4)	142 (21.6)	218 (25.7)	462 (37.1)	= 55
56-65	173 (36.6)	257 (38.6)	262 (39.9)	291 (34.2)	346 (27.8)	
>65	142 (30)	191 (28.7)	201 (30.6)	250 (29.4)	263 (21.1)	

Median Age = 60

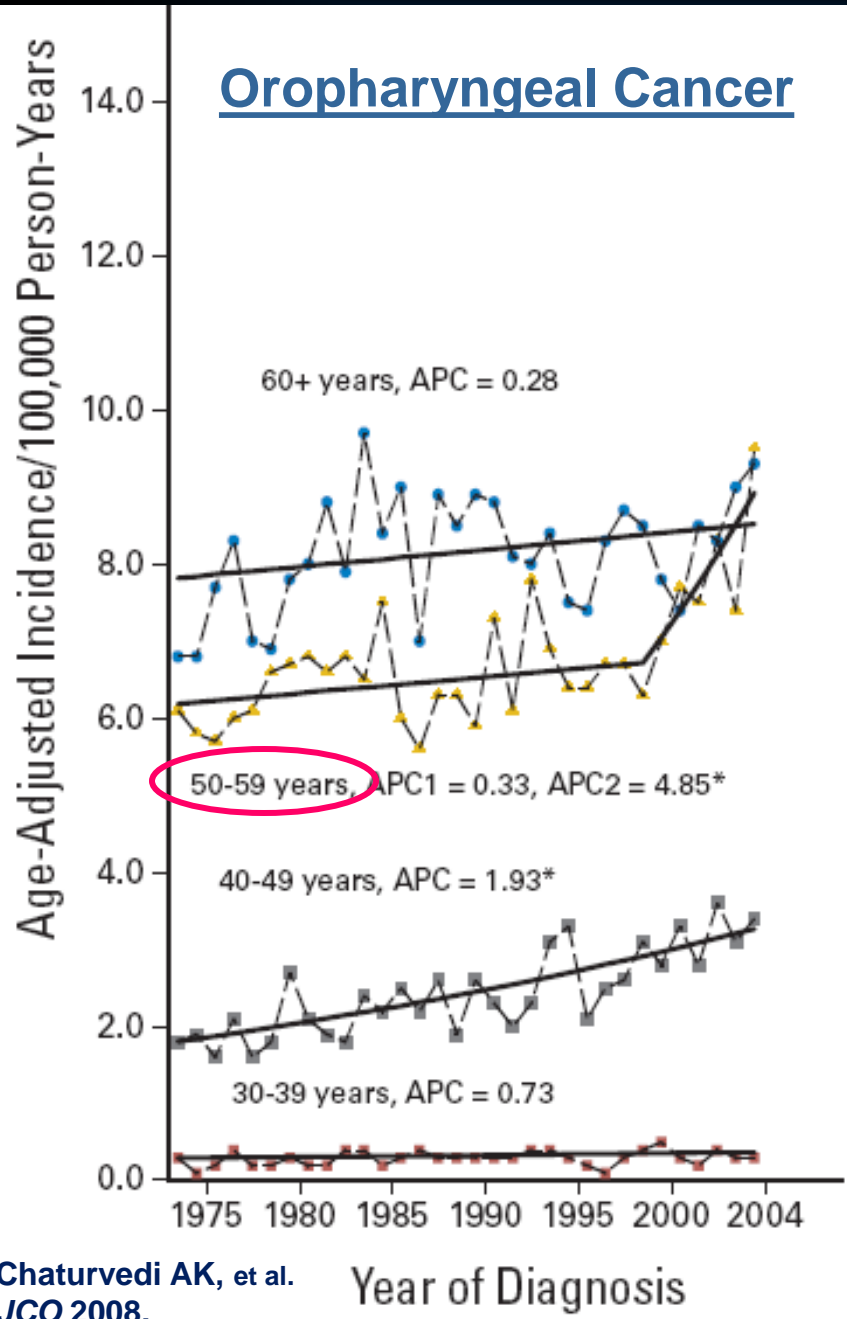
MDACC Prospective Database

(No. = 1,457)

Median Age = 55

Years: 95-99 00-04 05-09 10-14
Median: 54 55 56 56

Oropharyngeal Cancer SEER Age-adjusted Incidence

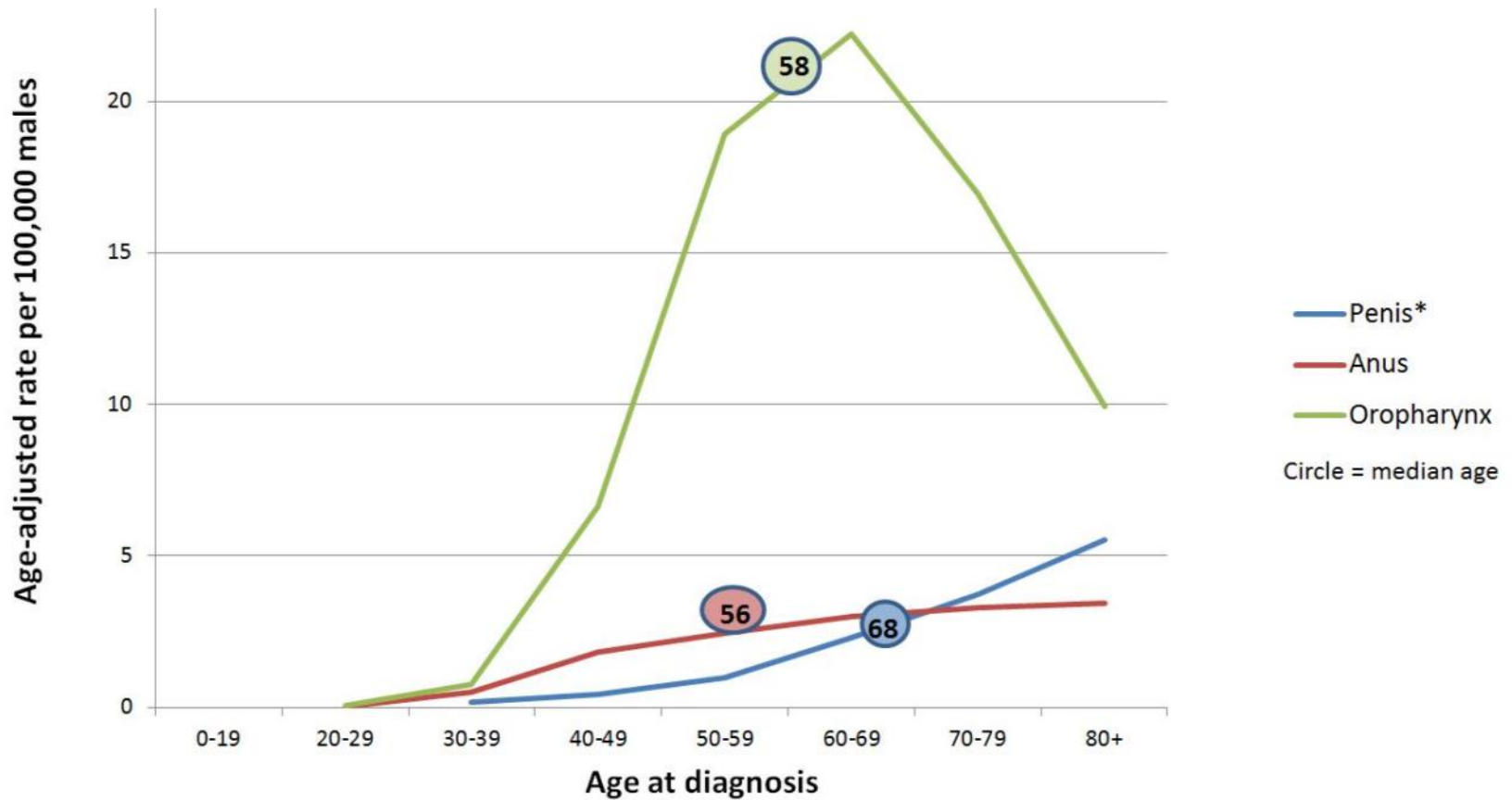


Chaturvedi AK, et al.
JCO 2008.

Chaturvedi AK, et al. JCO 2008.

HPV-Associated Cancer Incidence by Age & Median Age at Dx

Males, United States, 2004–2008

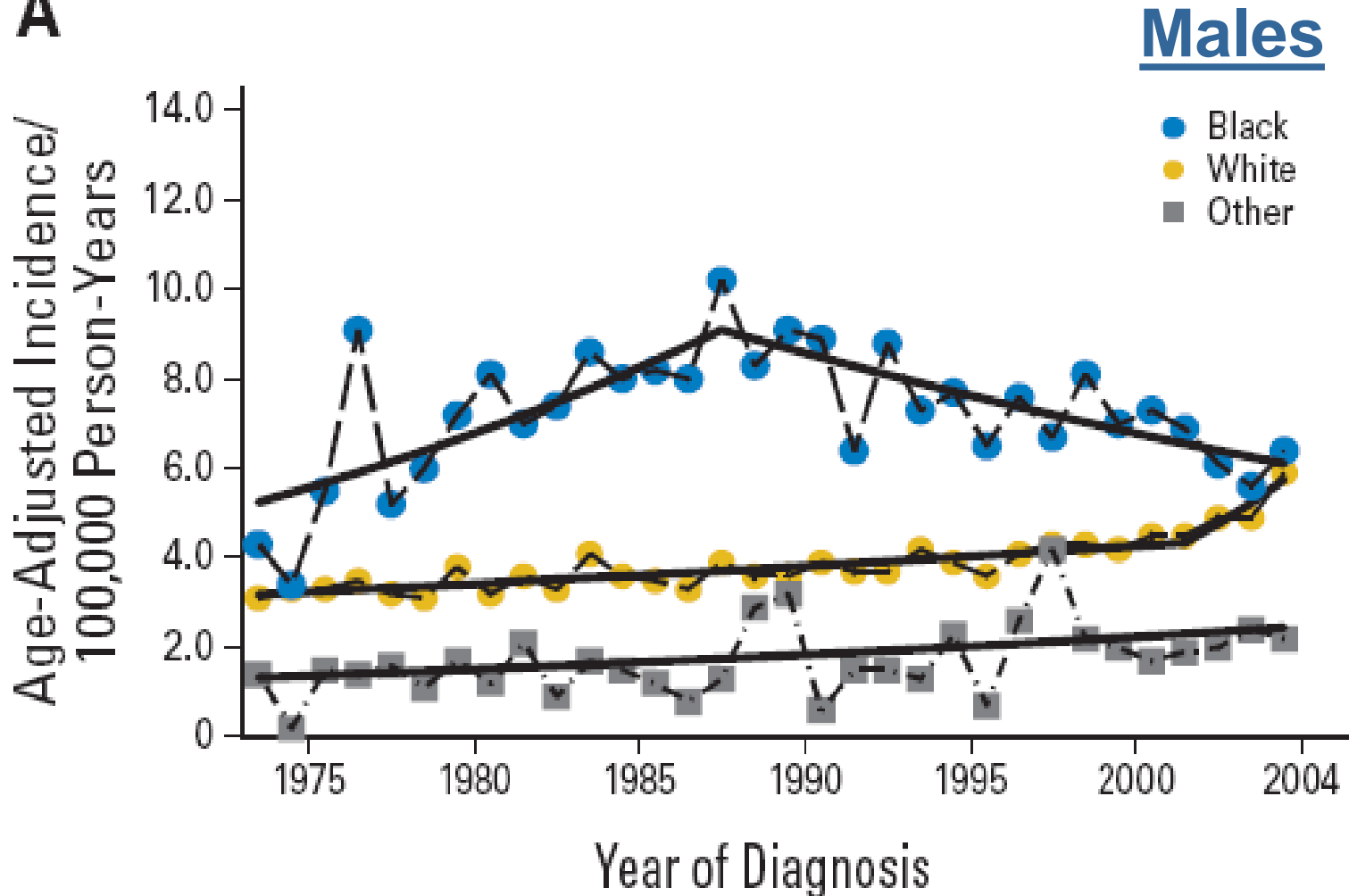


*Penile cancer statistics for men between the ages of 20 & 39 not shown because there were < 16 cases.

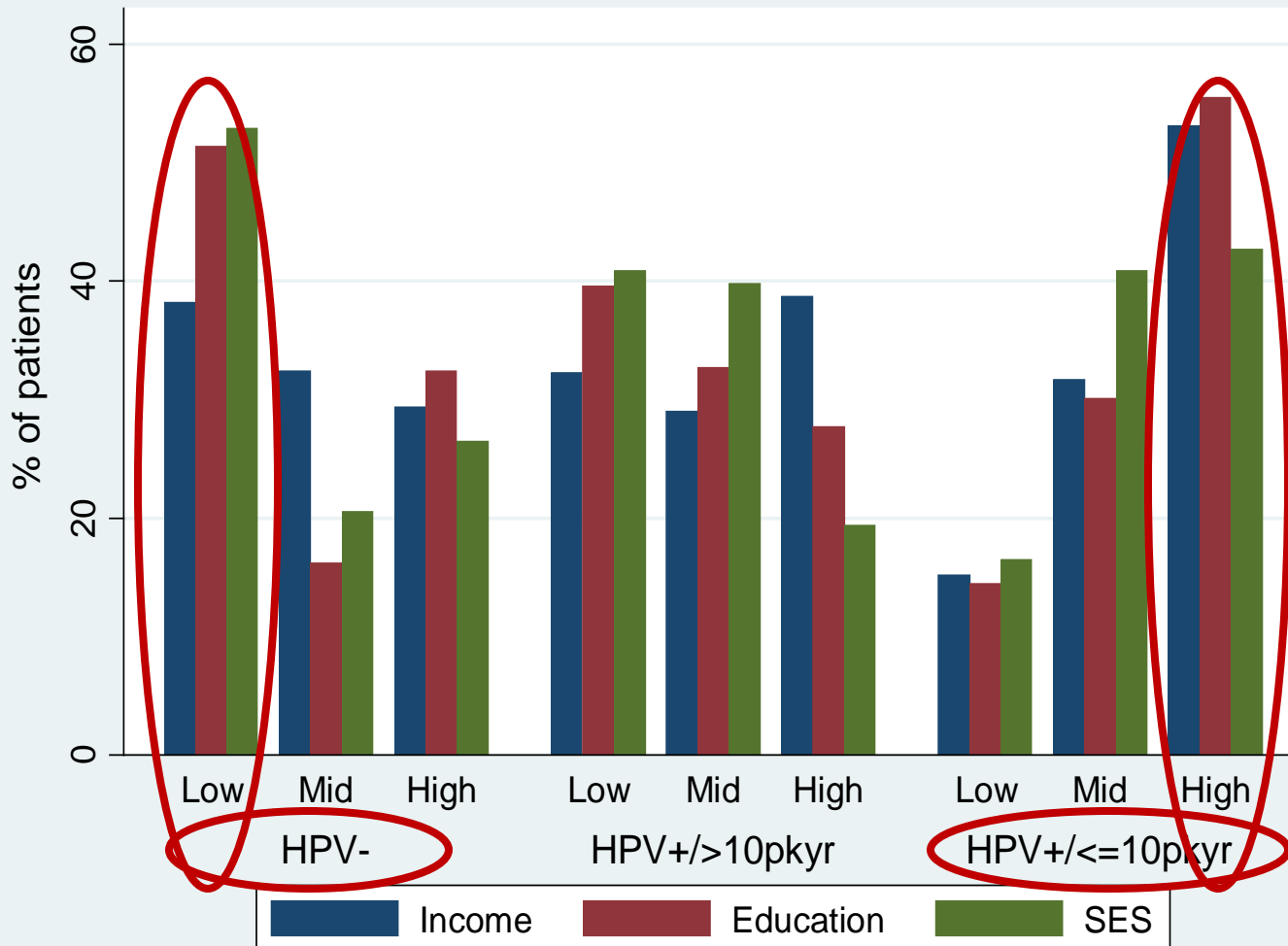
Watson et al. HPV-associated cancers—United States, 2004–2008. *MMWR* 2012;61:258–261.

Oropharyngeal Cancer SEER Age-adjusted Incidence

A



Socioeconomic Distribution



Income

Low: <\$50K
 Mid: \$50-\$100K
 High: >\$100K

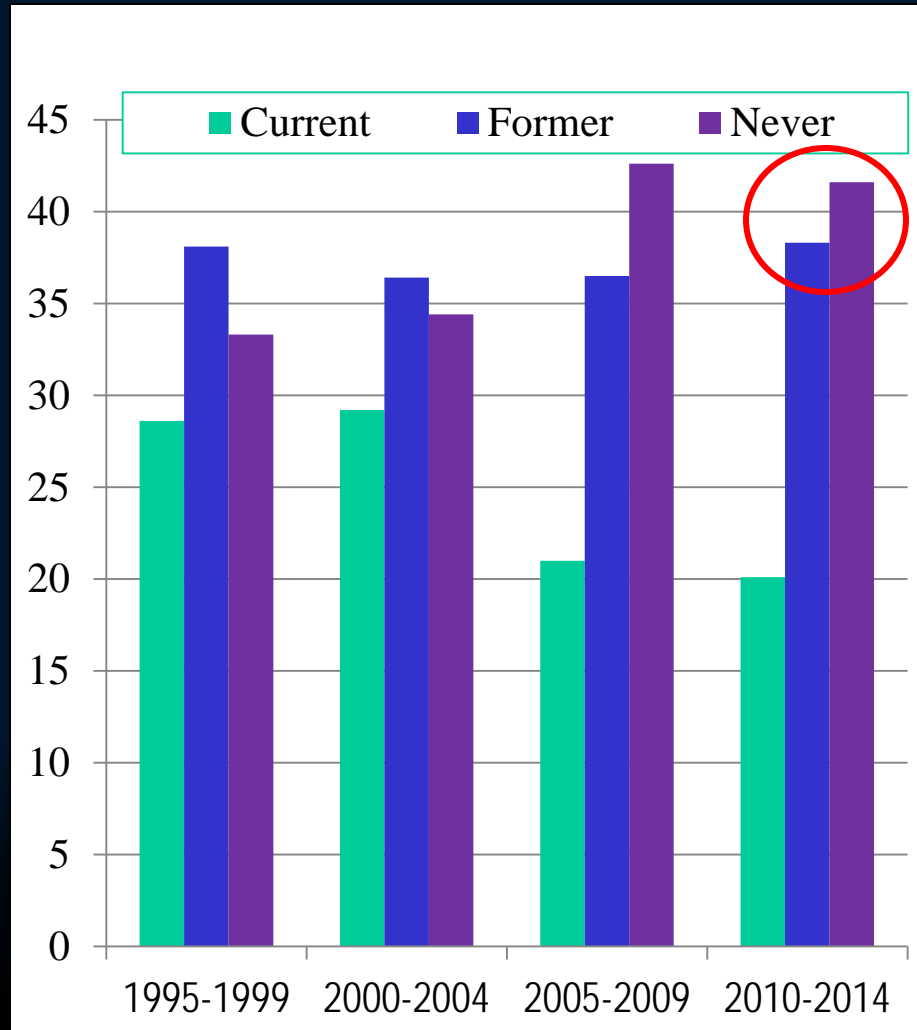
Education

Low: ≤HS/GED
 Mid: Tech/Voc
 High: ≥Bachelor's

SES Composite

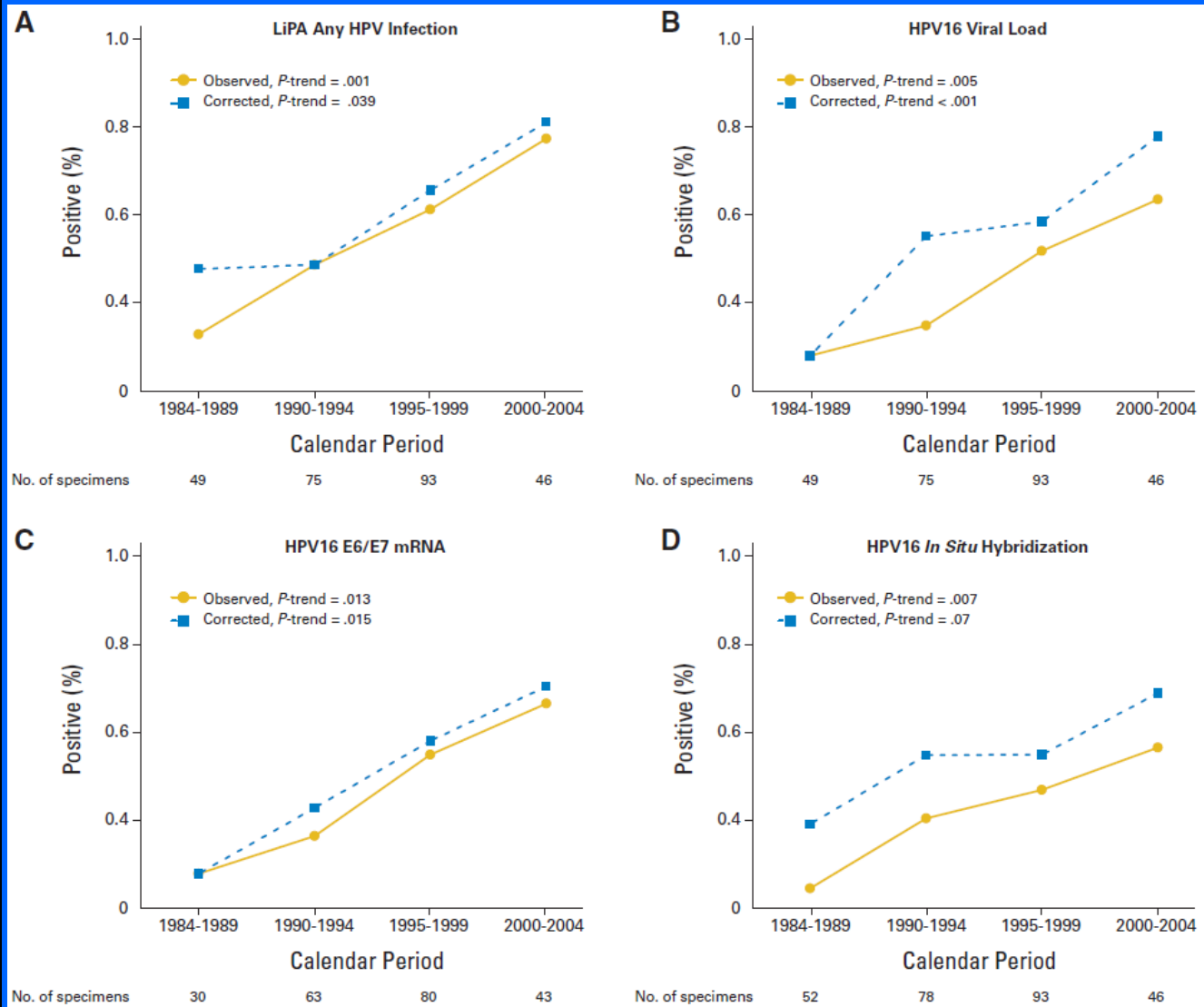
Low: Lowest 1/3
 Mid: Middle 1/3
 High: Highest 1/3

MDACC Prospective Database (No. = 1457)



80%

HPV+ Prevalence among 271 Oropharyngeal Cancers 1980-2004 Trends in SEER (Hawaii, L.A., Iowa)



Initial Symptoms in Patients With HPV-Positive and HPV-Negative Oropharyngeal Cancer

Wesley R. McIlwain, BS; Amit J. Sood, BA; Shaun A. Nguyen, MD, MA; Terry A. Day, MD

Table 3. Initial Chief Complaint Based on Human Papillomavirus (HPV) Status

Symptom	Total Patients (n = 88) ^a	No. (%)		P Value
		HPV Status		
		Positive (n = 71)	Negative (n = 17)	
Neck mass	39 (44)	36 (51)	3 (18)	.02
Sore throat	29 (33)	20 (28)	9 (53)	.09 ^b
Dysphagia	14 (16)	7 (10)	7 (41)	.005
Visualized mass	11 (13)	10 (14)	1 (6)	.60 ^b
Globus sensation	9 (10)	7 (9)	2 (12)	.81 ^b
Odynophagia	8 (9)	4 (6)	4 (24)	.04
Otalgia	6 (7)	6 (8)	0	.48 ^b
Pain (nonspecific)	6 (7)	4 (5)	2 (12)	.32 ^b
Bleeding	3 (3)	1 (1)	2 (12)	.09 ^b
Weight loss	3 (3)	1 (1)	2 (12)	.09 ^b
Change in voice	3 (3)	2 (2)	1 (6)	.48 ^b
Asymptomatic	2 (2)	2 (2)	0	.99 ^b
Fatigue	1 (1)	1 (1)	0	.99 ^b

Table 4. Initial Presenting Symptoms vs Positive Human Papillomavirus Status: Spearman Rank Order Correlation

Symptom	Correlation Coefficient	P Value
Neck mass	0.263	.01
Sore throat	-0.208	.05
Dysphagia	-0.338	.001
Odynophagia	-0.246	.02
Bleeding	-0.225	.03
Weight loss	-0.225	.03

^a Numbers do not all sum up to 100% because patients often present with multiple symptoms.

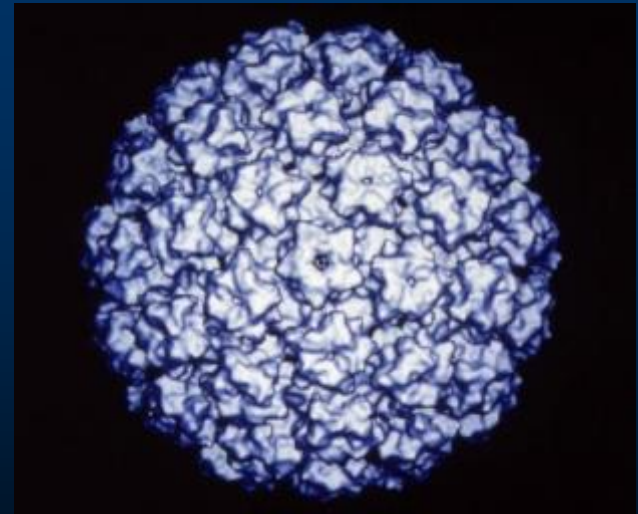
^b Nonsignificant P values.

Outline

- ❖ HPV in Men
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- ❖ **Prevention**
- ❖ **Screening**
- ❖ **Plan of Action**

HPV Prophylactic Vaccines

- Recombinant L1 capsid proteins that form “virus-like” particles
- Non-infectious and non-oncogenic
- Produce higher levels of neutralizing antibody than natural infection



HPV Virus-Like Particle

HPV Vaccines Currently Licensed in U.S.

	Bivalent 2vHPV (Cervarix)	Quadrivalent 4vHPV (Gardasil)	9-Valent 9vHPV (Gardasil 9)
Manufacturer	GSK	Merck	Merck
HPV Types Included	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Contraindications	Hypersensitivity to latex*	Hypersensitivity to yeast	Hypersensitivity to yeast
Dose Schedule	3 dose series: 0, 1, 6 months	3 dose series: 0, 2, 6 months	3 dose series: 0, 2, 6 months

~70% of
Cervical Cancers,
& ~90% of HPV+
OP & Anal Cancers

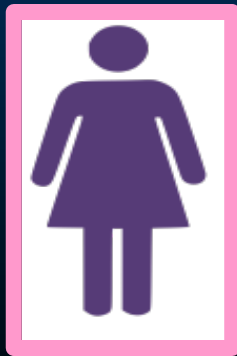
Genital Warts,
~70% of
Cervical Cancers,
& ~90% of HPV+
OP & Anal Cancers

Genital Warts,
~85% of
Cervical Cancers,
& ~90% of HPV+
OP & Anal Cancers

HPV Vaccine Recommendation

Girls and Boys can start HPV vaccination at age 9

Preteens should finish HPV vaccine series by 13th birthday



Catch-up Vaccination:
girls 13-26 years old who
have not started or finished
HPV vaccine series



Catch-up Vaccination:
boys 13-21 years old who
have not started or finished
HPV vaccine series

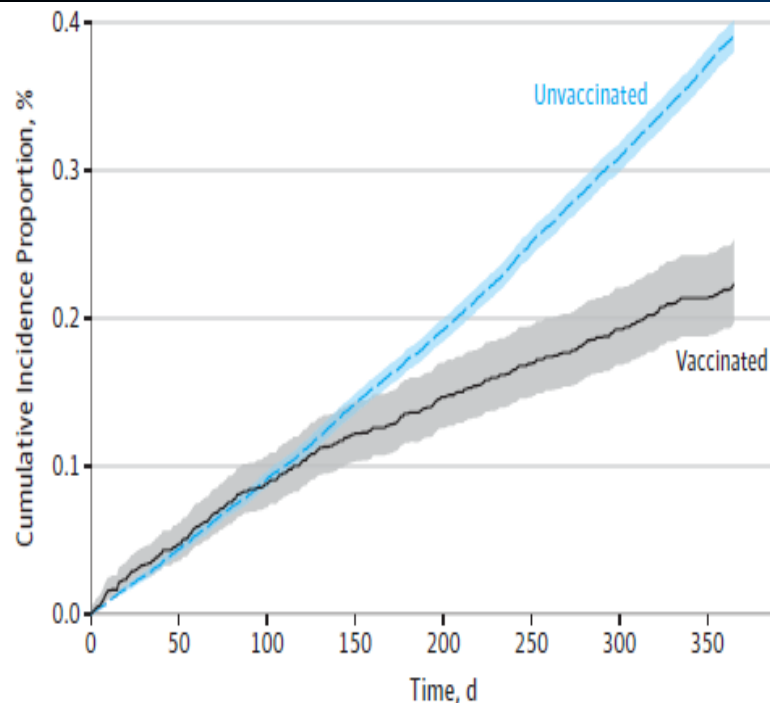
HPV Vaccination Is Safe, Effective, and Provides Lasting Protection

- **SAFE**
 - Benefits far outweigh any potential risks
 - Similar to safety reviews of MCV4 and Tdap vaccination
- **EFFECTIVE**
 - Population impact against early and mid outcomes are already being reported in multiple countries
- **LASTING PROTECTION**
 - No evidence of waning protection

Association of Varying Number of Doses of Quadrivalent Human Papillomavirus Vaccine With Incidence of Condyloma

Eva Herweijer, MSc; Amy Leval, PhD; Alexander Ploner, PhD; Sandra Eloranta, PhD; Julia Fridman Simard, ScD; Joakim Dillner, MD; Eva Netterlid, PhD; Pär Sparén, PhD; Lisen Arnheim-Dahlström, PhD

DESIGN, SETTING, AND PARTICIPANTS An open cohort of all females aged 10 to 24 years living in Sweden (n = 1 045 165) was followed up between 2006 and 2010 for HPV vaccination and first occurrence of condyloma using the Swedish nationwide population-based health data

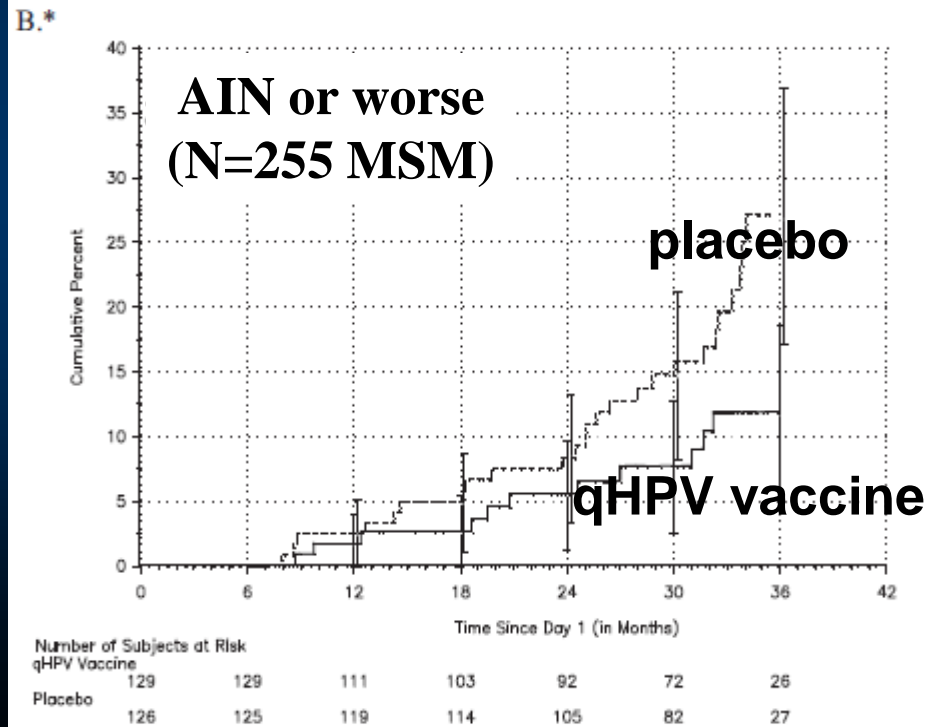
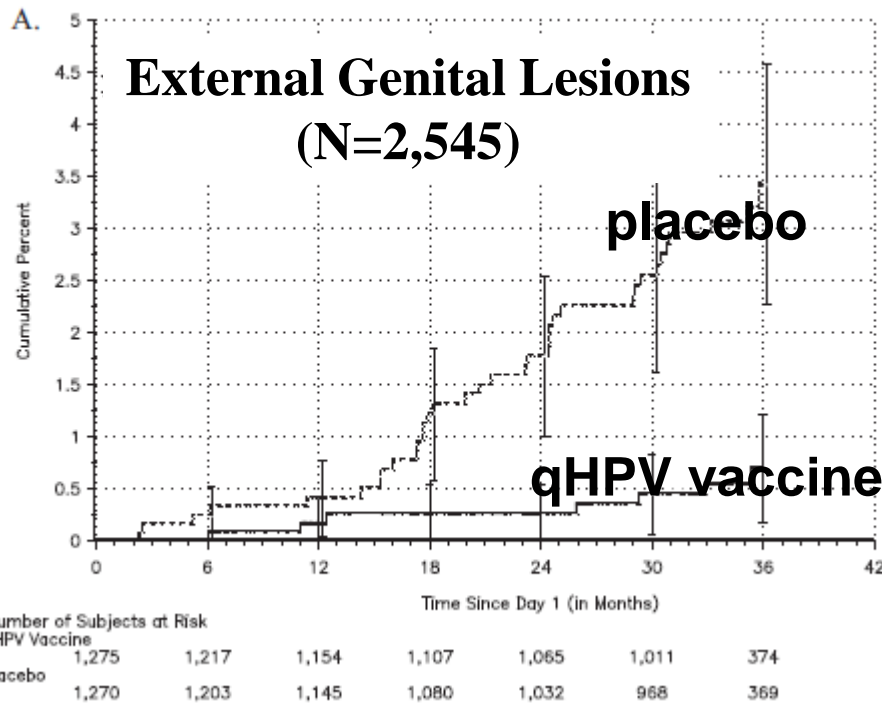


No. at risk	0	50	100	150	200	250	300	350
Unvaccinated	257 900	258 493	257 309	257 997	253 589	256 815	257 592	256 643
Vaccinated	119 046	117 515	114 723	111 659	107 991	103 305	98 327	93 283

	Individuals, No.	Events, No.	Person-Time, y	Crude Incidence Rate (95% CI) ^a
Age 10-13 y				
Unvaccinated	451 319	106	973 880	11 (9-13)
1 dose	11 703	0	1987	
2 doses	8028	0	1918	
3 doses	2978	0	875	
Age 14-16 y				
Unvaccinated	446 724	1460	796 219	183 (174-193)
1 dose	68 505	9	13 784	65 (34-125)
2 doses	63 513	19	21 664	88 (56-137)
3 doses	48 632	23	40 583	57 (38-85)
Age 17-19 y				
Unvaccinated	428 380	7110	780 134	911 (890-933)
1 dose	43 217	58	10 939	530 (410-686)
2 doses	48 247	54	20 037	269 (206-352)
3 doses	61 252	114	69 479	164 (137-197)
Age 20-21 y				
Unvaccinated	366 296	5496	520 363	1056 (1029-1084)
1 dose	1764	9	1028	875 (455-1682)
2 doses	2897	5	1720	291 (121-698)
3 doses	11 667	30	9400	319 (223-456)
Age 22-24 y				
Unvaccinated	398 910	5889	730 701	806 (786-827)
1 dose	109	0	73	
2 doses	192	1	129	773 (109-5487)
3 doses	1172	0	718	

Quadrivalent HPV vaccine efficacy against disease related to vaccine and non-vaccine HPV types in males[☆]

Stephen E. Goldstone^{a,*}, Heiko Jessen^b, Joel M. Palefsky^c, Anna R. Giuliano^d, Edson D. Moreira Jr.^e, Eftyhia Vardas^{f,g}, Carlos Aranda^h, Richard J. Hillmanⁱ, Daron G. Ferris^j, Francois Coutlee^k, J. Brooke Marshall^l, Scott Vuocolo^l, Richard M. Haupt^l, Dalya Guris^l, Elizabeth Garner^l



* Among MSM only.

(GARDASILTM, Merck & Co., Inc., Whitehouse Station, NJ) [13]. The study enrolled 3463 heterosexual males aged 16–24 years and 602 men who have sex with men (MSM) aged 16–27 years with less than six lifetime sexual partners (Fig. 1). The primary effi-

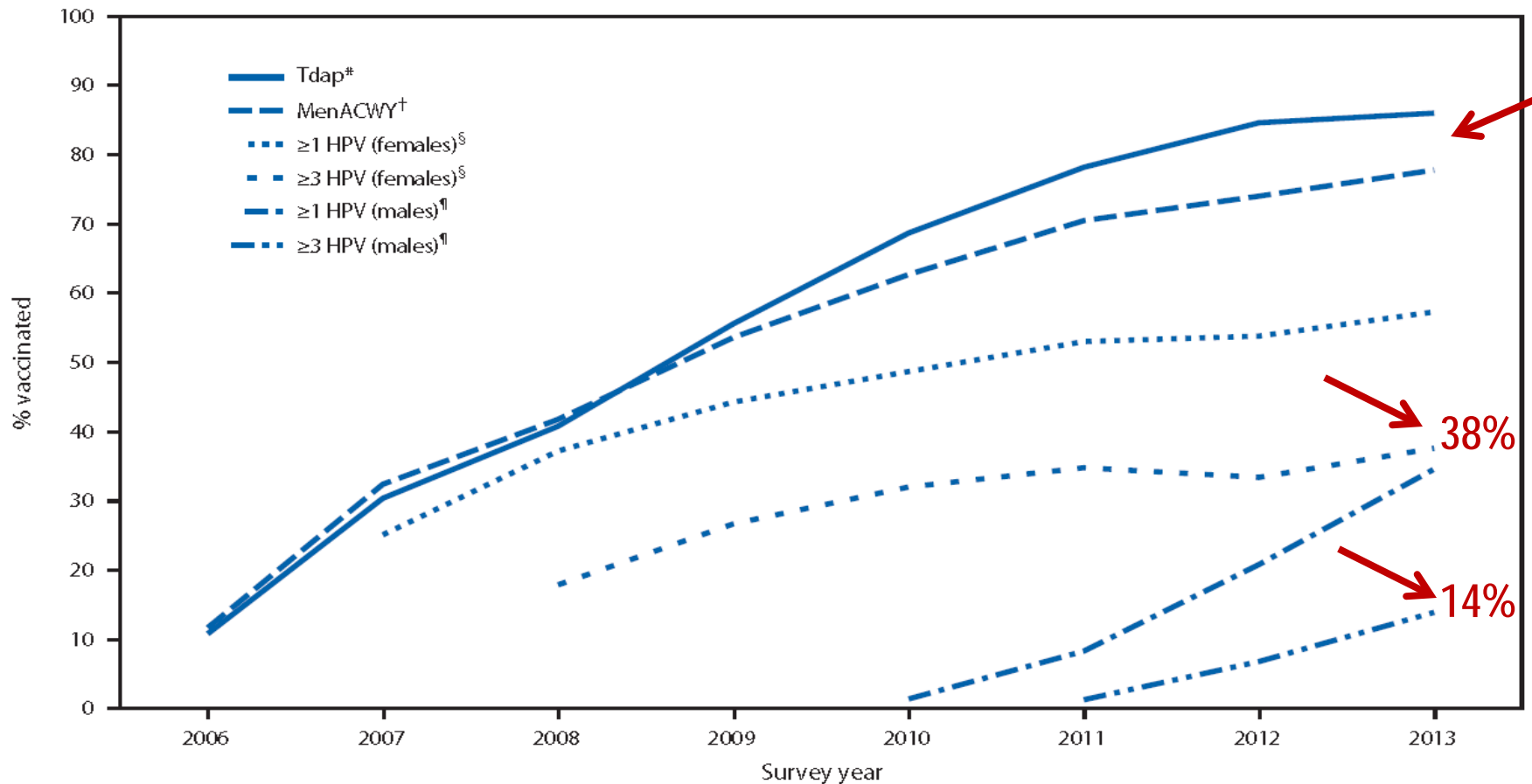
Fig. 2. Analysis of time to (A) EGL and (B) AIN or worse regardless of HPV detection among men in the naïve population.

Reduced Prevalence of Oral Human Papillomavirus (HPV) 4 Years after Bivalent HPV Vaccination in a Randomized Clinical Trial in Costa Rica

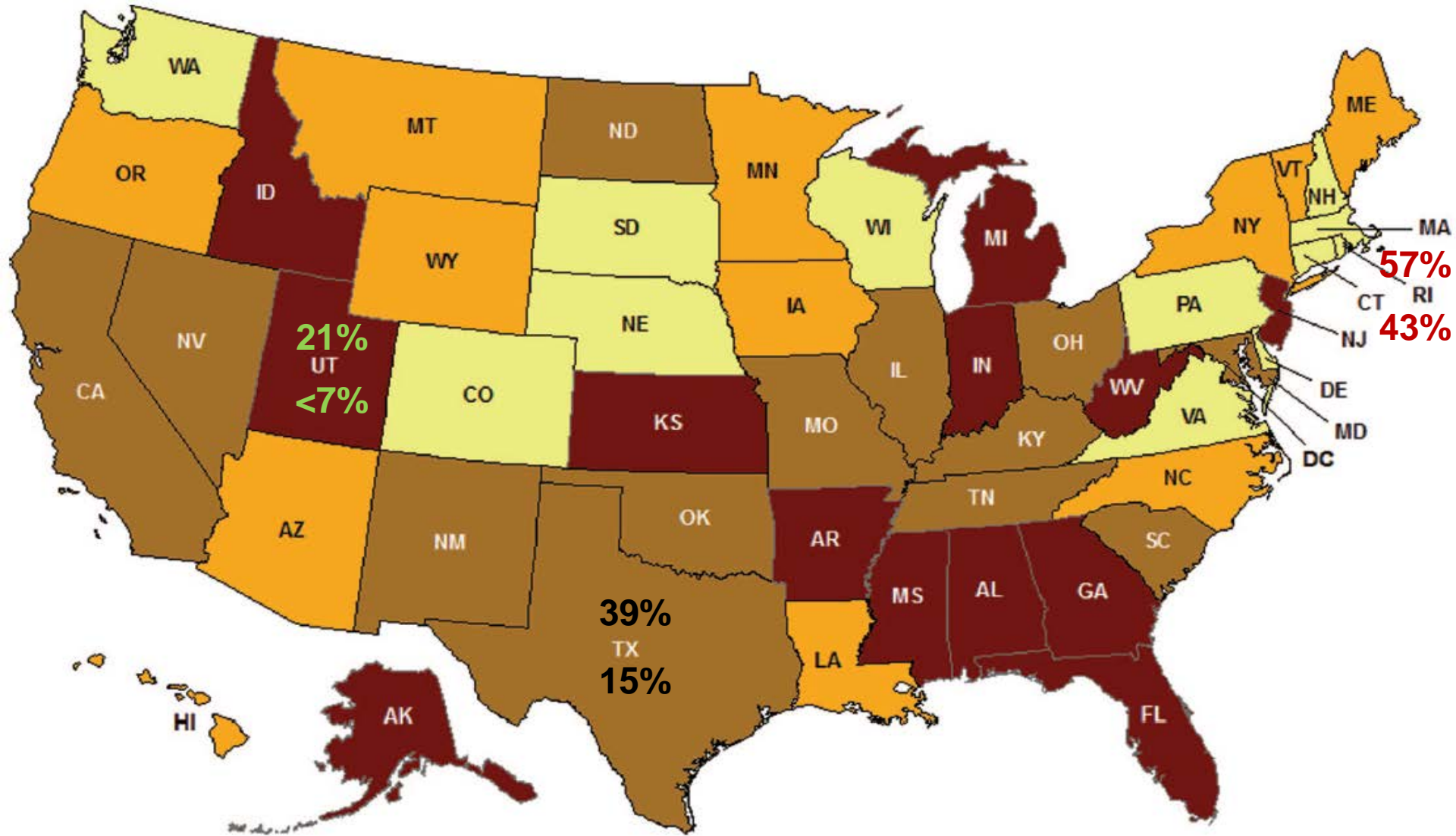
Rolando Herrero^{1*}, Wim Quint², Allan Hildesheim³, Paula Gonzalez⁴, Linda Struijk², Hormuzd A. Katki³, Carolina Porras⁴, Mark Schiffman³, Ana Cecilia Rodriguez⁴, Diane Solomon⁵, Silvia Jimenez⁴, John T. Schiller⁶, Douglas R. Lowy⁶, Leen-Jan van Doorn², Sholom Wacholder³, Aimée R. Kreimer³ for the CVT Vaccine Group[†]

Arm	Number of women	Number of women with infection*	Prevalence	95%CI	Vaccine efficacy	95%CI
Oral Infections						
HPV16/18[†]						
HPV	2910	1	0.0	0.0:0.2		
Control	2924	15	0.5	0.3:0.8	93.3%	62.5% to 99.7%
HPV16						
HPV	2910	1	0.0	0.0:0.2		
Control	2924	12	0.4	0.2:0.7	91.6%	51.7% to 99.6%
HPV18						
HPV	2910	0	0.0	0.0:0.1		
Control	2924	4	0.1	0.0:0.3	100%	-12.0% to 100%
Cervical Infections						
HPV16/18[†]						
HPV	2910	61	2.1	1.6:2.7		
Control	2924	219	7.5	6.6:8.5	72.0%	63.0% to 79.1%

FIGURE. Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13–17 years, by survey year — National Immunization Survey-Teen, United States, 2006–2013



Abbreviations: Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; MenACWY = meningococcal conjugate; HPV = human papillomavirus.
 * ≥1 dose Tdap vaccine on or after age 10 years.
 † ≥1 dose MenACWY vaccine.



13-17yo Girls in 2013:

38%

13-17yo Boys in 2013:

14%

Jemal A, et al. *J Natl Cancer Inst* 2013

Percentage of adolescent girls who received 3 doses of HPV vaccine

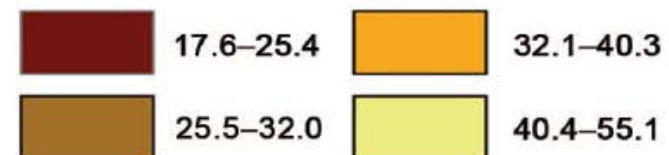


TABLE 2. Top five reasons for not vaccinating adolescents with human papillomavirus (HPV) vaccine* — National Immunization Survey-Teen, United States, 2013

Parents of girls			Parents of boys		
Reason	%	(95% CI)	Reason	%	(95% CI)
Lack of knowledge	15.5	(13.0–18.5)	Not recommended	22.8	(20.6–25.0)
Not needed or necessary	14.7	(12.5–17.3)	Not needed or necessary	17.9	(15.9–20.1)
Safety concern/Side effects	14.2	(11.8–16.8)	Lack of knowledge	15.5	(13.7–17.6)
Not recommended	13.0	(10.8–15.5)	Not sexually active	7.7	(6.4–9.2)
Not sexually active	11.3	(9.1–13.9)	Safety concern/Side effects	6.9	(5.6–8.5)

Abbreviation: CI = confidence interval.

* Analysis limited to parents reporting that they were not likely to seek HPV vaccination for their teen in the next 12 months or were unsure of their HPV vaccination plans.

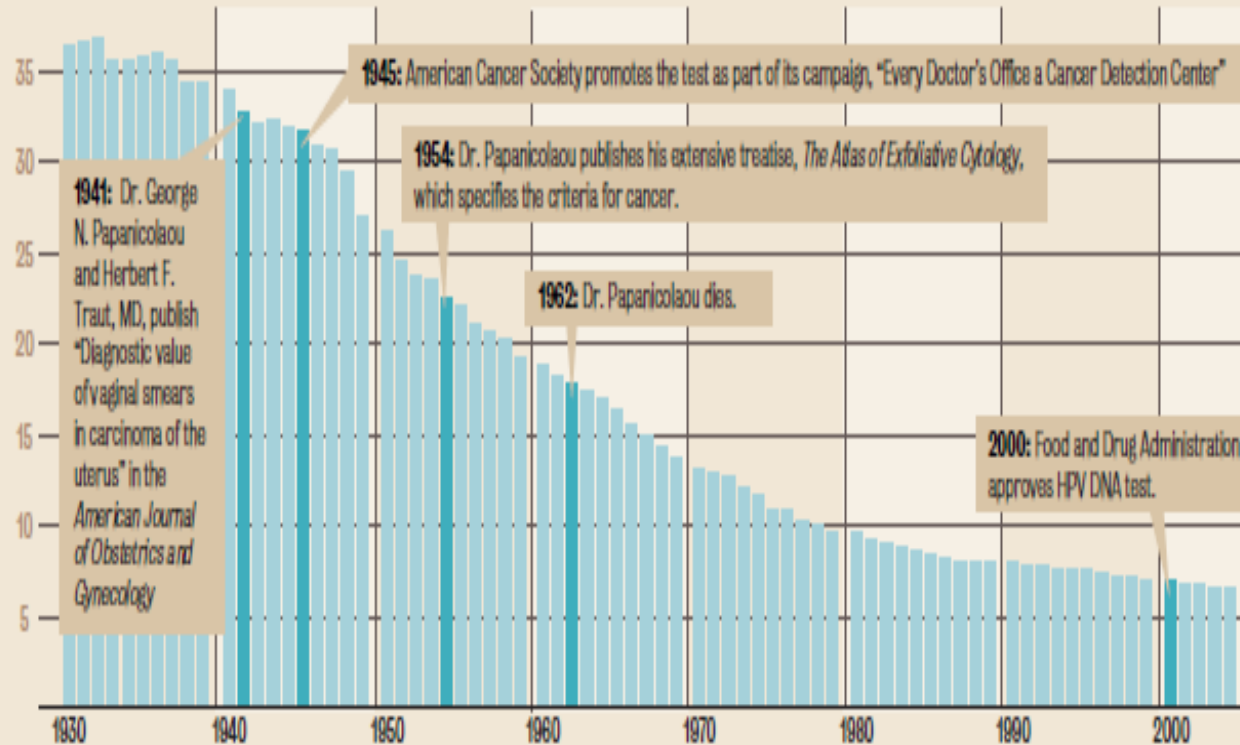
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**George Papanicolaou
(1883-1962)**

AGE-ADJUSTED DEATH RATE PER 100,000 (cervical and uterine cancer)



SOURCE: AMERICAN CANCER SOCIETY, CENTERS FOR DISEASE CONTROL AND PREVENTION

annual burden of genital HPV-related disease (U.S. females)

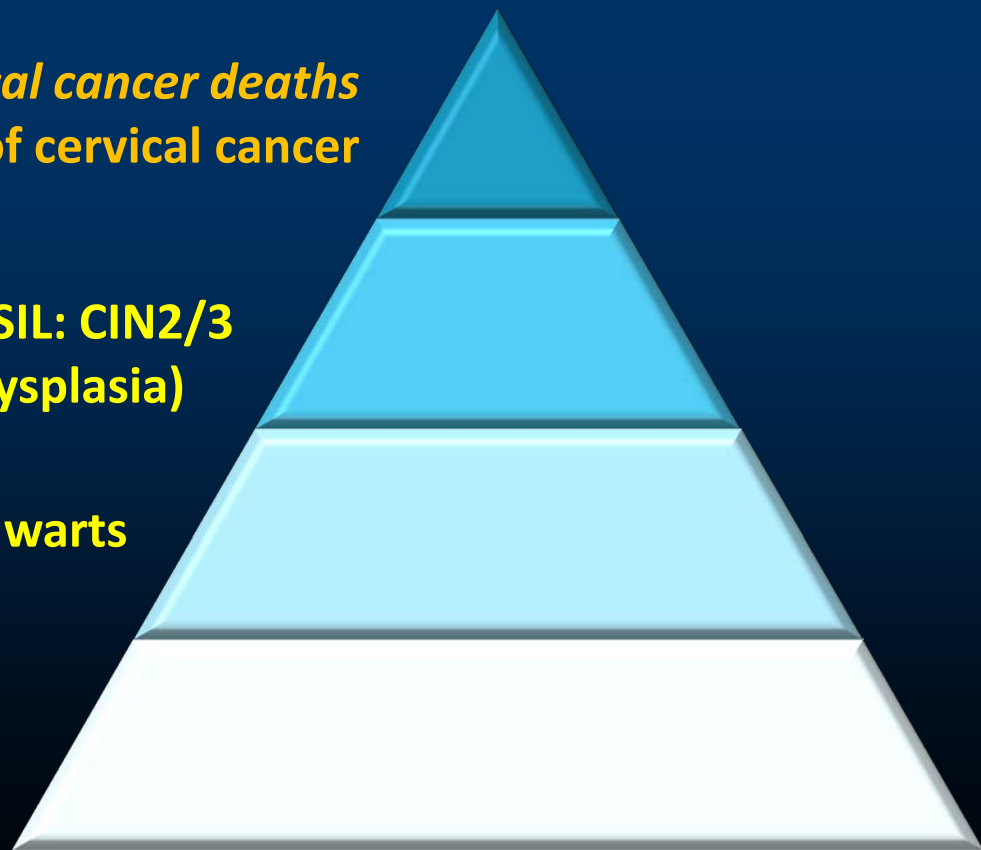
4,100 cervical cancer deaths
12,900 new cases of cervical cancer

330,000 new cases of HSIL: CIN2/3
(high grade cervical dysplasia)

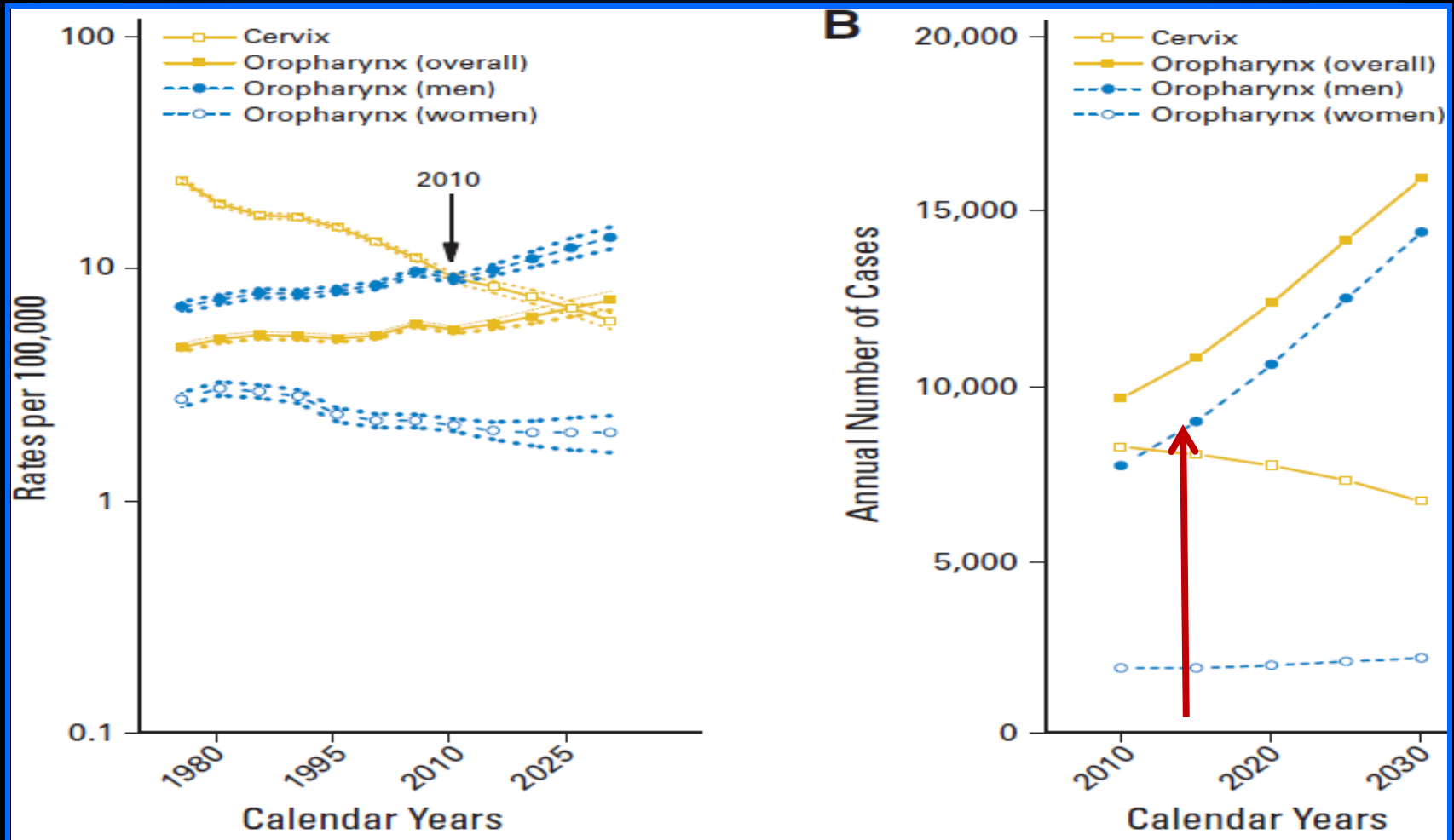
1 million new cases of genital warts

1.4 million new cases of LSIL: CIN1
(low grade cervical dysplasia)

3 million cases & \$7 billion



Trends in Cancer Incidence & Number Oropharynx vs. Cervix



Perspective

Perspective on Fakhry et al., p. 1378

Brush-based Cytology Screening in the Tonsils and Cervix: There Is a Difference!

Mark W. Lingen

A

Cervix

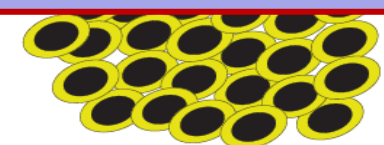
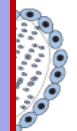
B

Oropharynx

Median Age at Presentation:

45yo

55yo



Outline

- ❖ HPV in Men
- ❖ Cancer Epidemic
- ❖ Prevention
- ❖ Screening
- ❖ **Plan of Action**

HPV-OAG (oral-anogenital) Lecture Series *established in 2012*

Open monthly meeting to discuss topics in HPV-associated malignancies

Attendees from across the Texas Medical Center

Founding Members:

- Cathy Eng (GI Medical Oncology)
- Lance Pagliaro (GU Medical Oncology)
- Curtis Pettaway (Urology)
- Kathleen Schmeler (Gyn Oncology)
- Erich Sturgis (H&N Surgery)

Charles and Daneen Stiefel Gift *established in 2013*

- **\$10 million gift (Randy Weber, Merrill Kies, and David Rosenthal)**
- **Create and leverage a central *infrastructure***
- **2014-2022 window: \$2M year one ► \$1M/year x 8years**
- **9 sections (prevention, infrastructure, discovery, and clinical trials)**

MDA Retreat on HPV-associated Cancers

Inaugural Retreat: 2014

- Co-Leaders: Cathy Eng, Lois Ramondetta, & Erich Sturgis
- Expert Panel:
 - Peter Howley (Dana-Farber)
 - Douglas Lowy (NCI)
 - Mona Saraiya (CDC)
 - John Schiller (NCI)
- Agenda:
 - I. Public Health & Prevention
 - II. Screening
 - III. Biology & Therapeutic Potentials
- Product: **Set of priorities and Action Items**

Six Priorities

1) Potential to eradicate BUT vaccination lagging

2) Cervical screening works BUT access not universal

3) No screening exists for oropharyngeal and rare sites

4) Pre-invasive treatment costly to individual and society

5) Std. treatment for invasive cancers works but...toxic

6) Recurrence is typically a disaster

MDA Pilot^(1 year) HPV Moon Shot

\$1.5 million Awarded: September, 2014

Education & Policy (Ramondetta)	Prevention & Screening (Schmeler)	Target Discovery & Novel Trials H&N (Glisson)	Target Discovery & Novel Trials GYN (Frumovitz)	Target Discovery & Novel Trials Rare Tumors (Eng)	
Cores/Platforms Cancer Prev. & Control (E.H.) Government Relations (M.M.) Provider Education (K.W.) Public Education (S.K.)		Cores/Platforms APOLLO Immunotherapy Genomics			CCCT Big Data Proteomics
Administrative Core (Sturgis)					

Steering Committee:

George Chang, John Heymach, Karen Lu, Jeff Myers, & Curtis Pettaway

Clinical Trials Oversight Committee:

clinical members from above (CE,BG,MF,LR,KS,&ES), Lance Pagliaro, & a representative from the Steering Committee.

External Advisory Committee: public health expert, premalignant clinical disease expert, expert clinicians for each disease site, HPV virology expert, & pt. advocate

HPV Full(5 year) Moon Shot

Submitted April 30, 2015 and Presented to SAB May 21, 2015

Flagship #1 Prevention & Screening

Policy & Education
(Lois M. Ramondetta)

Screening
(Kathleen M. Schmeler)

Cancer Prevention and Control Platform:

Health Policy
Government Relations
Professional Education
Public Education

Flagship #2 Discovery

Genomics
(Curtis R. Pickering)

Target Discovery
(Faye M. Johnson)

Platforms/Engines:

Cancer Genomics Lab
Institute for Applied Cancer Sciences

Flagship #3 Immunotherapy & Novel Trials

Rare Tumors
(Cathy Eng)

GYN
(Michael M. Frumovitz)

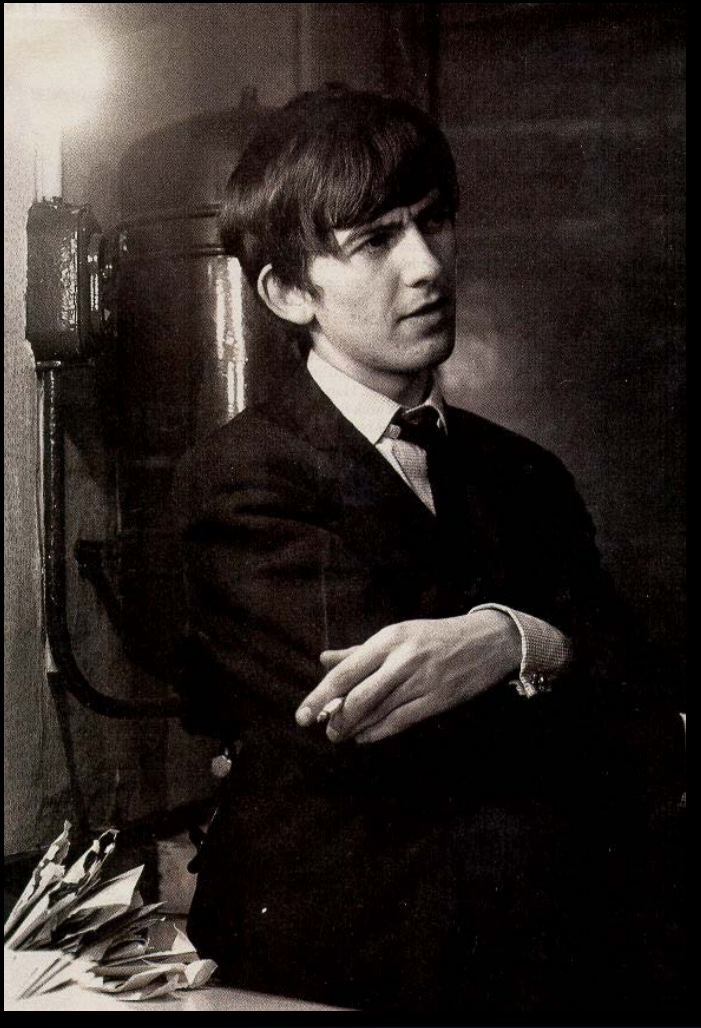
Head & Neck
(William N. William)

Platforms/Engines:

Center for Co-Clinical Trials
Immunotherapy

Conclusions

- ❖ HPV cancer epidemic – oropharyngeal, anal, & vulvar
- ❖ HPV vaccination is imperative:
Further Delay = Exponential Costs & Suffering
- ❖ Without novel screening/treatment of premalignancy:
30 years of increasing incidence
- ❖ Less toxic (& more effective) therapies are needed:
Must integrate our efforts across disease sites



George Harrison
1943 - 2001
Oropharynx Cancer



Thank You

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