Human Papilloma Virus Related Cancers – The changing spectrum of a preventable malignancy

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HPV Vaccination Symposium: Providers Are The Key
Saturday, March 3, 2018

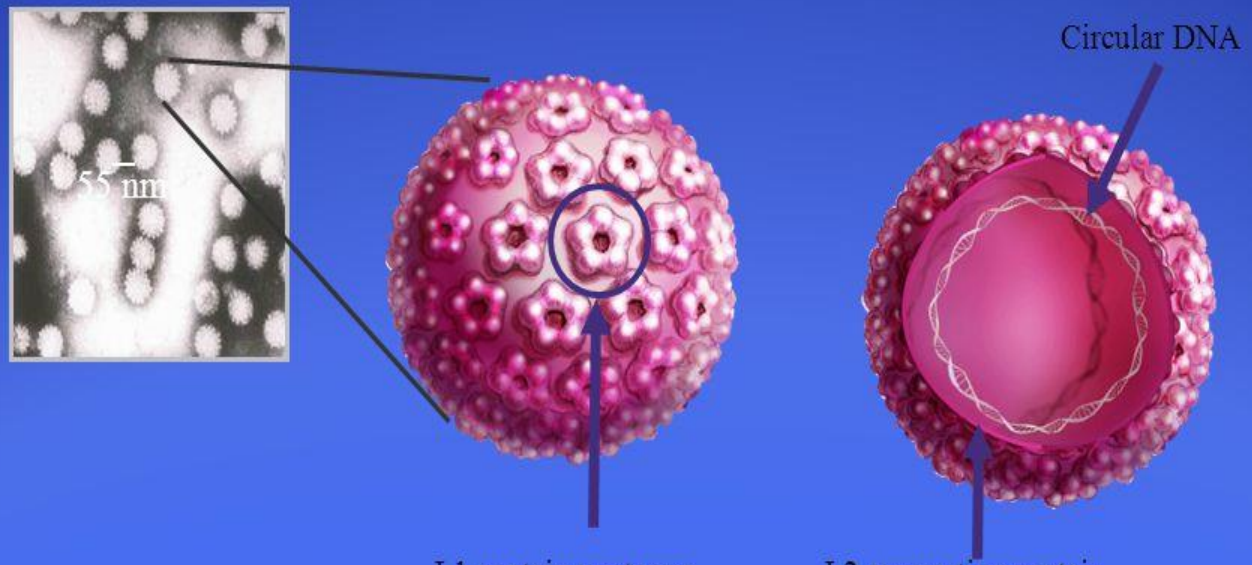
NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute

University of Maryland
Marlene and Stewart Greenebaum Comprehensive Cancer Center

What is HPV? - Epidemiology of HPV related cancers

Human papillomavirus structure

- HPV is a relatively small virus containing double-stranded DNA within a spherical shell (capsid)[1]
  - The capsid is composed of two proteins, the 'late' or structural proteins L1 and L2[1]



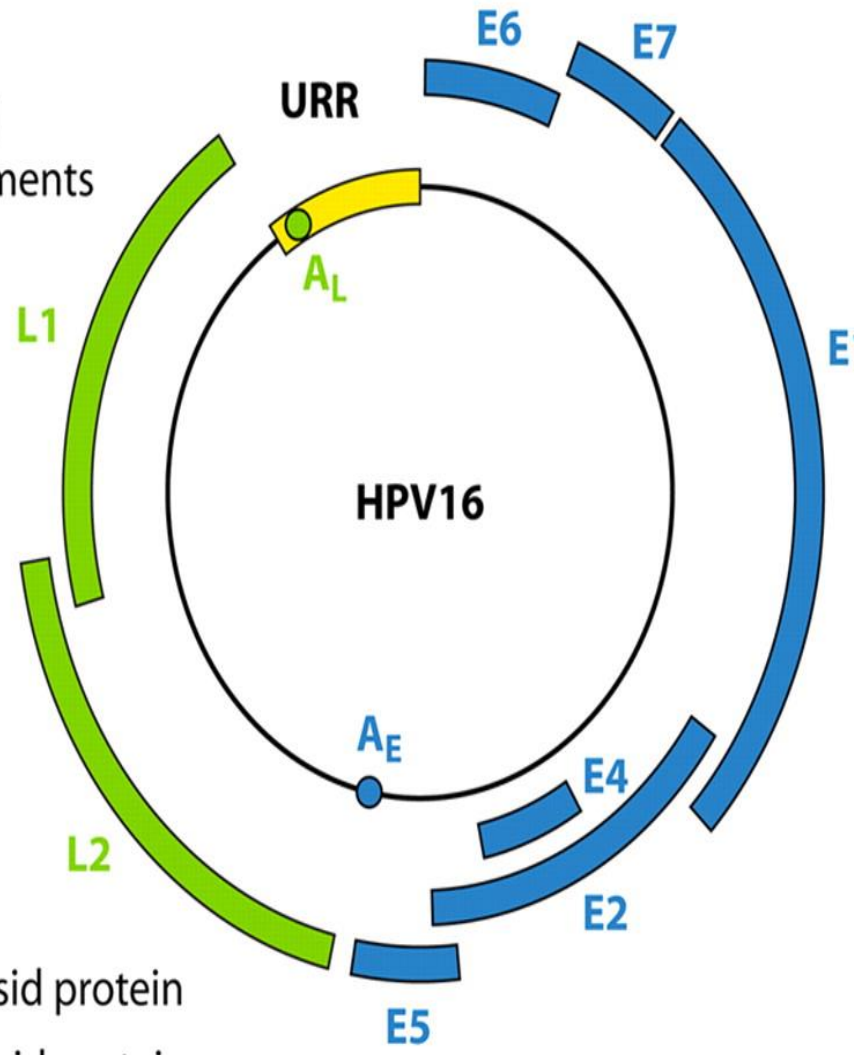
1. Burd EM. *Clin Microbiol Rev* 2003; 16:1–17.

HPV genome organization

URR

Promoter and enhancer elements

Viral ORI



Late genes

L1–Major capsid protein

L2–Minor capsid protein

Early genes

E1–Replication

E2–Replication and transcription

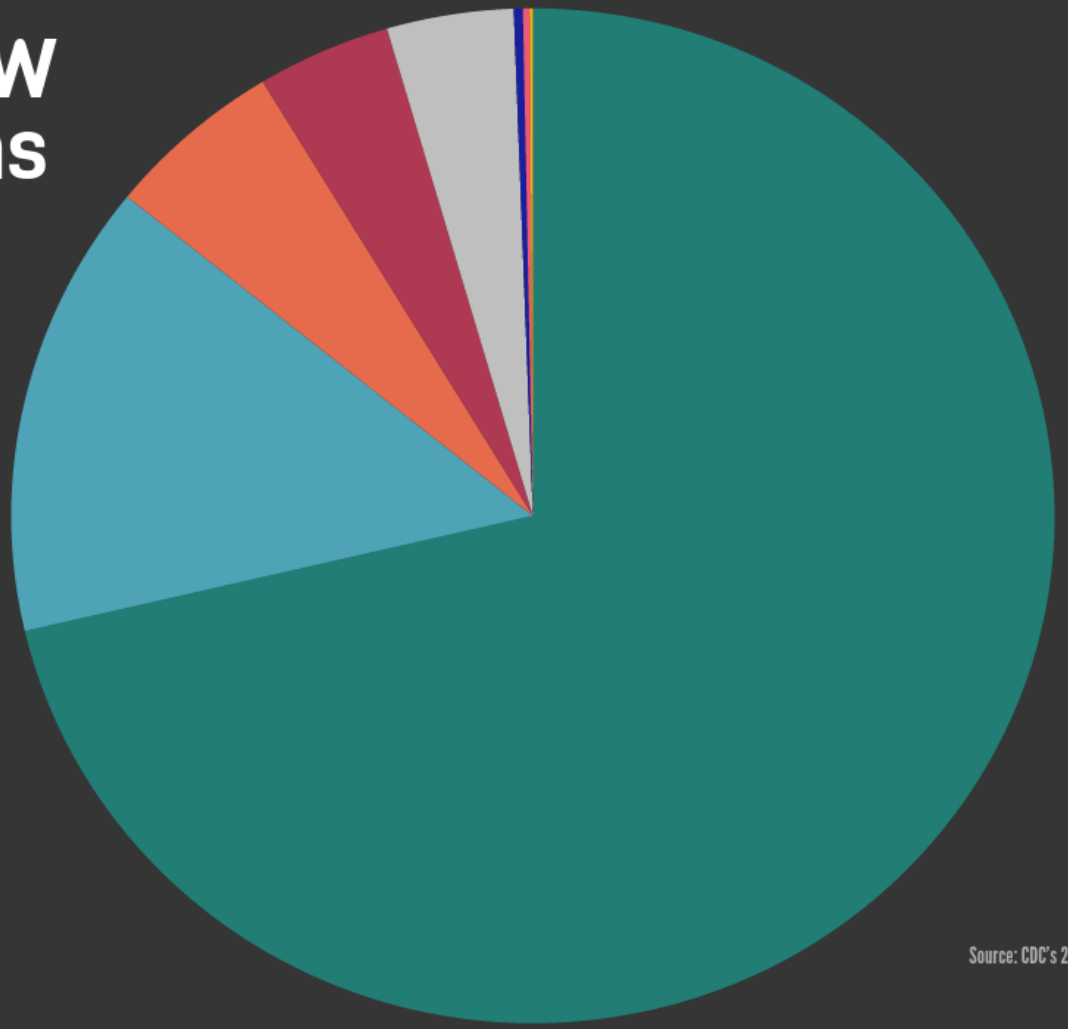
E4–Viral release

E5–Immune evasion

E6–Binds p53

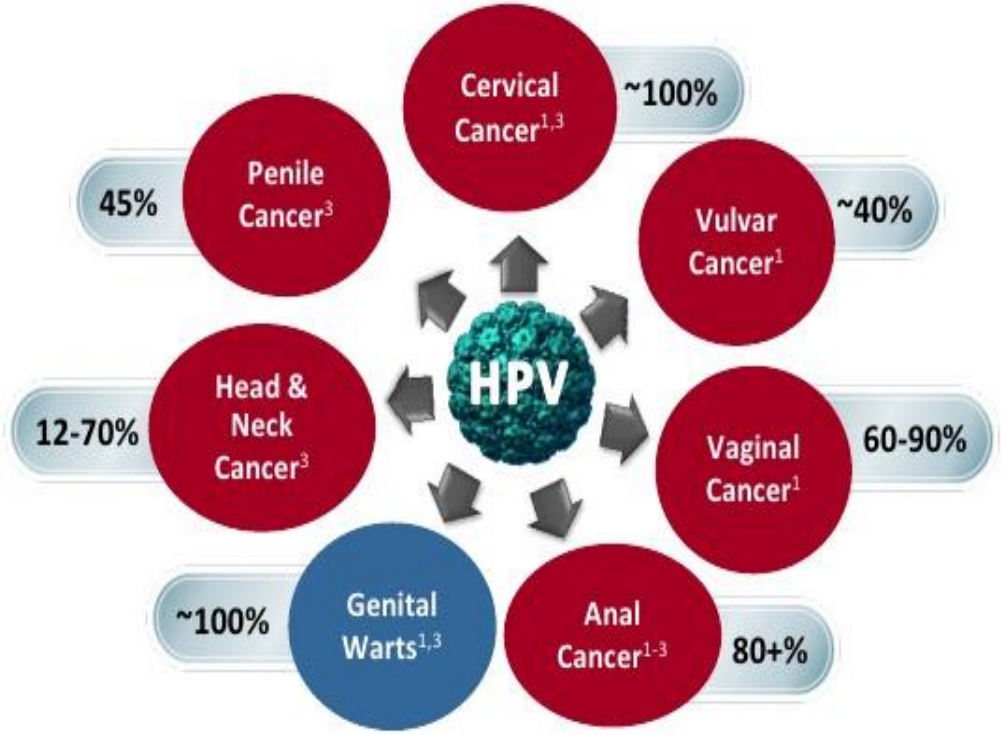
E7–Binds pRB

Estimated NEW STD Infections



Source: CDC's 2013 STD Fact Sheet

HPV causes more than cervical cancer



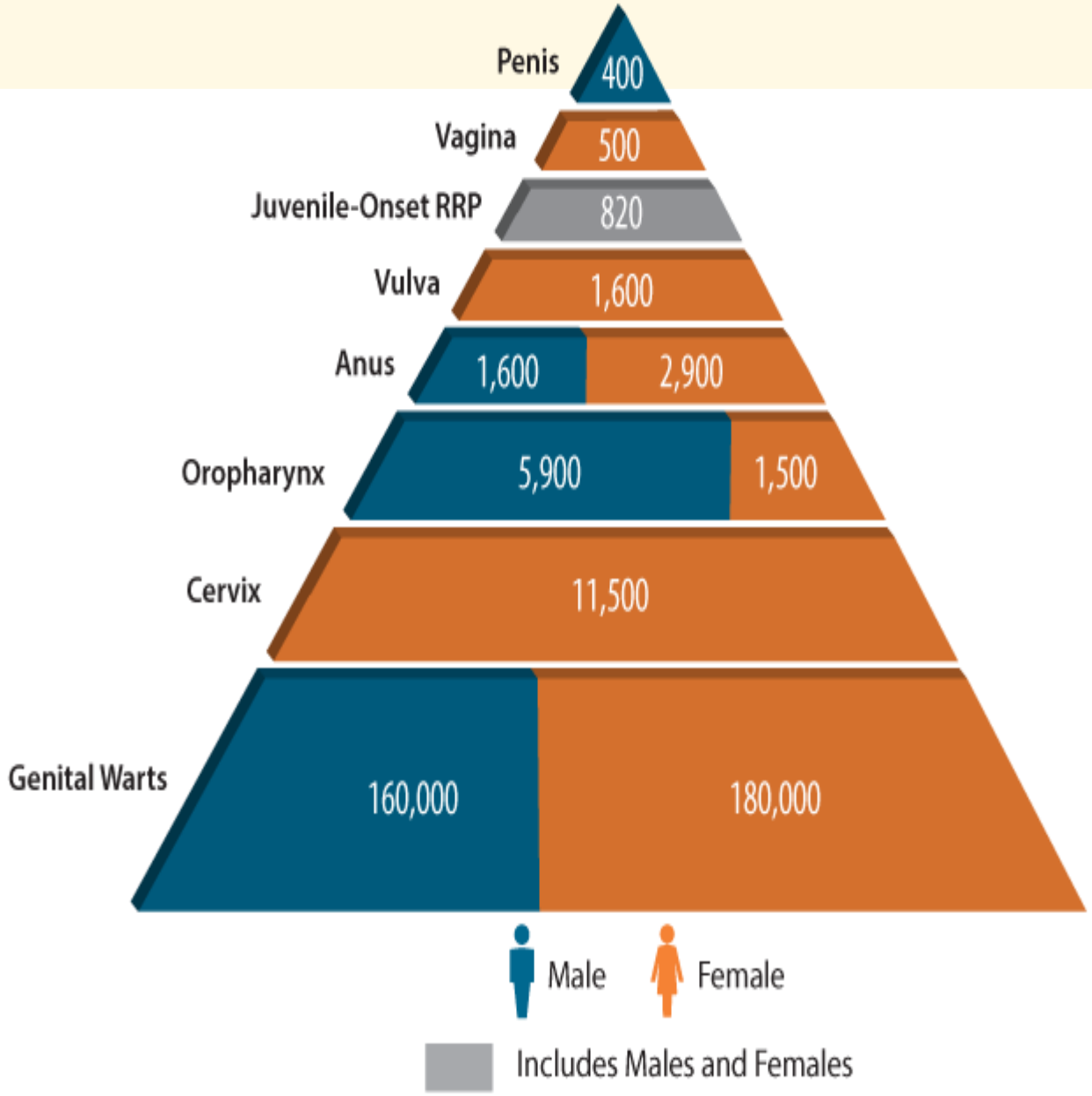
Percentages represent cases atrributable to HPV infection

Braaten KP et al. Rev Obstet Gynecol. 2008;1:2–10.

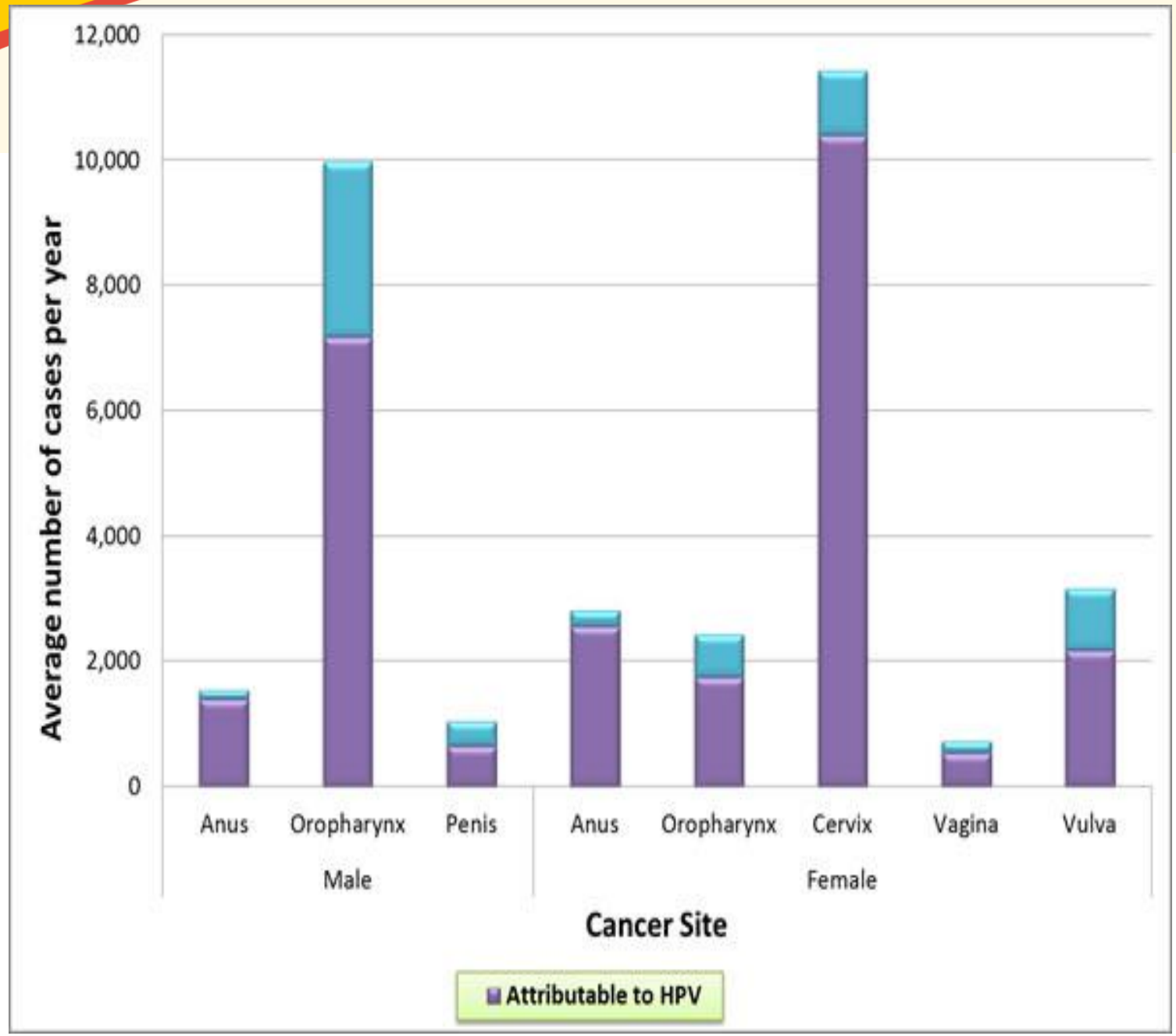
Hoots BE et al. Int J Cancer. 2009;124:2375–2383.

IARC. IARC monographs on the evaluation of carcinogenic risks to humans. Human papillomaviruses. Vol 90. Lyon, France: IARC, 2007.

Numbers of U.S. Cancers and Genital Warts Attributed to HPV Infections



Sources: Centers for Disease Control and Prevention. Human papillomavirus-associated cancers—United States, 2004-2008. MMWR. 2012 Apr 20;61(15):258-61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22513527; Hoy T, Singhal PK, Willey VJ, Insinga RP. Assessing incidence and economic burden of genital warts with data from a US commercially insured population. Curr Med Res Opin. 2009;25(10):2343-51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19650749; Chesson HW, Ekwueme DU, Saraiya M, Watson M, Lowy DR, Markowitz LE. Estimates of the annual direct medical costs of the prevention and treatment of disease associated with human papillomavirus in the United States. Vaccine. 2012;30(42):6016-9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22867718

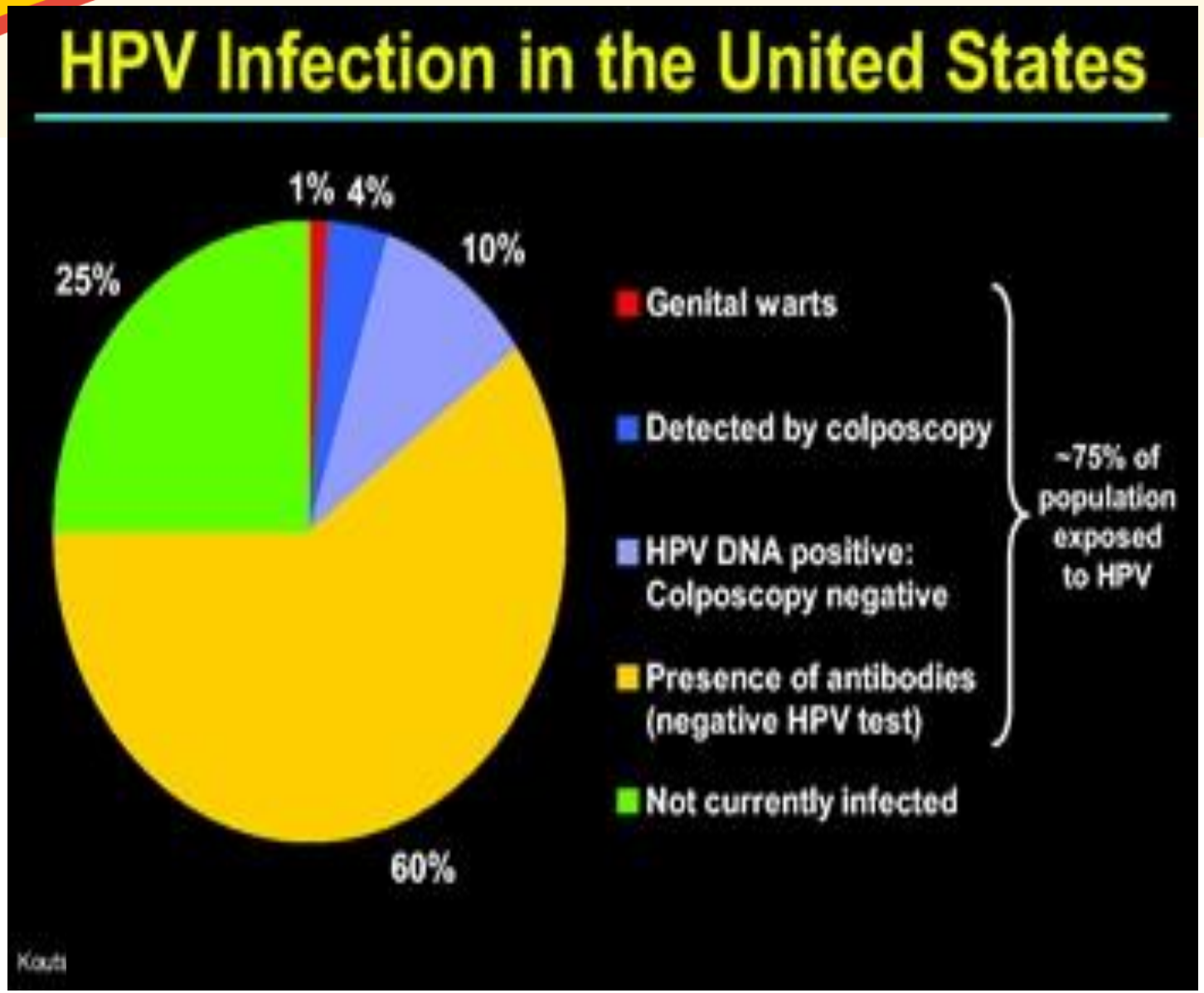

12,000
10,000
8,000
6,000
4,000
2,000
0
Average number of cases per year
Anus
Oropharynx
Penis
Anus
Oropharynx
Cervix
Vagina
Vulva
Male
Female
Cancer Site
Attributable to HPV

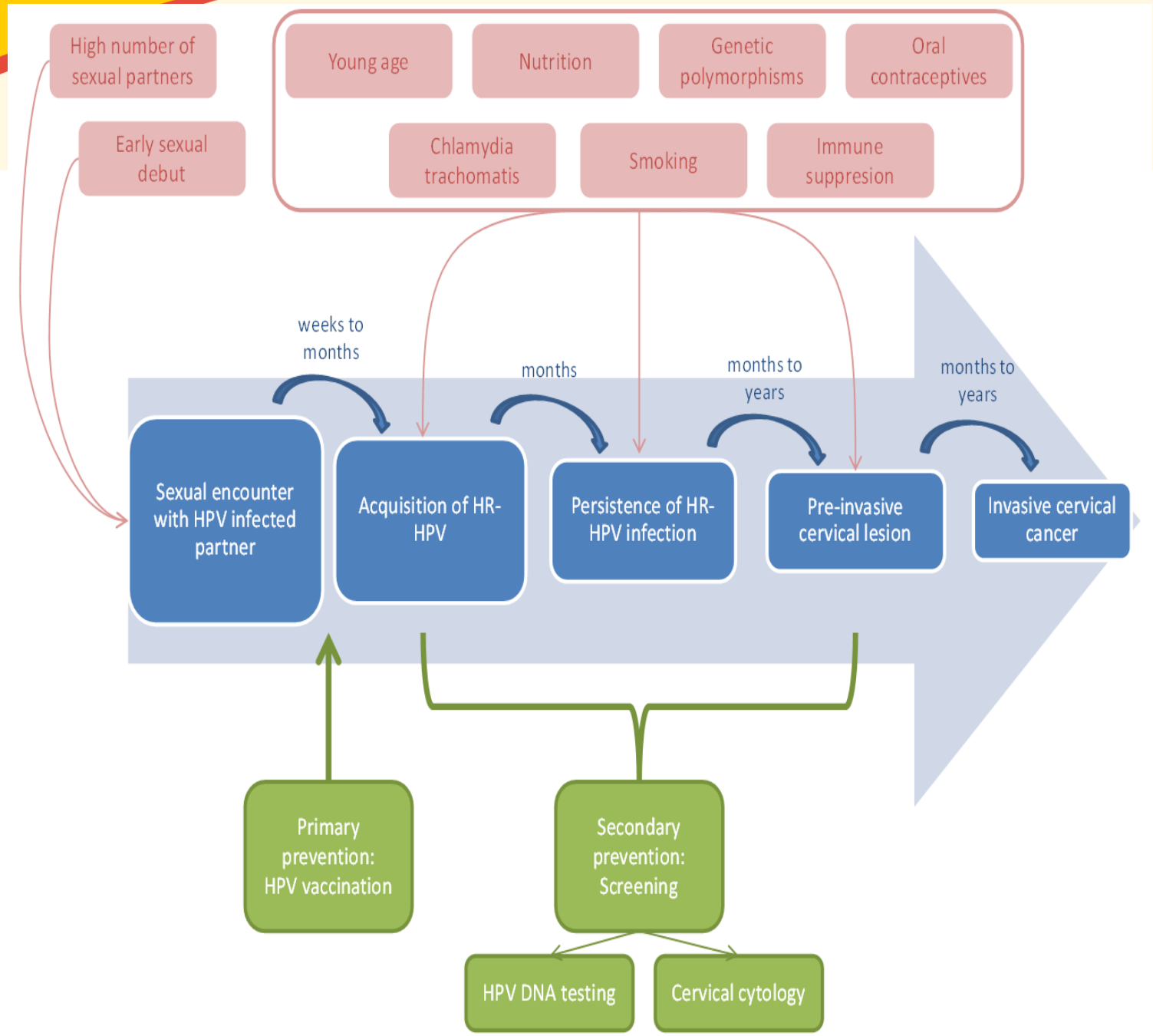
U.S. Cancers Attributed to HPV

Cancer Site	Average # Cancers Per Year at Site (a)	Percent Probably Caused by HPV (a)	Number Probably Caused by HPV (a)	Percent HPV Cancers Probably Caused by HPV16 or 18 (b)	Number Probably Caused by HPV16 or 18
Anus	4,767	93	4,500	93	4,200
Cervix	11,967	96	11,500	76	8,700
Oropharynx	11,726	63	7,400	95	7,000
Penis	1,046	36	400	87	300
Vagina	729	64	500	88	400
Vulva	3,136	51	1,600	86	1,400
TOTAL	**33,371**		**25,900**		**22,000**

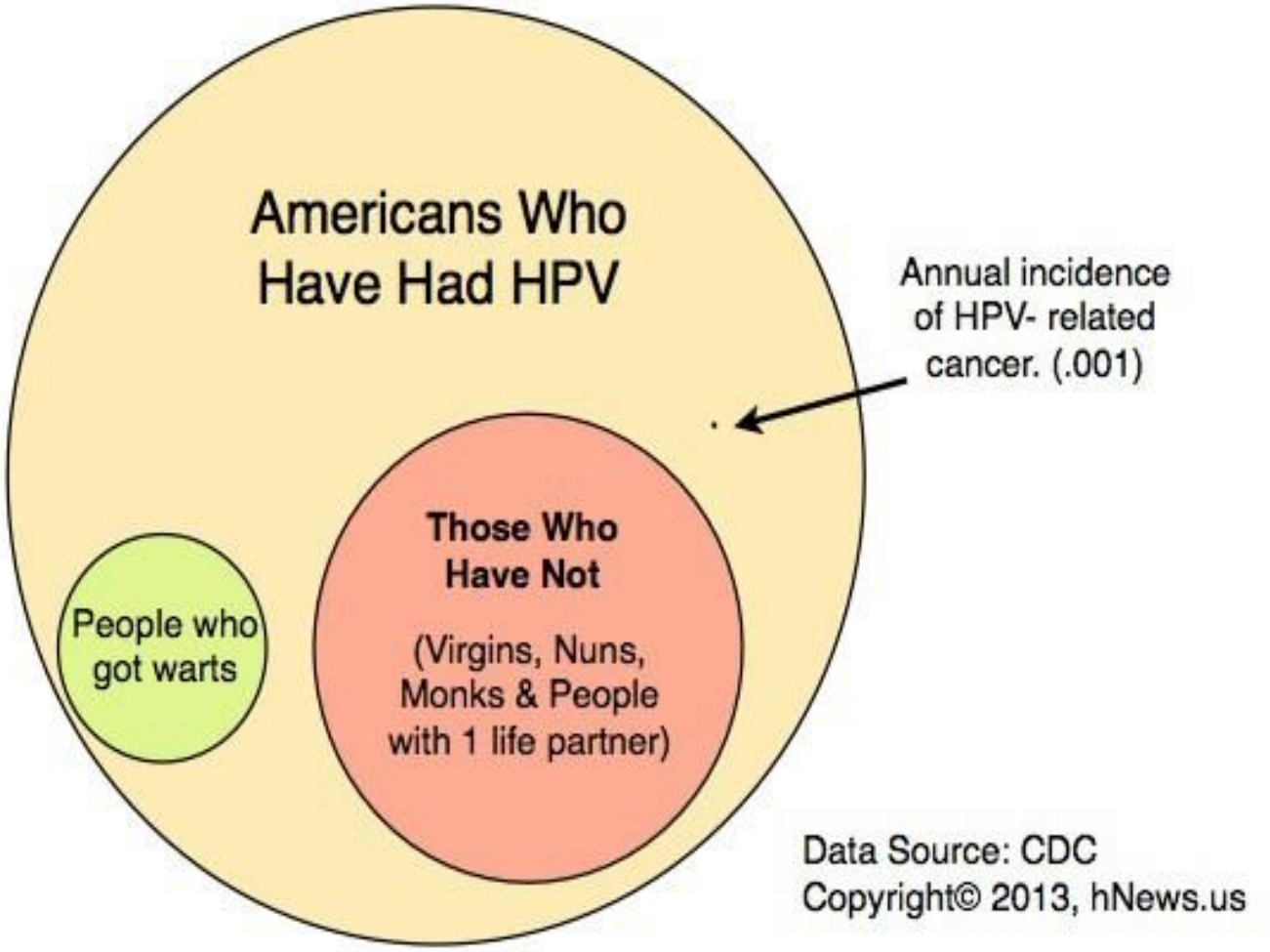
(a) Centers for Disease Control and Prevention. Human papillomavirus-associated cancers—United States, 2004-2008. MMWR. 2012 Apr 20;61(15):258-61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22513527

(b) Gillison ML, Chaturvedi AK, Lowy DR. HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. Cancer. 2008;113(10 Suppl):3036-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18980286

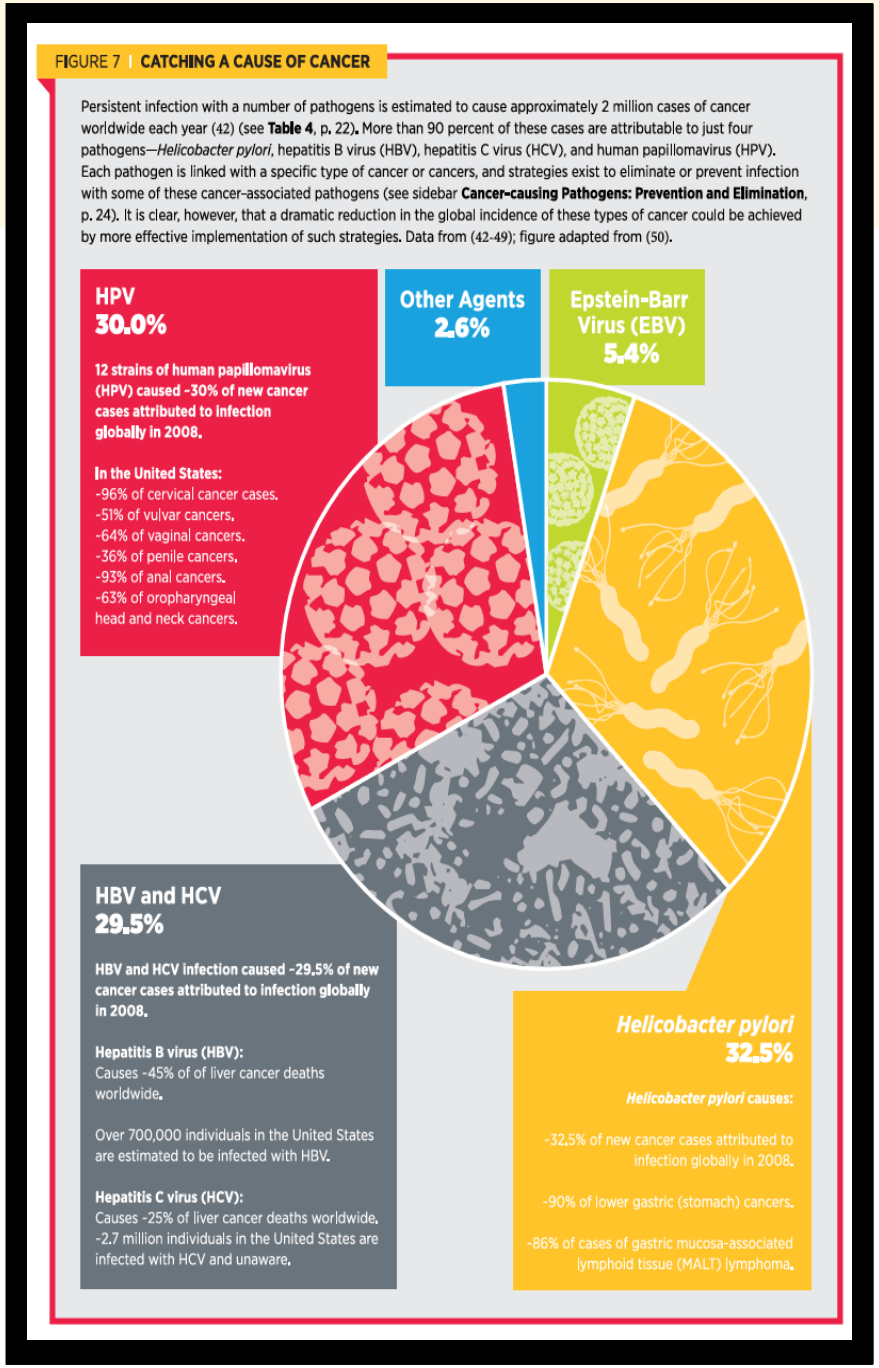

HPV Infection in the United States
1%
4%
10%
25%
60%
Genital warts
Detected by colposcopy
HPV DNA positive:
Colposcopy negative
Presence of antibodies
(negative HPV test)
Not currently infected
~75% of population exposed to HPV
Kouti


High number of sexual partners
Early sexual debut
Young age
Nutrition
Genetic polymorphisms
Oral contraceptives
Chlamydia trachomatis
Smoking
Immune suppresion
weeks to months
months
months to years
months to years
Sexual encounter with HPV infected partner
Acquisition of HR-HPV
Persistence of HR-HPV infection
Pre-invasive cervical lesion
Invasive cervical cancer
Primary prevention: HPV vaccination
Secondary prevention: Screening
HPV DNA testing
Cervical cytology

Americans & HPV



Data Source: CDC



http://cancerprogressreport.org/2014/Documents/AACR_CPR_2014.pdf

HPV vaccines – a remarkable success story

Richard Schlegel, M.D., Ph.D.

Papillomavirus Vaccine Development

- HPV monovalent (HPV 16) vaccine shown to protect against persistent infection 2002
- Schlegel lab (Georgetown) develops bivalent vaccine against HPV 16/18 – licensed through Medimmune to GSK

Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial

*Diane M Harper, Eduardo L Franco, Cosette Wheeler, Daron G Ferris, David Jenkins, Anne Schuind, Toufik Zahaf, Bruce Innis, Paulo Naud, Newton S De Carvalho, Cecilia M Roteli-Martins, Julio Teixeira, Mark M Blatter, Abner P Kom, Wim Quint, Gary Dubin, for the GlaxoSmithKline HPV Vaccine Study Group**

Summary

Background Vaccination against the most common oncogenic human papillomavirus (HPV) types, HPV-16 and HPV-18, could prevent development of up to 70% of cervical cancers worldwide. We did a randomised, double-blind, controlled trial to assess the efficacy, safety, and immunogenicity of a bivalent HPV-16/18 L1 virus-like particle vaccine for the prevention of incident and persistent infection with these two virus types, associated cervical cytological abnormalities, and precancerous lesions.

www.lancet.com Vol 364 November 13, 2004

Findings In the according-to-protocol analyses, vaccine efficacy was 91·6% (95% CI 64·5–98·0) against incident infection and 100% against persistent infection (47·0–100) with HPV-16/18. In the intention-to-treat analyses, vaccine efficacy was 95·1% (63·5–99·3) against persistent cervical infection with HPV-16/18 and 92·9% (70·0–98·3) against cytological abnormalities associated with HPV-16/18 infection. The vaccine was generally safe, well tolerated, and highly immunogenic.

Interpretation The bivalent HPV vaccine was efficacious in prevention of incident and persistent cervical infections with HPV-16 and HPV-18, and associated cytological abnormalities and lesions. Vaccination against such infections could substantially reduce incidence of cervical cancer.

www.lancet.com Vol 364 November 13, 2004

THE LANCET The Journal

Volume 364, Number 9447
13 November 2004

Vaccination against human papillomaviruses shows great promise

It took almost 10 years from the discovery of an association between human papillomavirus (HPV) and cervical cancer[1] to the finding of HPV type 16 in cervical cancer tissue.[2] It took another 10 years to show that past infection with HPV16 increases the risk for subsequent development of invasive cervical cancer,[3] and yet another decade to show that the seven most prevalent HPV types cause 87% of all cervical cancers.[4] By comparison, the creation of HPV virus-like-particle (VLP) vaccines has been a rapid breakthrough. VLPs mimic the true structure of the virion and induce a striking antibody response after vaccination.[5] 2 years ago, Koutsky et al[6] showed that vaccination with HPV16 VLPs protected 768 vaccinated women from persistent HPV16 infection.

In today's *Lancet*, Diane Harper and colleagues now expand this rapid development in a phase 2 trial in just over 1100 participants, a study that lasted 2·5 years. VLPs of the two most important oncogenic HPV types, HPV16 and HPV18, were combined in a preventive vaccine. According-to-protocol and intention-to-treat analyses showed high efficacy for this bivalent vaccine against both the incident and persistent HPV16 and HPV18 infections. This efficacy turned out to be excellent even though the most sensitive method, vaginal self-sampling, was used to define the endpoints.

HOW DO THE THREE FDA-APPROVED HPV VACCINES DIFFER?

13 **strains of HPV can cause cancer:** HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66.

3 **FDA-approved vaccines can prevent infection** with some of these strains.

CERVARIX

- Protects against infection with HPV16 and HPV18.
- FDA approved in 2009.
- FDA approved for:
  - preventing cervical cancer and precancers.
  - vaccination of females ages 9 to 25.

GARDASIL

- Protects against infection with HPV16 and HPV18, as well as HPV6 and HPV11, which cause genital warts.
- FDA approved in 2006.
- FDA approved for:
  - preventing anal, cervical, vaginal, and vulvar cancers and precancers, as well as genital warts.
  - vaccination of males and females ages 9 to 26.

GARDASIL 9

- Protects against infection with HPV6, 11, 16, 18, 31, 33, 45, 52, and 58.
- FDA approved in 2014.
- FDA approved for:
  - preventing anal, cervical, vaginal, and vulvar cancers and precancers, as well as genital warts.
  - vaccination of females ages 9 to 26 and males ages 9 to 15.

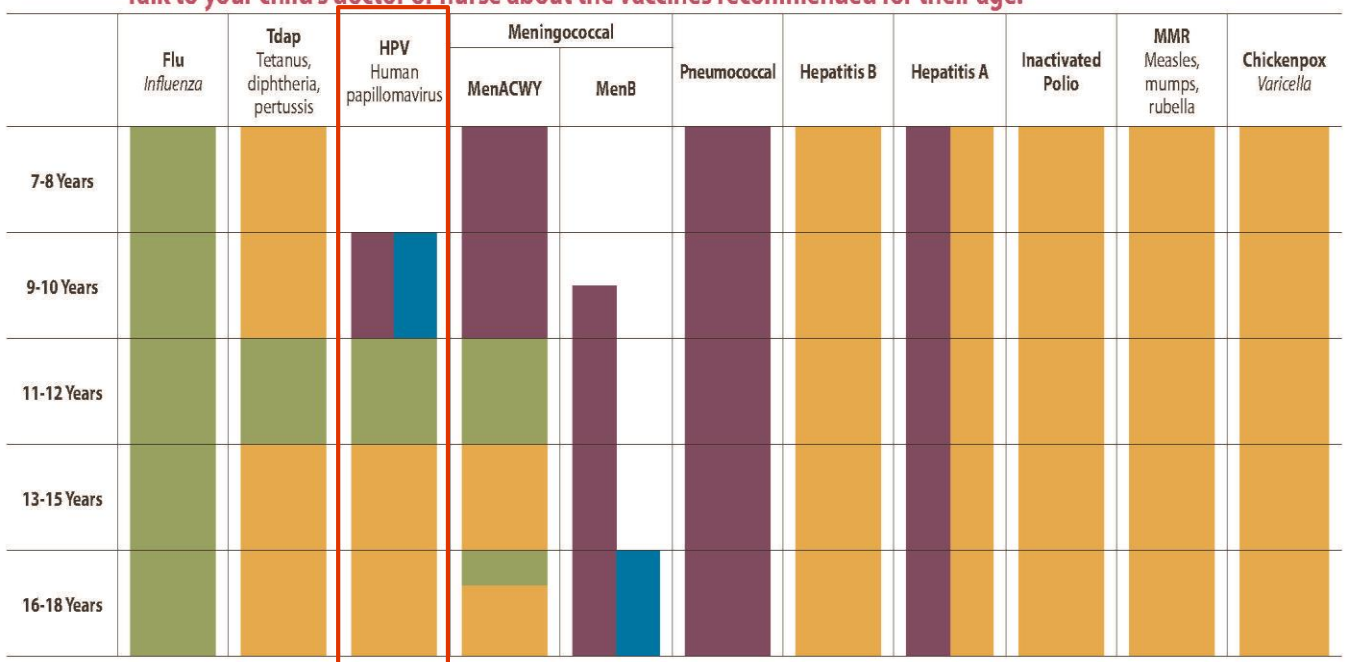
American Association for Cancer Research (AACR) Cancer Progress Report 2016

Information is current as of July 2016

INFORMATION FOR PARENTS

2017 Recommended Immunizations for Children 7-18 Years Old

Talk to your child's doctor or nurse about the vaccines recommended for their age.



More information:	Flu	Tdap	HPV	MenACWY	MenB
	Preteens and teens should get a flu vaccine every year.	Preteens and teens should get one shot of Tdap at age 11 or 12 years.	All 11-12 year olds should get a 2-shot series of HPV vaccine at least 6 months apart. A 3-shot series is needed for those with weakened immune systems and those age 15 or older.	All 11-12 year olds should get a single shot of a quadrivalent meningococcal conjugate vaccine (MenACWY). A booster shot is recommended at age 16.	Teens, 16-18 years old, **may** be vaccinated with a MenB vaccine.

These shaded boxes indicate when the vaccine is recommended for all children unless your doctor tells you that your child cannot safely receive the vaccine.

These shaded boxes indicate the vaccine should be given if a child is catching-up on missed vaccines.

These shaded boxes indicate the vaccine is recommended for children with certain health or lifestyle conditions that put them at an increased risk for serious diseases. See vaccine-specific recommendations at www.cdc.gov/vaccines/pubs/ACIP-list.htm.

This shaded box indicates the vaccine is recommended for children not at increased risk but who wish to get the vaccine after speaking to a provider.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

AMERICAN ACADEMY OF FAMILY PHYSICIANS
STRONG MEDICINE FOR AMERICA

HPV Vaccine Facts

for boys and girls

Every year **26,800** women and men in the U.S. develop HPV-related cancer.

The newest HPV vaccine protects against 9 HPV types and **6 kinds of cancer.**

90% of genital warts, 74% of all HPV cancers, and 81% of cervical cancers are prevented by the vaccine.

In the U.S., **79 million** are currently infected with HPV. Half of all new infections are in boys and girls aged 15-24.

Up to **80%** of sexually active individuals have had HPV. Safer sex practices like condoms and monogamy do not fully protect against HPV.

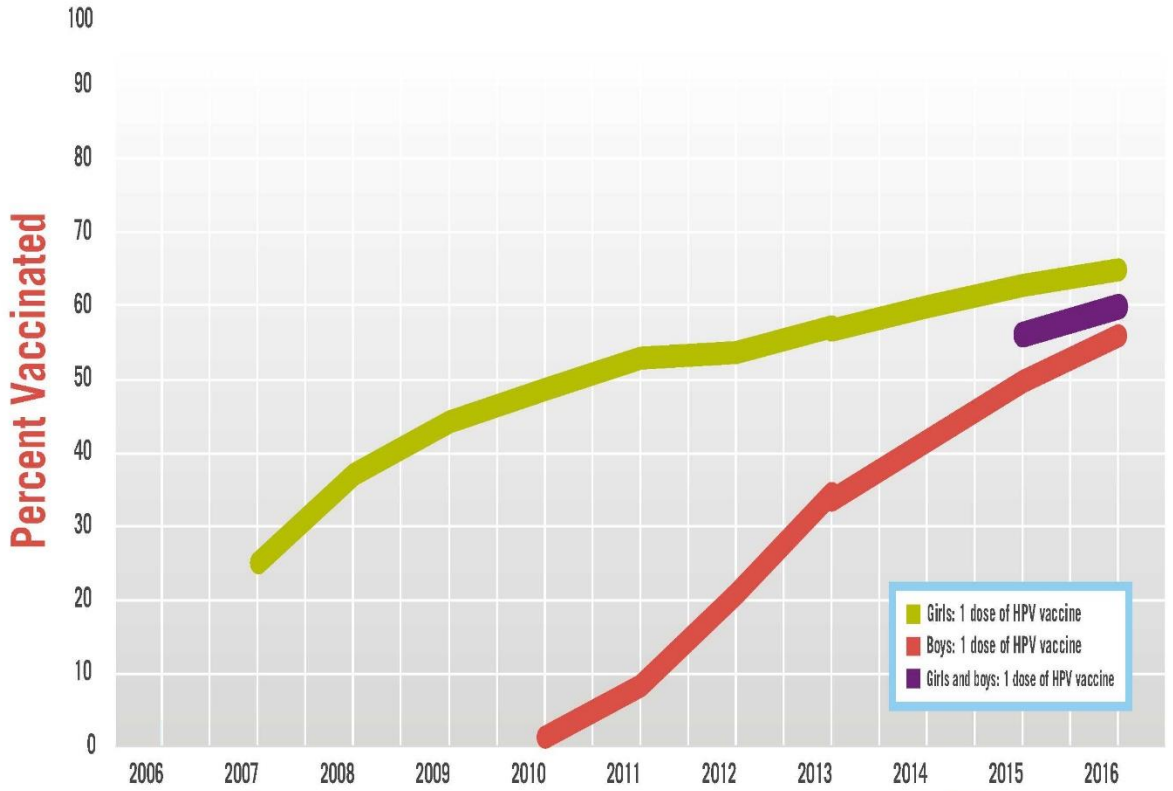
11-12 years is the optimal age for the vaccine because antibody production is highest, and it should be given long before any sexual contact to be most protective.

source: CDC MMWR 2015,64(11);300-304 and CDC 2013 Surveillance

Illustration by **Hannah Henry**, courtesy of **www.thevaccinepage.org**

HPV vaccination is the best way to protect your children from cancers caused by HPV

6 OUT OF 10 parents are choosing to get the human papillomavirus vaccine for their children



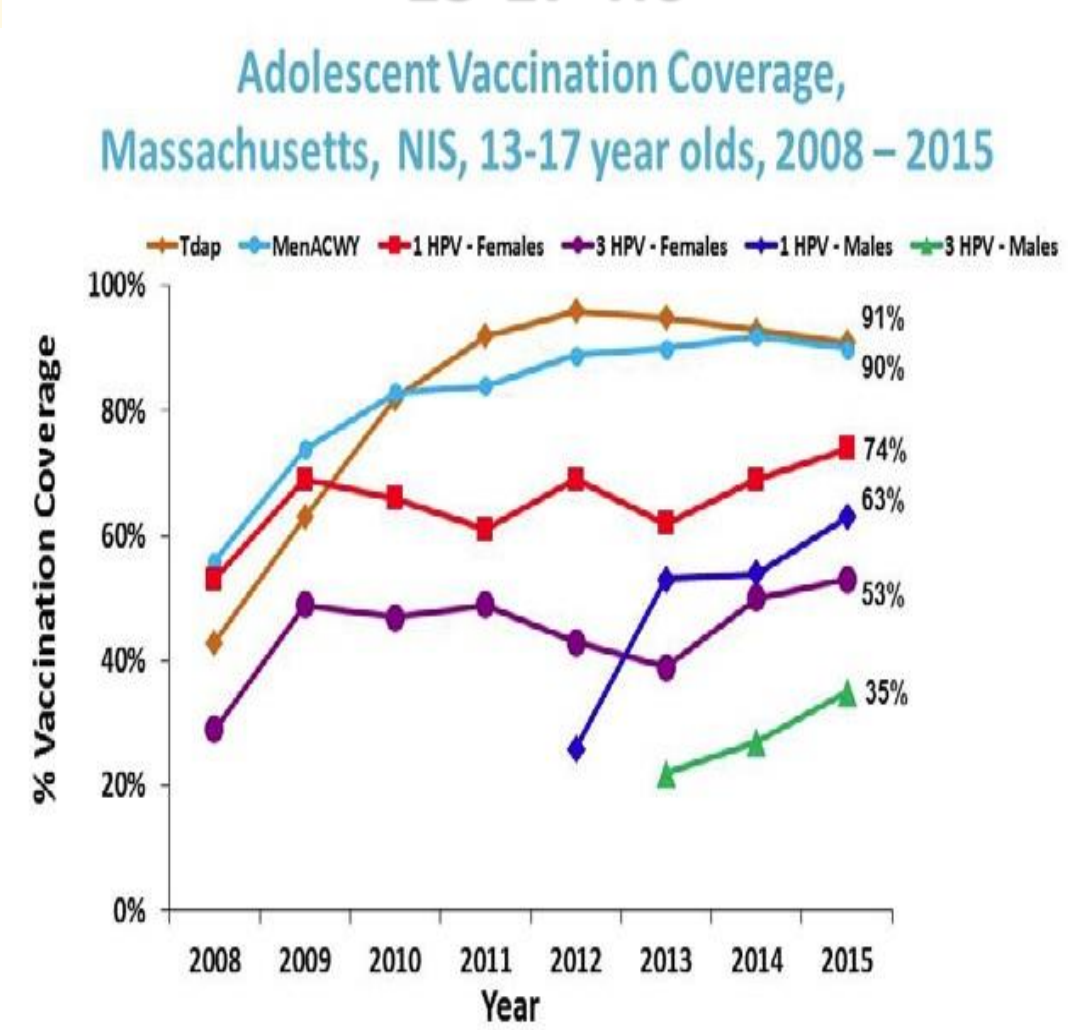
CDC RECOMMENDS THE HPV VACCINE AT AGES 11-12

Talk to your child's doctor about HPV cancer prevention

www.cdc.gov/hpv

Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13-17 years, by survey year – National Immunization Survey-Teen, United States, 2006 – 2016 Source: MMWR August 25, 2017

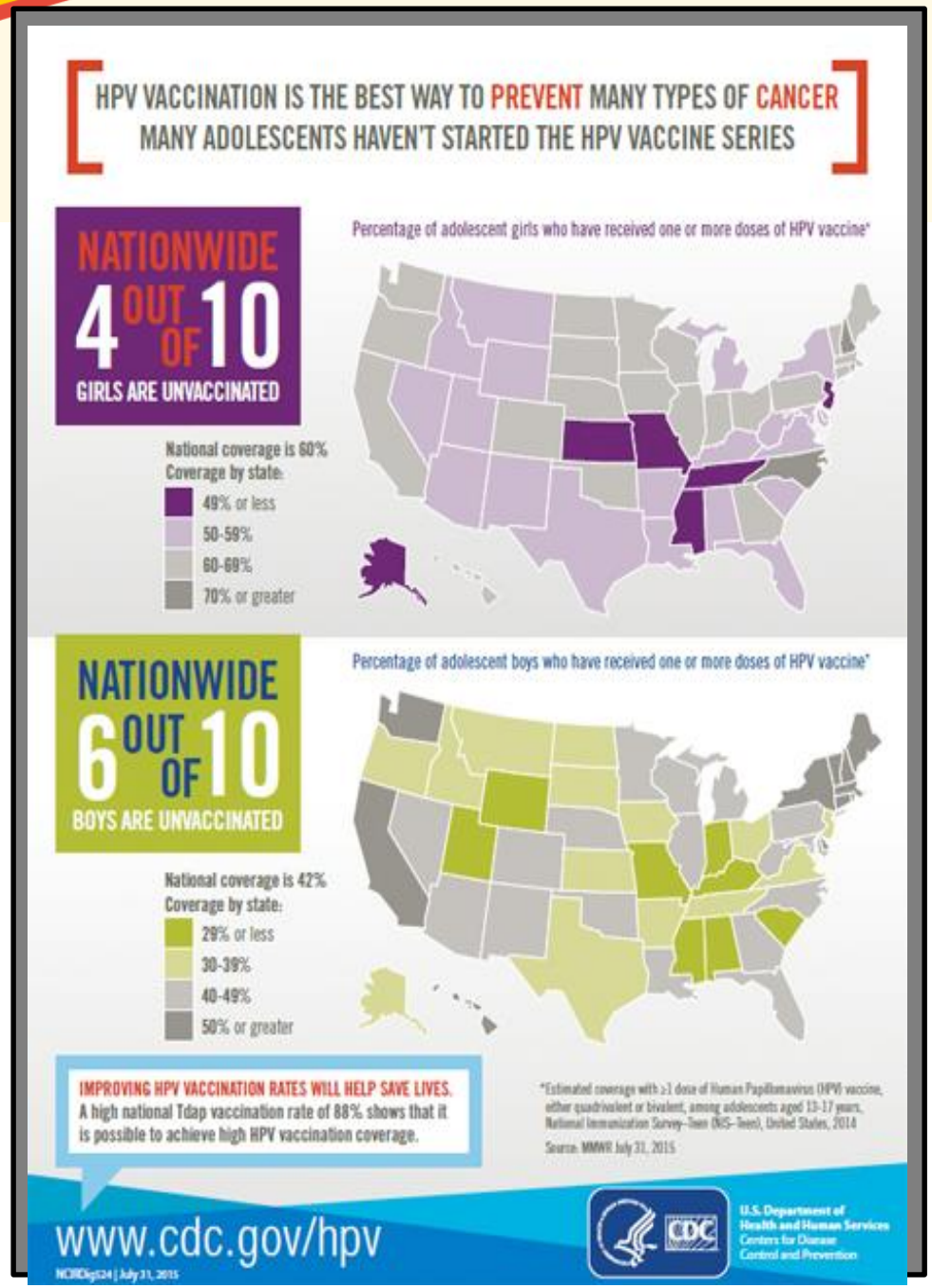
Trends in HPV Vaccination Rates: Ages 13-17 Yrs



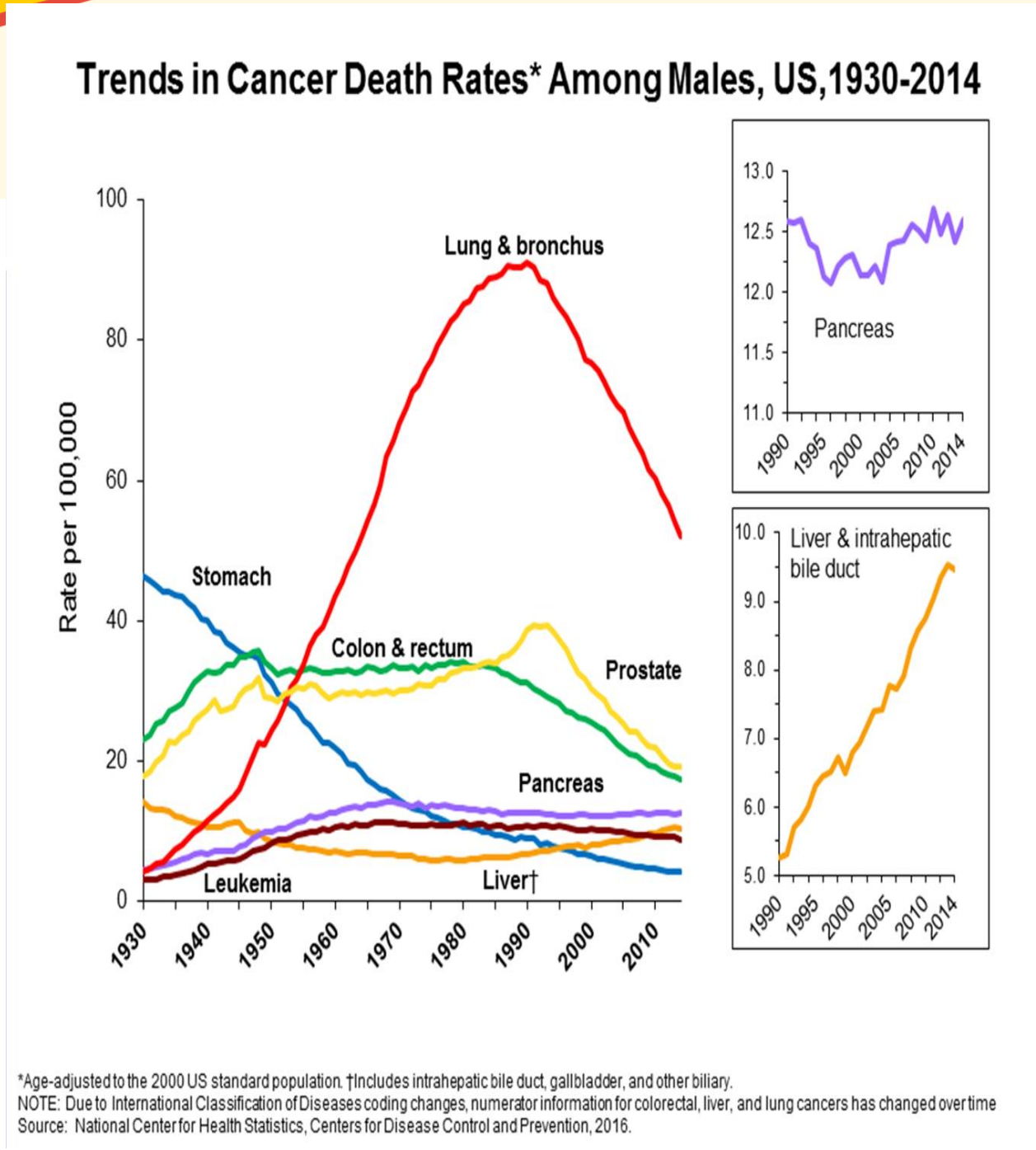
Note: For the purposes of comparability to 2014 estimates, 2013 estimates were revised by retrospectively applying the revised 2014 provider data definition to the 2013 NIS teen data and as a result, differ from those previously published.

NIS Data, CDC

YOU ARE THE KEY TO CANCER PREVENTION

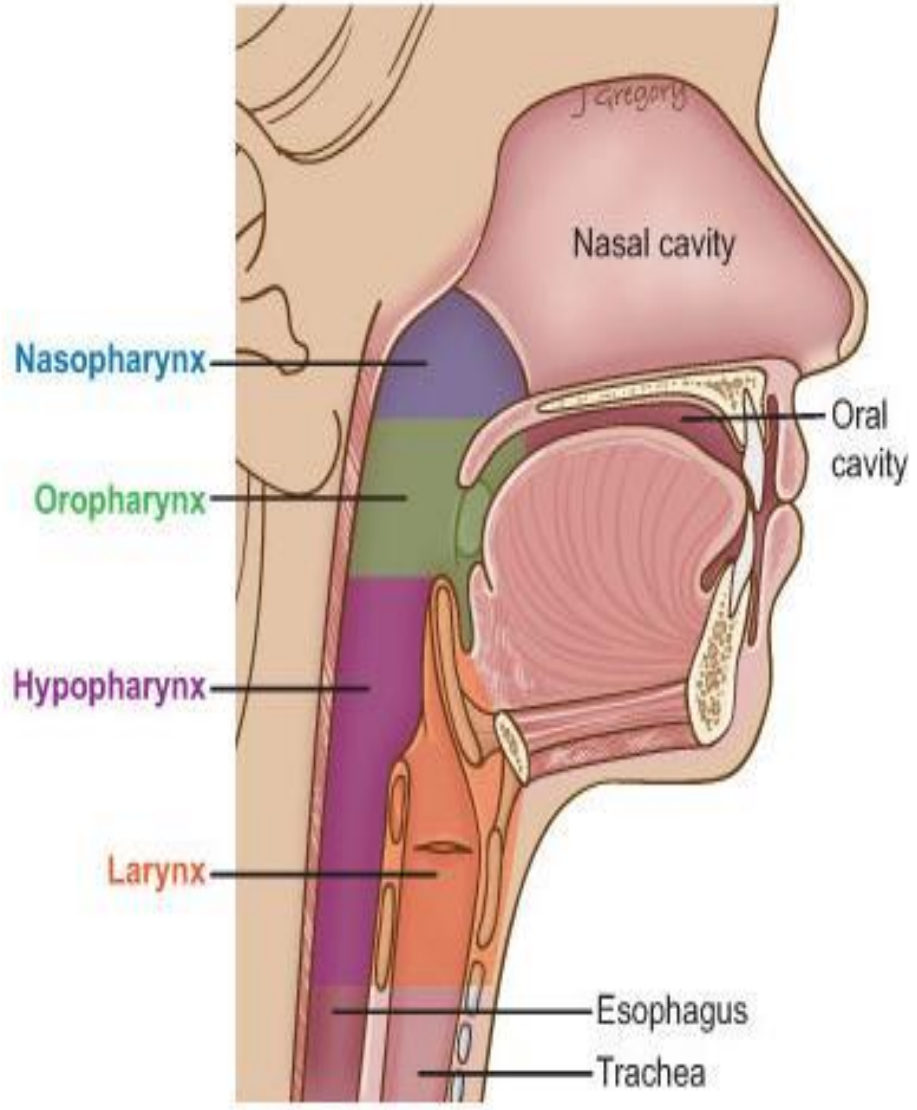

HPV VACCINATION IS THE BEST WAY TO PREVENT MANY TYPES OF CANCER
MANY ADOLESCENTS HAVEN'T STARTED THE HPV VACCINE SERIES
NATIONWIDE
4 OUT OF 10
GIRLS ARE UNVACCINATED
Percentage of adolescent girls who have received one or more doses of HPV vaccine*
National coverage is 60%
Coverage by state:
49% or less
50-59%
60-69%
70% or greater
NATIONWIDE
6 OUT OF 10
BOYS ARE UNVACCINATED
Percentage of adolescent boys who have received one or more doses of HPV vaccine*
National coverage is 42%
Coverage by state:
29% or less
30-39%
40-49%
50% or greater
IMPROVING HPV VACCINATION RATES WILL HELP SAVE LIVES.
A high national Tdap vaccination rate of 88% shows that it is possible to achieve high HPV vaccination coverage.
*Estimated coverage with ≥1 dose of Human Papillomavirus (HPV) vaccine, either quadrivalent or bivalent, among adolescents aged 13-17 years, National Immunization Survey-Teen (NIS-Teen), United States, 2014
Source: MMWR July 31, 2015
www.cdc.gov/hpv
NCIRDdg524 | July 31, 2015
CDC
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

The US cancer landscape is changing rapidly



*Age-adjusted to the 2000 US standard population. †Includes intrahepatic bile duct, gallbladder, and other biliary.
NOTE: Due to International Classification of Diseases coding changes, numerator information for colorectal, liver, and lung cancers has changed over time
Source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2016.

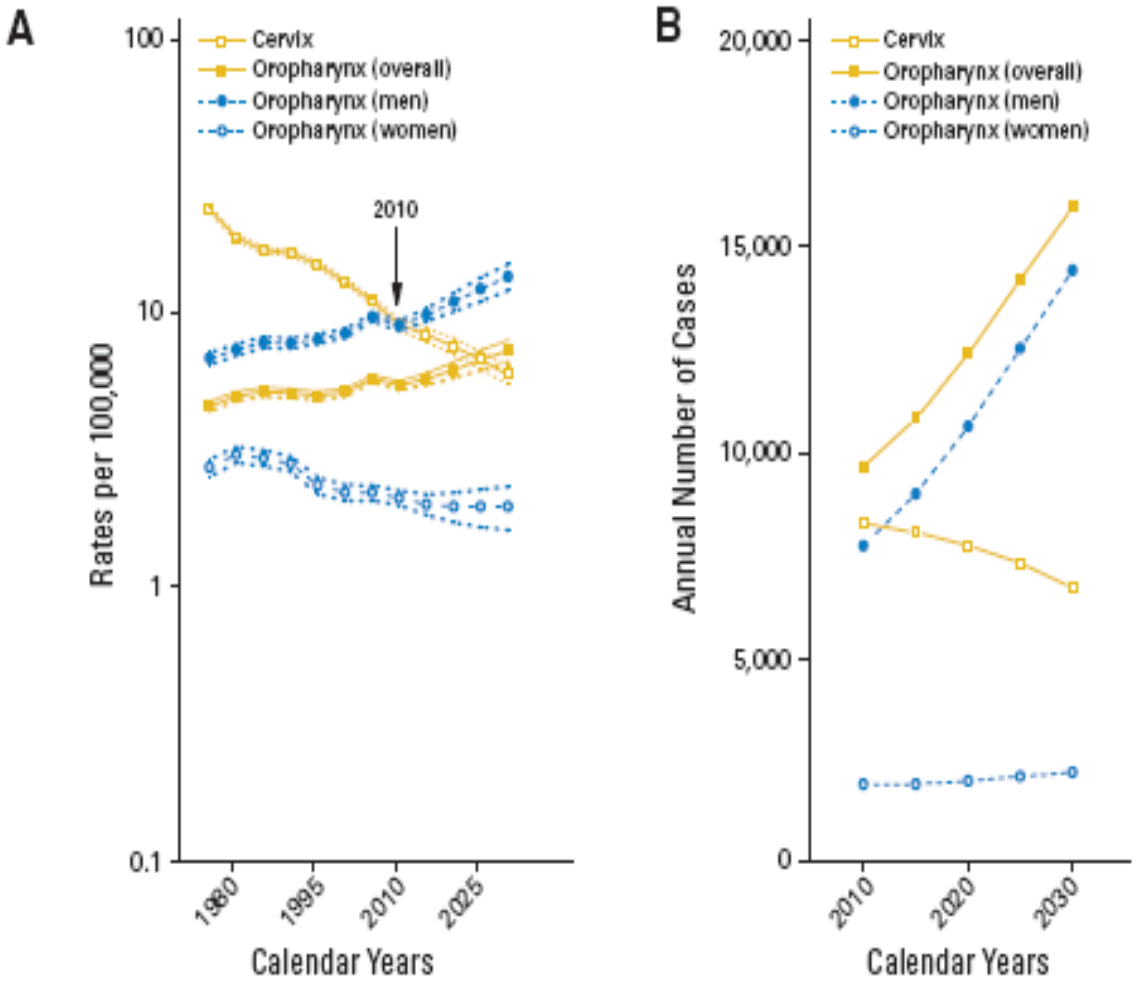
Head and Neck Cancer –
distinct anatomic sites with distinct biology



Papillomavirus and Head and Neck Cancer

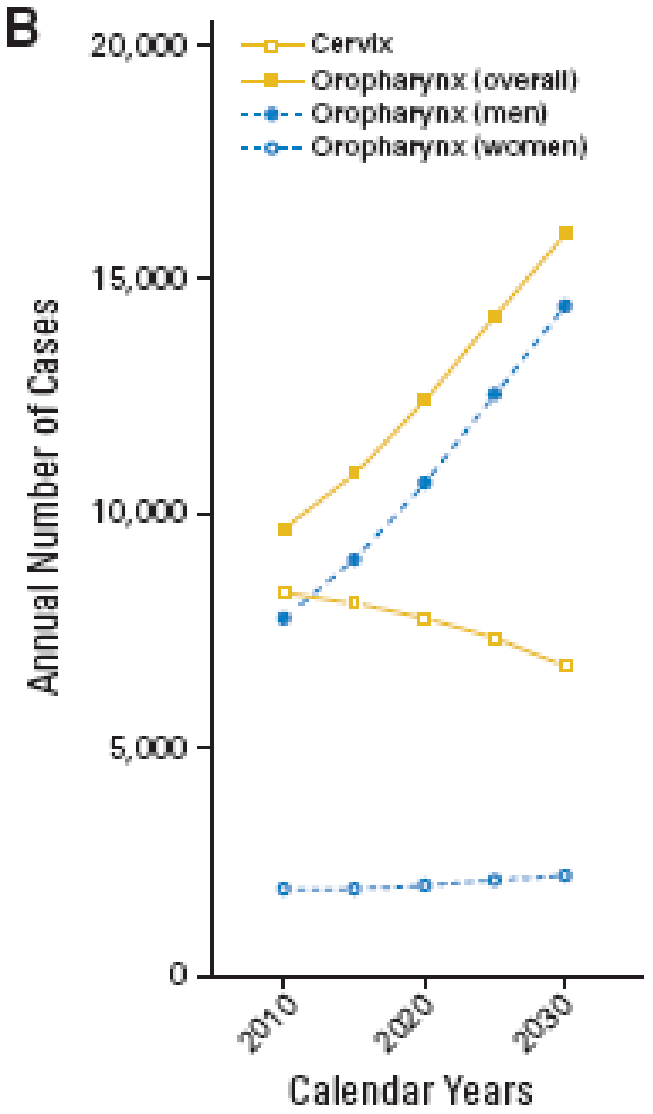
- 2/3 of oropharyngeal (tonsil and base of tongue) cancers contain detectable HPV DNA
- Almost all of these cancers associated with HPV 16
- HPV incidence increasing, now accounts for about 25% of all head and neck cancers
- Associated with other cancers as well

Oropharyngeal cancer cases in men now outnumbers cervical cancer cases in women



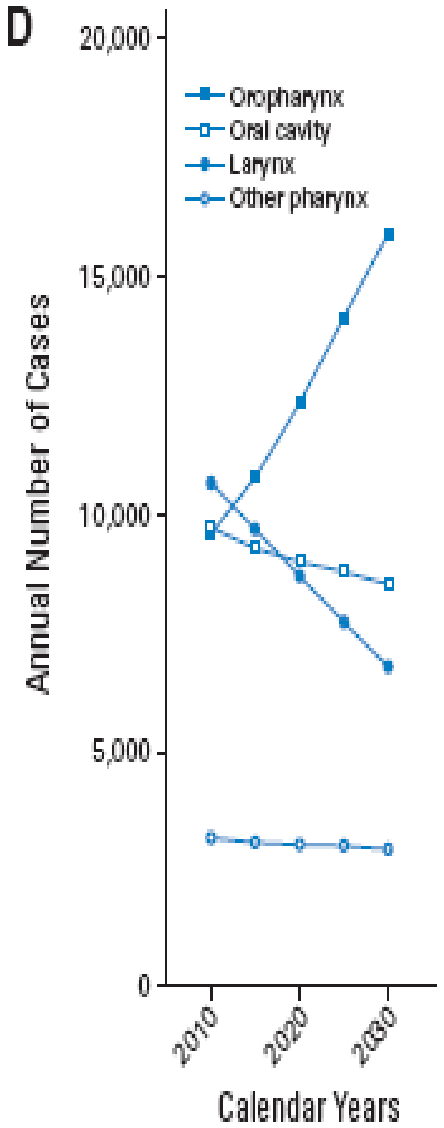
Chaturvedi *et al* JCO 29: 4294, 2011

By 2030 there will be four times as many cases of oropharyngeal cancer in U.S. men as cervical cancer in U.S. women



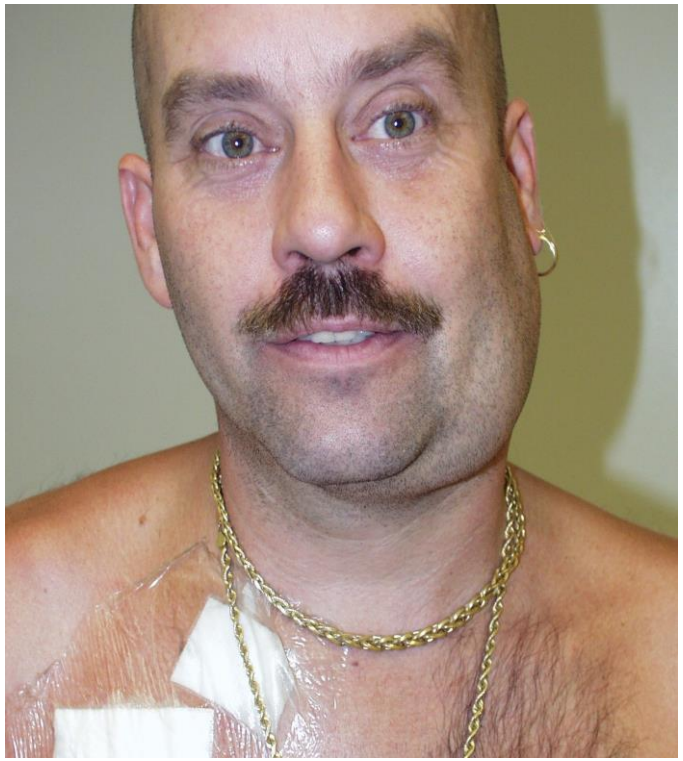
Chaturvedi *et al*
JCO 29: 4294, 2011

HPV associated head and neck cancer is climbing rapidly while smoking related head and neck cancer is declining

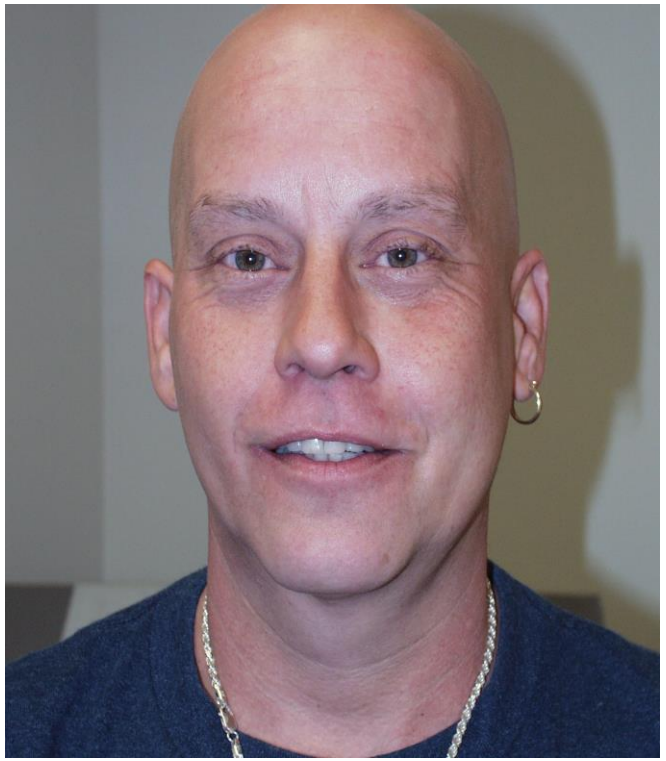


Chaturvedi *et al*
JCO 29: 4294, 2011

Oropharyngeal Cancer - Concomitant Cisplatin/RT

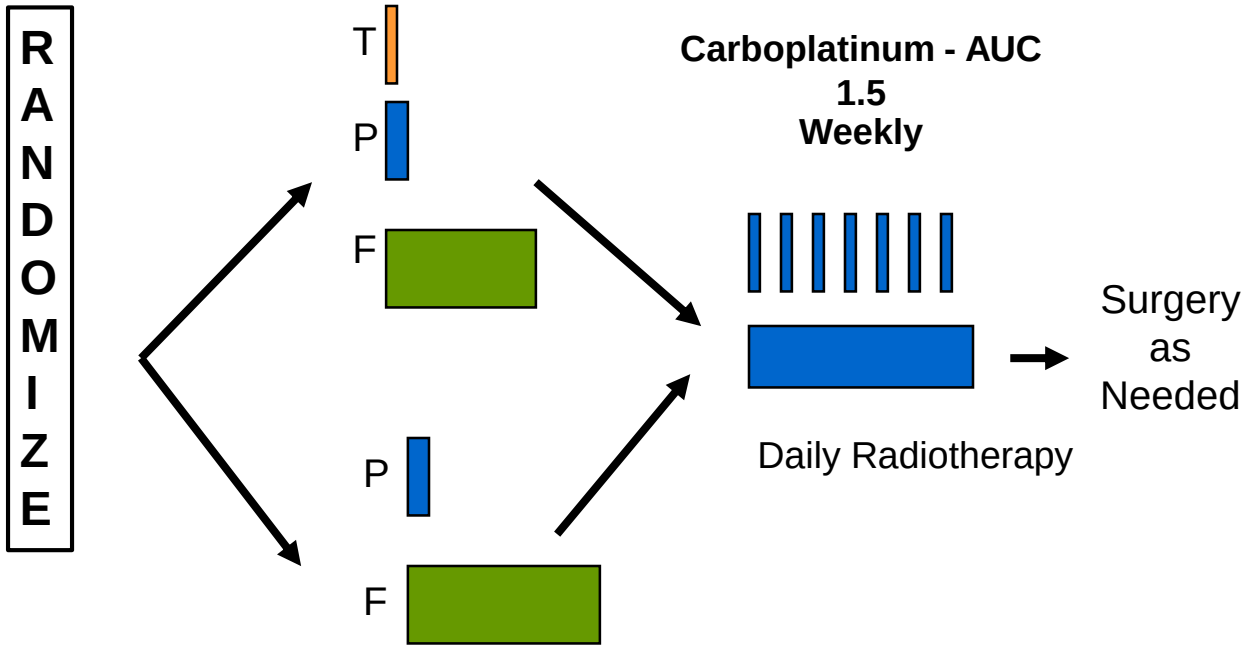


Pre Treatment



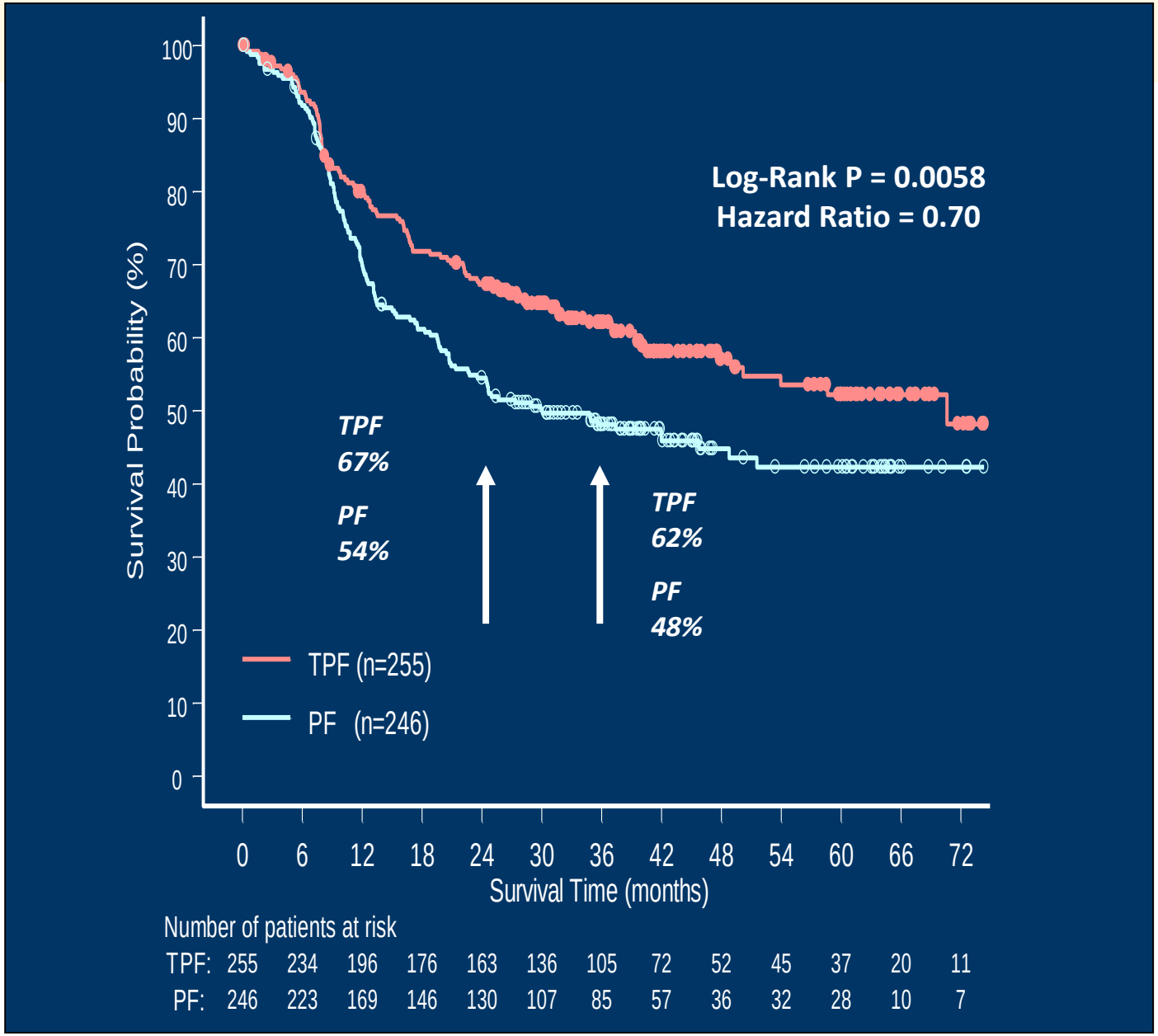
Post Treatment

TAX 324: Sequential Combined Modality Therapy
TPF *vs* PF Followed by Chemoradiotherapy

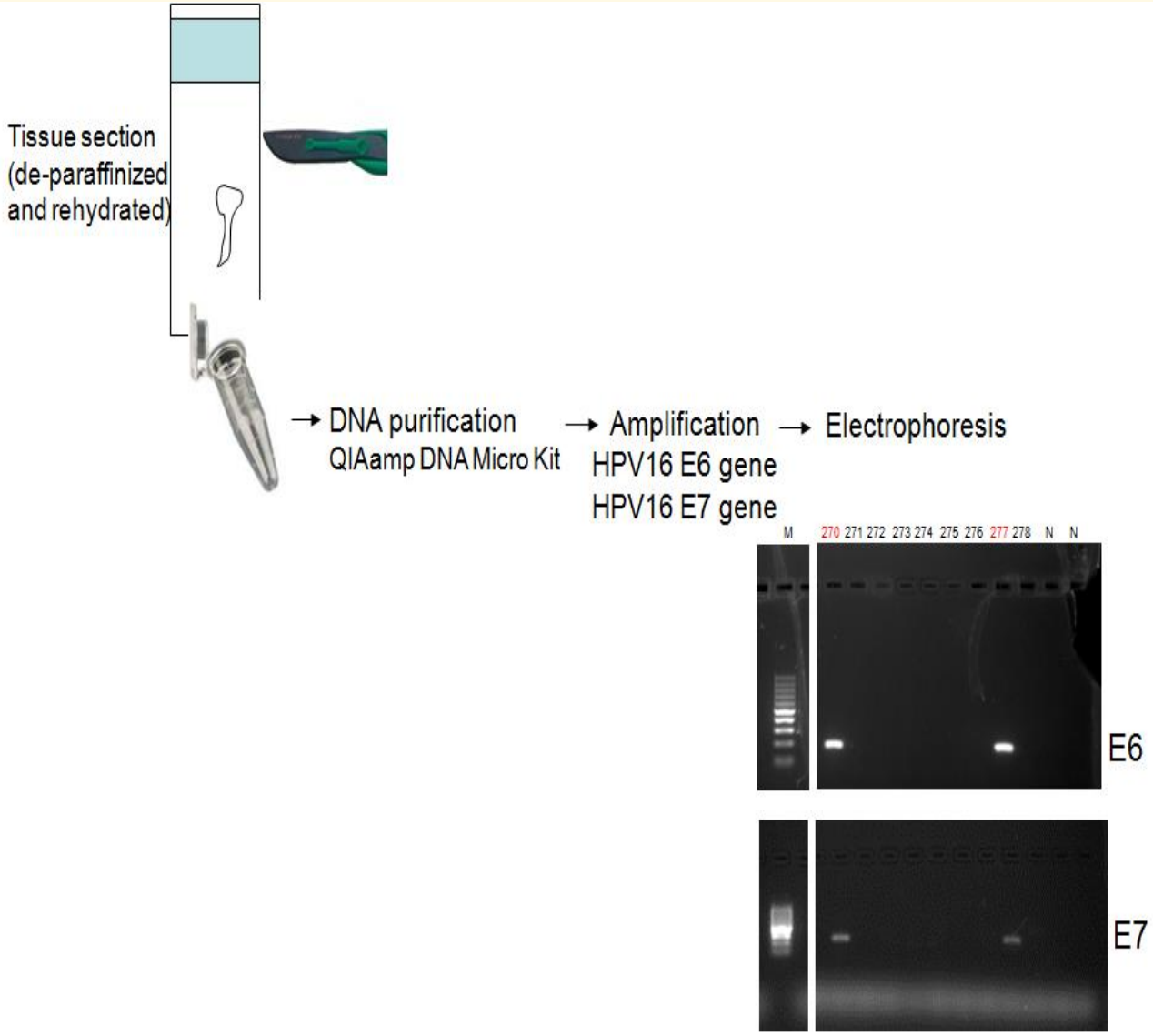


TPF: Docetaxel 75_{D1} + Cisplatin 100_{D1} + 5-FU 1000 $_{CI- D1-4}$ Q 3 weeks x3
PF: Cisplatin 100 $_{D1}$ + 5-FU 1000 $_{CI-D1-5}$ Q 3 weeks x 3

TAX324 : Survival



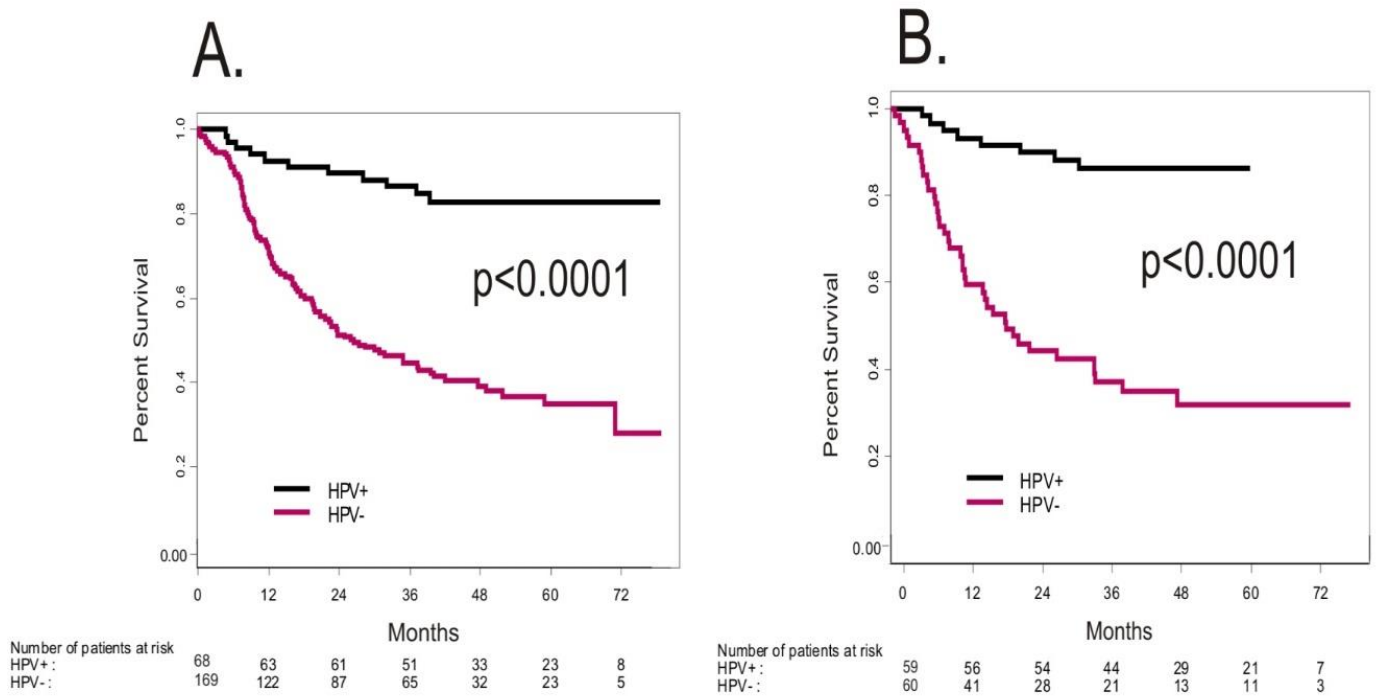
HPV Analysis – TAX 324



HPV Analysis – TAX 324

- 270 cases available (of 521)
- 269 yielded adequate DNA
- 238 interpretable HPV results
- Validation set (49 random cases repeated) error 0/49 for E6, 1/49 for E7
- 68 HPV positive, 170 HPV negative
- 59/68 positive cases oropharynx
- 49% of oropharynx HPV positive

HPV Positive Tumors Have Excellent Prognosis – TAX 324



All Patients

Oropharynx

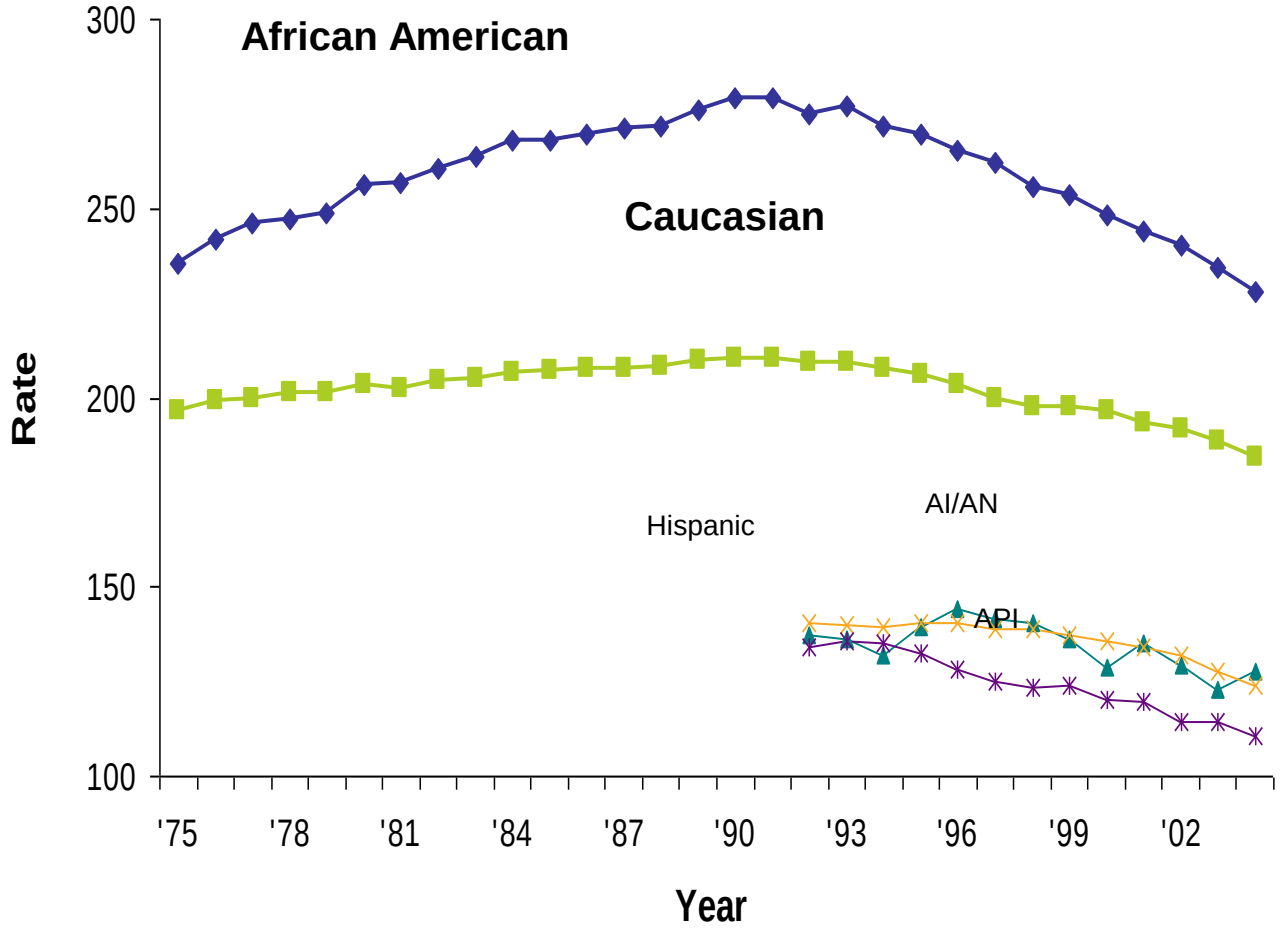
RACIAL DISPARITIES IN HEAD AND NECK CANCER

Racial Disparities in Head and Neck Cancer

"If you get cancer, whether you live or die shouldn't be determined by your zip code."

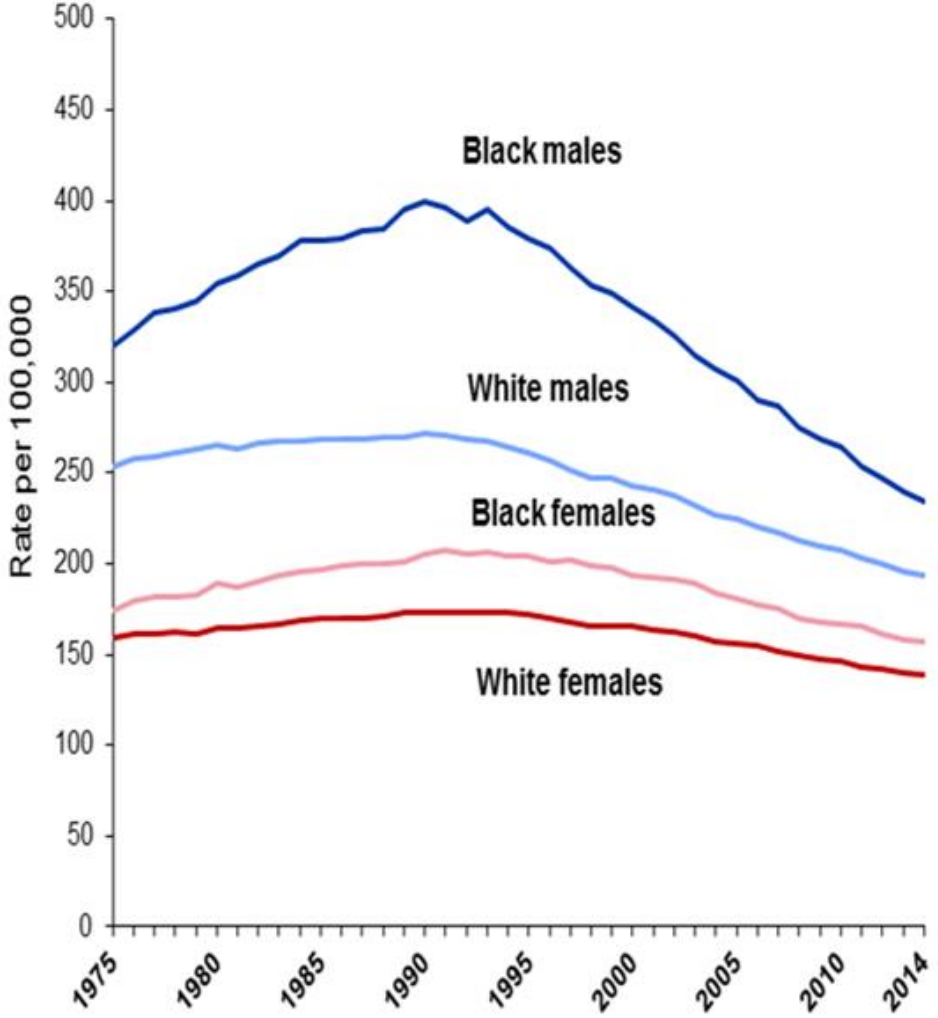
Stewart Greenebaum

All Sites – Cancer Mortality Rates 1973-2004
By Race, Males and Females



Incidence and mortality rates per 100,000 and age-adjusted to 2000 US standard population
SEER Cancer Statistics Review 1975-2004.

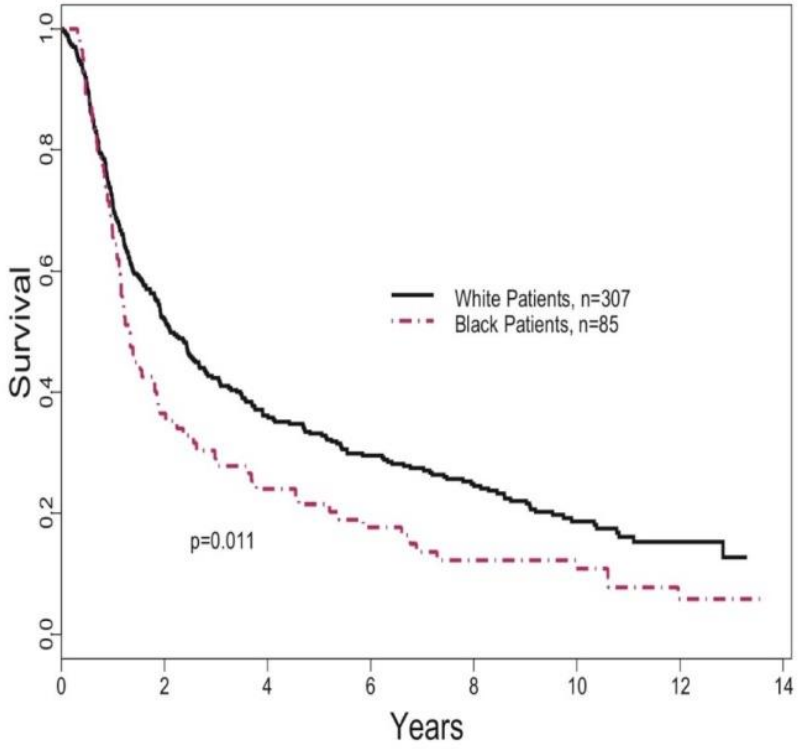
Trends in Cancer Death Rates* by Sex and Race, US, 1975-2014



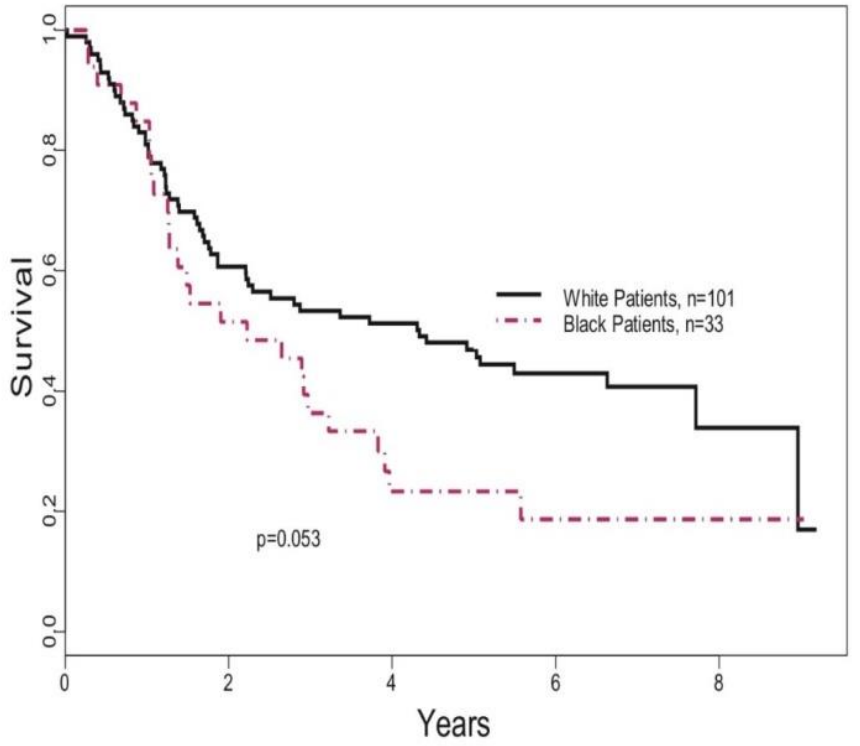
Age-adjusted to the 2000 US standard population.
Source: National Center for Health Statistics, Centers for Disease Control and Prevention

Black patients with locally advanced HNSCC show poor survival compared to whites – RTOG 9003, 9501

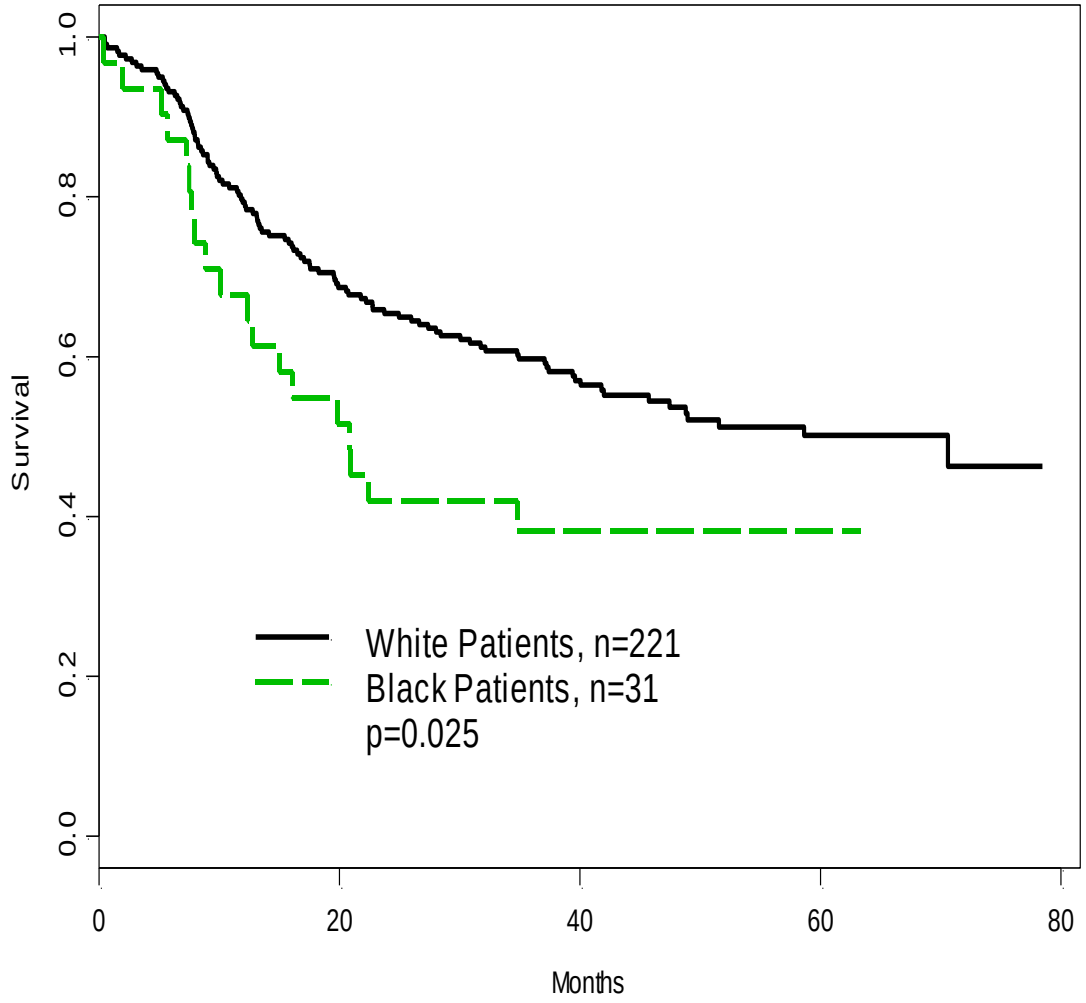
RTOG 9003



RTOG 9501



Black patients with locally advanced HNSCC show poor survival compared to whites – TAX 324



Cancer **Prevention** Research

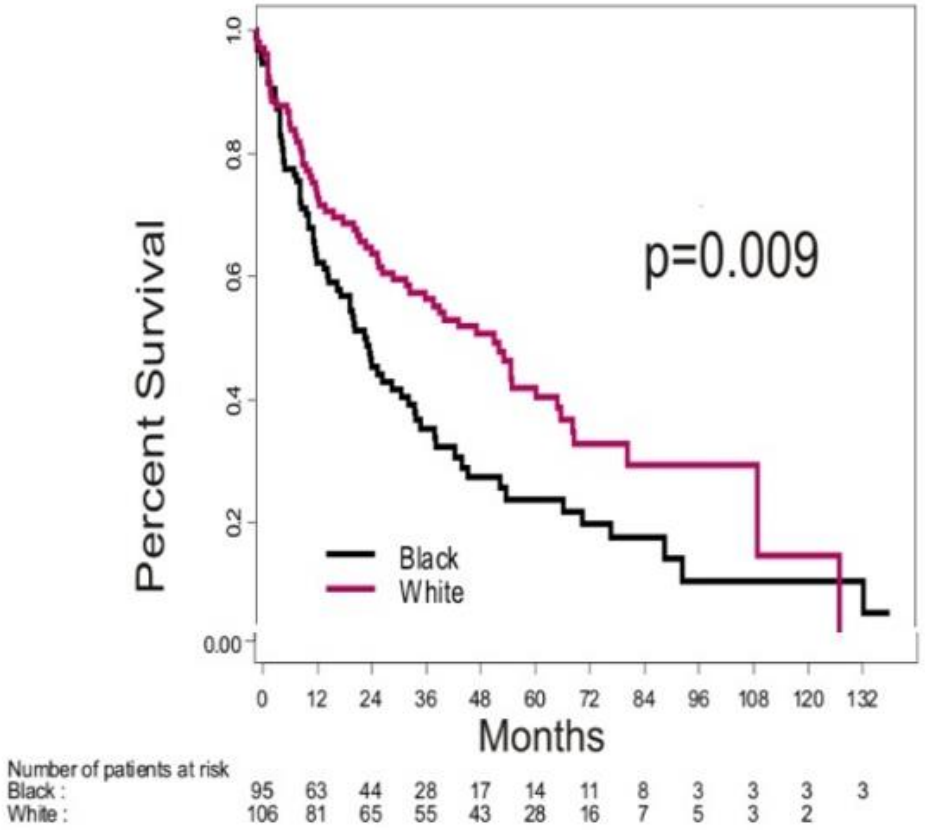
Racial Survival Disparity in Head and Neck Cancer Results from Low Prevalence of Human Papillomavirus Infection in Black Oropharyngeal Cancer Patients

Kathleen Settle,[1] Marshall R. Posner,[2] Lisa M. Schumaker,[1] Ming Tan,[1] Mohan Suntharalingam,[1] Olga Goloubeva,[1] Scott E. Strome,[1] Robert I. Haddad,[2] Shital S. Patel,[1] Earl V. Cambell III,[1] Nicholas Sarlis,[3] Jochen Lorch[2] and Kevin J. Cullen[1]

Cancer Prev Res 2009;2(9) September 2009

Impact of Race on Survival
University of Maryland

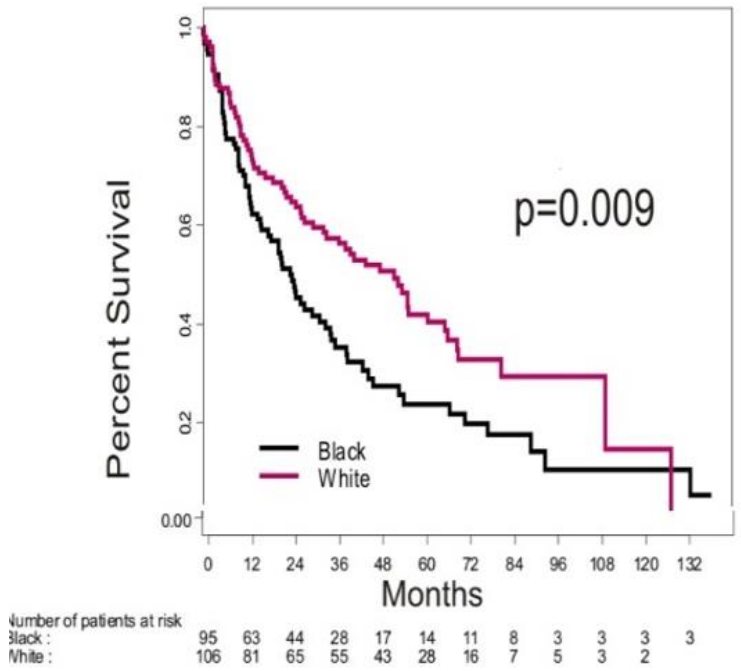
A.



All Patients

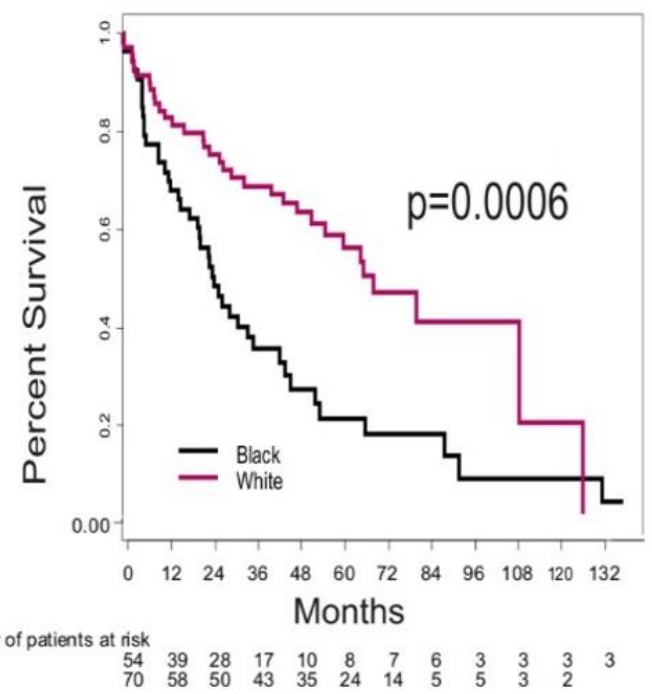
Impact of Race on Survival
University of Maryland

A.



All Patients

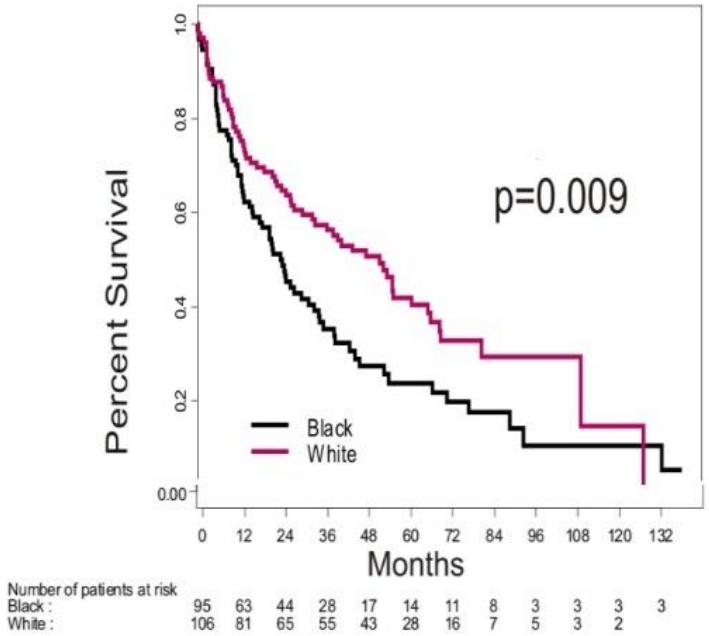
B.



Oropharynx

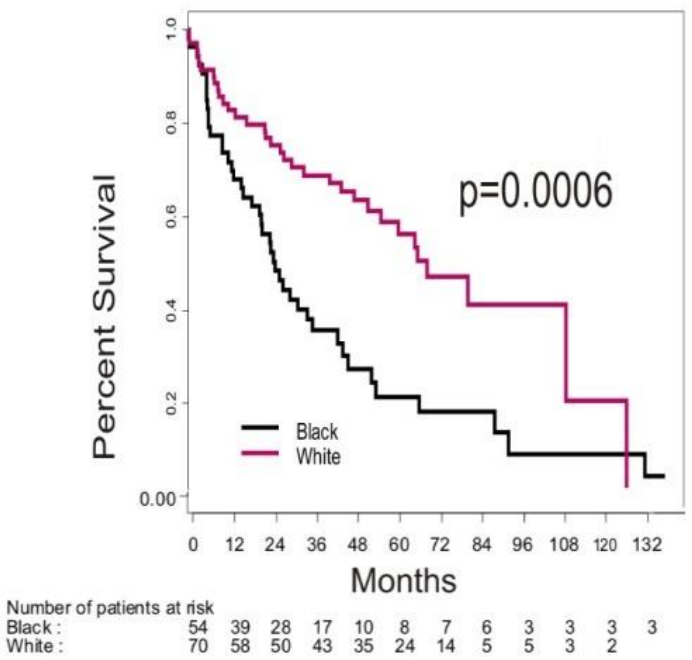
Impact of Race on Survival
University of Maryland

A.



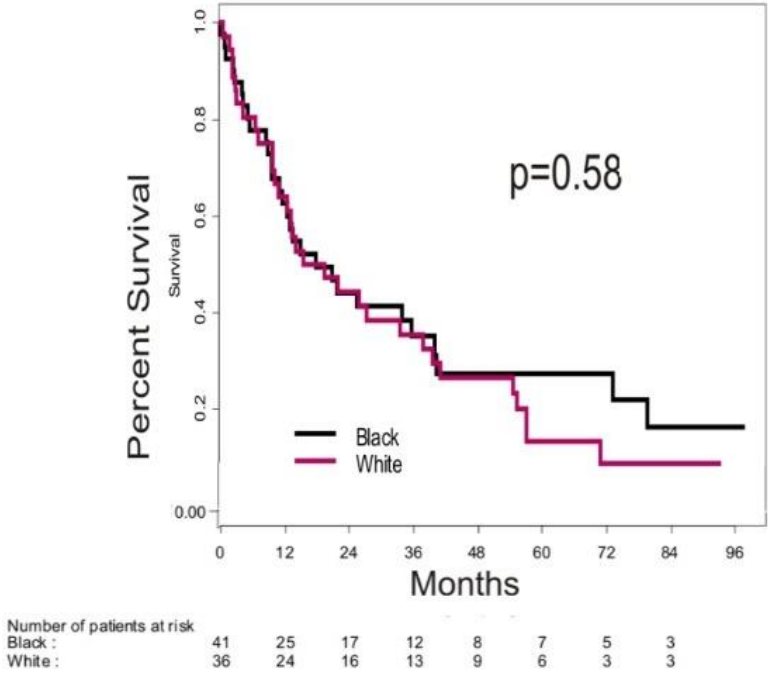
All Patients

B.



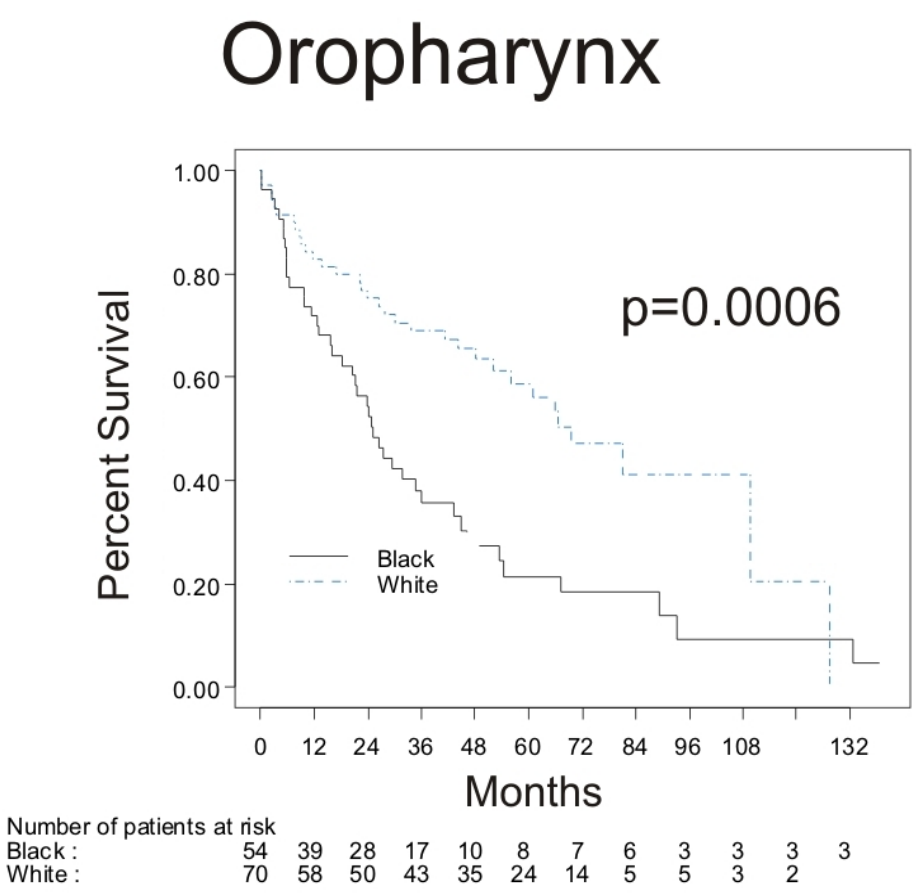
Oropharynx

C.

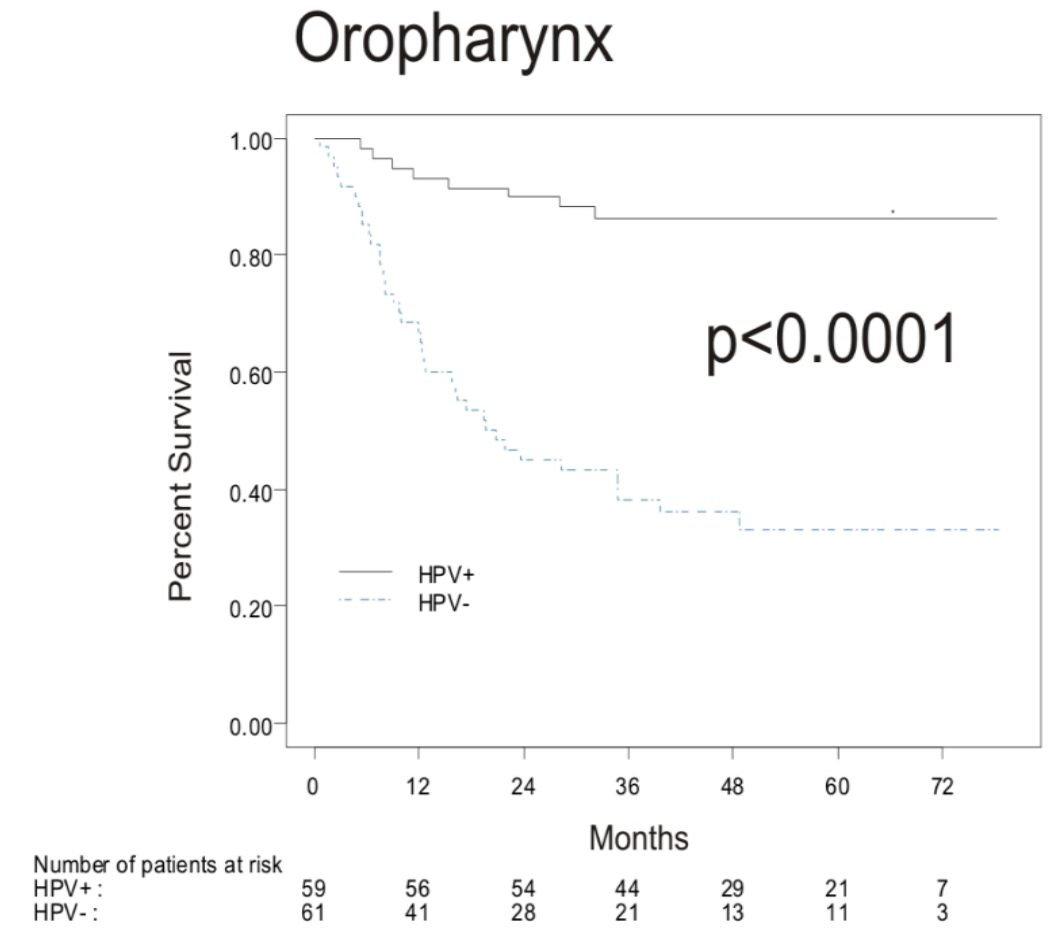


Non-Oropharynx

4am moment – “gee there is something similar about these curves….”



U of MD - Race



Tax 324 - HPV

HPV Positive Cases by Race – TAX 324

Race*	HPV negative	HPV positive	Total
White	130, 66%	66, 34%	196
Black	28, 97%	1, 3%	29
Total	158	67	225

HPV Positive Cases by Race – TAX 324

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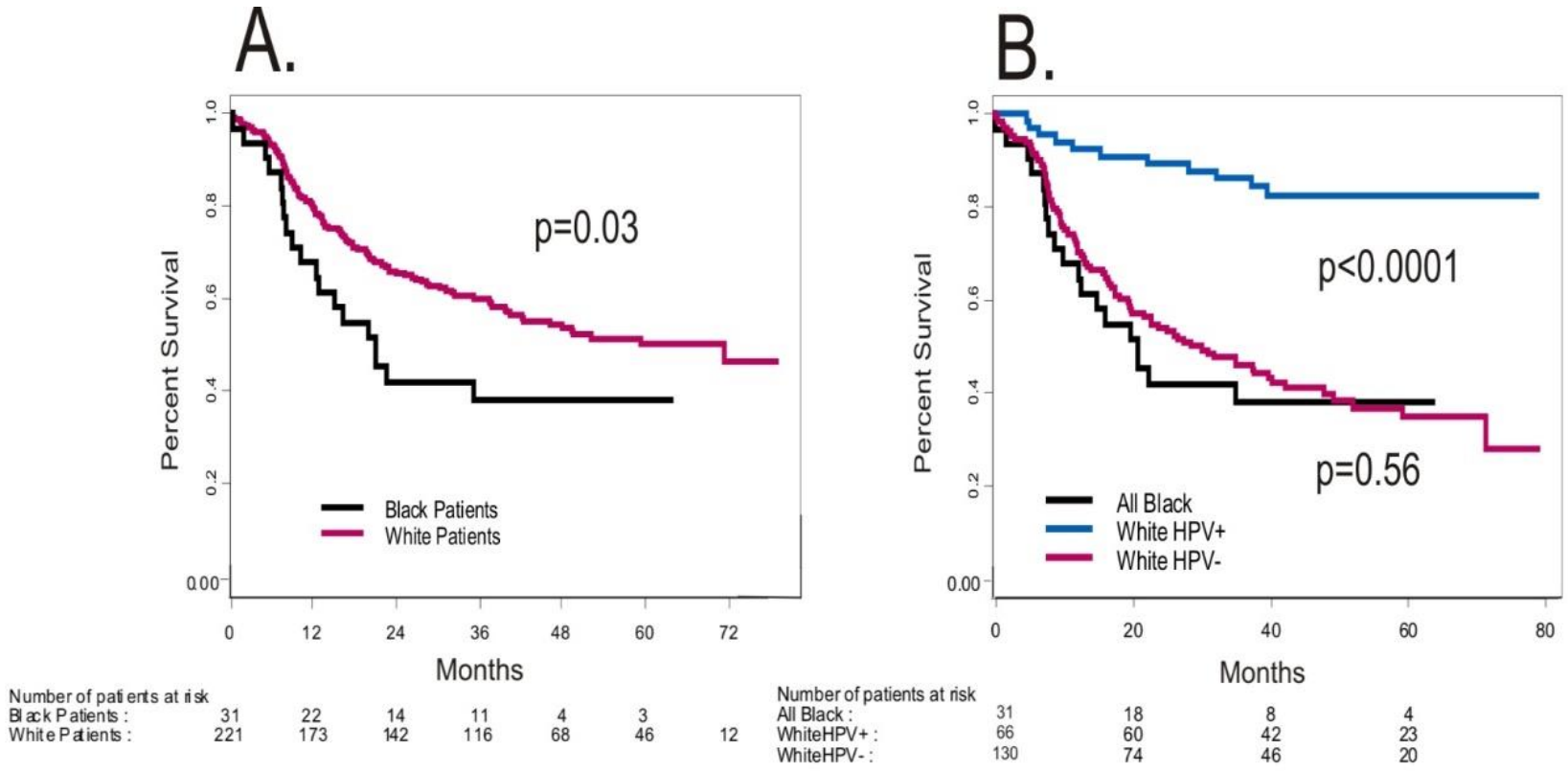
Whites 10 times more likely than blacks to be HPV positive p=0.0003

Impact of Race on Survival
TAX 324 Study



All Patients

Racial Disparities

Racial disparity is due to large number of white patients with good prognosis HPV positive tumors – rate of HPV positive tumors very low in blacks.

TUESDAY, AUGUST 4, 2009

Science Times

The New York Times

Findings May Explain Gap in Cancer Survival

By RONI CARYN RABIN

Scientists say they have made a discovery that may help explain the racial gap in cancer survival, providing clues to why white patients often outlive blacks even when they have what appear to be the same cancers.

The insights come from research at the University of Maryland into throat cancer and squamous-cell cancers of the head and neck, which have been increasing sharply in recent years, apparently because of the human papillomavirus — the same sexually transmitted virus that causes cervical cancer and is the target of a vaccine for girls.

The virus can also be spread through oral sex, causing cancer of the throat and tonsils, or oropharyngeal cancer.

A racial disparity may have roots in a tumor's cause.

The new research builds on earlier work suggesting that throat cancer tumors caused by the virus behave very differently from other throat cancers, and actually respond better to treatment. And the new research suggests that whites are more likely than blacks to have tumors linked to the virus, which may explain the poor outcomes of African-Americans with HPV-negative tumors.

University of Maryland researchers did the study after finding that their white patients with throat cancer were surviving 70 months on average, compared with 25 months for their black patients, even though all were treated at the same hospital.

The racial disparity in survival for oropharyngeal cancers explained most of the gap between blacks and whites for all head and neck cancers, the researchers said.

"We were shocked to see this in our own institution, where more than half of the patients we treat are African-American," said Dr. Kevin J. Cullen, director of the Greenebaum Cancer Center at University of Maryland and senior author of the new study, in the September issue of Cancer Prevention Research.

Around the same time, the Maryland researchers were analyzing specimens of head and neck tumors gathered from participants in a treatment trial called the TAX 324 study, to determine how many tumors were linked to HPV.

The results were striking: the TAX 324 patients whose tumors were caused by the virus responded much better to treatment with chemotherapy and radiation. And they were also overwhelmingly white.

While about one-half of the white patients' throat tumors were HPV-positive, only one of the black patients had a tumor caused by the virus, Dr. Cullen said.

"There was no difference in the survival between black and white patients in the TAX 324 trials if you subtracted out the HPV-positive patients," he said.

The racial gap has often been explained as a result of late diagnosis among African-Americans, lack of access to care and less aggressive treatment, but experts said that in the case of oropharyngeal cancer, there appeared to be distinct biological differences between the tumors.

This suggests that the racial gap in survival for this particular cancer may trace back to social and cultural differences between blacks and whites, including different sexual practices, experts said.

At a briefing for reporters, leading cancer experts called the new report a landmark paper that would transform the treatment of oropharyngeal cancers and challenge doctors to develop new treatment options for patients with HPV-negative tumors.

Dr. Otis Brawley, medical director of the American Cancer Society, who wrote an editorial accompanying the report, said that changing sexual practices were increasing rates of head and neck cancers, and perhaps others as well.

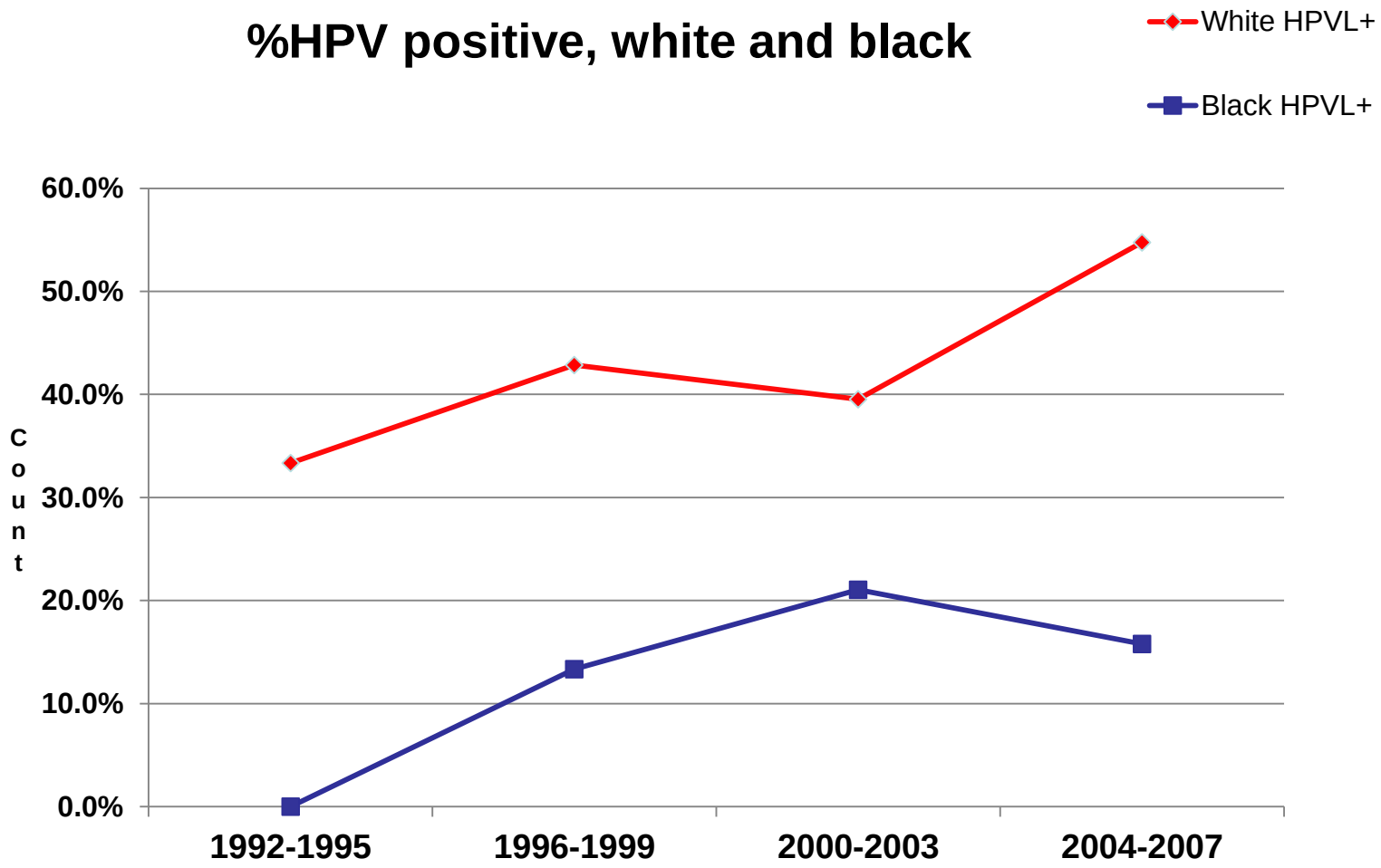
"There is a huge public health message here," he said.

HPV Summary – Tax 324 and U. Maryland

TAX 324				UMGCC OPC	
	HPV- (%)	**HPV +(%)**		HPV- (%)	**HPV+ (%)**
White	130 (66)	**66 (34)**		67 (53)	**54 (47)**
Black	27 (96)	**1 (4)**		62 (87)	**9 (13)**
Total	**157**	**67**		**129**	**63**

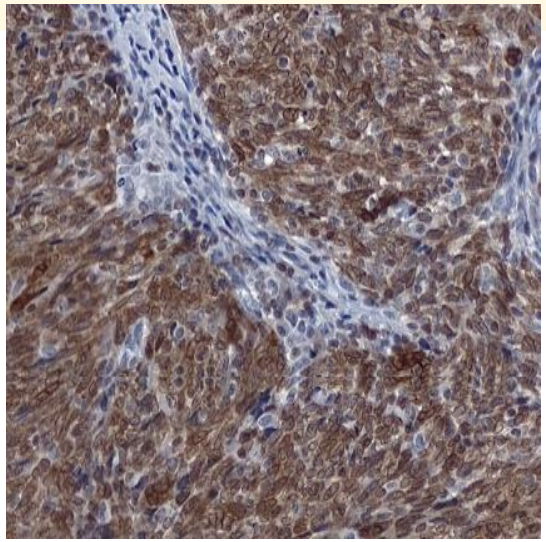
Combined TAX 324 +UMGCC		
	HPV - (%)	**HPV+ (%)**
White	197 (62)	**120 (38)**
Black	**99 (91)**	**10 (9)**

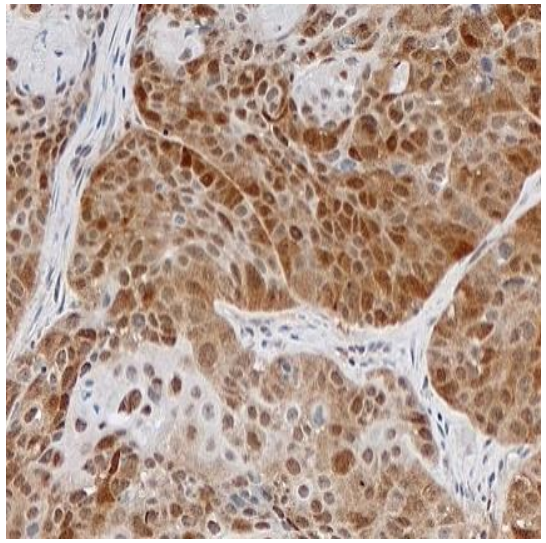
HPV 16 Positive Oropharyngeal Cancer 1992-2007, University of Maryland



Prognostic Markers in Oropharyngeal Cancer
Tax 324, U. of Maryland

Markers Analyzed (2)





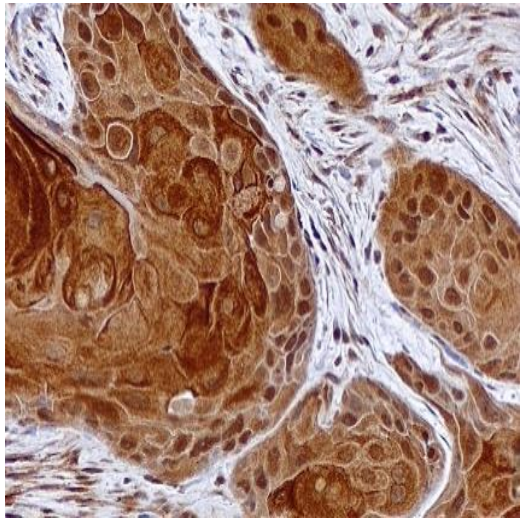
- Bcl-2
  - Resistance to apoptosis – favorable prognosis

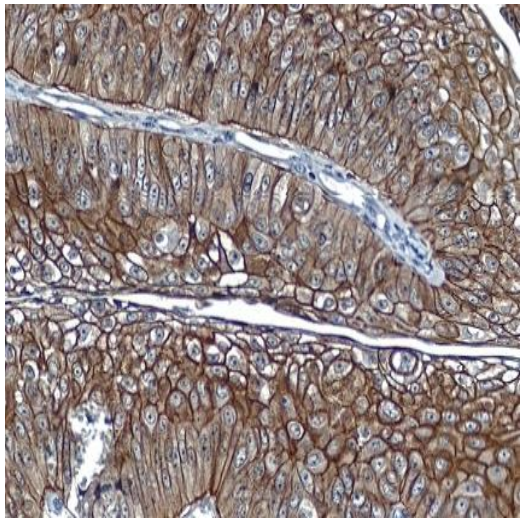
    (Dako 124)

- Thymidylate synthase
  - Resistance to 5-fluorouracil – adverse prognosis

    (Zymed TS 106)

Markers Analyzed (3)





- Beta-tubulin-II
  - Target of taxanes - ?adverse prognosis

    (Biogenex JDR 3B8)

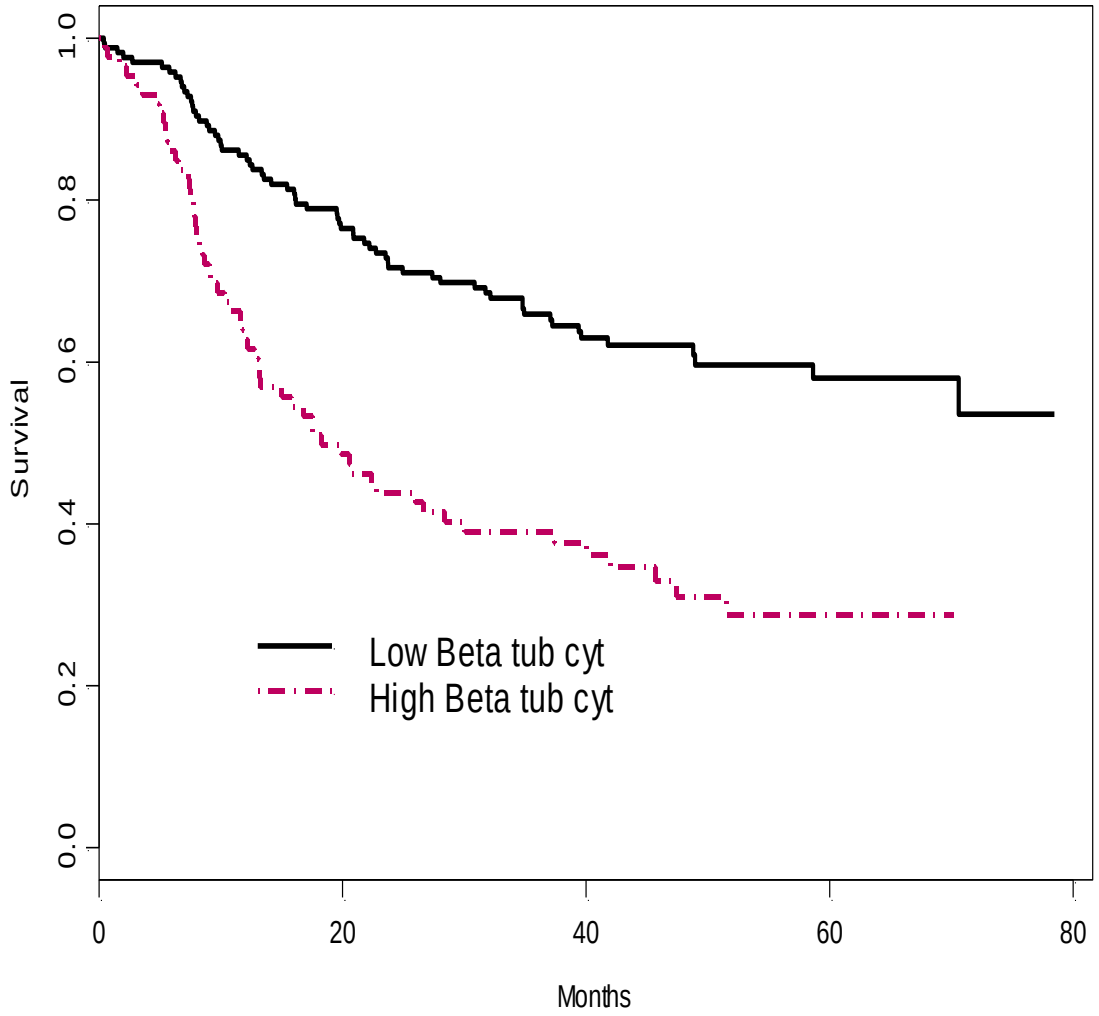
- Her-2 neu
  - Negative prognostic factor in several cancers

    (Dako A0485)

TAX 324 - Marker expression and survival – Univariate Analysis

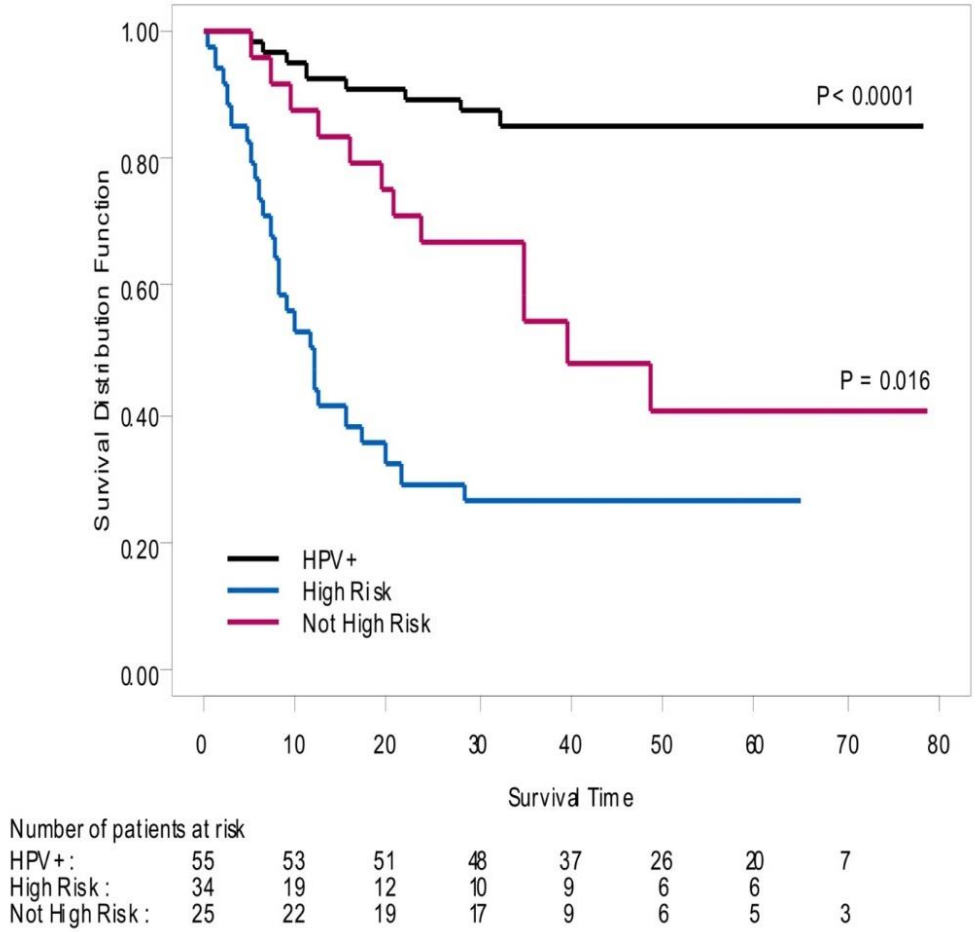
		OS			PFS		
Marker's category by intensity	N	HR (95% CI)	Median (95% CI)	P-Value	HR (95% CI)	Median (95% CI)	P-Value
P53							
≤ 1	136	1.0	—(39.59—)	0.066	1.0	34.46 (16.42—)	0.12
>1	127	1.39 (0.98-1.97)	—41.79 (21.78—)		1.29 (0.93-1.78)	16.82 (10.32-39.39)	
Bcl2							
≤1	178	1.0	39.39 (23.75—)	0.051	1.0	18.53 (11.60-31.18)	0.06
>1	77	0.67 (0.44-1.01)	— (48.79—)		0.70 (0.48-1.02)	55.82 (24.44—)	
TS							
≤ 1	153	1.0	51.55 (37.22—)	0.96	1.0	21.72 (13.53-45.73)	0.67
>1	109	1.01 (0.70-1.44)	— (25.95—)		0.93 (0.67-1.30)	25.95 (12.88—)	
GSTpi							
≤ 2	165	1.0	70.60 (47.44—)	0.04	1.0	39.39 (16.03—)	0.01
>2	96	1.44 (1.01-2.06)	37.22 (25.95-58.64)		1.32 (0.95-1.84)	19.32 (10.15-37.72)	
HER2							
≤ 1	135	1.0	58.64 (37.06—)	0.51	1.0	21.72 (13.60-47.44)	0.80
>1	122	1.13 (0.79-1.60)	48.95 (25.94—)		1.04 (0.75-1.45)	21.72 (12.12-55.82)	
β-tub Cytoplasmic							
≤ 2	169	1.0	— (58.64—)	<.0001	1.0	43.17 (24.44—)	<.0001
>2	86	2.39 (1.67-3.42)	18.27 (13.11-30.06)		1.99 (1.43-2.77)	9.82 (7.06-18.53)	

TAX 324 – Beta-Tubulin-II expression and overall survival



Median survival 58 months
v 18.2 months
(p<0.0001)

HPV status and biomarkers define risk groups in oropharyngeal cancer



Number of patients at risk

HPV+:	55	53	51	48	37	26	20	7
High Risk:	34	19	12	10	9	6	6	
Not High Risk:	25	22	19	17	9	6	5	3

High risk HPV negative – Beta tubulin positive or 2/3 other markers positive

Conclusions

- HPV is a growing cause of cancer worldwide – in women and in men.
- 75% of the US population has been exposed to HPV, nearly 15% have active asymptomatic infection
- The HPV vaccine is safe and effective and should be given to all children starting at age 9
- HPV associated oropharyngeal cancer has a good prognosis but can still be lethal
- HPV and other prognostic markers can be combined to tailor therapy
- HPV may explain some but not all outcome disparities in head and neck cancer and is the subject of ongoing research

Thanks to:

- UMGCC
  - Lisa Schumaker
  - Jia Yang
  - Sandy Liu
  - Ming Tan
  - Olga Goloubeva
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  - Rod Taylor
  - Bob Ord
  - Josh Lubeck
  - Mohan Suntha
  - Kathleen Settle
  - Arlene Davis
  - Dan Zandberg
- Dana Farber
  - Marshall Posner
  - Robert Haddad
- Johns Hopkins
  - Amber D'Souza
  - Carole Fakhry
- Sanofi aventis
  - Nick Sarlis
- Orokawa Foundation