

Consequences of the Tragic Underuse of the HPV Vaccine

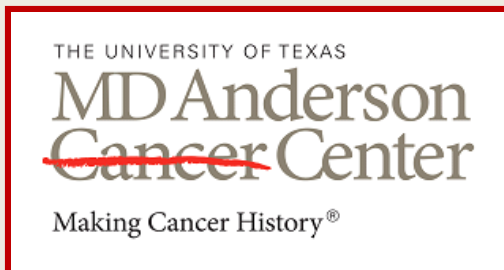
Lois M Ramondetta MD

Professor Gynecologic Oncology

Department of Gynecologic Oncology and Reproductive Medicine

Chief Gynecologic Oncology LBJ Hospital

UT MD Anderson Cancer Center & Harris Health System



Disclosures

- No conflicts of interest.
- Funded by the MD Anderson HPV Cancer Moon Shot.

The Burden of HPV Cancers

Objectives

1. Discuss range of HPV Associated Cancers
2. Review safety and effectiveness of HPV Vaccination
3. Talk about MD Anderson HPV Moonshot Efforts

My Service

- RD 46 (36)
- MH 33 (22)
- NW 45 (35)
- ML 36 (26)
- EGL 43(33)
- MG 42 (32)
- MH 61 (51)
- TC 48 (38)
- BB 31 (21)
- ML 52 (42)
- GB 61 (51)
- SJ 38 (28)
- LR 54 (44)
- CO 41 (31)

My Service

- RD 46 (36)
- MH 33 (22)
- NW 45 (35)
- ML 36 (26)
- EGL 43(33)
- MG 42 (32)
- MH 61 (51)
- TC 48 (38)
- BB 31 (21)
- ML 52 (42)
- GB 61 (51)
- SJ 38 (28)
- LR 54 (44)
- CO 41 (31)

HPV Infection & Disease: Understanding the Burden

- Almost ALL will be infected with at least 1 type HPV at some point
- Most will never know they've been infected
 - Can occur with any intimate sexual contact
 - Intercourse is not necessary for infection
- Estimated 79 million Americans currently infected
 - 14 million new infections/year in the US
 - HPV infection most common in teens - 20s



HPV Types Differ in their Disease Associations

~40 Types

Mucosal sites of infection

Cutaneous sites of infection

~ 80 Types

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

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

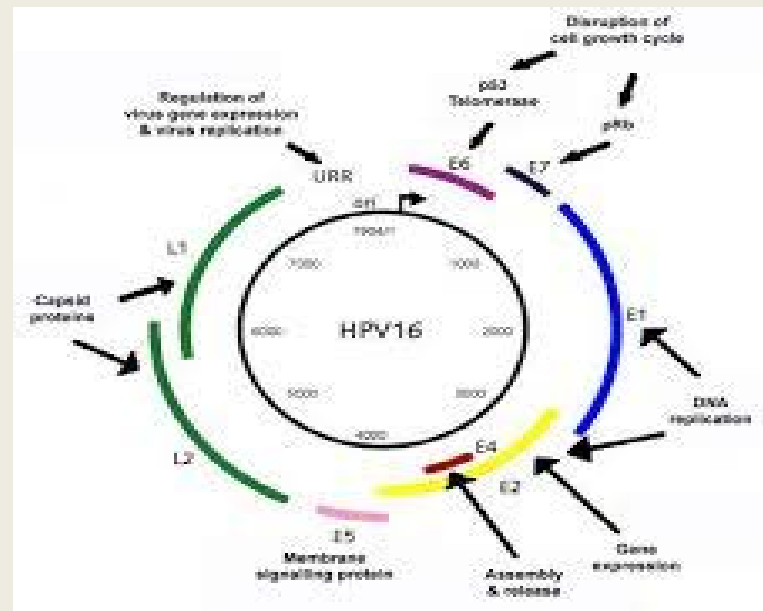
**Cervical Cancer
Anogenital Cancers
Oropharyngeal Cancer Cancer
Precursors
Low Grade Cervical Disease**

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

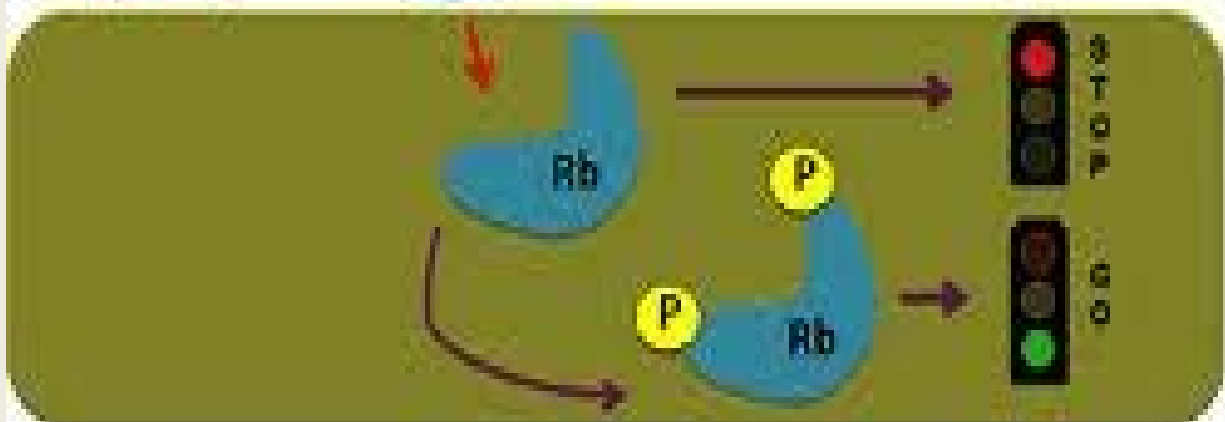
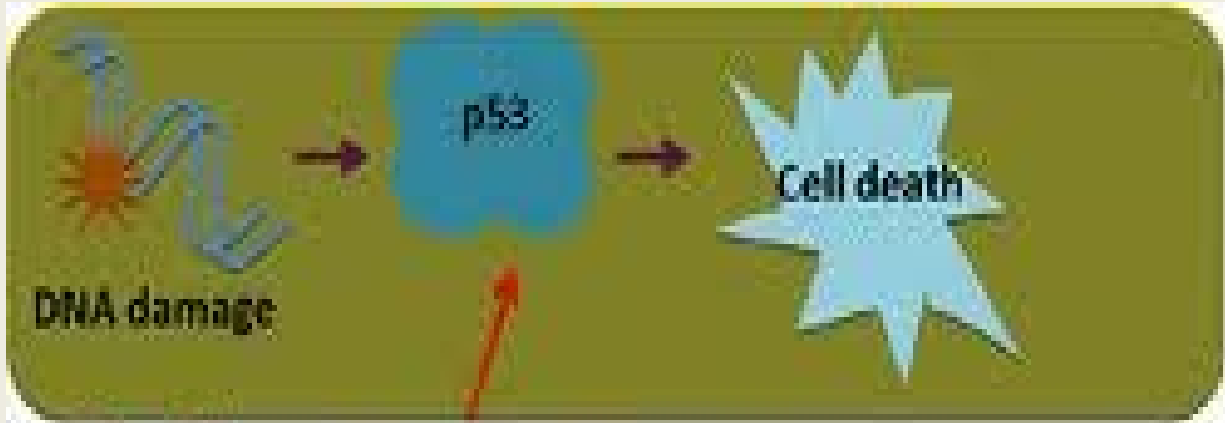
**"Common"
Hand and Foot
Warts**

HPV Types

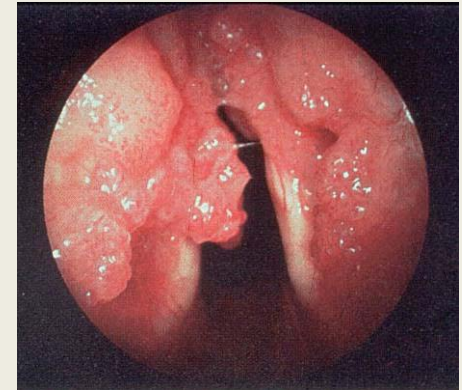
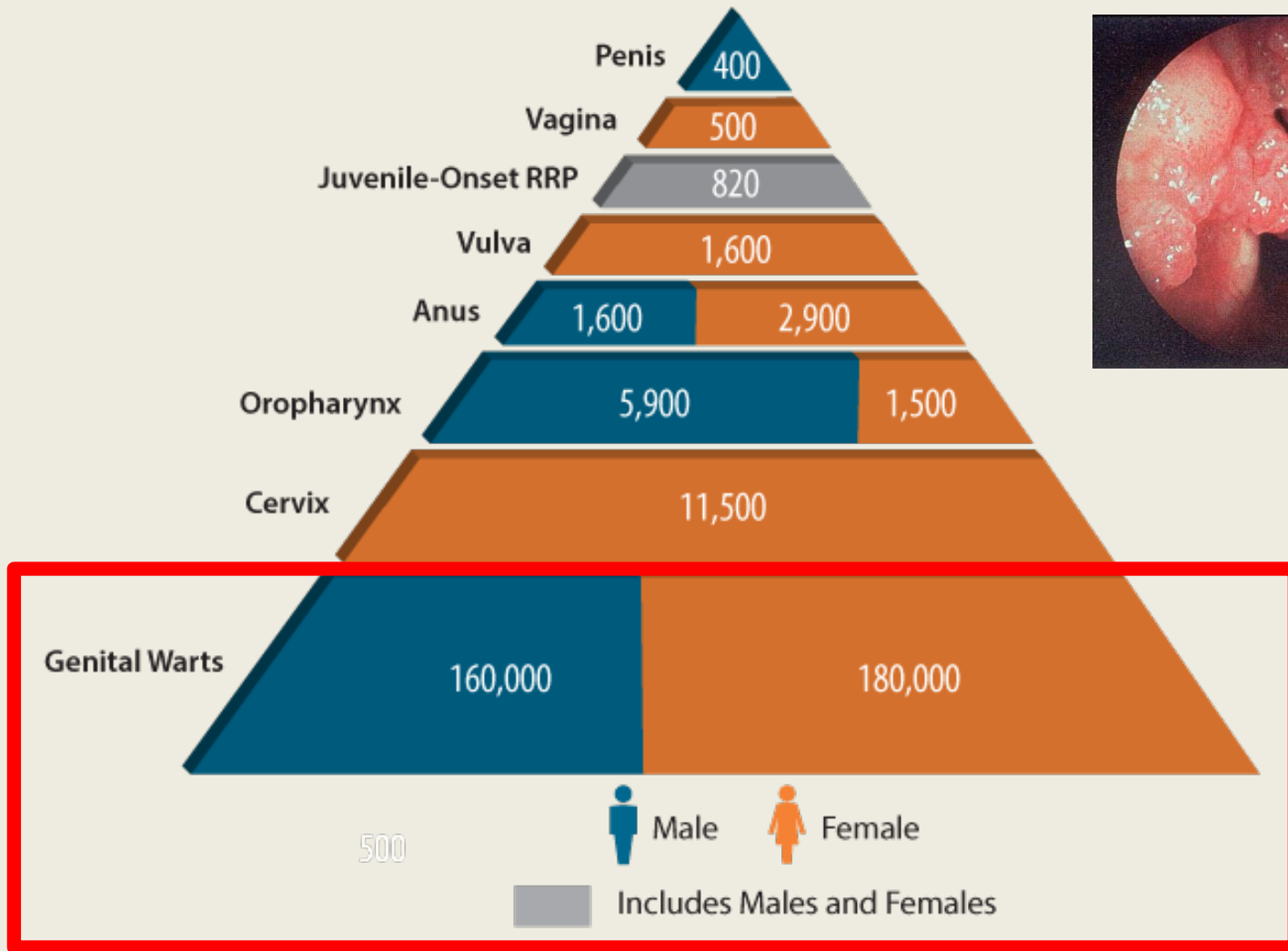
- HPV types 16 and 18 cause 70% of all cervical, anal, and genital cancers in women, and 70% of anal cancers in men.
- HPV types 6 and 11 cause 90% of all genital warts in men and women.
- Seventy percent of cancers of the oropharynx may be linked to HPV.



- Persistent infection and Integration in basal keratinocytes
- Viral genome (8 genes as circular double-stranded DNA) incorporated into host cell genome.
 - HPV genome disrupted at E2 gene so no more E2 protein made
 - E2 down-regulate two genes: E6 and E7.
 - Without functional E2, E6 and E7 expression is uncontrolled
 - E6 and E7 are oncogenes/oncoproteins.
 - E6 causes degradation of tumor suppressor protein 53.
 - E7 interferes with retinoblastoma protein and the host cell cycle.
 - E6 and E7 cause "immortalization" of these dysfunctional cells



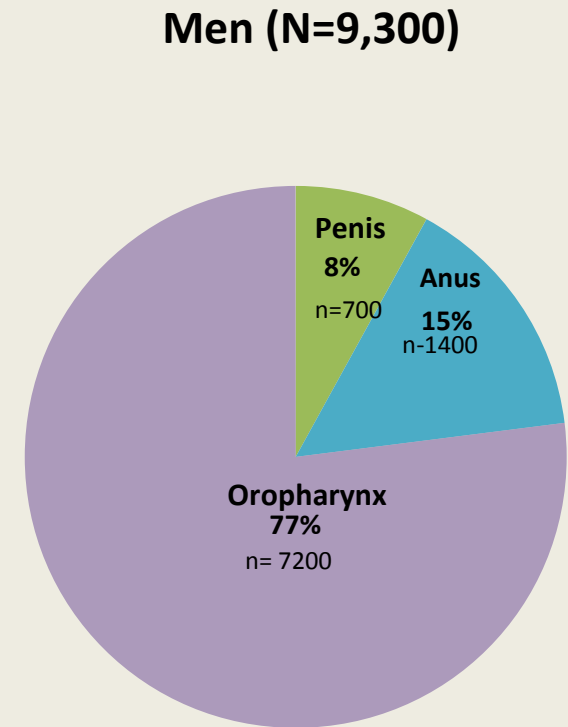
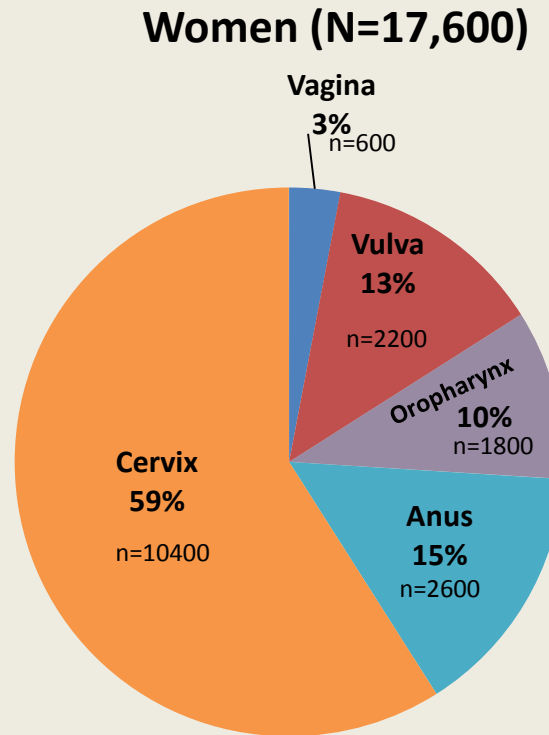
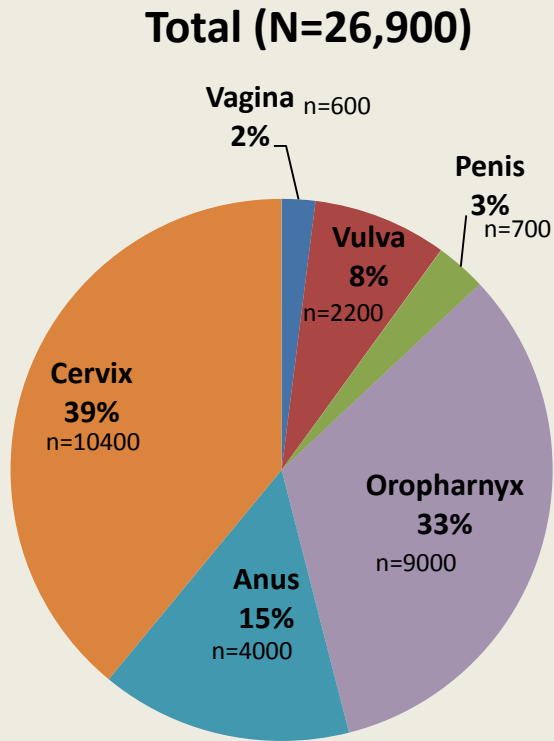
Numbers of Cancers and Genital Warts Attributed to HPV Infections, U.S.



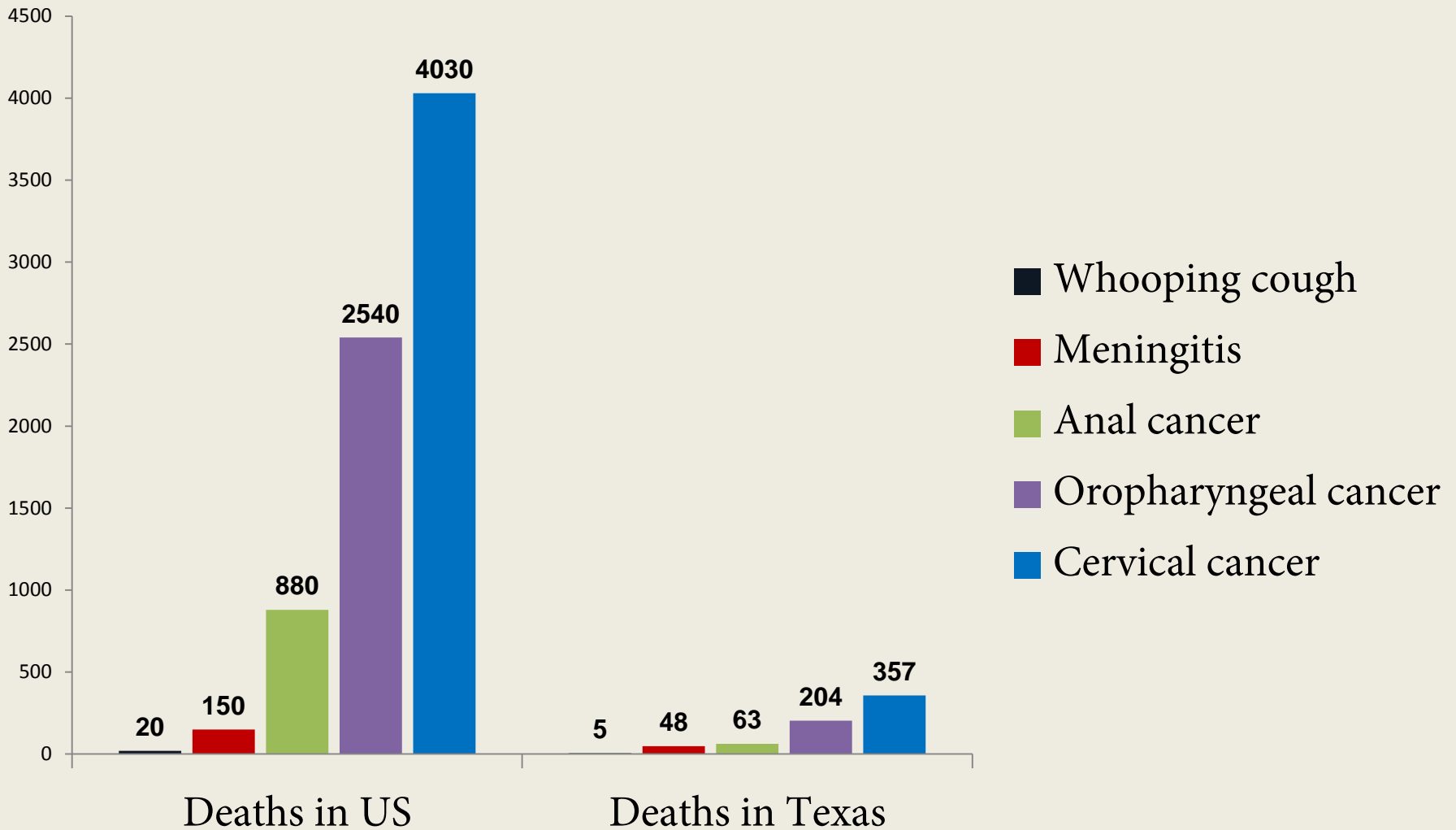
Cancers Caused by HPV, U.S.

Cancer site	Average number of cancers per year probably caused by HPV			Percentage Due to HPV
	Male	Female	Both Sexes	
Anus	1,400	2,600	4,000	91%
Cervix	0	10,400	10,400	91%
Oropharynx	7,200	1,800	9,000	72%
Penis	700	0	700	63%
Vagina	0	600	600	75%
Vulva	0	2,200	2,200	69%
TOTAL	9,300	17,600	26,900	

Average Number of New HPV-associated Cancers Overall, and by Sex, in the United States, 2006-2010



Annual Deaths From HPV-Related Cancers, 2012-2014



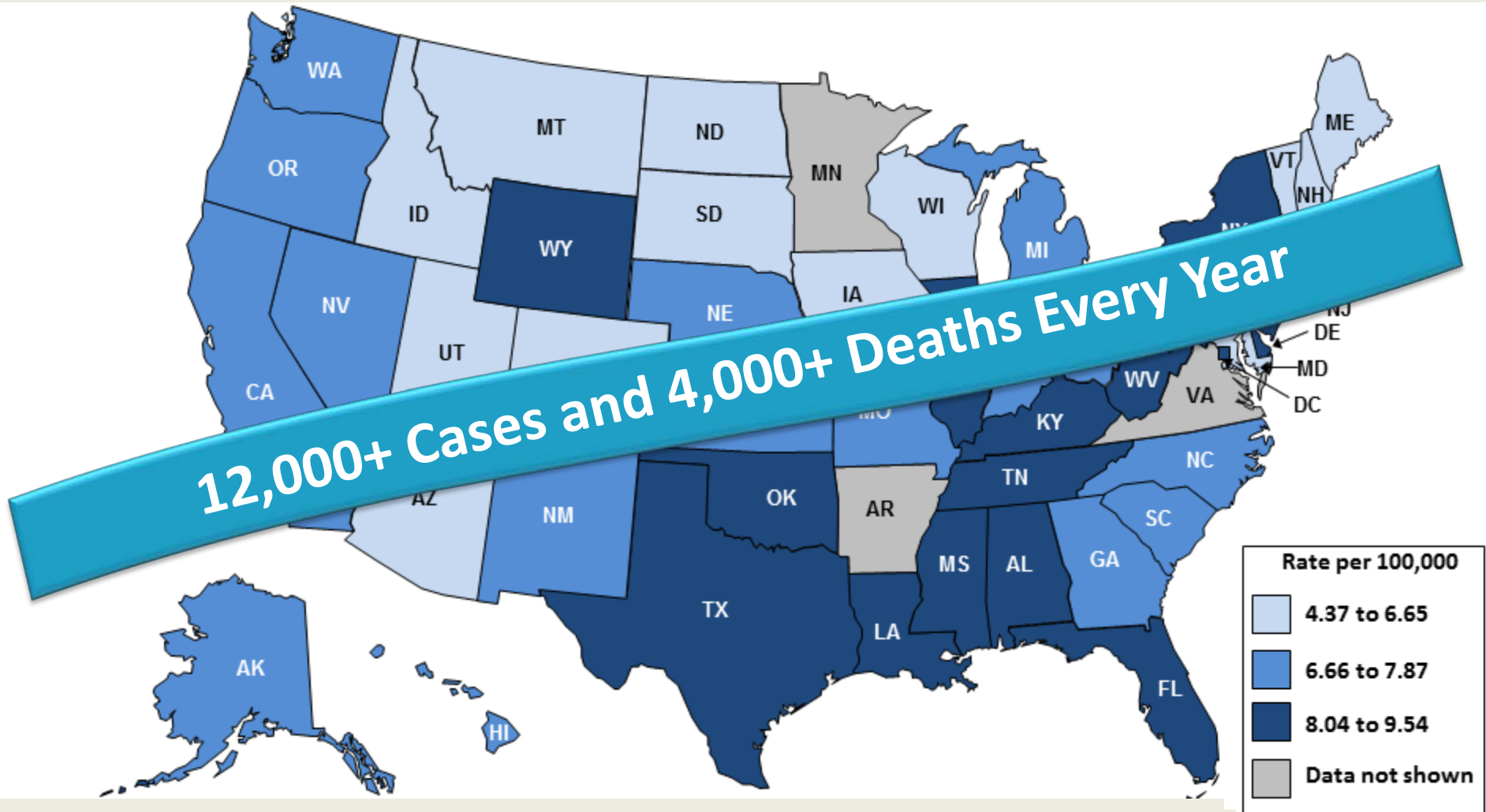
**Cervical Cancer has a defined avoidable etiology,
and if caught early is curable**

Despite these facts,

In 2014

12,360 new cases of cervical cancer in US

HPV-Associated Cervical Cancer Incidence Rates by State, United States, 2010-2012



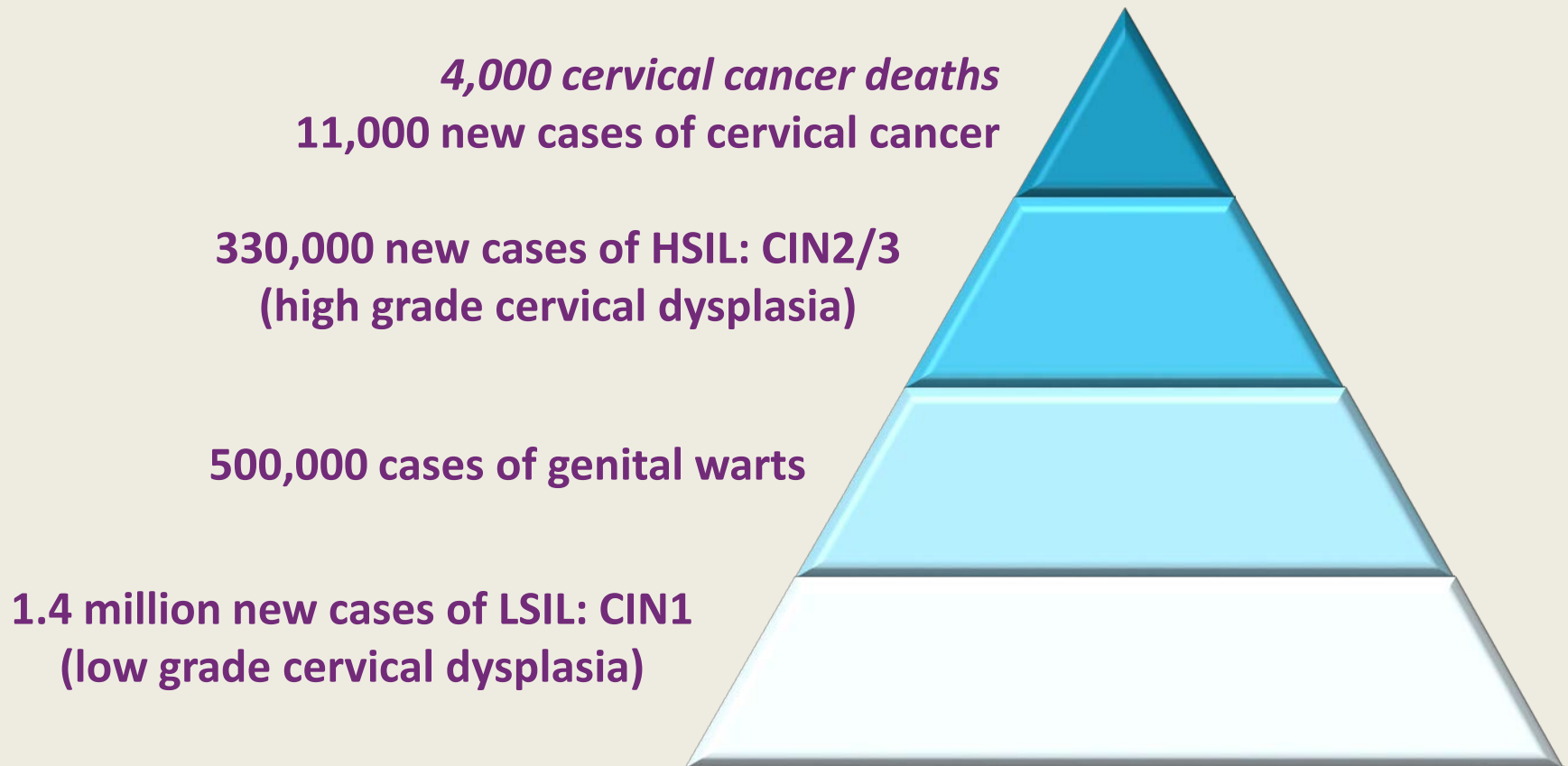
Correlation between HPV and cervical cancer is higher than that between smoking and lung cancer

Cervical Cancer

- Cervical cancer - most common HPV-associated cancer
 - 500,000 cases & 275,000 deaths world-wide in 2008
 - 12,000+ cases & 4,000+ deaths annually in the U.S.
- 37% cervical cancers occur between the ages of 20 - 44
 - 13% (or nearly 1 in 8) between 20 - 34
 - 24% (or nearly 1 in 4) between 35 - 44



Genital HPV disease in U.S. *Females*



2.25 million cases, costing \$7 billion

Oropharyngeal and Anal Cancer

Oropharynx is principal site of head & neck cancers

- HPV-related in 60-80% of cases
- HPV type 16 accounts for more than 90% of HPV positive cases
- In the US, 10,000-12,000 new cases yearly

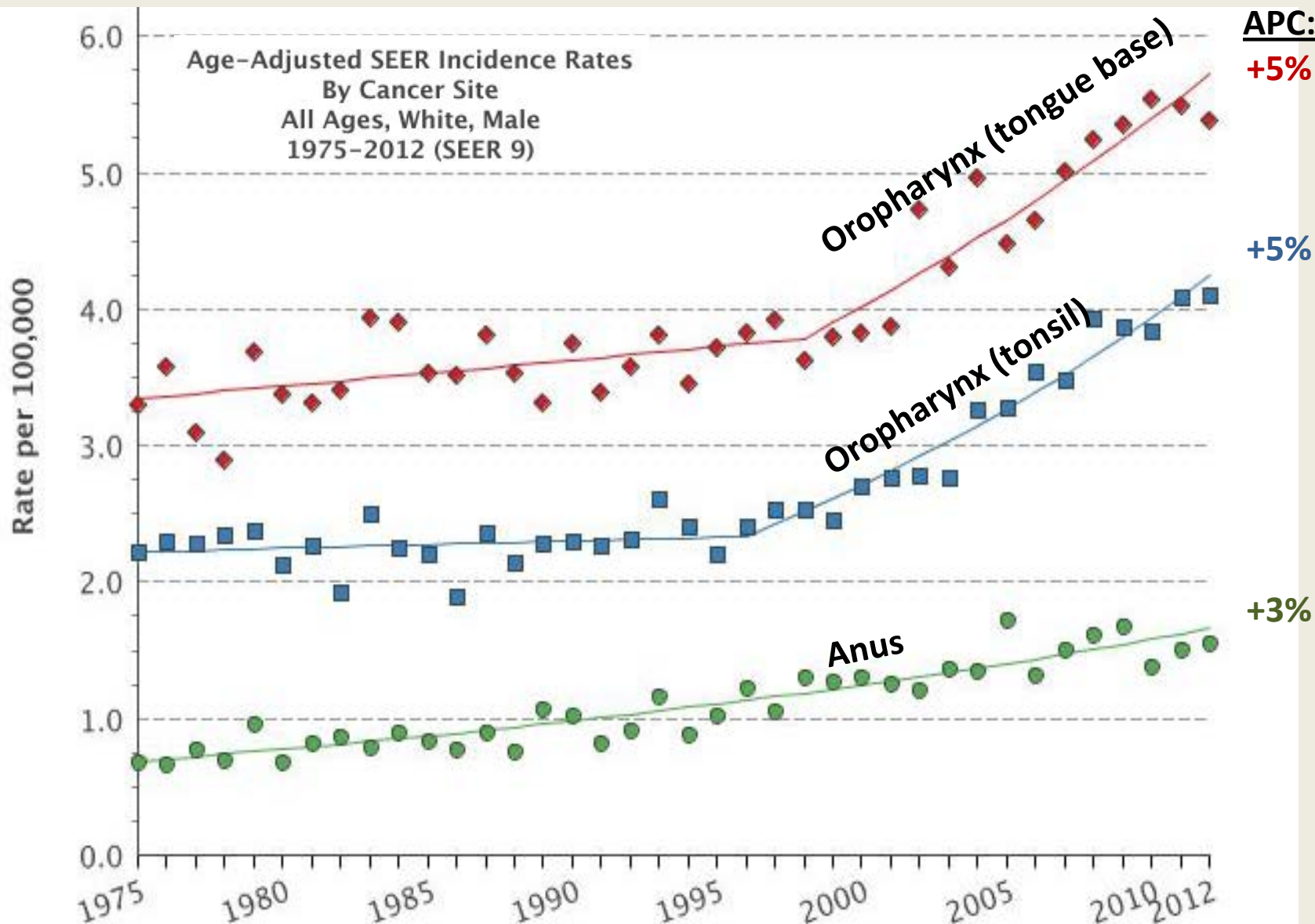


Anal Cancer

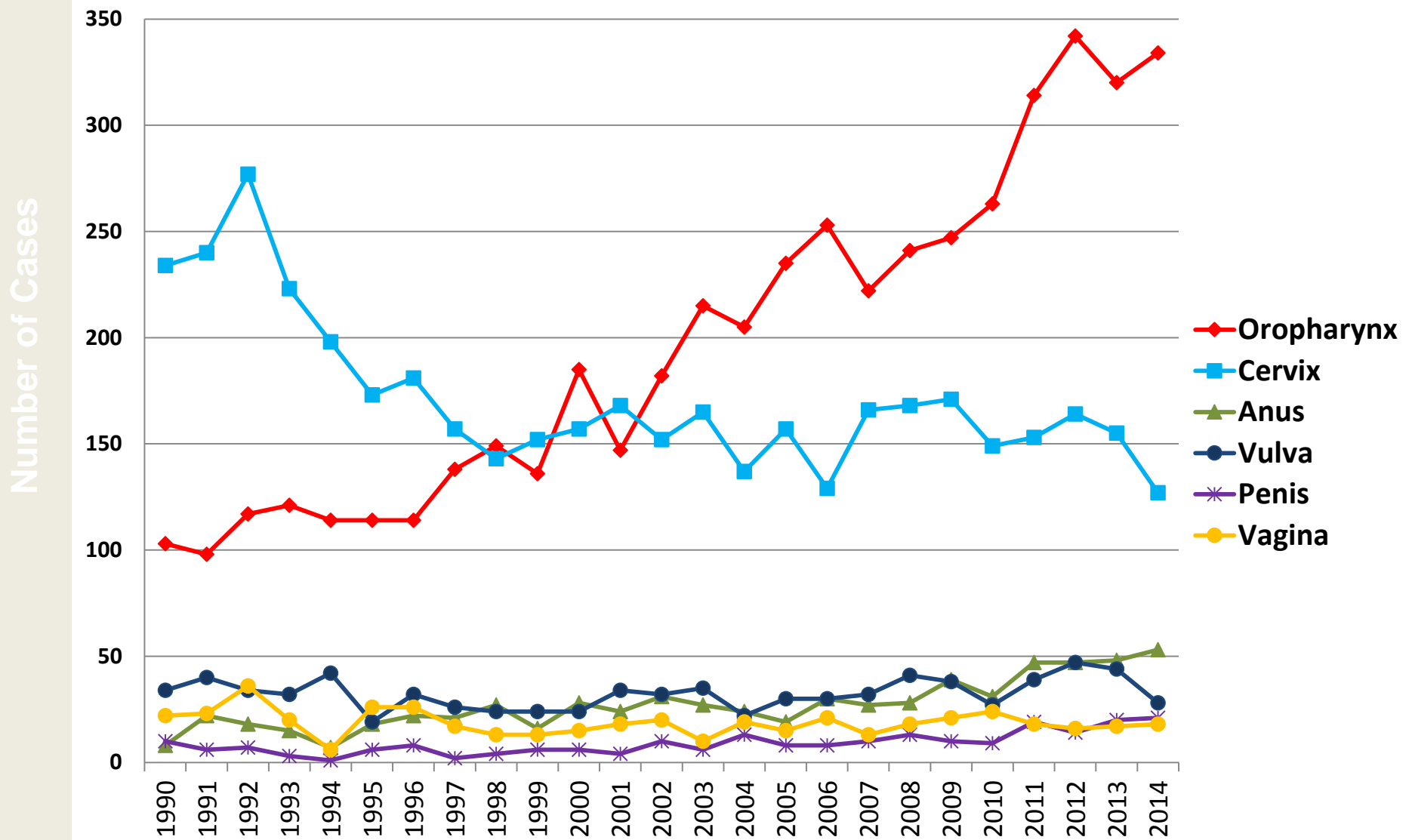
- In US, greater than 7,000 new cases yearly
 - More than 80% are HPV related (HPV16)
 - Anal cancer rates doubled from 1975 to 2009



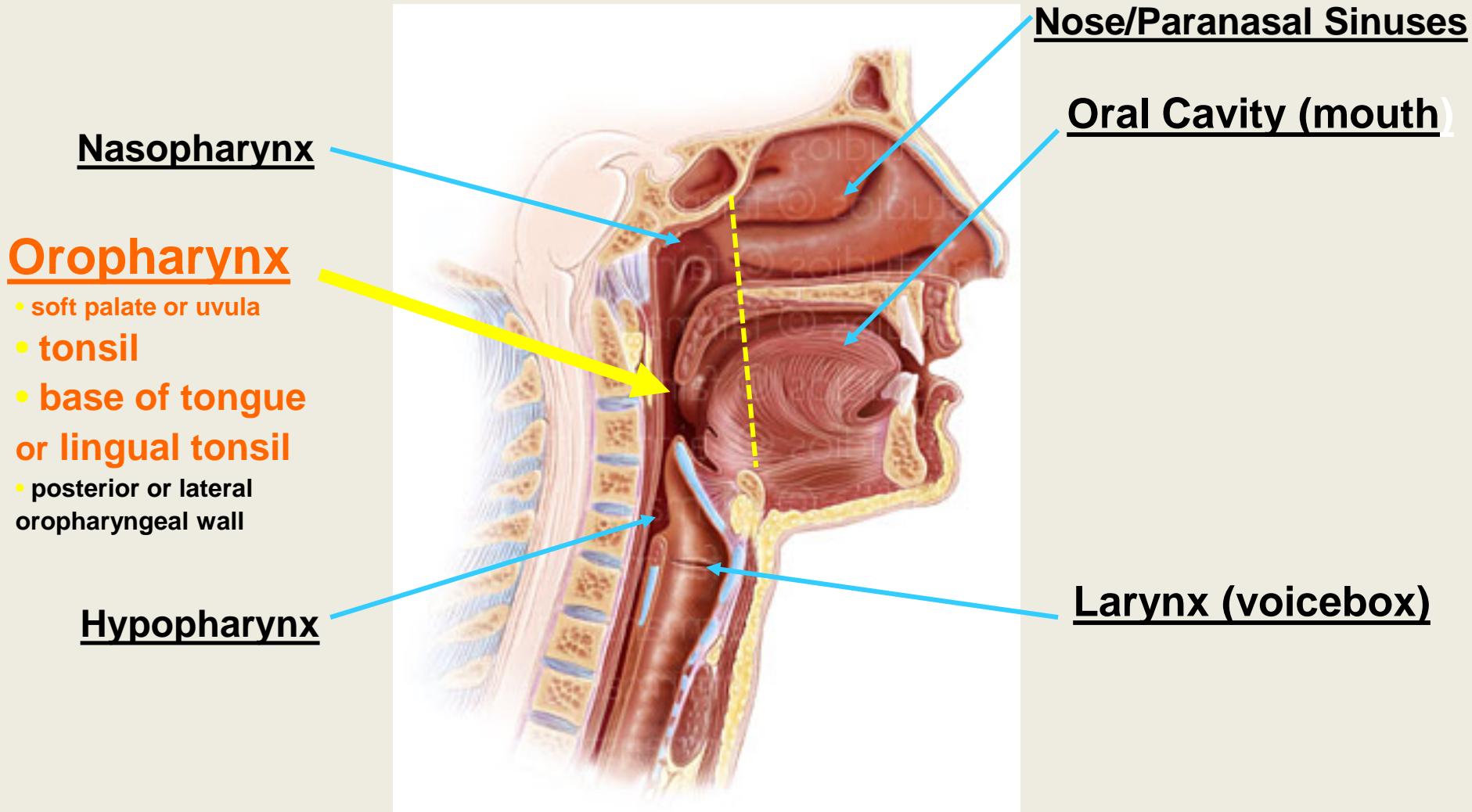
U.S. National Impending Crisis (HPV cancers in men)



Newly Diagnosed-Untreated Cases Presenting to MD Anderson Each Year



Head & Neck Cancer

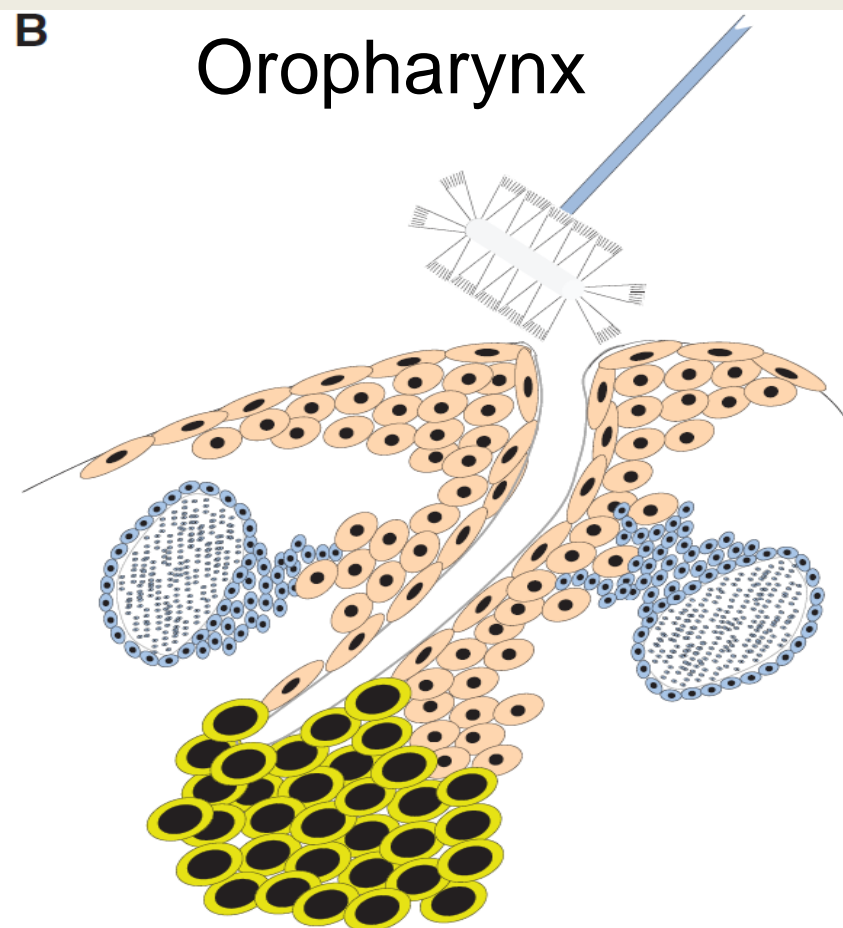
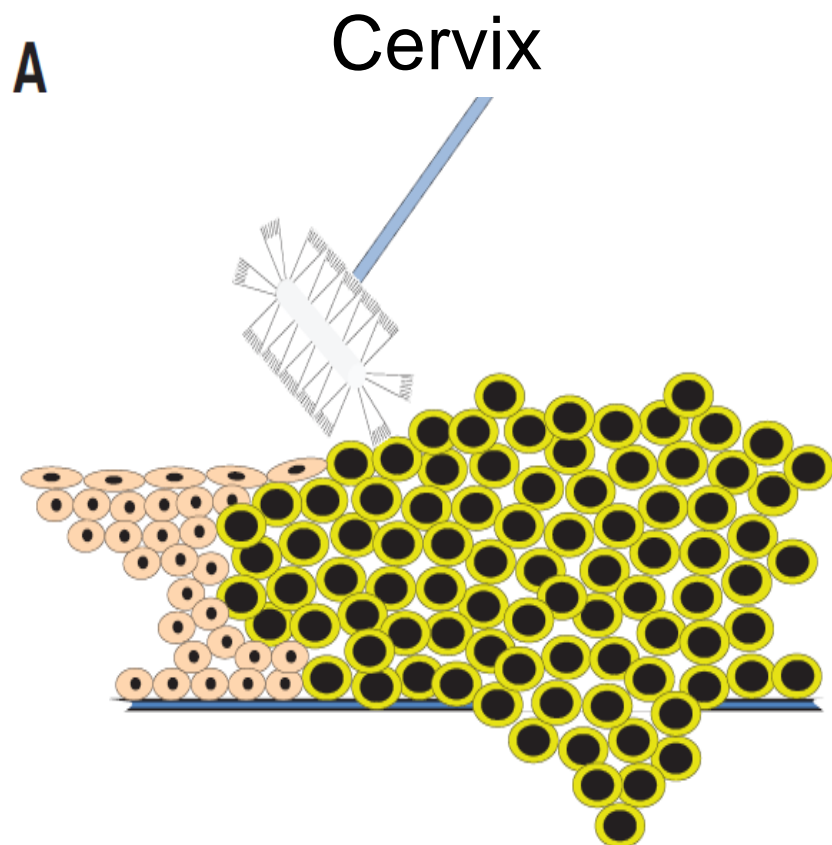


Perspective

Perspective on Fakhry et al., p. 1378

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

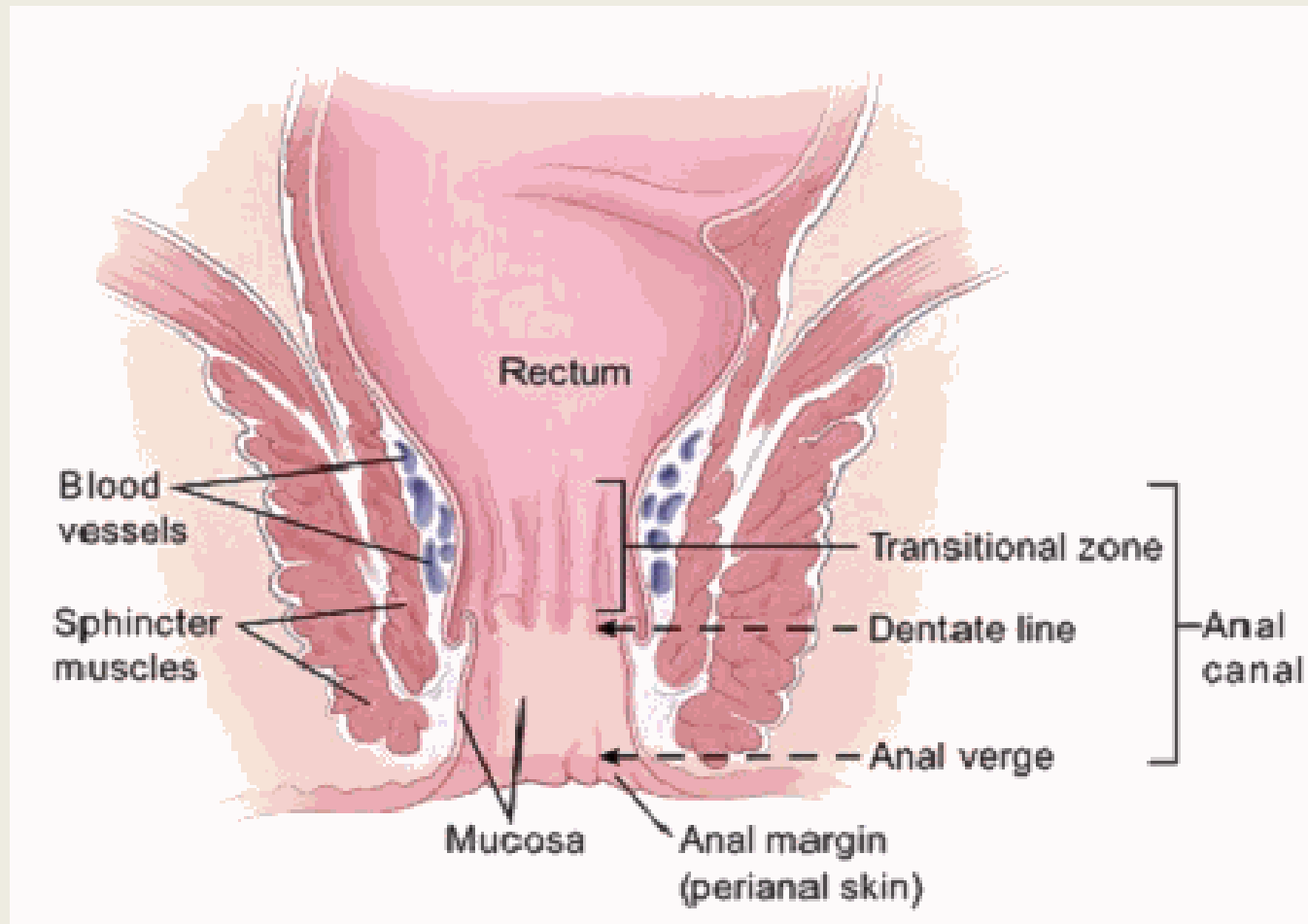
Mark W. Lingen



Oropharyngeal Cancer



Anal Cancer



Increased risk of anal cancer

- Women with a history of high-grade cervical, vulvar, vaginal dysplasia or cancer
- Individuals with a history of anal warts
- HIV-positive men and women
- Men who have sex with men
- Iatrogenic immunosuppression (eg, solid organ transplant recipients, long term oral corticosteroids)

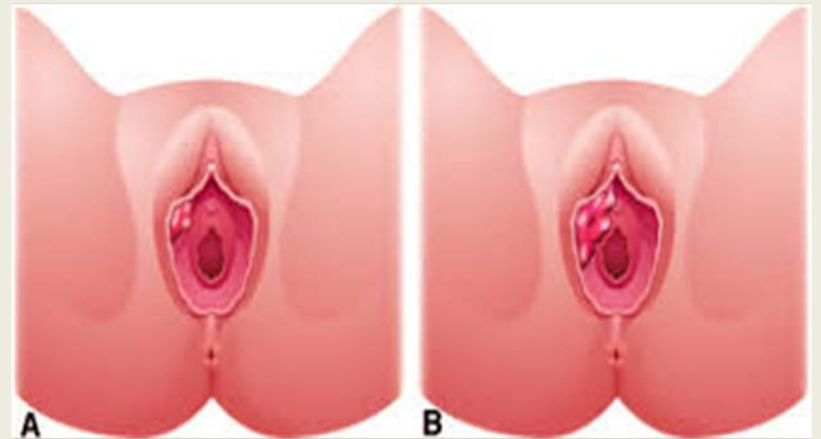
Anal Dysplasia and Anal Cancer



Dysplasia (*anal intraepithelial neoplasia (AIN)*)

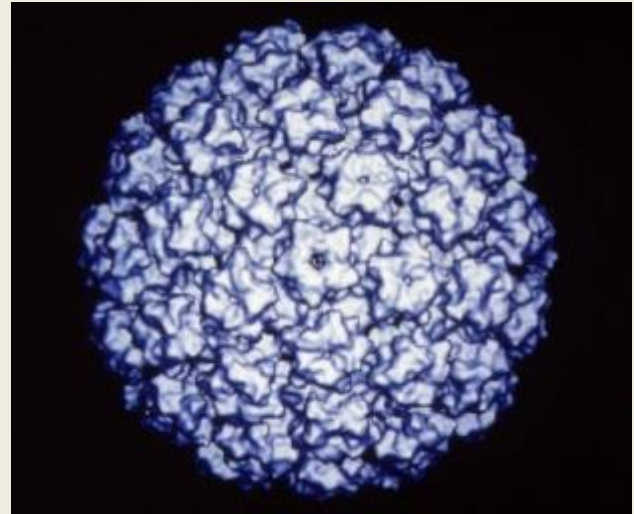
- Low-grade AIN (AIN1 or low-grade anal SIL):
 - often goes away without treatment-low chance of turning into cancer
- High-grade AIN (AIN2 or AIN3, or high-grade anal SIL):
 - less likely to go away without treatment and could eventually become cancer, so it needs to be watched closely or treated
- Carcinoma in situ
 - Most advanced pre cancer
- Anal cancer
 - Most anal cancers in the United States are squamous cell carcinomas

Penile Cancer, Vulvar/Vaginal Cancer



HPV Prophylactic Vaccines

- Recombinant L1 capsid proteins that form “virus-like” particles (VLP)
- 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	GlaxoSmithKline	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

* only contained in pre-filled syringes, not single-dose vials

Boys Need the HPV Vaccine Too

Girls & Boys can start HPV vaccination at age 9

Preteens should finish HPV vaccine series by age 13



Plus girls 13-26 years old who haven't started or finished HPV vaccine series



Plus boys 13-21 years old who haven't started or finished HPV vaccine series

Vaccination Recommendations

Clinicians should recommend HPV vaccine on the **same day and in the same way** as the other vaccines for preteens.

Frequent Questions

- **Two Doses or Three?**
 - ACIP will formally review data on 2-dose schedules when this summer
 - 3 for now is recommended!
- **Already Exposed?**
 - Do not withhold!
- **Restart the series?**
 - Never

The HPV Vaccine is Safe

Extensive safety testing of HPV Vaccine

- No serious side effects
- As safe as meningococcal and Tdap vaccine
- 90 Million Doses in the US
- 200 Million Doses World Wide

Most HPV vaccine side effects are mild

- Most common side effects are pain and redness
- Sitting during and for 15 minutes after shot reduces fainting that can cause injury

The HPV Vaccine Works and it Lasts

HPV Vaccine WORKS extremely well!

- HPV vaccine provides close to 100% protection against HPV infections and related precancers
- HPV vaccination decreases HPV infection in teens

HPV Vaccine LASTS

- Excellent protection lasts at least 10 years
- No sign that protection will decrease
- Made like the Hepatitis B vaccine which gives lifelong protection

Medical Ethics

- If you are not recommending the vaccine, you are not doing your job
 - Substandard care
- It's the equivalent of having patients over 50 and not recommending a colon screening or mammogram, and then seeing them diagnosed with colon or breast cancer

Healthy People 2020 goal is 80%

Worldwide HPV Vaccination Rates^{10,13,14}



Rwanda
99%



United Kingdom
86%



Belgium
82%



Portugal
87%



Denmark
82%



Australia
73%



United States
39.7%

Healthy People 2020 goal is 80%

United States

13- to 17-year old girls in

2014

1 dose = 60%

3 dose = 40%

Texas

50%

34%

Houston

69%

44%

13- to 17-year old boys in

2014

1 dose = 42%

3 dose = 22%

Texas

37%

20%

Houston

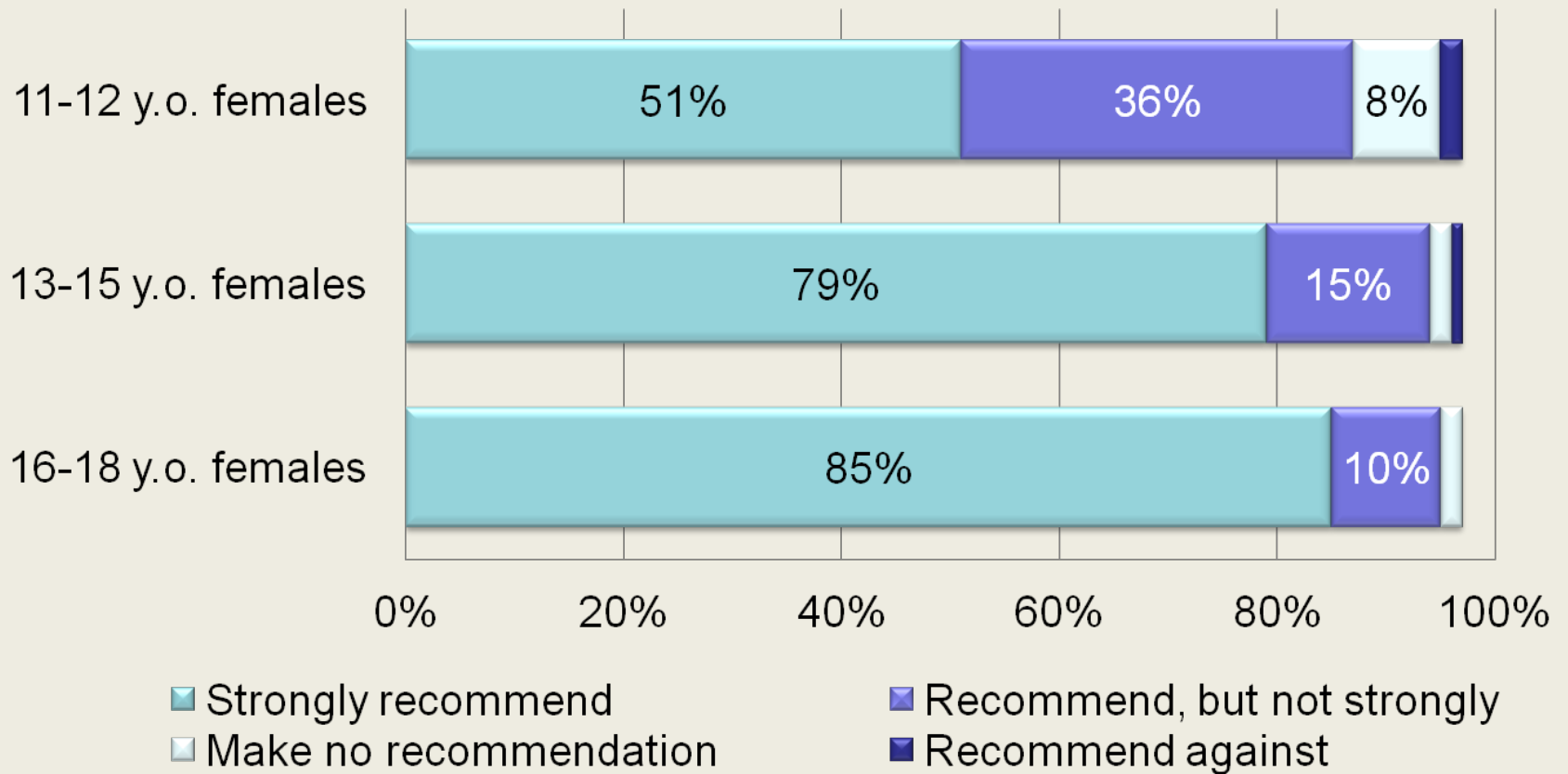
54%

27%

Why are rates so low?

- Providers:
 - Don't recommend (many reasons)
 - Lack knowledge about HPV or vaccine
 - Recommend too late
 - Miss opportunities (few visits for adolescents)
 - Ineffective communication skills
- ***A clear recommendation from YOU-the provider- is the main reason parents decide to vaccinate***

Strength of HPV Vaccine Recommendation



UT MD Anderson Cancer Center HPV Cancer Moon Shot

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)

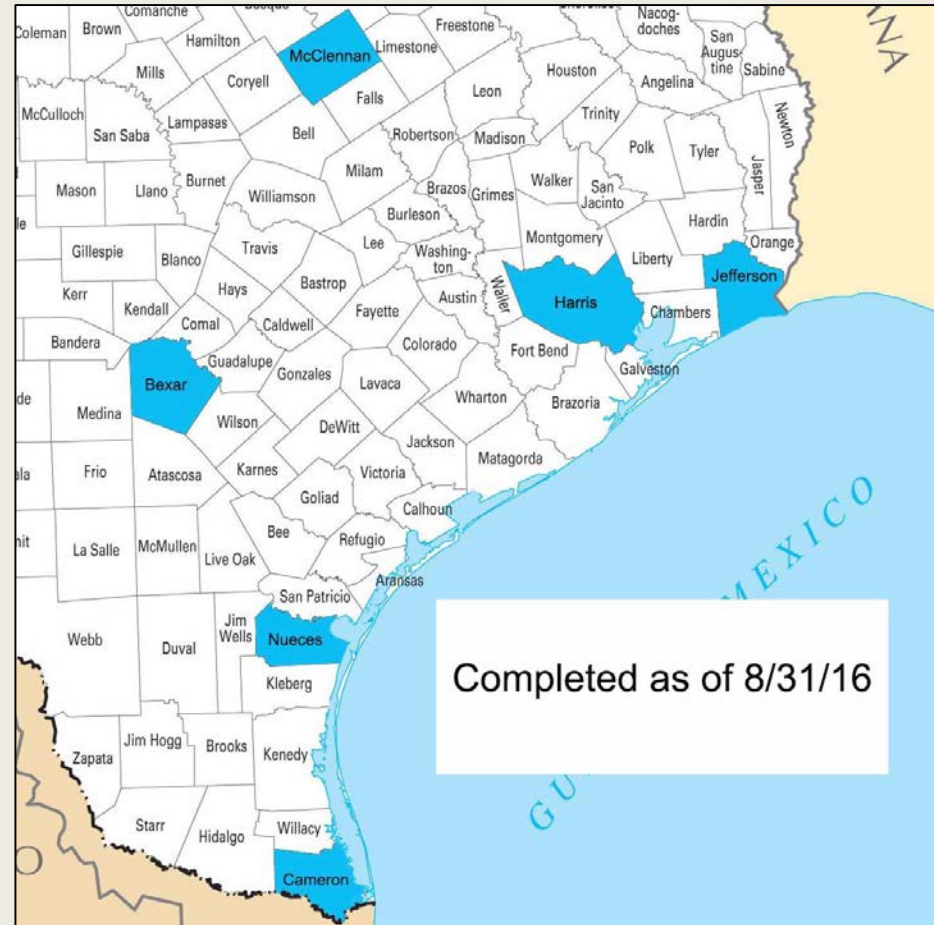
Platforms/Engines:
Center for Co-Clinical Trials
Immunotherapy

Flagship 1 Goals

- **Increase HPV vaccination rates in Texas to 80 percent by 2020;**
- **Improve access to cervical cancer screening in underserved populations both in the United States and globally;**
- **Develop new screening paradigms for non-cervical HPV-related malignancies**

Progress

- Information Transfer Demonstration Project
- Geographic Reach
- Professional Lectures
- Public talks
- UT Medical School PBLs



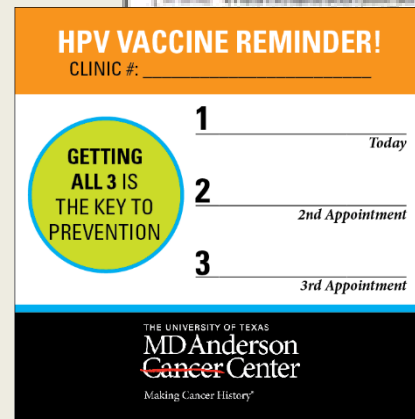
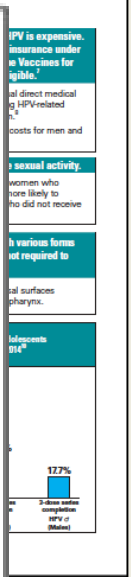
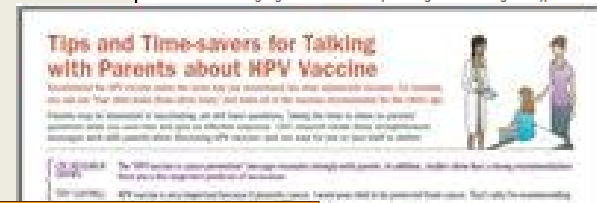
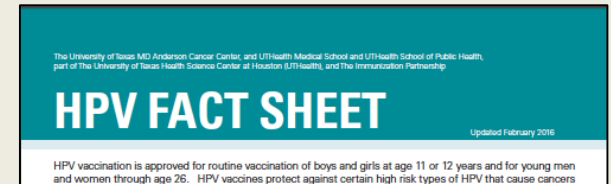
Key Materials

Patients/Parents:

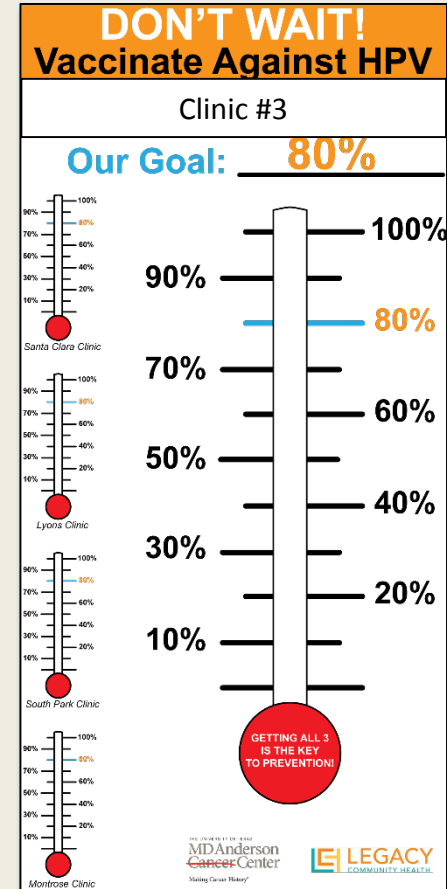
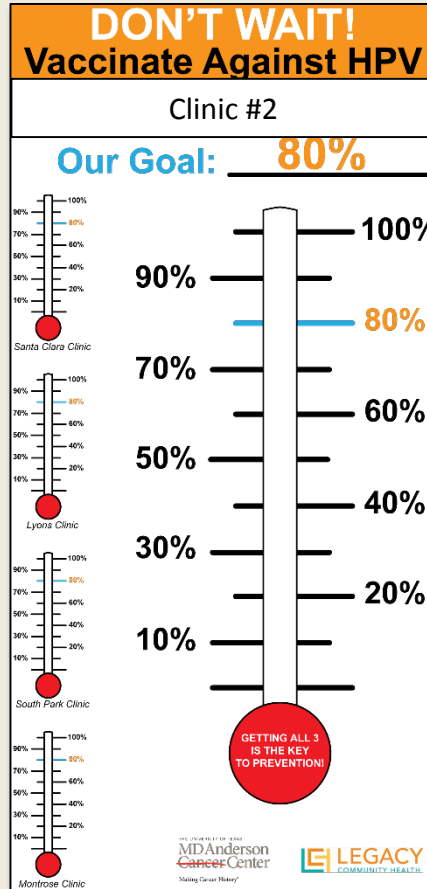
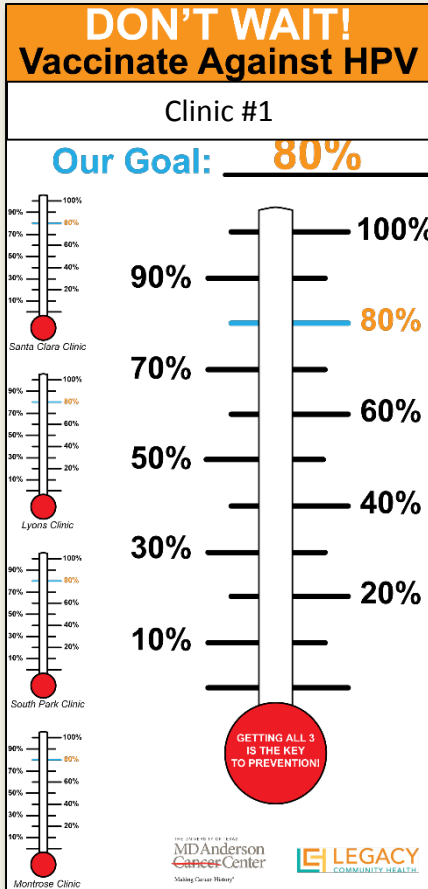
- Magnets (write-on)
- Posters in clinic (CDC and TMA)
- Patient information

Providers:

- Tips and Time Savers
- HPV Fact Sheet
- Clinic/System baseline rates



Internal Competition



Progress

- Policy

- Senate Bill 200 Passed – Requires Texas HPV Strategic Plan
- Economic Model Development
- Held NCI Designated Cancer Center meeting resulting in HPV Consensus Statement
- Completed Environmental Scan of Texas-Facilitators and Barriers to vaccination
- MD Anderson's HPV Vaccination Clinic (starts June 11, 2016)
- Harris Health to offering HPV vaccine through Adult Safety Net

- Infrastructure Support and Development

- City, State, National coalition building

- Environmental

- Mass-reach social marketing campaign for back-to-school (summer) expected Summer 2016
- Survivor mobilization

NCI-designated Cancer Centers Urge HPV Vaccination for the Prevention of Cancer

Approximately 79 million people in the United States are currently infected with a human papillomavirus (HPV) according to the Centers for Disease Control and Prevention (CDC), and 14 million new infections occur each year. Several types of high-risk HPV are responsible for the vast majority of cervical, anal, oropharyngeal (middle throat) and other genital cancers. The CDC also reports that each year in the U.S., 27,000 men and women are diagnosed with an HPV-related cancer, which amounts to a new case every 20 minutes. Even though many of these HPV-related cancers are preventable with a safe and effective vaccine, HPV vaccination rates across the U.S. are low. Together, the National Cancer Institute (NCI)-designated Cancer Centers, recognize these low rates of HPV vaccination as a serious public health threat. HPV vaccination represents a rare opportunity to prevent many cases of cancer that is tragically underused. As national leaders in cancer research and clinical care, we are compelled to jointly issue this call to action.

According to a 2015 CDC report, only 40 percent of girls and 21 percent of boys in the U.S. are receiving the recommended three doses of the HPV vaccine. This falls far short of the goal of 80 percent by the end of this decade, set forth by the U.S. Department of Health and Human Services' Healthy People 2020 mission. Furthermore, U.S. rates are significantly lower than those of countries such as Australia (75 percent), the United Kingdom (84-92 percent) and Rwanda (93 percent), which have shown that high vaccination rates are currently achievable.

The HPV vaccines, like all vaccines used in the U.S., passed extensive safety testing before and after being approved by the U.S. Food and Drug Administration (FDA). The vaccines have a safety profile similar to that of other vaccines approved for adolescents in the U.S. Internationally, the safety of HPV vaccines has been tested and approved by the World Health Organization's Global Advisory Committee on Vaccine Safety.

CDC recommends that boys and girls receive three doses of HPV vaccine at ages 11 or 12 years. The HPV vaccine series can be started in preteens as early as age 9 and should be completed before the 13th birthday. The HPV vaccine is more effective the earlier it is given; however, it is also recommended for young women until age 26 and young men until age 21.

The low vaccination rates are alarming given our current ability to safely and effectively save lives by preventing HPV infection and its associated cancers. Therefore, the 69 NCI-designated Cancer Centers urge parents and health care providers to protect the health of our children through a number of actions:

- We encourage all parents and guardians to have their sons and daughters complete the 3-dose HPV vaccine series before the 13th birthday, and complete the series as soon as possible in children aged 13 to 17. Parents and guardians should talk to their health care provider to learn more about HPV vaccines and their benefits.
- We encourage young men (up to age 21) and young women (up to age 26), who were not vaccinated as preteens or teens, to complete the 3-dose HPV vaccine series to protect themselves against HPV.
- We encourage all health care providers to be advocates for cancer prevention by making strong recommendations for childhood HPV vaccination. We ask providers to join forces to educate parents/guardians and colleagues about the importance and benefits of HPV vaccination.

HPV vaccination is our best defense in stopping HPV infection in our youth and preventing HPV-related cancers in our communities. The HPV vaccine is CANCER PREVENTION. More information is available from the [CDC](http://www.cdc.gov).



Present Activities & Future Plans

- Provider Education - Information Transfer Demonstration Project
 - Expansion across the state of Texas
 - Expansion nationwide via a train-the-trainer program with Cancer Network members
 - Texas HPV residency challenge
- Environmental Change
 - Mass-reach social marketing campaign
 - MD Anderson employee education campaign
 - MD Anderson patient education campaign
 - Survivor mobilization

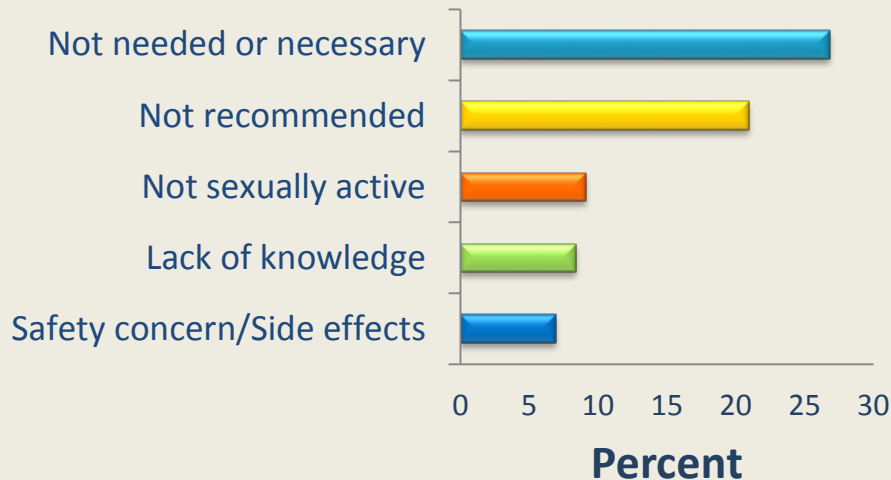
Present Activities & Future Plans

- Policy Change
 - MD Anderson's HPV vaccination clinic
 - Continue economic model development
- Infrastructure Support
 - Texas HPV Strategic Plan (Senate Bill 200)
 - Texas HPV Network growth
 - Statewide HPV meeting hosted by MD Anderson
 - Continue work with NCI cancer centers

MD Anderson employee vaccination rates (completed 3-dose series)

Women

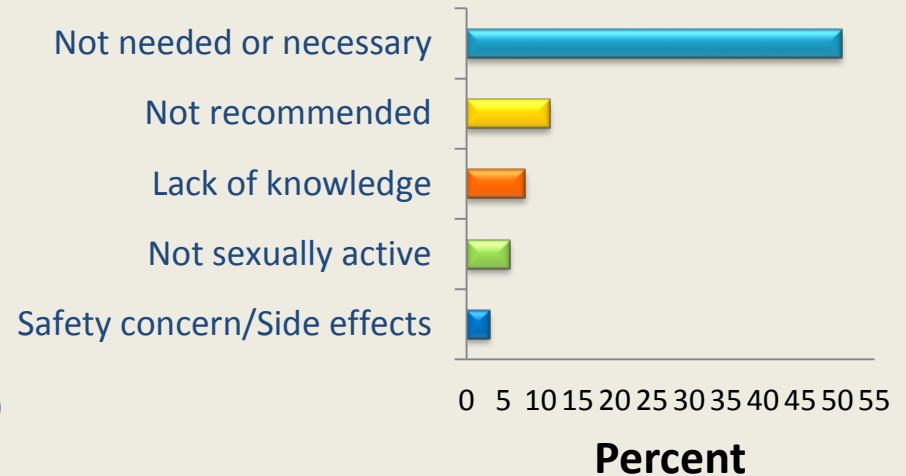
- ▶ 33% of responding eligible women vaccinated
- ▶ Health care providers more likely to be vaccinated: 40% vs 30% ($p < .001$)



Health care providers less likely to state “didn’t know it was needed” and “safety concerns”

Men

- ▶ 13% of responding eligible men vaccinated
- ▶ No difference between providers and non-providers: 14% vs 13% ($p = .632$)

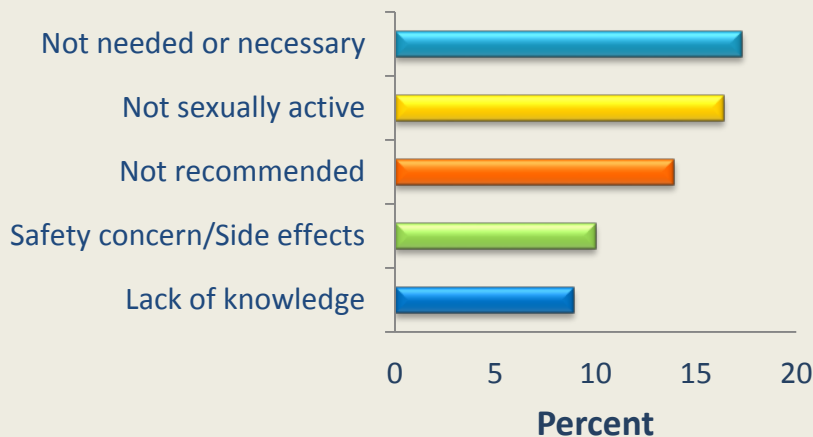


Men: No difference between health care providers and non-providers

Vaccination rates for children of MD Anderson employees (completed 3-dose series)

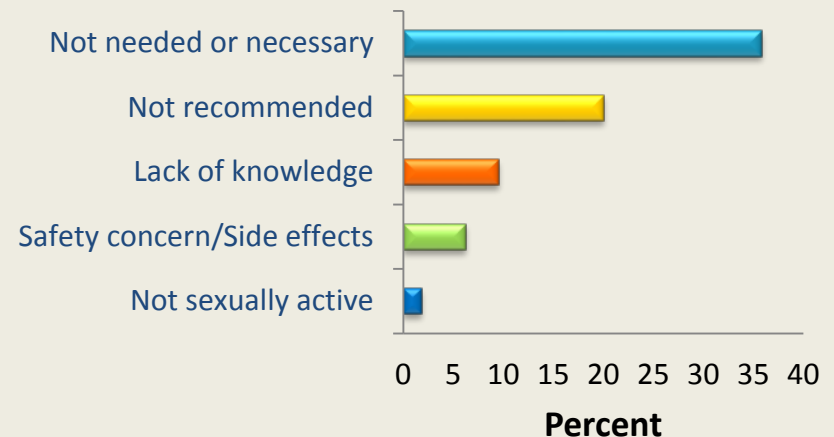
Girls

- 44% of girls vaccinated
 - Compared with: U.S., 40%; Houston, 44%
- Daughters of health care providers more likely: 48% vs 42% (p=.004)



Boys

- 24% of girls vaccinated
 - Compared with: U.S., 18%; Houston, 27%
- Sons of health care providers more likely : 29% vs 22% (p<.001)



- Majority of employees plan to have their young children vaccinated (sons, 79% and daughters, 82%)
 - Health care providers more likely to plan on vaccinating when child is old enough

Acknowledgments

Dr. Lewis Foxhall – Office of Health Policy

Dr. Ernest Hawk – Cancer Prevention and Population Sciences

Mark Moreno – Government Relations

Wesley Duncan – Government Relations

Erich Sturgis- Head and Neck Surgery

The HPV Vaccine Team (Office of Health Policy)

- Rosalind Bello
- Lori Stevens
- Melissa Mims
- Mehwish Javaid
- Dana Ashrawi
- Rachel Harris
- Carolyn Bernard
- Zeena Shelal
- Rachel Landgren

Leadership

- Dr. Ronald DePinho



Questions

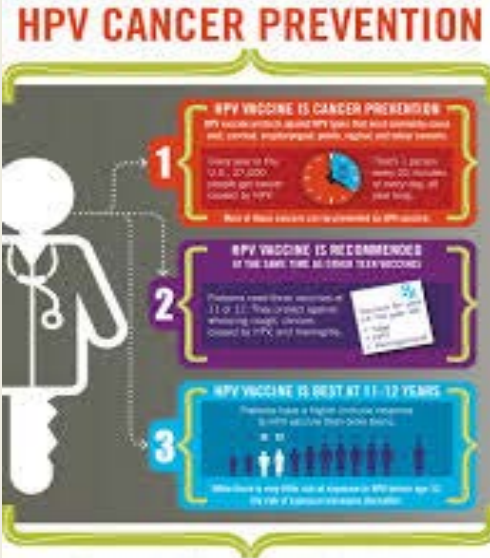
Lois Ramondetta, MD

Professor, Department of Gynecologic Oncology and
Reproductive Medicine

The University of Texas MD Anderson Cancer Center

Chief, Division of Gynecologic Oncology
Lyndon Baines Johnson General Hospital
Harris Health System

lramonde@mdanderson.org



HPV CANCER PREVENTION

1 HPV VACCINE IS CANCER PREVENTION
HPV vaccine prevents almost all HPV types that cause cervical cancer and certain anal, penile, vaginal, and throat cancers.
Only one in five (19.4%) of 20,000 women get cancer caused by HPV.
That's 3 percent every 100 women of every age, all year long.
Most of those cancers can be prevented by HPV vaccine.

2 HPV VACCINE IS RECOMMENDED AT THE SAME TIME AS OTHER TEEN VACCINES
Preteens need other vaccines at 11 or 12. They protect against whooping cough, tetanus, diphtheria, and polio.
HPV vaccine is recommended at the same time.

3 HPV VACCINE IS BEST AT 11-12 YEARS
Preteens have a higher immune response to HPV vaccine than older teens.
HPV vaccine is most effective when given to preteens ages 11-12.
By age 17, immunity decreases.

Parents and healthcare professionals are the key to protecting adolescents from HPV cancers.

VACCINATE YOUR 11-12 YEAR OLDS.

www.cdc.gov/vaccines/teens

YOU CAN DO THIS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

HPV EXPOSURE IS PART OF BEING HUMAN

**PROTECT YOURSELF, YOUR CHILDREN,
AND YOUR PATIENTS!**





HPV vaccine is cancer prevention.

Talk to the doctor
about vaccinating
your 11–12 year old
sons and daughters
against HPV.

#UCanStopHPV

Evidence-Based HPV Disease Prevention

HPV VACCINE

THE UNIVERSITY OF TEXAS
MDAnderson
~~Cancer~~ Center
Making Cancer History®