



# **HPV Vaccine: Hesitancy and Recommendations**

23<sup>rd</sup> Annual Family Medicine Fall Update-2019

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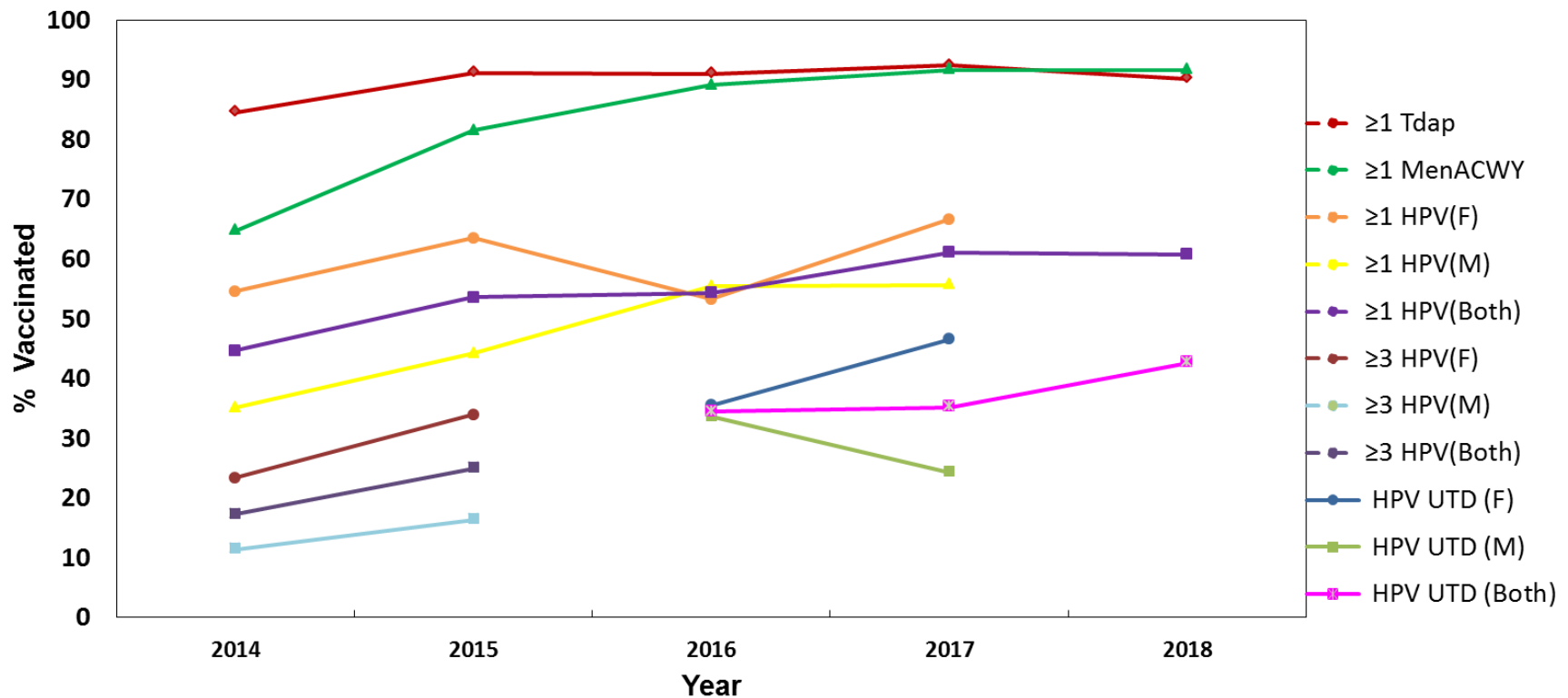
Medical Director, Immunizations

# Disclosures

- Dr. Dillaha has no financial or other conflicts of interest to disclose.

# Adolescent Vaccination for Selected Vaccines Arkansas, 2014-18

Estimated Vaccination Coverage Among Adolescents Aged 13-17  
Years, NIS-Teen, Arkansas



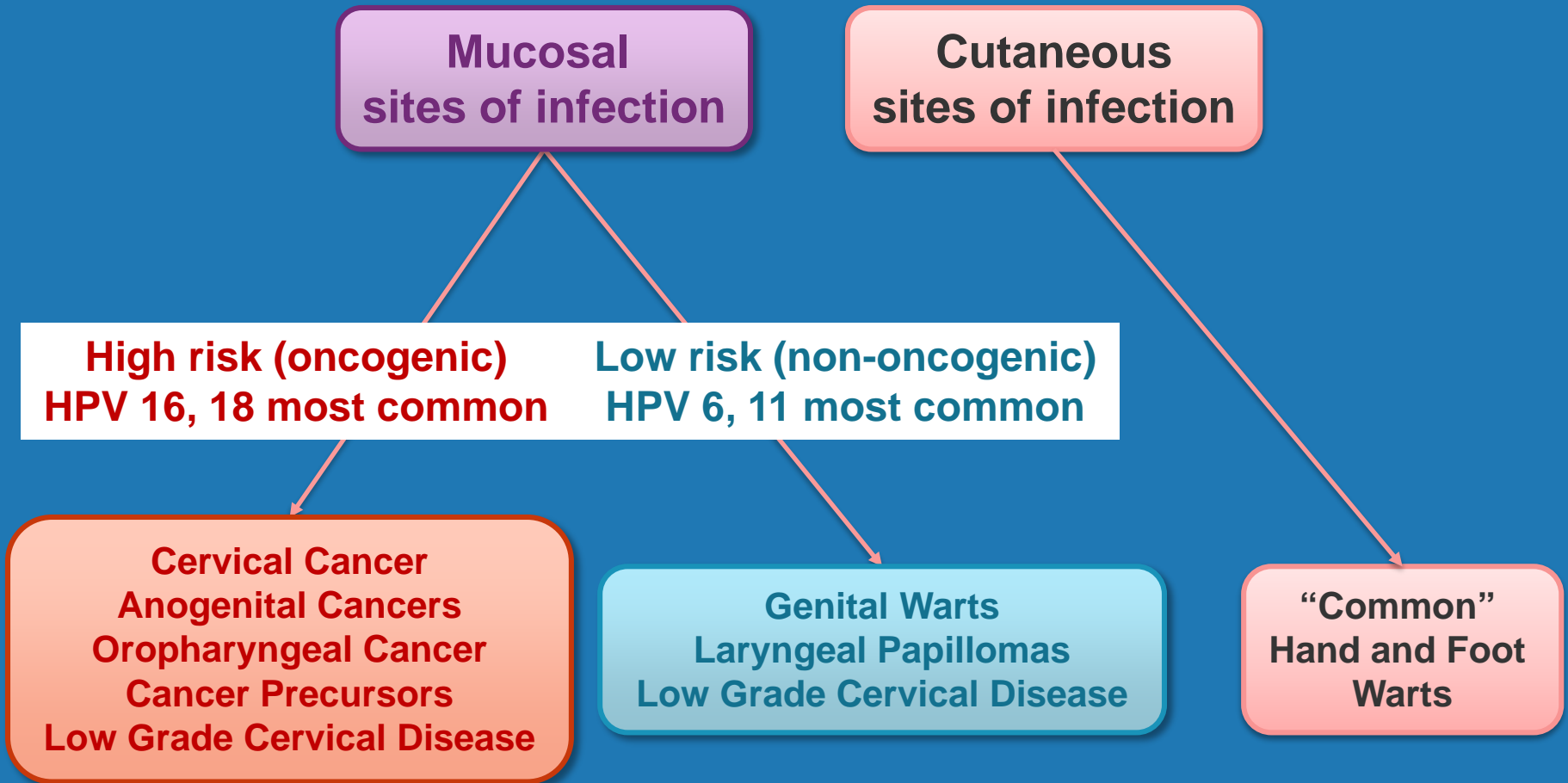
# Purpose of Presentation

- Review the epidemiology of HPV-associated cancers in Arkansas
- Review the current recommendations for preventing HPV infection through vaccination
- Review the current HPV vaccination rates in Arkansas
- Engage you in Arkansas' efforts to decrease the impact of HPV-related cancers in Arkansas

# Human Papilloma Virus

- Double-stranded DNA virus that belongs to the *Papillomaviridae* family
- Mucosal types have specific affinity for genital skin and mucosa
- Produces epithelial tumors of skin and mucous membranes
- Over 200 human specific HPV types
- Infection identified by the detection of HPV DNA

# HPV Types Differ in their Disease Associations

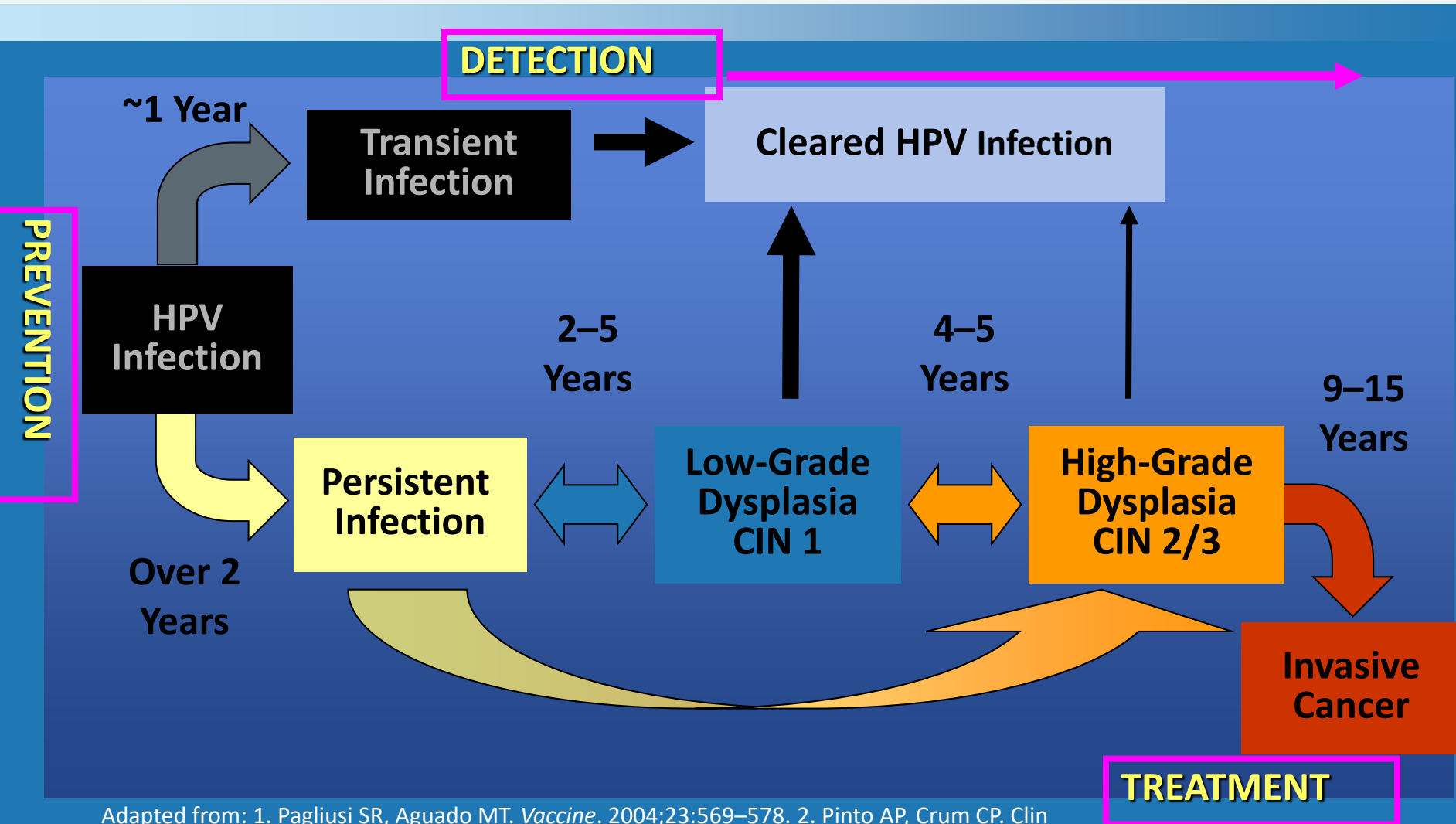


# HPV Infection

- Most females and males will be infected with at least one type of mucosal HPV at some point in their lives
  - Estimated 79 million Americans currently infected
  - 14 million new infections/year in the U.S.
  - HPV infection is most common in people in their teens and early 20s
- Most people will never know that they have been infected



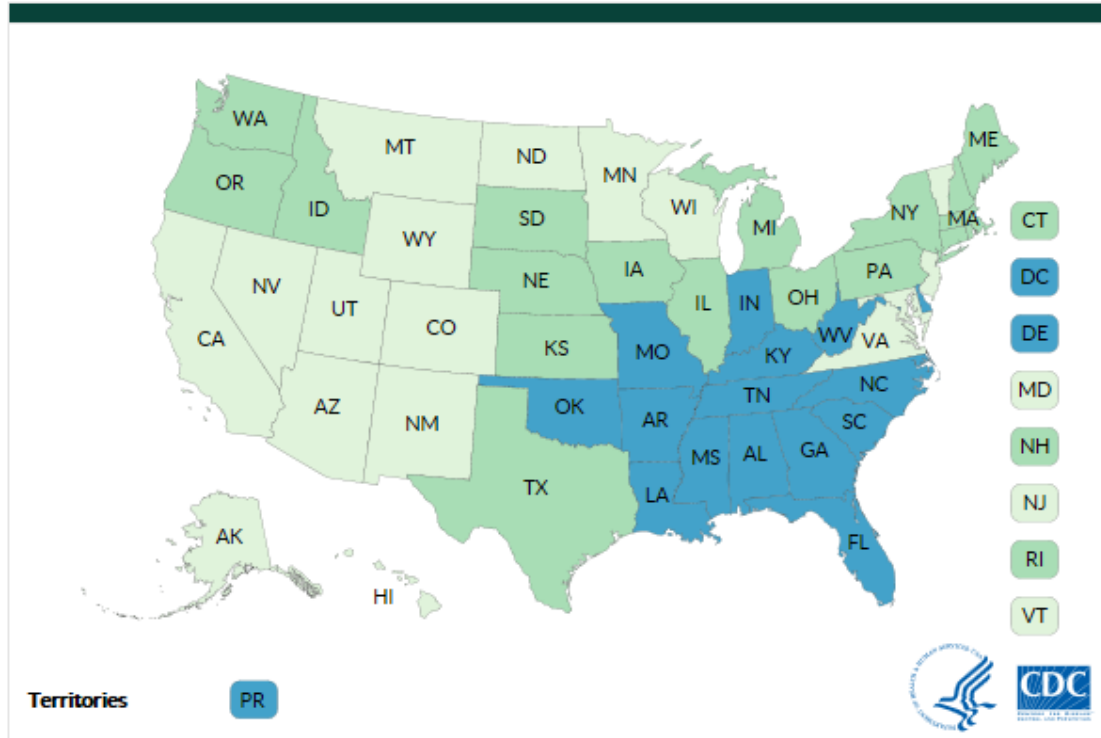
# Natural History of High-Risk HPV Infection and Potential Progression to Cervical Cancer<sup>1,2</sup>



Adapted from: 1. Pagliusi SR, Aguado MT. *Vaccine*. 2004;23:569–578. 2. Pinto AP, Crum CP. *Clin Obstet Gynecol*. 2000;43:352–362.



# HPV-Associated Cancer Rates by State, 2011-2015 Combined



## Interval

- 8.05 to 11.33
- 11.34 to 13.08
- 13.09 to 15.67

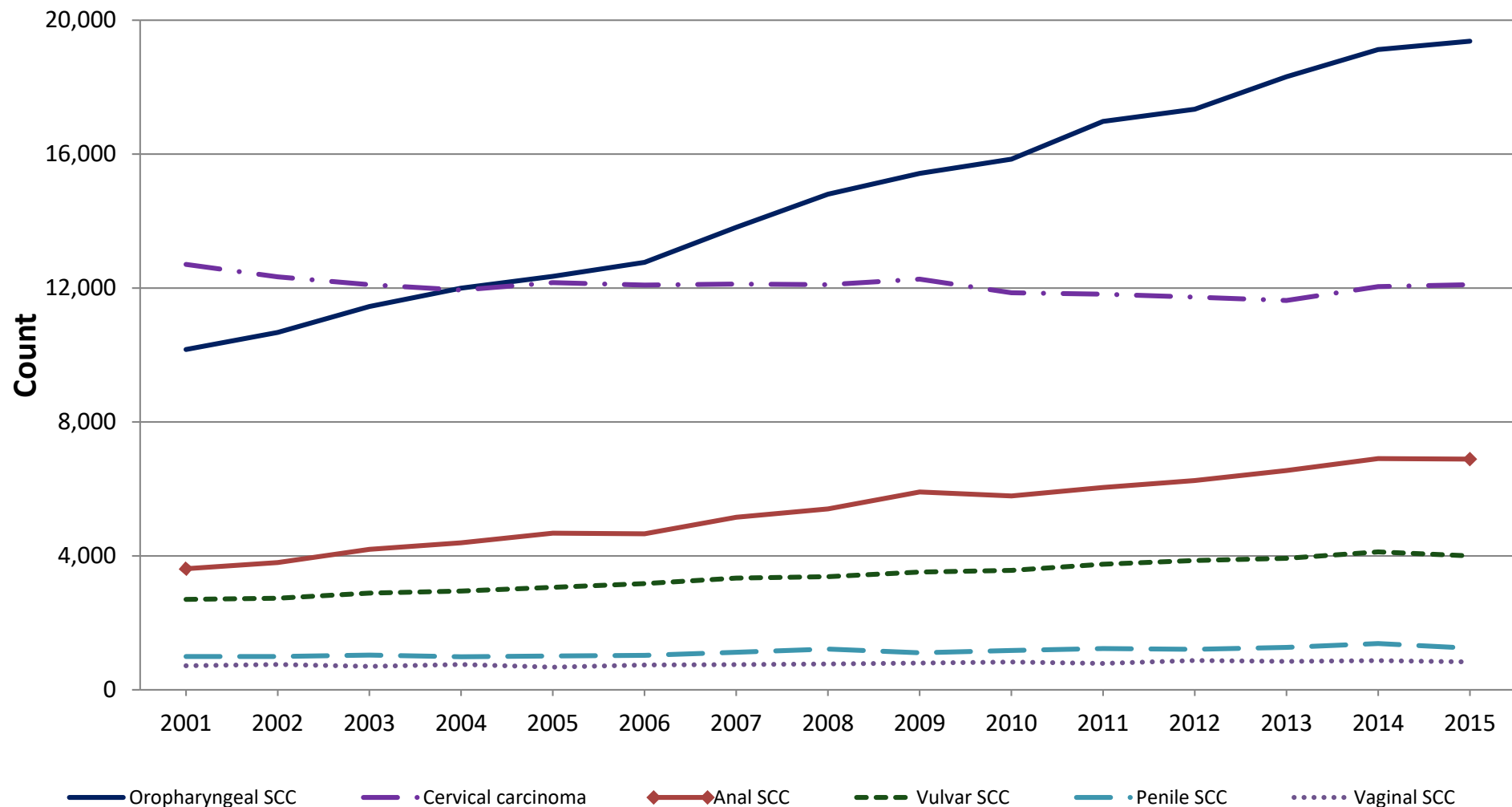
State	Rate
1. KY	15.67
2. WV	14.94
3. MS	14.39
4. FL	14.27
5. AR	14.18
6. LA	13.91
7. DC	13.89
8. TN	13.79
9. PR	13.61
10. MO	13.57

Notes: Rates per 100,000, age –adjusted to the 2000 U.S. Standard Population.

Data source: National Program of Cancer Registries SEER\*Stat Database: U.S. Cancer Statistics Incidence Analytic file 1998–2015. United States Department of Health and Human Services, Centers for Disease Control and Prevention. Released June 2018, based on the November 2017 submission.

Adapted from *HPV-Associated Cancer Rates by State*, by Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, 2018, retrieved from <https://www.cdc.gov/cancer/hpv/statistics/state/index.htm> on 10/31/2018.

# Number of Incident HPV-Associated Cancers by Site, United States, 2001-2015

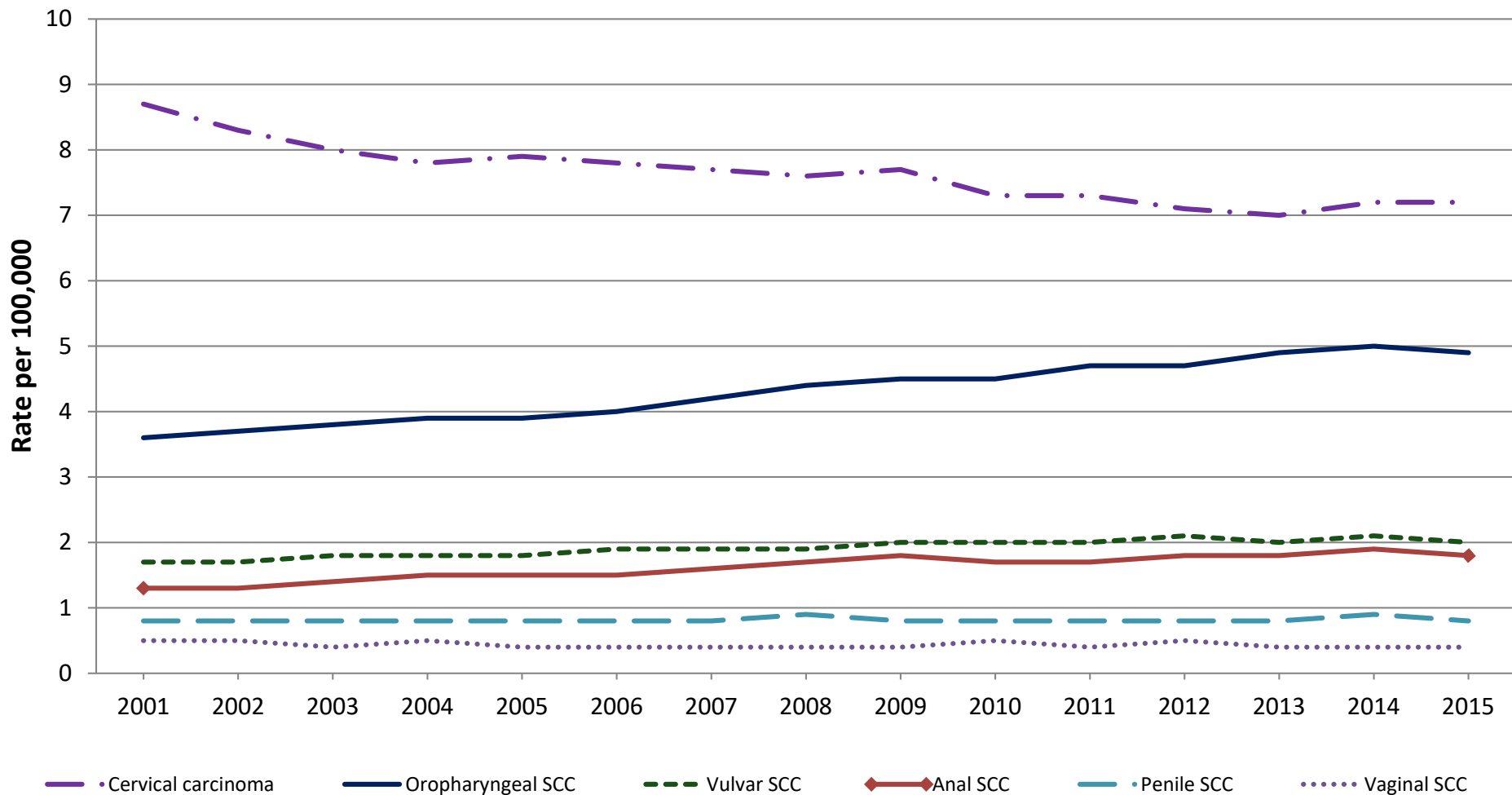


**Abbreviations:** SCC = squamous cell carcinoma

Software: Surveillance Research Program, National Cancer Institute SEER\*Stat software ([www.seer.cancer.gov/seerstat](http://www.seer.cancer.gov/seerstat)) version 8.3.5.

Data: SEER\*Stat Database: NPCR and SEER Incidence – U.S. Cancer Statistics Public Use Database, Nov 2017 submission (2001-2015). Created on 12/04/2018.

# Trends in Age-Adjusted HPV-Associated Cancer Incidence by Site, United States, 2001-2015



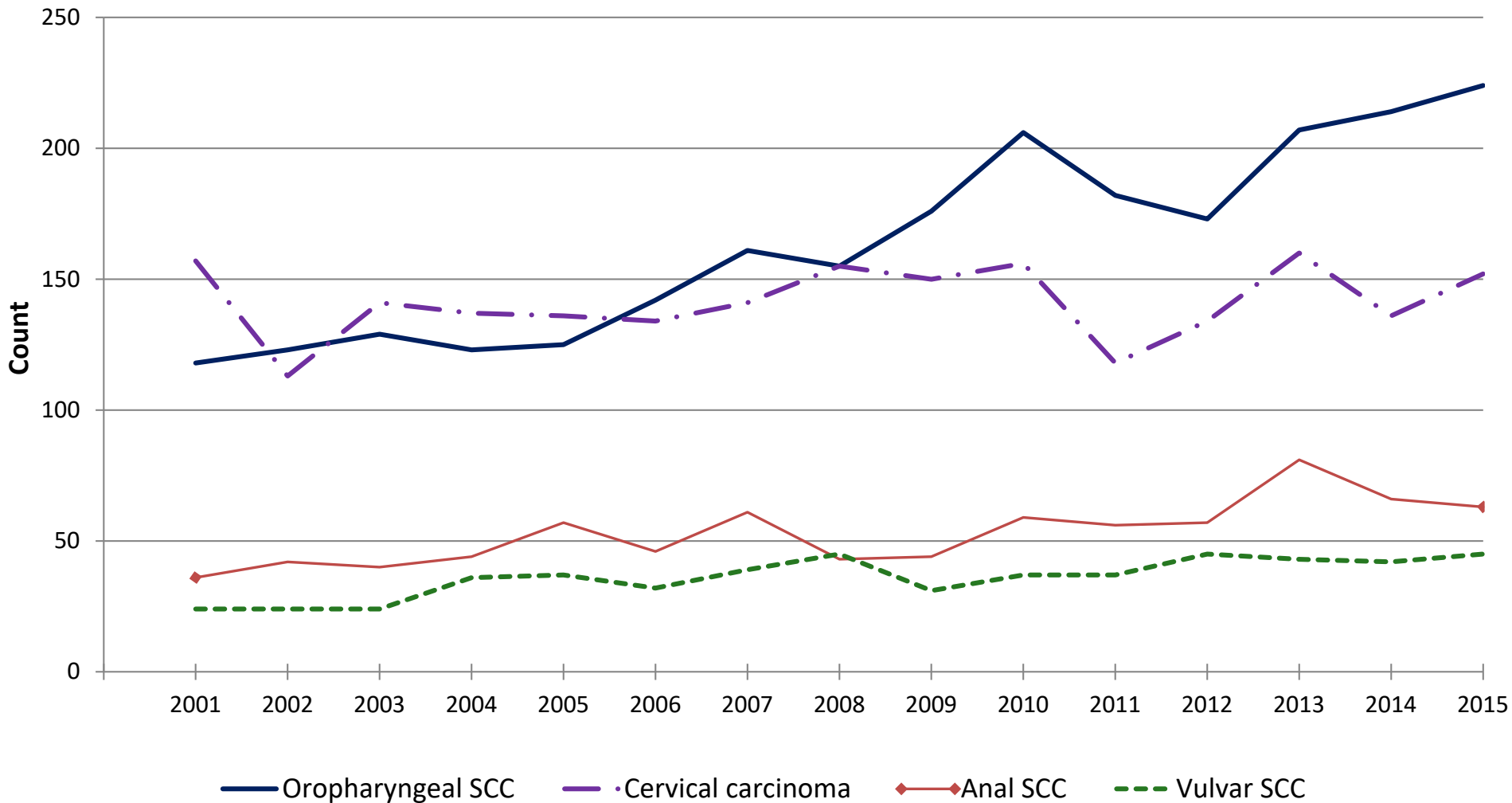
**Abbreviations:** SCC = squamous cell carcinoma

Notes: Trend rates per 100,000 population age-adjusted to the 2000 U.S. Standard Population.

Dataset: NPCR and SEER Incidence – U.S. Cancer Statistics Public Use Database, Nov 2017 submission (2001-2015).

Created on 12/04/2018.

# Number of Incident HPV-Associated Cancers by Site\*, Arkansas, 2001-2015



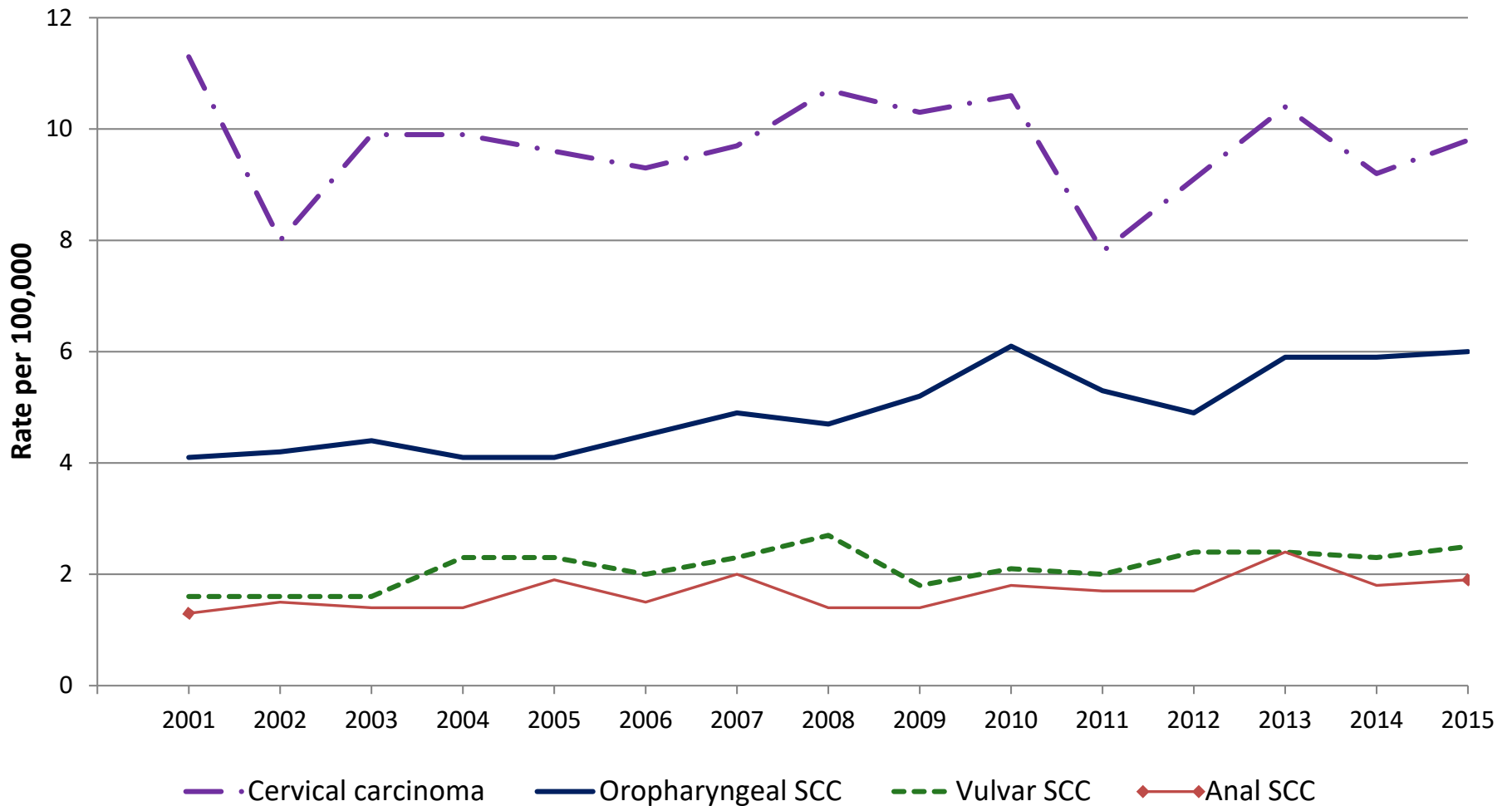
\*Vaginal SCC and penile SCC statistics not displayed due to fewer than 16 cases per year.

**Abbreviations:** SCC = squamous cell carcinoma

Dataset: NPCR and SEER Incidence – U.S. Cancer Statistics Public Use Database, Nov 2017 submission (2001-2015).

Created on 09/21/2018.

# Trends in Age-Adjusted HPV-Associated Cancer Incidence by Site\*, Arkansas, 2001-2015



\* Vaginal SCC and penile SCC not displayed due to fewer than 16 cases per year in multiple years.

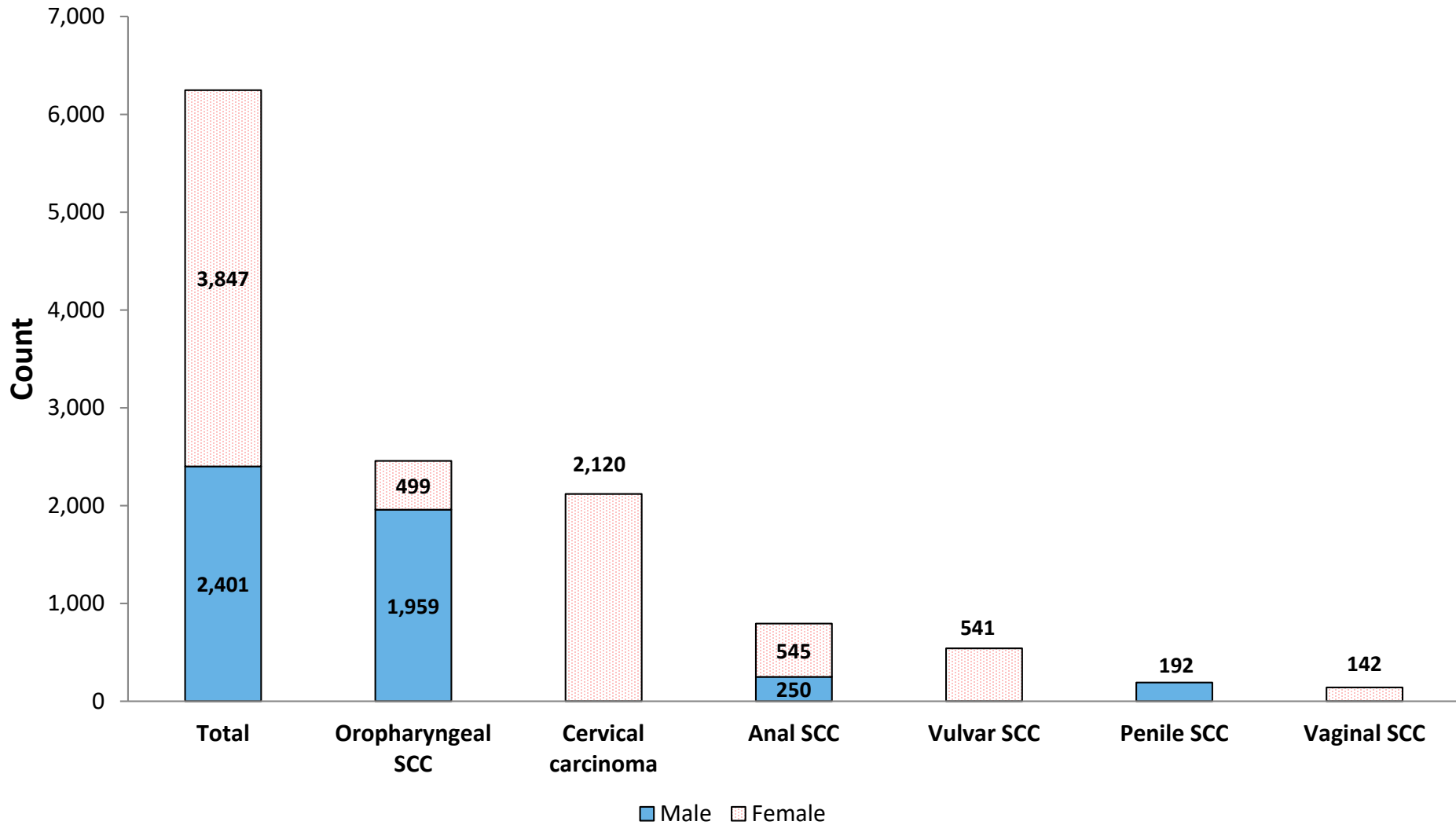
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Notes: Trend rates per 100,000 population age-adjusted to the 2000 U.S. Standard Population.

Dataset: NPCR and SEER Incidence – U.S. Cancer Statistics Public Use Database, Nov 2017 submission (2001-2015).

Created on 09/21/2018.

# Number of HPV-Associated Cancers Diagnosed in Arkansas by Cancer Type, 2001-2015 Combined

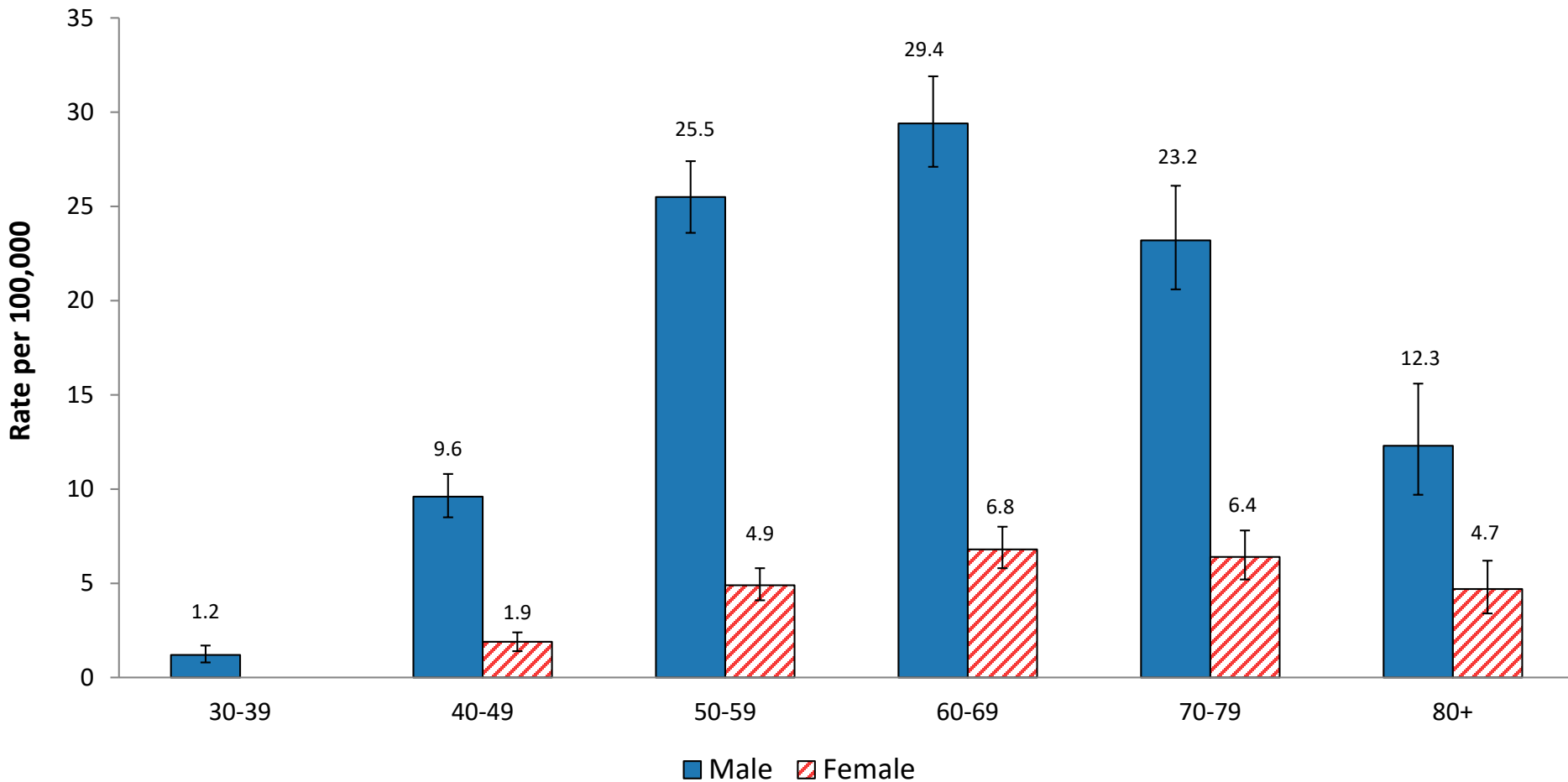


**Abbreviations:** SCC = squamous cell carcinoma

Dataset: NPCR and SEER Incidence – U.S. Cancer Statistics Public Use Database, Nov 2017 submission (2001-2015).

Created on 12/04/2018.

## Age-Adjusted Oropharyngeal SCC Rates\* Among Males and Females by Age, Arkansas, 2001-2015 Combined



\*Data suppressed for rates when the number of cases was <16 for a given category.

**Abbreviations:** SCC = squamous cell carcinoma

Notes: Trend rates per 100,000 population age-adjusted to the 2000 U.S. Standard Population.

Dataset: NPCR and SEER Incidence – U.S. Cancer Statistics Public Use Database, Nov 2017 submission (2001-2015).

Created 11/13/2018.

# Associated vs. Attributable HPV Cancers

## HPV-Associated Cancer

- Specific cellular type of cancer that can be caused by HPV
- Diagnosed in a body site where HPV is commonly found

## HPV-Attributable Cancer

- Proportion of HPV-associated cancers determined to be caused by HPV
- Based on CDC study that looked for HPV DNA in cancer tissue



# HPV-Attributable Fraction

HPV is the attributable cause of the following proportion of cancers:

- Cervical - 91%
- Oropharyngeal - 71%
- Anal - 92%
- Vulvar - 69%
- Penile - 63%
- Vaginal - 75%
- *Any HPV-Associated Cancer -79%*

Source: Centers for Disease Control and Prevention, 2016 <https://www.cdc.gov/mmwr/volumes/65/wr/mm6526a1.htm>

# Incidence of HPV-Associated Cancer and Estimated Number of Cancers Attributable to HPV by Site Arkansas, 2001-2015

Cancer	No.	Attributable to Any HPV Type	Attributable to HPV 16/18	Attributable to HPV 31/33/45/52/58	Attributable to HPV 16/18/31/33/45/52/58
		No. (%)	No. (%)	No. (%)	No. (%)
Cervical carcinoma	2,120	1,900 (90.6)	1,400 (66.2)	300 (14.7)	1,700 (80.9)
Oropharyngeal SCC	2,458	1,700 (70.1)	1,500 (60.2)	100 (5.7)	1,600 (65.9)
Anal SCC	795	700 (91.1)	600 (79.4)	100 (8.2)	700 (87.6)
Vulvar SCC	541	400 (68.8)	300 (48.6)	100 (14.2)	300 (62.8)
Penile SCC	192	100 (63.3)	100 (47.9)	- (9.0)	100 (56.9)
Vaginal SCC	142	100 (75.0)	100 (55.1)	- (18.3)	100 (73.4)
<b>Total</b>	<b>6,248</b>	<b>5,000</b>	<b>3,900</b>	<b>600</b>	<b>4,500</b>

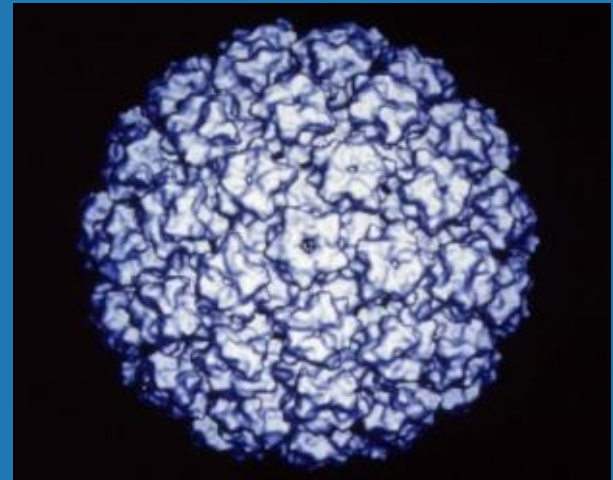
4,500



Preventable cancer cases with 9-valent HPV vaccine

# HPV Prophylactic Vaccines

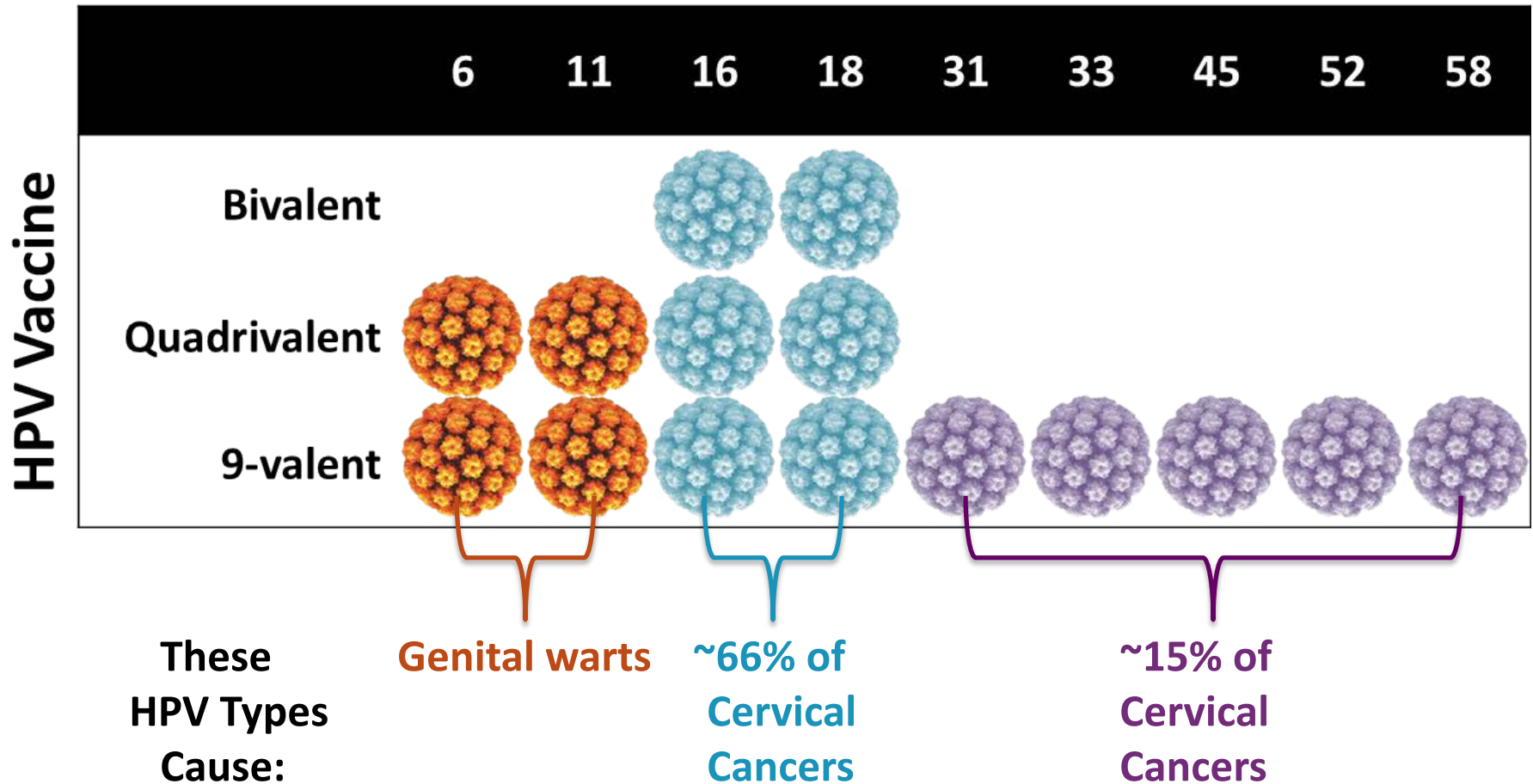
- Recombinant L1 capsid proteins that form “virus-like” particles
- Non-infectious and non-oncogenic
- Produce higher levels of neutralizing antibody than natural infection



**HPV Virus-Like Particle**

# HPV Vaccine Comparison

## HPV Types Included in Vaccine



# ACIP Recommendations for HPV Vaccination

- Routine vaccination at age 11 or 12 years
- May begin at age 9 years
- Recommended through age 26 for females and males not previously vaccinated
- Recommended for females and males age 27 through 45 based on shared clinical decision-making with their physician, if not adequately vaccinated

MMWR 2019;68:698-702

# ACIP Recommendations:

## Timing of the Series for Persons Under Age 15

- For males and females aged 9 through 14 years at time of first dose
- 9vHPV administered in a 2-dose schedule
  - ✓ Interval between doses 1 and 2 is 6-12 months
  - ✓ Minimum interval between doses 1 and 2 is 5 months
- If the second dose is delayed, the series does not need to be restarted
- Persons with immunocompromising conditions should follow the 3-dose schedule regardless of age.

MMWR 2016;64:1405-1408

# ACIP Recommendations: Timing of the Series for Persons Age 15 and Older

- For males and females aged 15 through 26 years at time of first dose
- 9vHPV administered in a 3-dose schedule
  - ✓ Interval between doses 1 and 2 is 1-2 months
  - ✓ Interval between doses 1 and 3 is 6 months
  - ✓ Minimum interval between doses 1 and 2 is 4 weeks
  - ✓ Minimum interval between doses 2 and 3 is 12 weeks
- If the vaccine schedule is interrupted, the series does not need to be restarted.

MMWR 2016;64:1405-1408

# Considerations for Persons Age 26-45

## Shared Clinical Decision-making

- HPV is a very common sexually transmitted infection.
- Most sexually active adults have been exposed to some HPV types, but not all of the HPV types in the vaccine.
- At any age, having a new sex partner is a risk factor for acquiring a new HPV infection.
- Persons in a long-term monogamous sexual partnership are not likely to acquire a new HPV infection.

MMWR 2016;64:1405-1408



# Considerations for Shared Clinical Decision-making

- HPV vaccine efficacy is high among person who have not been exposed to vaccine-type HPV before vaccination.
- Vaccine effectiveness might be low among persons with risk factors for HPV infection or disease, as well as among persons with certain immunocompromising conditions.
- HPV vaccine is prophylactic. It does not prevent progression of HPV infection to disease, clear HPV infection, or treat HPV disease.

MMWR 2016;64:1405-1408

# Case #1

- A 35 year-old woman
- Recently divorced
- Married to same man for 15 years

# Case #2

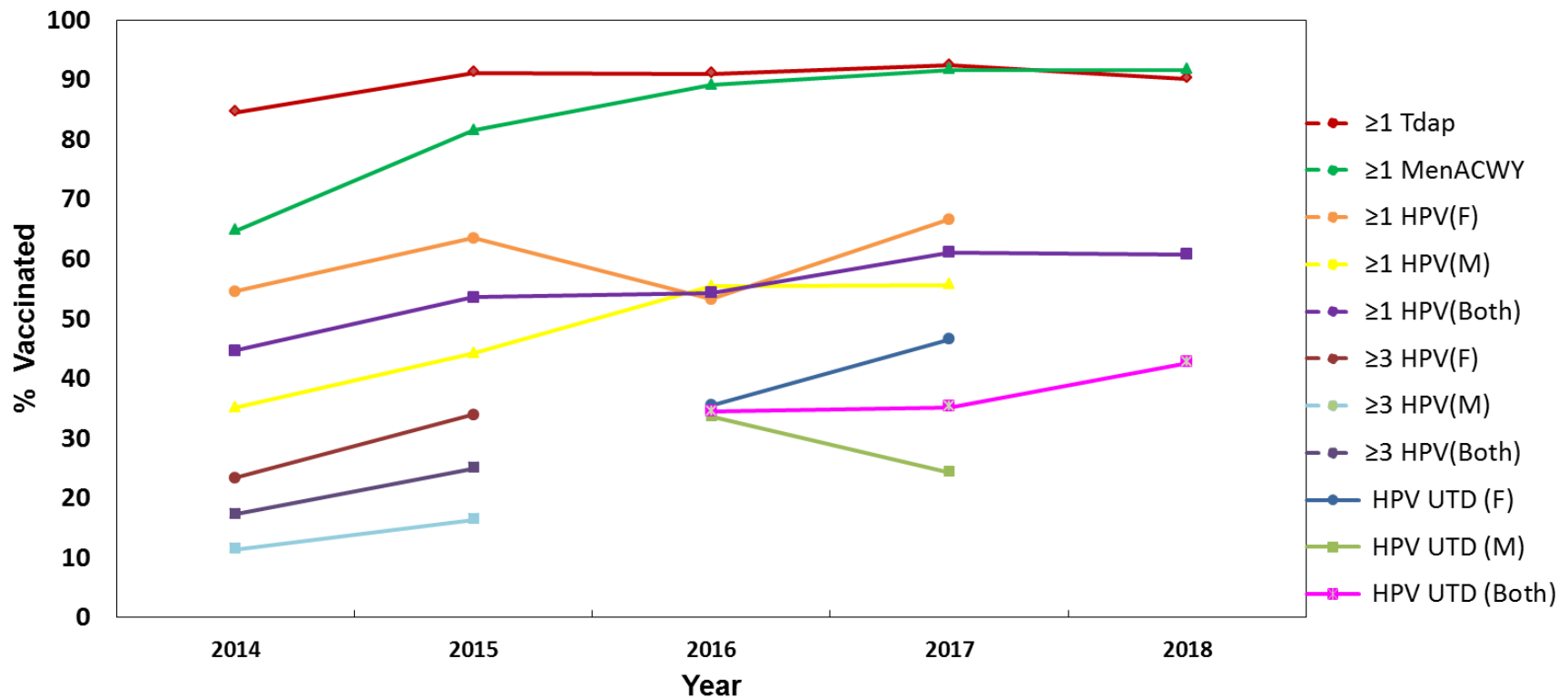
- A 42 year-old man
- Never married

# Case #3

- A 29 year-old man
- Has sex with men
- Does not have a current partner

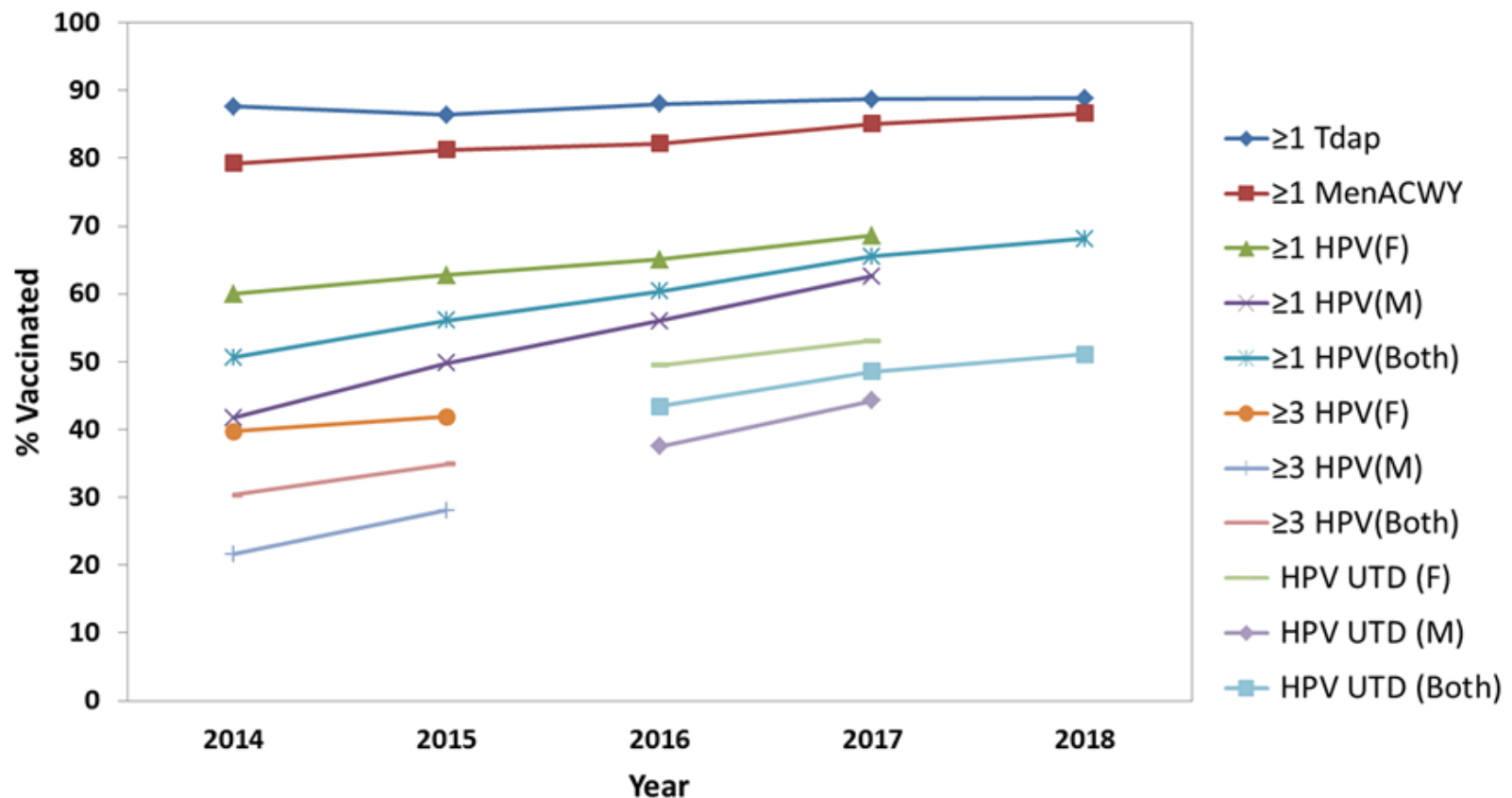
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Estimated Vaccination Coverage Among Adolescents Aged 13-17  
Years, NIS-Teen, Arkansas

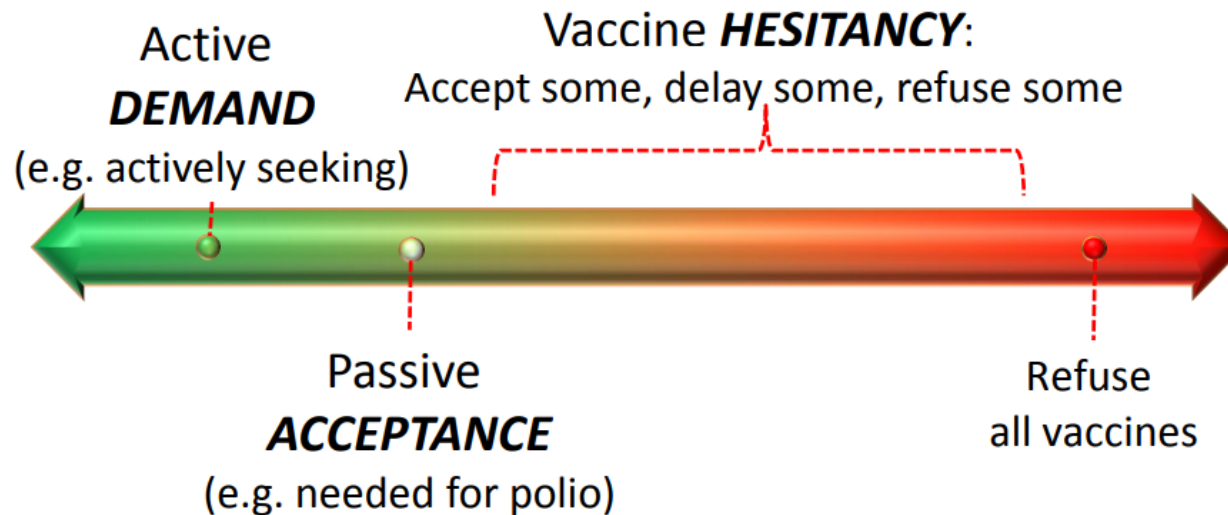


# Adolescent Vaccination for Selected Vaccines United States, 2014-18

Estimated Vaccination Coverage Among Adolescents Aged 13-17  
Years, NIS-Teen, United States



# Core concepts: A continuum of attitudes and behaviours



**Vaccine hesitancy: a delay in acceptance or refusal of vaccines, despite available services. Is complex and context specific, varying across time, place, and vaccine**

SAGE Working Group on Vaccine Hesitancy, Final Report. October 2014.  
MacDonald NE and SAGE Working Group on Vaccine Safety. Vaccine 2015; 33(34): 4161-4

# The Advisory Committee on Immunization Practices (ACIP)

- The Centers for Disease Control and Prevention (CDC) sets the US immunization schedules based on recommendations from the ACIP
- The ACIP considers many factors before recommending a vaccine, including safety and effectiveness
- The recommendations include:
  - Age(s) when the vaccine should be given
  - Number of doses needed
  - Amount of time between doses
  - Precautions and contraindications



# The Advisory Committee on Immunization Practices (ACIP)

- 15 medical and public health experts serve as voting members
- 8 ex officio members who represent other federal agencies with responsibility for immunization programs in the US
- 30 non-voting representatives of liaison organizations that bring related immunization expertise
- Members and representatives serve voluntarily

# Vaccine Safety Monitoring

## Vaccine Adverse Event Reporting System (VAERS)

- An early warning public health system where people report adverse health events following vaccination

## Vaccine Safety Datalink (VSD)

- Collaboration between CDC and several health care organizations which uses de-identified health records to monitor and evaluate adverse events following vaccination

## Post-Licensure Rapid Immunization Safety Monitoring (PRISM)

- FDA system that uses data from health plans with data from state and city immunization registries to monitor the safety of vaccines.

## Clinical Immunization Safety Assessment (CISA)

- Collaboration between CDC and several medical research centers in the U. S. to conduct research to understand how adverse events might be caused by vaccines

<http://www.cdc.gov/vaccinesafety/vaccines/HPV/index.html#monitor>

# HPV Vaccine Safety

- Prelicensure trials
- 10 years of post-licensure monitoring and evaluation
- No deaths identified from spontaneous reporting systems were causally linked to HPV vaccination.
- Vaccine Safety Datalink 2005-2011
  - 1,335,535 doses in females aged 9-26 years
  - Rate of death in HPV recipients was lower than expected
  - No deaths causally associated with HPV vaccine

Phillips A, et al. Safety of human papillomavirus vaccines: an updated review. *Drug Saf.* 2018. 41:329-346.

# 9vHPV vs 4vHPV Vaccine

- Data from clinical trials reported similar safety profile
- Overall injection site reactions were more frequent with the 9vHPV vaccine
- Adverse events were similar
  - Headache most common
- Syncope (8-10 per 100,000 doses)
- Anaphylaxis (<1 per 100,000 doses)

Phillips A, et al. Safety of human papillomavirus vaccines: an updated review. Drug Saf. 2018. 41:329-346.

# Conditions Not Associated with HPV Vaccination

- Venous thromboembolic events
- New-onset autoimmune disease
- Neurological autoimmune conditions, including paralysis
- Seizure
- Nerve palsies
- Complex regional pain syndrome
- Postural orthostatic tachycardia syndrome
- Chronic fatigue syndrome

Phillips A, et al. Safety of human papillomavirus vaccines: an updated review. *Drug Saf.* 2018. 41:329-346.

# Population Impact

- Systematic review and meta-analysis
- 60 million individuals
- Up to 8 years of post-vaccination follow-up
- Decrease in HPV infections and CIN2+ among girls and women
- Decrease in anogenital warts diagnosis among girls, women, boys, and men
- Countries with higher vaccination rates had quicker and greater direct impact and herd effects.

Drolet M, et al. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. *Lancet*. 2019. 394:497-509

# Herd Immunity-Oral HPV Infection

- Oral HPV infections in unvaccinated US men and women age 18 to 59 years
- 4 cycles of the NHANES (2009-2016)
- Prevalence of 4 vaccine types and 33 non-vaccine types
- Vaccine-type oral HPV prevalence declined from 2.7% to 1.6% in unvaccinated men; no change in non-vaccine type
- Vaccine and non-vaccine type HPV prevalence remained unchanged in unvaccinated women

Chaturvedi AK, et al. Prevalence of oral HPV infection in unvaccinated men and women in the United States. JAMA. 2019. 322:977-979

# HPV Vaccination Is Safe, Effective, and Provides Lasting Protection

- HPV Vaccine is SAFE
  - Benefits of HPV vaccination far outweigh potential risks
  - Safety studies findings for HPV vaccination similar to safety reviews of MCV4 and Tdap vaccination
- HPV Vaccine WORKS
  - Population impact against early and mid outcomes have been reported in multiple countries
- HPV Vaccine LASTS
  - Studies suggest that vaccine protection is long-lasting
  - No evidence of waning protection



# HPV Knowledge Among Persons Aged 18-26 Years

- Fewer men vs women were knowledgeable
  - About HPV: 54% vs 80%
  - About HPV vaccine: 53% vs 79%
- 69% of men and 32% of women did not know HPV causes cervical cancer
- 85% of men and 78% of women did not know HPV causes oral cancer
- Fewer men (19%) than women (31.5%) received an HPV vaccine recommendation from a health care professional

Suk et al. Public Knowledge of Human Papillomavirus and Receipt of Vaccination Recommendations. JAMA Pediatrics. Published online Sept 16, 2019

# Strengthen Our Recommendation?

- One of the strongest predictors of vaccine acceptance is whether the patient's physician recommends the HPV vaccine.
- Presumptive style
  - 65% Pediatricians
  - 42% Family Physicians

Kempe et al. HPV Vaccine Delivery Practices by Primary Care Physicians. *Pediatrics*. 144(4). Oct 2019

# Help Patients Who Are Hesitant about HPV Vaccine?


- Allow patients to express their specific concerns
- Treat their concerns seriously
- Know the HPV vaccine well enough to address their concerns
- Give a strong recommendation
  
- <http://www.immunize.org/talking-about-vaccines/>

# Strengthen Office Processes that Support HPV Vaccination?

- All staff are involved
- Routine identification of patients in need of HPV vaccine
- All staff give a strong recommendation
- Standing orders
- Routine referral for vaccination
- Reminder/Recall

# Give a Unified Message?

- All health professionals make a strong recommendation for HPV vaccination
- Unified message: HPV vaccine is cancer prevention
  - Family Medicine, Pediatrics, Internal Medicine
  - Dentists, Dental Hygienists
  - Otolaryngologists (Ear Nose & Throat)
  - Obstetrician/Gynecologists
  - Gastroenterologists (GI)
  - Oncologists and oncologic surgeons



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# HPV VACCINE IS CANCER PREVENTION

**#WeCanStopHPV**



# ARKANSAS DEPARTMENT OF HEALTH

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