Trends in Human Papillomavirus (HPV)-Associated Cancers, Arkansas, 2001-2015

Kristyn Vang, MPH
Outline

• Purpose
• Background
  – Defining HPV-associated cancers
• U.S. Trends
• AR Trends
  – Incidence
  – Cancer by site
  – Demographics
    • Age, Sex, Race
• Associated vs. Attributable Risk
• Immunization Rates in AR
Purpose

- Analyze state-specific trends in HPV-associated cancers
- Describe current HPV vaccination rates in Arkansas
- Specify target populations
  - Cancer risk
  - Vaccination
Background

- Estimated 79 million HPV infections in U.S., 2008
- Most infections are transient, clear spontaneously
- Persistent infection can lead to cancer
  - Progression from infection to invasive cervical cancer: 10-15 years
- HPV causes cancer of the following sites:
  - Cervix
  - Vagina
  - Vulva
  - Anus/Rectum
  - Penis
  - Oropharynx (including base of tongue, tonsils, and back of throat)
- HPV vaccine publicly available in U.S. starting June 2006
HPV-Associated Cancer Rates by State, 2011-2015 Combined

<table>
<thead>
<tr>
<th>State</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>KY</td>
<td>15.67</td>
</tr>
<tr>
<td>WV</td>
<td>14.94</td>
</tr>
<tr>
<td>MS</td>
<td>14.39</td>
</tr>
<tr>
<td>FL</td>
<td>14.27</td>
</tr>
<tr>
<td>AR</td>
<td>14.18</td>
</tr>
<tr>
<td>LA</td>
<td>13.91</td>
</tr>
<tr>
<td>DC</td>
<td>13.89</td>
</tr>
<tr>
<td>TN</td>
<td>13.79</td>
</tr>
<tr>
<td>PR</td>
<td>13.61</td>
</tr>
<tr>
<td>MO</td>
<td>13.57</td>
</tr>
</tbody>
</table>

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

The majority of cancer registries across the United States report to one of the following:

- CDC National Program of Cancer Registries (NPCR)
  - Arkansas Central Cancer Registry
- National Cancer Institute’s (NCI) Surveillance, Epidemiology, and End Results (SEER) Program

NPCR recently collaborated with the Surveillance, Epidemiology, and End Results (SEER) Program to generate a high-quality population-based cancer incidence database for the entire United States.
Data Analysis for this Report


Software: Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.3.5
  - Incident cases only
    • Year listed = year of diagnosis
  - Software automatically suppresses data and analysis if <16 cases in a group

Note: Some data, including county-level and survival information, sourced directly from Arkansas Central Cancer Registry and analyzed in the Central Cancer Registry Database Management System, CancerCORE v2.
## Predefined Variables

### Human Papillomavirus-Associated Cancers

<table>
<thead>
<tr>
<th>Cancer</th>
<th>ICD-O-3 site codes</th>
<th>ICD-O-3 histology codes</th>
<th>Additional restrictions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinoma of the oropharynx</td>
<td>C01.9, 02.4, 02.8, 05.1–05.2, 09.0–09.1, 09.8–09.9, 10.0–10.9, 10.8–10.9, 14.0, 14.2, 14.8</td>
<td>8050–8084, 8120–8131</td>
<td>Restrict to microscopically confirmed</td>
</tr>
<tr>
<td>Squamous cell carcinoma of the anus</td>
<td>C21.0–21.8, 20.9</td>
<td>8050–8084, 8120–8131</td>
<td>Restrict to microscopically confirmed</td>
</tr>
<tr>
<td>Squamous cell carcinoma of the vulva</td>
<td>C51.0–51.9</td>
<td>8050–8084, 8120–8131</td>
<td>Restrict to females and restrict to microscopically confirmed</td>
</tr>
<tr>
<td>Squamous cell carcinoma of the vagina</td>
<td>C52.9</td>
<td>8050–8084, 8120–8131</td>
<td>Restrict to females and restrict to microscopically confirmed</td>
</tr>
<tr>
<td>Carcinoma of the cervix</td>
<td>C53.0–53.9</td>
<td>8010–8671, 8940–8941</td>
<td>Restrict to females and restrict to microscopically confirmed</td>
</tr>
<tr>
<td>Squamous cell carcinoma of the penis</td>
<td>C60.0–60.9</td>
<td>8050–8084, 8120–8131</td>
<td>Restrict to males and restrict to microscopically confirmed</td>
</tr>
</tbody>
</table>

Notes: Table showing which International Classification of Disease for Oncology (ICD-0)-3 site codes, histology codes, and other restrictions used for the predefined SEER*Stat variables. Adapted from *Predefined SEER*Stat Variables for Calculating the Number of Associated Cancers for Selected Risk Factors*, by Centers for Disease Control and Prevention, 2017, retrieved from https://www.cdc.gov/cancer/npcr/pdf/public-use/predefined-seer-stat-variables.pdf
National Trends

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

Abbreviations: SCC = squamous cell carcinoma
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.
Created on 12/04/2018.
Arkansas Trends

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

Abbreviations: SCC = squamous cell carcinoma
Created on 11/6/2018.
Number of HPV-Associated Cancers Diagnosed in Arkansas by Cancer Type, 2001-2015 Combined

Abbreviations: SCC = squamous cell carcinoma
Created on 12/04/2018.
Percentage of HPV-Associated Cancer by Type, Arkansas, 2013-2015 Combined

- Oropharyngeal SCC: 42.9%
- Cervical carcinoma: 29.8%
- Anal SCC: 14.0%
- Vulvar SCC: 8.6%
- Penile SCC: 2.5%
- Vaginal SCC: 2.2%

Abbreviations: SCC = squamous cell carcinoma
Created on 10/19/2018.
Age-Adjusted Incidence of HPV-Associated Cancer by Site, Arkansas

**Abbreviations:** SCC = squamous cell carcinoma

HPV-associated cancers in males include oropharyngeal SCC, anal SCC, and penile SCC. HPV-associated cancers in females include oropharyngeal SCC, anal SCC, vaginal SCC, vulvar SCC, and cervical carcinoma.

* Significant at p<0.05. Trends were measured with APC in rates and were considered to increase or decrease if p<0.05.

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

**Abbreviations:** APC = annual percentage change; SCC = squamous cell carcinoma.


Created 11/14/18.
Age-Adjusted Incidence* of HPV-Associated Cancer by Site and Race, Arkansas, 2011-2015 Combined

*Rates suppressed if <16 cases per category.

**Abbreviations:** SCC = squamous cell carcinoma

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


Created on 10/19/2018.
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

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.

**Abbreviations:** SCC = squamous cell carcinoma

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


Created on 09/21/2018.
Trends in Age-Adjusted Incidence of Cervical Carcinoma Among Females and Oropharyngeal SCC Among Males and Females, Arkansas, 2001-2015

*Cervical carcinoma; APC = -0.2  Oropharyngeal SCC; APC = 3.0*

* Significant at p<0.05. Trends were measured with APC in rates and were considered to increase or decrease if p<0.05.

**Abbreviations:** APC = annual percentage change; SCC = squamous cell carcinoma.

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


Created on 09/21/2018.
Trends in Age-Adjusted Oropharyngeal SCC Rates by Sex, Arkansas, 2001-2015

Abbreviations: SCC = squamous cell carcinoma
Notes: Trend rates per 100,000 population age-adjusted to the 2000 U.S. Standard Population.
Created on 09/21/2018.
Age-Adjusted Oropharyngeal SCC Rates Among Males and Females, Arkansas, 2011-2015 Combined

Abbreviations: SCC = squamous cell carcinoma
Notes: Trend rates per 100,000 population age-adjusted to the 2000 U.S. Standard Population.
Created 10/29/2018.
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.


Created 11/13/2018.
Age-Adjusted Oropharyngeal SCC Rates* Among Males and Females by Race and 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.


Created 10/29/2018.
Trends in Age-Adjusted Incidence of Cervical Carcinoma Among Females and Oropharyngeal SCC Among Men, Arkansas, 2001-2015

* Significant at p<0.05. Trends were measured with APC in rates and were considered to increase or decrease if p<0.05.

**Abbreviations**: APC = annual percentage change; SCC = squamous cell carcinoma.

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


Created on 09/21/2018.
**Trends in Age-Adjusted HPV-Associated Cancer Incidence by Cancer Type and Sex, Arkansas, 2001-2015**

* Significant at p<0.05. Trends were measured with APC in rates and were considered to increase or decrease if p<0.05.

**Abbreviations:** APC = annual percentage change; SCC = squamous cell carcinoma.

Notes: Anal SCC rates in males suppressed before 2010 when the number of cases was <16 per year. Vaginal SCC and penile SCC not displayed due to <16 cases per year in multiple years.

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


Created on 09/21/2018.
Trends in Age-Adjusted Anal SCC Incidence by Sex, Arkansas, 2001-2015

Notes: Counts for males 2001-2008 suppressed due to <16 cases per year for multiple years.

Abbreviations: SCC = squamous cell carcinoma
Trend rates per 100,000 population age-adjusted to the 2000 U.S. Standard Population.
Created on 09/21/2018.
# Annual Age-Adjusted Rates and Trends in HPV-Associated Cancer, Arkansas and United States, 2001-2015

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Arkansas</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Period of Diagnosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rate (No.)</td>
<td>Rate (No.)</td>
</tr>
<tr>
<td>All HPV-associated cancers</td>
<td>13.0 (362)</td>
<td>15.0 (510)</td>
</tr>
<tr>
<td>Male</td>
<td>9.0 (120)</td>
<td>12.2 (211)</td>
</tr>
<tr>
<td>Female</td>
<td>16.7 (242)</td>
<td>17.9 (299)</td>
</tr>
<tr>
<td>Oropharyngeal SCC</td>
<td>4.1 (118)</td>
<td>6.0 (224)</td>
</tr>
<tr>
<td>Male</td>
<td>7.2 (96)</td>
<td>9.9 (177)</td>
</tr>
<tr>
<td>Female</td>
<td>1.4 (22)</td>
<td>2.5 (47)</td>
</tr>
<tr>
<td>Anal SCC</td>
<td>1.3 (36)</td>
<td>1.9 (63)</td>
</tr>
<tr>
<td>Male</td>
<td>~</td>
<td>1.4 (21)</td>
</tr>
<tr>
<td>Female</td>
<td>1.5 (25)</td>
<td>2.4 (42)</td>
</tr>
<tr>
<td>Vulvar SCC</td>
<td>1.6 (24)</td>
<td>2.5 (45)</td>
</tr>
<tr>
<td>Vaginal SCC</td>
<td>~</td>
<td>~</td>
</tr>
<tr>
<td>Penile SCC</td>
<td>~</td>
<td>~</td>
</tr>
<tr>
<td>Cervical carcinoma</td>
<td>11.3 (157)</td>
<td>9.8 (152)</td>
</tr>
</tbody>
</table>

* Significant at p<0.05. Trends were measured with AAPC in rates and were considered to increase or decrease if p<0.05.

~ Data suppressed for rates when the number of cases was <16 per year.

**Abbreviations:** AAPC = average annual percentage change; SCC = squamous cell carcinoma.

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


Associated vs. Attributable
HPV Cancers
Definition

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

Source: Centers for Disease Control and Prevention, 2018 https://www.cdc.gov/cancer/hpv/pdf/USCS-DataBrief-No4-August2018-508.pdf
HPV is the attributable cause of the following proportion of cancers:

- Cervical - 91%
- Oropharyngeal - 71%
- Anal/Rectal - 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

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

**Preventable cancer cases with 9-valent HPV vaccine**

Notes: Estimates for attributable fraction were based on studies that used population-based data from cancer tissue to estimate the percentage of those cancers probably caused by HPV. The estimated number of HPV-attributable cancers was calculated by multiplying the HPV-associated cancer counts by the percentage of each cancer attributable to HPV. Estimates were rounded to the nearest 100. Estimates less than 100 are not presented. Individual counts may not sum to the total count because of rounding.

Created on 10/19/2018.
HPV Vaccination Rates

Jennifer Dillaha, MD
Estimated vaccination coverage with selected vaccines among adolescents aged 13-15 years, by survey year, NIS-Teen, United States and Arkansas, 2008-2017

**U.S.**

**Arkansas**

Survey year

% Vaccinated

Revised APD Definition

Survey year

% Vaccinated

Revised APD Definition
Estimated vaccination coverage with selected vaccines and doses among adolescents aged 13-15 years, by survey year, NIS-Teen, Arkansas, 2008-2017

<table>
<thead>
<tr>
<th>Survey Year</th>
<th>≥1 Tdap*</th>
<th>≥2 VAR*</th>
<th>≥1 MenACWY®</th>
<th>≥1 HPV® (F)</th>
<th>≥1 HPV® (M)</th>
<th>≥2 HPV® (Both)</th>
<th>≥3 HPV® (F)</th>
<th>≥3 HPV® (M)</th>
<th>≥3 HPV® (Both)</th>
<th>HPV UTD* (F)</th>
<th>HPV UTD* (M)</th>
<th>HPV UTD* (Both)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy People 2020 Target</td>
<td>80.0%</td>
<td>90.0%</td>
<td>80.0%</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>80.0%</td>
<td>80.0%</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>31.3±7.1</td>
<td>20.2±6.8</td>
<td>20.3±6.1</td>
<td>25.2±9.5</td>
<td>NA</td>
<td>NA</td>
<td></td>
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<tr>
<td>2009</td>
<td>38.4±7.7</td>
<td>25.3±10.6</td>
<td>21.2±6.3</td>
<td>33.1±11.0</td>
<td>NA</td>
<td>NA</td>
<td></td>
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<tr>
<td>2010</td>
<td>47.0±8.4</td>
<td>27.1±8.5</td>
<td>32.0±7.9</td>
<td>32.6±11.9</td>
<td>NA</td>
<td>18.6±9.2</td>
<td></td>
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</tr>
<tr>
<td>2011</td>
<td>56.4±10.1</td>
<td>54.1±12.4</td>
<td>30.0±9.0</td>
<td>27.5±14.5</td>
<td>NA</td>
<td>15.7±8.1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>2012</td>
<td>73.9±7.8</td>
<td>56.1±9.9</td>
<td>37.9±8.4</td>
<td>41.6±12.6</td>
<td>16.1±9.1</td>
<td>30.0±8.3</td>
<td>18.4±8.7</td>
<td>NA</td>
<td>12.4±5.4</td>
<td></td>
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<tr>
<td>2013</td>
<td>84.7±5.8</td>
<td>61.6±9.4</td>
<td>40.2±8.6</td>
<td>44.2±12.2</td>
<td>NA</td>
<td>28.7±8.1</td>
<td>21.1±10.3</td>
<td>NA</td>
<td>12.9±5.9</td>
<td></td>
<td></td>
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<tr>
<td>2013 Revised®</td>
<td>82.4±6.3</td>
<td>57.9±9.4</td>
<td>39.6±8.3</td>
<td>43.0±12.1</td>
<td>NA</td>
<td>28.2±7.8</td>
<td>20.2±9.8</td>
<td>NA</td>
<td>12.3±5.5</td>
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<tr>
<td>2014™</td>
<td>87.9±5.8</td>
<td>71.2±8.7</td>
<td>65.4±7.9</td>
<td>54.0±12.1</td>
<td>38.7±11.6</td>
<td>45.9±8.5</td>
<td>23.7±10.6</td>
<td>12.4±7.1</td>
<td>17.7±6.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>91.0±4.6</td>
<td>88.0±5.5</td>
<td>83.0±5.7</td>
<td>60.2±11.2</td>
<td>39.7±10.3</td>
<td>50.0±7.8</td>
<td>31.3±10.5</td>
<td>14.6±6.8</td>
<td>23.0±6.4</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2016</td>
<td>91.1±3.9</td>
<td>92.2±4.1</td>
<td>89.0±4.6</td>
<td>47.1±12.1</td>
<td>48.8±10.5</td>
<td>48.0±8.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2017</td>
<td>93.5±3.6</td>
<td>91.0±4.5</td>
<td>91.0±4.9</td>
<td>64.5±12.1</td>
<td>55.6±11.2</td>
<td>59.7±8.3</td>
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</tr>
</tbody>
</table>
Vaccination Rate per County for 11-14 Years-old with 2 or More HPV Vaccine, Arkansas 2018

Date: October 11, 2018
Source: Arkansas Department of Health
Author: Haytham Safi, Epidemiologist

Percent UTD
- > 80 (HP2020)
- 60.1 - 80
- 40.1 - 60
- 20.1 - 40
- 0 - 20
Conclusion

• While cervical carcinoma rates have remained stable over time, other HPV-associated cancers are being diagnosed more frequently.

• Both males and females need to be vaccinated for HPV.

• Improved vaccination rates could reduce the burden of disease in Arkansas.
Contact Information

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Arkansas Department of Health

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