HPV-Related Cancers and Vaccination in Appalachia: Implications for Disparities

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Outline

- HPV and HPV Vaccine
- Cancer Registry Project
- NIS-Teen Vaccination Project
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HPV

- HPV is the most common STI in the U.S.
  - 43% of females and >20% of males have current infection
- >30 strains cause cancer and genital warts
  - 6% of US adults report history of genital warts
- High concordance between sexual partners
  - About 38% of partners of HPV-positive individuals have 1+ types of HPV

Hariri et al. 2011, JID
Dunne et al. 2006, JID
Dinh et al. 2008, STD
Reiter, Pendergraft & Brewer 2010, CEBP
HPV Causes Cancer

![Bar chart showing the annual number of cases worldwide due to HPV-induced cancers in different body parts. The chart highlights the significant impact on the cervix, with a much lower occurrence in the anus, vagina/vulva, penis, mouth, and throat.]
HPV Cancer Burden

- HPV causes about 19,000 cases of these cancers each year in the U.S.
  - Similar to brain cancer and the most common types of leukemia
- Substantial economic burden
  - About $400 million annually

Gillison et al. 2008, Cancer
Chaturvedi et al. 2010, JAH
## HPV Vaccines

<table>
<thead>
<tr>
<th></th>
<th>HPV4</th>
<th>HPV2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other Names</strong></td>
<td>Gardasil, quadrivalent</td>
<td>Cervarix, bivalent</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>3 doses (months 0, 2, 6)</td>
<td>3 doses (months 0, 1, 6)</td>
</tr>
<tr>
<td><strong>Approval</strong></td>
<td>2006</td>
<td>2009</td>
</tr>
<tr>
<td><strong>Recommendation</strong></td>
<td>Routine; ages 11-12 with catch up for ages 13-26</td>
<td>Routine; ages 11-12 with catch up for ages 13-25</td>
</tr>
<tr>
<td><strong>Recommendation</strong></td>
<td>Routine; ages 11-12 with catch up for ages 13-26</td>
<td>Not available</td>
</tr>
<tr>
<td><strong>Types 16 &amp; 18</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Types 6 &amp; 11</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Approved to Prevent</strong></td>
<td>Cervical, vaginal, vulvar, and anal cancers; genital warts</td>
<td>Cervical cancer</td>
</tr>
</tbody>
</table>
HPV Vaccine Coverage

- 2011 estimates (females ages 13-17)
  - Vaccine initiation: 53%
  - Vaccine completion: 35%
- Steady improvements from 2008
  - 37% and 18%
- Still much lower than other developed countries
  - Australia: >80% vaccine initiation and >70% vaccine completion

CDC 2011, MMWR
Appalachia

- 400+ counties in 13 states
- Mostly rural region with 70% of counties considered non-metropolitan
- Lower levels of education and higher levels of poverty
- Poorer health and health behaviors
Cancer in Appalachia

- Appalachia has a higher cancer burden compared to rest of U.S.
- All cancer sites combined
  - Males: 569 vs. 539 cases per 100,000
  - Females: 415 vs. 399 cases per 100,000
- Disparities include:
  - Lung cancer (males and females)
  - Colorectal cancer (males and females)
  - Cervical cancer

Wingo et al. 2008, Cancer
Hopenhayn et al. 2008, Cancer
Lengerich et al. 2005, J Rural Health
HPV Vaccine in Appalachia

- Despite high cervical cancer rates, little is known about HPV vaccine in Appalachia
  - Most adults are accepting of HPV vaccine for adolescent females (about 70%)
  - Most healthcare facilities in Appalachia offered HPV vaccine by 2008
  - Modest vaccination (initiation: <50%; completion: <5%) among adult women in Kentucky offered free vaccine

Hopenhayn et al. 2007, Can Causes Control
Christian et al. 2009, JAH
Katz et al. 2009, Vaccine
Huey et al. 2009, Prev Chronic Dis
Crosby et al. 2011, J Rural Health
State of Appalachian Research

What We Know
- High cervical cancer rates
- Pretty high parental acceptance of HPV vaccine for adolescent females
- Vaccine is readily available

What We Don’t Know
- Burden of other HPV-related cancers among females
- Burden of HPV-related cancers among males
- HPV vaccine uptake among adolescent females

Cancer Registry Project
NIS-Teen Vaccination Project
Outline

- HPV and HPV Vaccine
- Cancer Registry Project
- NIS-Teen Vaccination Project
Goal

- To assess the total burden of HPV-related cancers among females and males in Appalachia
- To compare Appalachian areas with non-Appalachian areas
Data Sources

- Incidence data (1996-2008) from cancer registries for three Appalachian states
  - Ohio
  - Kentucky
  - West Virginia

- National data from SEER 9 cancer registries (1996-2008)
  - Represents about 10% of U.S. population
Defining Appalachia

- Ohio: 29 out of 88 counties
- Kentucky: 51 out of 120 counties
- West Virginia: all 55 counties (only state that is completely Appalachian)

Note: 3 counties in OH and KY were added to Appalachia in 2008 but were not classified as Appalachian here since 2008 was the last year of data examined
Cancer Outcomes

- Each HPV-related cancer type separately
  - Cervical, vaginal, vulvar, penile, anal, and oral cavity/pharyngeal cancers

- All HPV-related cancers combined (total burden)
  - **Females:** cervical, vaginal, vulvar, anal, and oral cavity/pharyngeal cancers
  - **Males:** penile, anal, and oral cavity/pharyngeal cancers
Rates

- SEER*Stat to calculate age-adjusted incidence rates
- Rates (all races included) calculated for:
  - Entire state (or SEER 9)
  - Appalachian vs. non-Appalachian regions of each state
  - Counties within states
- Statistical significance inferred by non-overlapping 95% confidence intervals (CIs)
  - Conservative approach

Schenker et al. 2001, *The American Statistician*
Maps

- Mapped county-level incidence rates for all HPV-related cancers combined for both females and males
- Data suppressed for counties with fewer than five cases to prevent misinterpretation of rates
- ArcGIS (ArcMap 10.0) used to generate all maps
HPV Cancer Burden (1996-2008)

- **KY**:
  - Females: 6663
  - Males: 5436

- **OH**:
  - Females: 15813
  - Males: 11638

- **WV**:
  - Females: 3200
  - Males: 2418
Females – All HPV Cancers

Incidence Rate (Cases per 100,000)

KY
OH
WV
SEER 9

Appalachia
Non-Appalachia
Females – All HPV Cancers

Age-adjusted incidence rate per 100,000

- 10.1 - 17.8
- 17.9 - 20.3
- 20.4 - 23.4
- 23.5 - 25.9
- 26.0 - 39.4

Cases < 5

Appalachia
Appalachian females have higher rates of all HPV-related cancers, but what cancers are causing these disparities?
Females – Cervical Cancer

Incidence Rate (Cases per 100,000)

KY
OH
WV
SEER 9

APPalachia
Non-APPalachia
Females – Vulvar Cancer

Incidence Rate (Cases per 100,000)

KY
OH
WV
SEER 9

Appalachia
Non-Appalachia
Females – Anal Cancer

Incidence Rate (Cases per 100,000)

KY
OH
WV
SEER 9

Appalachia
Non-Appalachia
Females – Other Cancers

- Geographic areas did not differ greatly in terms of:
  - Vaginal cancer (all rates <1.0)
  - Oral cavity/pharyngeal cancer (all rates between 5.4 and 6.5)
Males – All HPV Cancers

Incidence Rate (Cases per 100,000)

KY
OH
WV
SEER 9

- Appalachia
- Non-Appalachia
Males – Oral Cavity/Pharyngeal

Incidence Rate (Cases per 100,000)

KY, OH, WV, SEER 9

Appalachia  Non-Appalachia
Males – Penile Cancer

Incidence Rate (Cases per 100,000)

KY
OH
WV
SEER 9

Appalachia
Non-Appalachia
Males – Other Cancers

- Geographic areas did not differ greatly in terms of:
  - Anal cancer (all rates between 1.1 and 1.3)
How Do They Compare?

Females

Males

Age-adjusted incidence rate per 100,000

Cases < 5

Appalachia
Conclusions

- Substantial burden of HPV-related cancers in Appalachia
- Disparities among females beyond cervical cancer
  - Vulvar and anal cancers
- Disparities not as present among males
  - Penile cancer
  - KY has high rates regardless; Appalachian OH has higher rates than non-Appalachian OH
Conclusions

- HPV vaccine is a potentially important public health strategy for reducing disparities
  - Currently approved to prevent cervical, vaginal, vulvar, and anal cancers
  - If vaccination is lower, disparities could worsen

- Limitations
  - Health behaviors (e.g., tobacco use)
  - Did not have HPV status of cancers
Outline

- HPV and HPV Vaccine
- Cancer Registry Project
- NIS-Teen Vaccination Project
Goal

- Examine HPV vaccination among adolescent females from Appalachia
- Compare Appalachian areas with non-Appalachian areas
Data Source

- National Immunization Survey – Teen (NIS-Teen)
- National survey conducted yearly by CDC
- Examines vaccination coverage among adolescents ages 13-17
- Complex stratified sampling strategy that identifies parents through RDD
  - Parents complete survey on vaccination and demographics
Data Source

- Obtains vaccination data from adolescents’ healthcare providers to produce estimates
  - Gold standard of vaccination data in the U.S.
- Examined data for 2008-2010
  - All publicly available years for HPV vaccination
  - Total of 27,419 females with provider-verified vaccination records
Disclaimer

The findings and conclusions in this paper are those of the author(s) and do not necessarily represent the views of the Research Data Center, National Center for Health Statistics, Centers for Disease Control and Prevention.
Defining Appalachia

- Most recent definition of Appalachia since all data were 2008 or more recent
  - 420 counties in 13 states
- 1,951 (7%) of all females classified as living in Appalachia based on current county of residence
Variables

- **Outcomes (all yes or no)**
  - HPV vaccine initiation (1 or more doses)
  - HPV vaccine completion (3 doses)
  - HPV vaccine follow-through (completion among those who initiate the series)

- **Main Independent Variable**
  - Appalachian residence (yes or no)

- **Covariates**
  - Demographics and health-related variables (awareness of HPV, HPV vaccine, etc.)
Data Analysis

- Logistic regression to determine if Appalachian residence was associated with three HPV vaccine outcomes
  - Controlled for covariates
- Examined temporal trends and differences by Appalachian subregion
- SAS Version 9.2
  - Applied sampling weights for complex design
  - Appropriate subpopulation methods
## Demographics

<table>
<thead>
<tr>
<th></th>
<th>Appalachian (n=1951)</th>
<th>Non-Appalachian (n=25468)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daughter Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 13-15</td>
<td>60%</td>
<td>61%</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>81%**</td>
<td>58%</td>
</tr>
<tr>
<td><strong>Mother Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 45+</td>
<td>39%**</td>
<td>46%</td>
</tr>
<tr>
<td>Some College or More</td>
<td>56%*</td>
<td>60%</td>
</tr>
<tr>
<td>Married</td>
<td>74%</td>
<td>73%</td>
</tr>
<tr>
<td><strong>Household Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than $75,000</td>
<td>30%**</td>
<td>40%</td>
</tr>
<tr>
<td>Rural (Non-MSA)</td>
<td>37%**</td>
<td>15%</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.001
## Health-Related Variables

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<th>Appalachian (n=1951)</th>
<th>Non-Appalachian (n=25468)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daughter Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visited Doctor in Last Year</td>
<td>85%</td>
<td>84%</td>
</tr>
<tr>
<td>Covered by Private Insurance</td>
<td>63%</td>
<td>64%</td>
</tr>
<tr>
<td><strong>Parent Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heard of HPV</td>
<td>84%</td>
<td>84%</td>
</tr>
<tr>
<td>Heard of HPV Vaccine</td>
<td>95%**</td>
<td>91%</td>
</tr>
<tr>
<td>Provider Recommendation for HPV Vaccine</td>
<td>56%</td>
<td>53%</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.001
HPV Vaccination: 2008-2010

- Initiation
  - Appalachia: 41% (n=1951)
  - Non-Appalachia: 44% (n=25468)

- Completion

- Follow-Through

Legend:
- Dark blue: Appalachia
- Pale blue: Non-Appalachia
HPV Vaccination: 2008-2010

Initiation

- Appalachia: 41% (n=1951)
- Non-Appalachia: 44% (n=25468)

Completion

- Appalachia: 28% (n=1951)
- Non-Appalachia: 25% (n=25468)

Follow-Through

- Appalachia: (n=1951)
- Non-Appalachia: (n=25468)
HPV Vaccination: 2008-2010

- Initiation: Appalachia (n=1951) 41% vs. Non-Appalachia (n=25468) 44%
- Completion: Appalachia (n=1951) 28% vs. Non-Appalachia (n=25468) 25%
- Follow-Through: Appalachia (n=1951) 68% vs. Non-Appalachia (n=25468) 58%
### HPV Vaccination: 2008-2010

#### Multivariate ORs and 95% CIs

<table>
<thead>
<tr>
<th></th>
<th>Initiation</th>
<th>Completion</th>
<th>Follow-Through</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appalachian</td>
<td>0.92 (0.79-1.07)</td>
<td>1.12 (0.95-1.32)</td>
<td>1.36 (1.07-1.72)*</td>
</tr>
<tr>
<td>Non-Appalachian</td>
<td>ref.</td>
<td>ref.</td>
<td>ref.</td>
</tr>
</tbody>
</table>

* *p<0.05, **p<0.001

Note. Multivariate ORs adjusted for demographic and health-related characteristics.
On the surface, Appalachia and non-Appalachia are somewhat similar. But, are there differences by time or place?
HPV Vaccination By Year

Followed Through Initiation

- Appalachia
- Non-Appalachia
Subregions - Initiation

Non-App: 44%
App: 41%

50%
39%
29%*
40%
36%*
Subregions - Completion

Non-App: 25%
App: 28%

38%*
25%
16%*
30%
20%*
Subregions – Follow-Through

Non-App: 58%
App: 68%*

76%*
63%
55%
76%*
55%
West Virginia

- HPV vaccination is lacking
  - Initiation=38%
  - Completion=23%
  - Follow-Through=61%

- Ranks in bottom half of Appalachian states for all outcomes
  - Similar to OH, KY, and TN
Conclusions

- First estimates of HPV vaccination among adolescent females in Appalachia
- On the surface, HPV vaccination in Appalachia is similar to non-Appalachia
  - Similar in terms of vaccine initiation and completion
  - Better follow-through
- Time trends have been pretty consistent across these three outcomes
Conclusions

- It makes a big difference where you live in Appalachia!
  - Northern and South Central subregions are promising areas
  - North Central, Central, and Southern subregions are more problematic areas

- So, what does this mean for cervical cancer (and maybe other HPV-related) disparities?
Conclusions

Cervical Cancer Incidence 1995-2004

HPV Vaccine Completion 2008-2010

Non-App: 25%
App: 28%
If this pattern continues, cervical cancer disparities will persist and maybe even worsen!
What Can We Do?

- Need programs to increase HPV vaccination in Appalachia
  - Focus on high-risk regions within Appalachia
  - OSU multilevel intervention (PI: Paskett)

- Ideal that multiple states partner with one another
  - Example: OH, WV, and KY
  - Contiguous states that have similar HPV-related problems (high cancer rates, low vaccination rates)
Acknowledgements

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Thomas Tucker (KY)

NIS Teen Vaccination Project
Mira Katz
Electra Paskett
Patricia Barnes (CDC)
Vijay Gambhir (CDC)

Grants
NCI: P50CA105632, P30CA016058, and U01CA114622
CDC: Cooperative agreement number U58/CCU000768)

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Thank you for your time!

Questions?