HPV Associated Cancers
It’s More Than Cervical Cancer

BCCCP/WiseWoman/MiCRC
Annual Conference
Friday May 10th
Grand Traverse Resort

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Topics to be Covered

- What is MCSP?
- HPV Associated Cancer Incidence and Trend
- Surveillance of Preinvasive Cervical Cancer
- HPV Prevalence in Cancer Tumor Tissue
- Strategy for Assessing Vaccine Impact
Twenty-Seven Years of Surveillance Data

- Covers the State of Michigan
- Population-based
- 1.3 million patients
- 1.5 million tumors
- Geocoded pop-based data
- Complete for 1985-2010
- Facilitated 115 research protocols
Collection Methods

- Passive Reporting
  - Quality Assurance Reviews
- Electronic or Paper Reports
  - Accept NAACCR formatted files
- Reports Initiated by Facilities
- Physicians contacted as needed
Information Collected

- Basic Identifiers
- Patient Demographics
- Site, Histology, Stage
- Method of Diagnosis
- Treatment Information
- Supplemental Information
  - Mortality Data – Cause and Occupation
  - Geocoding
Registry Uses

- Basic Statistics
  - Incidence/Mortality/Survival
- Cluster Investigations
- Cohort Studies
- Case Finding and Recruiting
HPV Associated Cancers*

- Uterine Cervix
- Vagina
- Penis
- Vulva
- Anal
- Specific Head and Neck Sites
  - Pharynx, oropharynx, tonsil, base of tongue


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HPV Associated Cancers
Michigan - 2010

- Cervix Uteri  344
- Vagina     44
- Vulva   170
- Anus     83
- Head & Neck  521
- Penis    43
Age-adjusted Pre-invasive Cervical Cancer Rates
Michigan, 1995-2010
Focus of 2013 Report to the Nation

HPV Vaccine

- Quadrivalent Vaccine Approved 6/2006
  - Females 9-26
    - Recommended for females 11-12

- Bivalent Vaccine Approved 10/2009
  - Females 9-26
    - Recommended for females 11-12

- Quadrivalent Vaccine Approved 10/2009
  - Males 9-26
    - Recommended for males 11-12
HPV Types Targeted

- Quadrivalent
  - 6, 11, 16, 18

- Bivalent
  - 16, 18

- 16 and 18 have cancer association

Vaccination Rates Creeping Up

- For 13-15 year old females in 2011
  - 55 percent w 1 or more shots
  - 32 percent complete 3 shot series
Surveillance of Cervical Lesions

Multi-state Collaboration
Supported by CDC
Preinvasive Cervical Cancer Data

- Available Population-based Data Very Limited
- Reportable across the Country until 1996.
  - Concerns over cost and classification problems
- Michigan Continued to Collect
- HPV Vaccine has Created a Need for Data
- Feasibility Study Proposed by CDC
  - Demonstration project to develop surveillance approach
  - Enlisted Michigan, Kentucky and Louisiana
  - Began operation for the 2009 incidence year
CDC Initiative

- Re-establish Surveillance of CIS
- Recruited Kentucky and Louisiana
- Demonstrate feasibility
- Promote Nationally
Develop Uniform Approach

- Develop a uniform case definition
- Agree on a standard data set
- Create diagnostic terms for case-finding
- Establish case-finding and reporting
- Agree on a standard approach to QA
  - Edit rules
  - Follow-back process
## Issues with Classification Systems

<table>
<thead>
<tr>
<th>Dysplasia System</th>
<th>CIN System</th>
<th>Bethesda System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Inflammatory or reactive atypia</td>
<td>Inflammatory or reactive atypia</td>
<td>Normal or ASCUS</td>
</tr>
<tr>
<td>Koilocytotic or condylomatous atypia</td>
<td>Koilocytotic or condylomatous atypia</td>
<td>Low-grade SIL</td>
</tr>
<tr>
<td>Mild dysplasia</td>
<td>CIN 1</td>
<td>Low-grade SIL</td>
</tr>
<tr>
<td>Moderate dysplasia</td>
<td>CIN 2</td>
<td>High-grade SIL</td>
</tr>
<tr>
<td>Severe dysplasia</td>
<td>CIN 3</td>
<td>High-grade SIL</td>
</tr>
<tr>
<td>Carcinoma in situ (CIS)</td>
<td>CIN 3</td>
<td>High-grade SIL</td>
</tr>
<tr>
<td>Invasive squamous carcinoma</td>
<td>Invasive squamous carcinoma</td>
<td>Invasive squamous carcinoma</td>
</tr>
</tbody>
</table>
# Case Definition

<table>
<thead>
<tr>
<th>Site (ICD-O-3)</th>
<th>C53.0 (endocervix), C53.1 (exocervix), C53.8 (overlapping lesions of cervix uteri) and C53.9 (cervix uteri)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavior</td>
<td>2 (in situ or noninvasive)</td>
</tr>
</tbody>
</table>
| Histology     | 8010/2 Carcinoma in situ, NOS  
8050/2 Papillary carcinoma in situ  
8052/2 Papillary squamous cell carcinoma, non-invasive  
8070/2 Squamous cell carcinoma in situ, NOS  
8071/2 Sq. cell carcinoma, keratinizing, NOS, in situ  
8072/2 Sq. cell carcinoma, lg. cell, non-ker., in situ  
8076/2 Sq. cell carc. in situ with question stromal invas.  
8077/2 Squamous intraepithelial neoplasia grade III  
8140/2 Adenocarcinoma in situ  
*Other histologies are acceptable, but only after careful review. |
| Pathologic Classification | CIN III, CIS, AIS, severe dysplasia |

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LAST Project
Lower Anogenital Squamous Terminology

- Released in January
- CAP and ASCCP effort
  - Address reliability/consistency issues
  - Improve information relative to management
- Cervical, Anal, Vulvar, Penile, Vaginal
- Material from Teresa Darragh, UCSF


http://www.asccp.org/PracticeManagement/LASTProject/tabid/10967/Default.aspx

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Spectrum of HPV Disease

Morphologic Continuum
Biology: Infection vs Precancer

Schematic Representation of SIL

<table>
<thead>
<tr>
<th></th>
<th>Low-grade squamous intraepithelial lesion (LSIL)</th>
<th>High-grade squamous intraepithelial lesion (HSIL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condyloma</td>
<td>CIN/AIN grade 1</td>
<td>CIN/AIN grade 2</td>
</tr>
<tr>
<td>Very mild to mild dysplasia</td>
<td>Moderate dysplasia</td>
<td>Severe dysplasia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In Situ carcinoma</td>
</tr>
</tbody>
</table>

Biology & Management

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Biomarkers: Further reduce diagnostic variation
Approaches Followed

- E-Path software installed in several pathology labs had to be updated
- Rapid Case Ascertainment
- Web Plus
- Direct reporting by hospitals/labs
# Results from Year 1 - 2009

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Kentucky</th>
<th>Louisiana</th>
<th>Michigan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytic Sample (Total)</strong></td>
<td>5537  100.0</td>
<td>1613  100.0</td>
<td>1255  100.0</td>
<td>2669  100.0</td>
</tr>
<tr>
<td><strong>Histology Terminology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AIS</td>
<td>214    3.9</td>
<td>52   3.2</td>
<td>24    1.9</td>
<td>138   5.2</td>
</tr>
<tr>
<td>CIN III</td>
<td>3971  71.7</td>
<td>916  56.8</td>
<td>917  73.1</td>
<td>2138  80.1</td>
</tr>
<tr>
<td>CIS</td>
<td>524    9.5</td>
<td>170  10.5</td>
<td>129  10.3</td>
<td>225   8.4</td>
</tr>
<tr>
<td>Severe dysplasia</td>
<td>828    15.0</td>
<td>475  29.4</td>
<td>185  14.7</td>
<td>168   6.3</td>
</tr>
</tbody>
</table>

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## Data by Race

<table>
<thead>
<tr>
<th>Race</th>
<th>Total</th>
<th>Kentucky</th>
<th>Louisiana</th>
<th>Michigan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td><strong>Analytic Sample (Total)</strong></td>
<td>5537</td>
<td>100.0</td>
<td>1613</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>3715</td>
<td>67.1</td>
<td>1301</td>
<td>80.7</td>
</tr>
<tr>
<td>Black</td>
<td>885</td>
<td>16.0</td>
<td>82</td>
<td>5.1</td>
</tr>
<tr>
<td>American Indian</td>
<td>14</td>
<td>0.3</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>36</td>
<td>0.7</td>
<td>4</td>
<td>0.2</td>
</tr>
<tr>
<td>Other</td>
<td>33</td>
<td>0.6</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Unknown</td>
<td>854</td>
<td>15.4</td>
<td>226</td>
<td>14.0</td>
</tr>
</tbody>
</table>

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## Data by Source

<table>
<thead>
<tr>
<th>Reporting Source</th>
<th>Total</th>
<th>Kentucky</th>
<th>Louisiana</th>
<th>Michigan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytic Sample (Total)</td>
<td>5537</td>
<td>100.0</td>
<td>1613</td>
<td>100.0</td>
</tr>
<tr>
<td>Hospital</td>
<td>1504</td>
<td>27.2</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Radiation or Medical Oncology Center</td>
<td>2</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Laboratory</td>
<td>3360</td>
<td>60.7</td>
<td>1613</td>
<td>100.0</td>
</tr>
<tr>
<td>Physician</td>
<td>670</td>
<td>12.1</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Other hospital or outpatient unit/surgery center</td>
<td>1</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>
## Assessment of Completeness

### Reported and Expected Cases and Incidence Rates of Pre-Invasive Cervical Lesions, by State

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Kentucky</th>
<th>Louisiana</th>
<th>Michigan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported Cases (January-December 2009)</td>
<td>5537</td>
<td>1613</td>
<td>1255</td>
<td>2669</td>
</tr>
<tr>
<td>Annual Incidence Rate*</td>
<td>0.00065</td>
<td>0.00083</td>
<td>0.00062</td>
<td>0.00059</td>
</tr>
<tr>
<td>Expected Cases Over 12 Months</td>
<td>5326</td>
<td>1228</td>
<td>1337</td>
<td>2763</td>
</tr>
<tr>
<td>Annual Incidence Rate*</td>
<td>0.00063</td>
<td>0.00063</td>
<td>0.00066</td>
<td>0.00061</td>
</tr>
<tr>
<td>Ratio of Reported/Expected Cases</td>
<td>1.04</td>
<td>1.31</td>
<td>0.94</td>
<td>0.97</td>
</tr>
</tbody>
</table>
Directions

- Continue surveillance
- Expand to other states
- Maintain a baseline to assess trends
- Adapt to changes in classification
Collaborators

- Won Silva, Jetty Alverson, Michelle Hulbert, Elaine Snyder – MCSP
- Joanne Whitlock, Ann Schwartz - DMCSS
- Debina Datta, Mona Saraiya, Meg Watson, Elaine Flagg – CDC
- Kentucky, Louisiana and Los Angeles Collaborators – Tom Tucker, Ed Peters and Dennis Deapen

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Monitoring the Impact of a Prophylactic HPV Vaccine on HPV Types in Cervical Cancer: Using Tissues from Central Cancer Registries
Project to Assess HPV Type

- Document HPV in Cancer Tissue
- Assess HPV Type
- Evaluate All HPV Associated Cancers
- Use Population-based Approach
- Collect Patient Demographics
Basics

- CDC Funded
- Florida, Kentucky, Louisiana and Michigan
- Tissue preparation alternatives
  - In facility or by state central lab
- Labs reimbursed for tissue prep
- HPV Detection and typing by CDC
- De-identified data sent to CDC with tissue
CRs Identify Eligible Cases, Create Random ID

Tissue Sample Request Form

Hospitals / Path Labs Prepare Tissue Samples

Linkage Documents maintained at the local Hospitals/Path Labs

Shipping Reports Sent to CDC HPV Lab and Battelle (only contain random CR ID and Specimen IDs)

Samples Shipping QA/QC

Tissue Samples Shipped to CDC (only Specimen IDs are used to identify samples)

CDC HPV Lab Confirms Receipt and Conducts HPV Typing Analysis

CRs prepare De-Identified Database (only random CR IDs are used to identify case information)

Submit Data Files to Battelle (only Specimen IDs are used)

Battelle Merges Data Files and Prepares Final Database (assigns Battelle random IDs to replace Specimen IDs)

Final De-Identified Database Provided to CDC

Exception: CR has obtained IRB approval to link the genotyping results to individual records in the CR database and requested the data with CR ID. Battelle will provide the genotyping results (individual CR only) with the CR ID to the requested CR.

*First Stage of De-Identification: Using Random CR IDs and Specimen IDs

*Second Stage of De-Identification: Using Battelle Random IDs

01-16-08
Monitoring the Impact of a Prophylactic HPV Vaccine on HPV Types in Cervical and Other HPV-associated Cancers: Using Tissues from Central Cancer Registries
Attachment 3
SOP 103: Sample Selection Procedures

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Michigan</th>
<th>Louisiana</th>
<th>Kentucky</th>
<th>Florida**</th>
<th>Total by State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix (invasive)</td>
<td>140</td>
<td>176</td>
<td>176</td>
<td>176</td>
<td>668</td>
</tr>
<tr>
<td>In Situ Cervical Cancer (Michigan only)</td>
<td>300</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>300</td>
</tr>
<tr>
<td>Vagina (invasive)</td>
<td>20</td>
<td>40</td>
<td>38</td>
<td>62</td>
<td>160</td>
</tr>
<tr>
<td>Vulva (invasive)</td>
<td>20</td>
<td>46</td>
<td>50</td>
<td>44</td>
<td>160</td>
</tr>
<tr>
<td>Penis (invasive)</td>
<td>20</td>
<td>40</td>
<td>50</td>
<td>44</td>
<td>160</td>
</tr>
<tr>
<td>Anus (invasive)*</td>
<td>20</td>
<td>50</td>
<td>47</td>
<td>44</td>
<td>161</td>
</tr>
<tr>
<td>Head &amp; Neck, HPV-Related*</td>
<td>180</td>
<td>194</td>
<td>194</td>
<td>224</td>
<td>792</td>
</tr>
</tbody>
</table>

* Including both male and female.
** Palm Beach, Broward and Dade counties.
Registry Role

- Select Cases for Inclusion
  - 2004 and 2005 cases
- Determine if Tissue Remains
- Trace Location of Tissue Block
- Negotiate Participation by Lab
  - Determine Reimbursement Rate
- Train Lab in Protocol
- Provide Lab with Specimen Information
- Arrange for Collection Kits to Lab
Michigan Lab Responsibilities

- Select Best Tissue Block
  - Representative of primary
  - Highest tumor to non-tumor ratio
  - Minimal necrosis
  - Best preservation
  - Sufficient residual tumor
Preparation of Each Block

- Clean Microtome
- Use New Microtome Blade for Each Block
- Cut six 5-um serial sections
  - Section 1 for slide 1 for confirmation
  - Sections 2 and 3 for tube 1 for PCR assay
  - Sections 4 and 5 for tube 2 for PCR assay
  - Section 6 for slide 2 for confirmation
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Preparing to Ship

- Report on site and behavior
- Report on specimen quality
- Insert material in zip lock per subject
- Place in insulated mailer
- Ship with supplied cool packs
- Tape transmittal form to mailer
- Ship Fed Ex

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# Overall Results

## Tissue Sample Summary by Cancer Site

*From 9/1/2003 to 10/5/2010*

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Florida</th>
<th>Kentucky</th>
<th>Louisiana</th>
<th>Michigan</th>
<th>Total CDC Received</th>
<th>Target Number</th>
<th>% of Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>178</td>
<td>181</td>
<td>108</td>
<td>116</td>
<td>583</td>
<td>668</td>
<td>87.3%</td>
</tr>
<tr>
<td>Anal</td>
<td>50</td>
<td>50</td>
<td>27</td>
<td>16</td>
<td>143</td>
<td>161</td>
<td>88.8%</td>
</tr>
<tr>
<td>Vaginal</td>
<td>15</td>
<td>15</td>
<td>16</td>
<td>15</td>
<td>61</td>
<td>160</td>
<td>38.1%</td>
</tr>
<tr>
<td>In situ-cervix</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>417</td>
<td>300</td>
<td>139.0%</td>
</tr>
<tr>
<td>Penile</td>
<td>30</td>
<td>15</td>
<td>13</td>
<td>16</td>
<td>74</td>
<td>160</td>
<td>46.3%</td>
</tr>
<tr>
<td>Vulvar</td>
<td>38</td>
<td>57</td>
<td>41</td>
<td>21</td>
<td>157</td>
<td>160</td>
<td>98.1%</td>
</tr>
<tr>
<td>H&amp;N HPV</td>
<td>151</td>
<td>129</td>
<td>123</td>
<td>168</td>
<td>571</td>
<td>792</td>
<td>72.1%</td>
</tr>
<tr>
<td><strong>Project Totals</strong></td>
<td><strong>462</strong></td>
<td><strong>447</strong></td>
<td><strong>328</strong></td>
<td><strong>769</strong></td>
<td><strong>2006</strong></td>
<td><strong>2401</strong></td>
<td><strong>83.5%</strong></td>
</tr>
</tbody>
</table>

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## Michigan Results

<table>
<thead>
<tr>
<th>Cancer Registry</th>
<th>Cancer Site</th>
<th>Kits Requested</th>
<th>Sample Submitted</th>
<th>CDC Received</th>
<th>Target Number</th>
<th>% of Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michigan</td>
<td></td>
<td>803</td>
<td>770</td>
<td>769</td>
<td>700</td>
<td>109.9%</td>
</tr>
<tr>
<td>Cervix</td>
<td></td>
<td>126</td>
<td>117</td>
<td>116</td>
<td>140</td>
<td>82.9%</td>
</tr>
<tr>
<td>Anal</td>
<td></td>
<td>19</td>
<td>16</td>
<td>16</td>
<td>20</td>
<td>80.0%</td>
</tr>
<tr>
<td>Vaginal</td>
<td></td>
<td>17</td>
<td>15</td>
<td>15</td>
<td>20</td>
<td>75.0%</td>
</tr>
<tr>
<td>In situ-cervix</td>
<td></td>
<td>428</td>
<td>418</td>
<td>417</td>
<td>300</td>
<td>139.0%</td>
</tr>
<tr>
<td>Penile</td>
<td></td>
<td>19</td>
<td>16</td>
<td>16</td>
<td>20</td>
<td>80.0%</td>
</tr>
<tr>
<td>Vulvar</td>
<td></td>
<td>21</td>
<td>21</td>
<td>21</td>
<td>20</td>
<td>105.0%</td>
</tr>
<tr>
<td>H&amp;N HPV</td>
<td></td>
<td>173</td>
<td>167</td>
<td>168</td>
<td>180</td>
<td>93.3%</td>
</tr>
</tbody>
</table>

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Added Iowa, Hawaii, Los Angeles

- Leverage existing tissue repositories
- Not true population-based
- Roughly doubled samples
- Expanded to more in situ cases
Initial Results

- Retrieved 2796 cases from 5,084 identified
- Adequate samples for 2,698
- HPV detected in 78% of all samples
- Current vaccine prevalence was 57%
- Cancer type affects prevalence
### HPV Prevalence by Type and Percent HPV 16 or 18

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Cases</th>
<th>HPV Prevalence %</th>
<th>Current Vaccine %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penis</td>
<td>79</td>
<td>63%</td>
<td>48%</td>
</tr>
<tr>
<td>Vulva</td>
<td>176</td>
<td>69%</td>
<td>49%</td>
</tr>
<tr>
<td>Vagina</td>
<td>60</td>
<td>75%</td>
<td>55%</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>574</td>
<td>72%</td>
<td>62%</td>
</tr>
<tr>
<td>Cervix (invasive)</td>
<td>777</td>
<td>91%</td>
<td>66%</td>
</tr>
<tr>
<td>Anus</td>
<td>146</td>
<td>91%</td>
<td>79%</td>
</tr>
<tr>
<td>Other Head and Neck</td>
<td>309</td>
<td>26%</td>
<td>14%</td>
</tr>
<tr>
<td>CIS</td>
<td>481</td>
<td>99%</td>
<td>60%</td>
</tr>
<tr>
<td>VIS</td>
<td>68</td>
<td>97%</td>
<td>81%</td>
</tr>
</tbody>
</table>

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Collaborators

- Mona Saraiya, Deblina Datta, Meg Watson, Elizabeth R. Unger  - CDC
- Won Silva, Jetty Alverson, Michelle Hulbert  - MCSP
- Lana Ashley MDCH Epidemiology
- Dr. Samuel Hirsch – St Joseph Mercy AA
- Colleagues in Kentucky, Florida, Louisiana, Los Angeles, Iowa and Hawaii
Monitoring the Impact HPV Vaccines on Precancerous Cervical Lesions

A Feasibility Study
Collaborators

- Rachel Potter and Robert Swanson
  - Michigan Care Improvement Registry
- Deblina Datta
  - STD Prevention, CDC
- Mona Saraiya
  - Cancer Prevention and Control, CDC
- Elaine Flagg
  - STD Prevention, CDC
- Benita O’Colmain
  - Macro International

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Assess Feasibility of Measuring HPV Vaccine Impact

- CDC Approached Michigan with an Idea
  - Can existing Michigan resources be leveraged to assess early impact of HPV vaccinations?

- Unique Situation in Michigan
  - Existing surveillance of pre-invasive cervical lesions
  - Established statewide vaccine registry

- Preinvasive Cervical Lesions of Special Interest
  - Would be evident ahead of any decline in invasive disease

- Established a Collaborative Project
  - Objective was to gauge feasibility
Strategy

- Monitor Incidence of Pre-invasive Cervical Lesions
- Monitor HPV Vaccinations
- Assess Precancerous Lesions Relative to Vaccine Use
  - Link cases to immunization registry
  - Identify vaccination status
- Establish a Continuous Resident Cohort
  - Within the cohort compare
    - Vaccination history
    - Prevalence of pre-invasive cervical lesions
- Compare Vaccination Status for Continuous Residents
  - Women with and without pre-invasive cervical lesions
Resources Available

- **Michigan Cancer Surveillance System**
  - Statewide registry since 1985
  - Includes pre-invasive cervical lesions

- **Michigan Care Improvement Registry**
  - Vaccination registry established in 1998
  - Includes information of HPV vaccinations

- **Michigan Birth Registry**
  - Statewide registry of all live births
What is Practical

- Link of Pre-invasive Cervical Cases to Births
- Link Vaccine Registry to Births
- Crosslink Registries
- Assess Residence of Females in Vaccine Registry
Data Used in Analysis

- Pre-invasive Cervical Cases in 2006
  - 1,358 in situ cases

- Vaccine Data on Women and Girls
  - 1,274,316 females aged 10-30
    - As of 12/31/2006

- Live Birth Files
  - 1,439,859 live born Michigan females
    - Birth year cohorts 1976 through 1996
Tools

- LinkPlus 2.0
- Accurint On-Line Locator Service
- Willing Staff to Validate Results
Birth Link Success Percentages by Birth Year for Pre-Invasive Cervical Lesion Cases and Vaccine Registry Cases

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Use of Accurint to Assess Residence

- LexisNexis Company
- Built on Collection of Interlinked Databases
  - Corporate, Financial, Governmental
  - Public and Private

- Widely Used Service
  - Background Checks
  - Credit Checks
  - Work Histories
  - Locator Service

- Can Provide Address Histories on Individuals

- http://www.accurint.com/

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Residence Histories

- **Selected Sample Cases**
  - Sampled matched birth to vaccine registry cases

- **Sample cases randomly selected**
  - Selected 810 cases from each of 7 birth intervals
  - Selected a Total of 5,670 cases Generating 21,632 Records
    - Child, Mother with Married, Mother with Maiden, Father

- **Prepare File of Mother, Father and Child**

- **Submit to Accurint**
Females born between 1976 and 1996 in the Michigan Care Improvement Registry (MCIR): 1,274,282

Cervical carcinoma *in situ* cases diagnosed in 2006 in the Michigan Cancer Surveillance Program (MCSP): 1,358

Females born between 1976 and 1996 in the Live Birth File (LBF)

863,880 confirmed MCIR-LBF matches

830 confirmed MCSP-LBF linkages

452 MCSP-LBF matches merged into matching MCIR-LBF records

Exclude 378 MCSP-LBF matches not also matching the MCIR-LBF records

Cohort: 863,880 confirmed MCIR-LBF linkages, 452 with cancer diagnosis data from the MCSP

Analytical file: 5,670 stratified random sample of cohort for Accurint search
Results of Accurint Link

- 98.4% submitted cases with 1 or more links
  - 14.1% Percent using Child’s Name
  - 92.4% Percent of Mother’s Maiden Name
  - 96.0% Percent of Mother’s “Current” Name
  - 94.5% Percent of Father’s Name
    - 4,633 of 5670 births had fathers information
Percent with One or More Accurint Link
by Birth Year Interval

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### Residence History Detail

<table>
<thead>
<tr>
<th>Birth Year Interval</th>
<th>Total</th>
<th>One or More</th>
<th>No match</th>
<th>Any Michigan</th>
<th>Any Last not Michigan</th>
<th>Both MI and Not MI</th>
<th>All Michigan</th>
<th>% of Linked Always Michigan</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Years</td>
<td>5670</td>
<td>5578</td>
<td>92</td>
<td>5251</td>
<td>788</td>
<td>461</td>
<td>4790</td>
<td>85.9</td>
</tr>
<tr>
<td>1976-78</td>
<td>809</td>
<td>780</td>
<td>29</td>
<td>739</td>
<td>109</td>
<td>68</td>
<td>671</td>
<td>86.0</td>
</tr>
<tr>
<td>1979-81</td>
<td>809</td>
<td>786</td>
<td>23</td>
<td>753</td>
<td>122</td>
<td>89</td>
<td>664</td>
<td>84.5</td>
</tr>
<tr>
<td>1982-84</td>
<td>811</td>
<td>800</td>
<td>11</td>
<td>759</td>
<td>103</td>
<td>62</td>
<td>697</td>
<td>87.1</td>
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<tr>
<td>1985-87</td>
<td>812</td>
<td>796</td>
<td>16</td>
<td>755</td>
<td>100</td>
<td>59</td>
<td>696</td>
<td>87.4</td>
</tr>
<tr>
<td>1988-90</td>
<td>810</td>
<td>803</td>
<td>7</td>
<td>756</td>
<td>116</td>
<td>69</td>
<td>687</td>
<td>84.8</td>
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<tr>
<td>1991-93</td>
<td>810</td>
<td>806</td>
<td>4</td>
<td>757</td>
<td>101</td>
<td>52</td>
<td>705</td>
<td>87.5</td>
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<tr>
<td>1994-96</td>
<td>809</td>
<td>807</td>
<td>2</td>
<td>732</td>
<td>137</td>
<td>62</td>
<td>670</td>
<td>83.0</td>
</tr>
</tbody>
</table>
Results

- Able to Identify a Resident Cohort
- Able to Merge
  - Vaccination status
  - Cancer status
- Able to Calculate Relative Risk

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Feasibility Assessment

- Appears feasible and economical
- Need to:
  - Assess unlinked cases
  - Assess continuous residence reliability
- Could be Done Statewide or on a Sample
- Resources
  - Statewide immunization registry since mid 90s
  - Statewide surveillance of preinvasive cervical lesions
  - Ability to link to live births
  - Access to Accurint
Australian Study

- Vaccination Status
  - Coverage of 85/81/75% for 12 year olds
  - 82/77/70% in 15-17 year olds

- High grade cervical abnormalities
  - Women <18 years
    - 0.85% in 2006 to 0.22% in 2009
  - Women 18-20 years
    - 1.2% in 2006 to 0.99% in 2009

http://www.vccr.org/stats.html
DOI: 10.1016/S0140-6736(11)60551-5)
More Good News from “Down Under”

- Incidence of genital warts way down
  - 90% in adolescent/teen girls
  - 70% in women 21 to 30
  - 50-80% decline in hetero boys and young men

- Barton S, O'Mahony C "HPV vaccination -- Reaping the rewards of the appliance of science" BMJ 2013; DOI: 10.1136/bmj.f2184.
HPV Vaccine Coverage by Birth Year Cohort
Michigan Resident Females in Michigan Immunization Registry

Percent of Resident Females

Age on June 30, 2012

10 11 12 13 14 15 16 17 18 19 20

1 or more shots
2 or more shots
3 or more shots

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When will any impact be detectable?

<table>
<thead>
<tr>
<th>Birth Year/Age in 2012</th>
<th>Resident Cases</th>
<th>Vaccination Rate as a Percent</th>
<th>Vaccinated Resident Cases</th>
<th>Observed Unvaccinated Preinvasion Cervical Lesion Rate</th>
<th>Expected Cervical Lesions</th>
<th>Expected Lesions in Vaccinated</th>
<th>Cumulative Cervical Lesions</th>
<th>Cumulative Vaccinated Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997/15</td>
<td>64000</td>
<td>34.6</td>
<td>22136</td>
<td>0.5</td>
<td>3.2</td>
<td>1.1</td>
<td>3.2</td>
<td>1.1</td>
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<td>1996/16</td>
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<td>31.0</td>
<td>20076</td>
<td>1.1</td>
<td>7.1</td>
<td>2.2</td>
<td>10.3</td>
<td>3.3</td>
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<tr>
<td>1995/17</td>
<td>64984</td>
<td>22.5</td>
<td>14627</td>
<td>3.1</td>
<td>20.1</td>
<td>4.5</td>
<td>30.5</td>
<td>7.8</td>
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<tr>
<td>1994/18</td>
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<td>12.9</td>
<td>8594</td>
<td>5.9</td>
<td>39.2</td>
<td>5.1</td>
<td>59.4</td>
<td>12.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Birth Year/Age in 2013</th>
<th>Resident Cases</th>
<th>Vaccination Rate as a Percent</th>
<th>Vaccinated Resident Cases</th>
<th>Observed Unvaccinated Preinvasion Cervical Lesion Rate</th>
<th>Expected Cervical Lesions</th>
<th>Expected Lesions in Vaccinated</th>
<th>Cumulative Cervical Lesions</th>
<th>Cumulative Vaccinated Lesions</th>
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<tbody>
<tr>
<td>1998/15</td>
<td>64000</td>
<td>36.8</td>
<td>23567</td>
<td>0.5</td>
<td>3.2</td>
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<td>1997/16</td>
<td>64000</td>
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<td>1996/17</td>
<td>64686</td>
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<td>20076</td>
<td>3.1</td>
<td>20.1</td>
<td>6.2</td>
<td>30.3</td>
<td>9.8</td>
</tr>
<tr>
<td>1995/18</td>
<td>64984</td>
<td>22.5</td>
<td>14627</td>
<td>5.9</td>
<td>38.3</td>
<td>8.6</td>
<td>58.4</td>
<td>18.5</td>
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<tr>
<td>1994/19</td>
<td>66524</td>
<td>12.9</td>
<td>8594</td>
<td>10.2</td>
<td>67.9</td>
<td>8.8</td>
<td>126.2</td>
<td>27.2</td>
</tr>
</tbody>
</table>

≈ 50% Decline Detectable using 2012 Incidence
≈ 40% Decline Detectable using 2013 Incidence
assuming similar incidence and vaccination rates by age

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Contact Information

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