Reduction in HPV-Associated High Grade Cervical Lesion Incidence in Connecticut, 2008-14: Evidence for Herd Immunity

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Background

• Annually responsible for ~12,000 cases/yr of cervical cancer and >200,000 cases of high grade cervical cancer precursor lesions (CIN2+)

• CIN2+ (and cervical cancer) became vaccine preventable in 2006
  – HPV vaccine recommended for girls 11-12 yrs in 3-dose series
  – Catch-up for women up to 26 yrs
  – >95% effective in preventing CIN2+ (cervical interepithelial neoplasia grades 2 and higher, adenocarcinoma in situ)

Surveillance – HPV IMPACT

• In 2008, CDC STD staff and five EIP sites (CA, CT, OR, TN, NY) established active, population-based surveillance for CIN2+
  – Pathology-laboratories
  – In CT, CIN 2+ made reportable statewide

Study Objectives

• Determine trends in CIN 2+ incidence in Connecticut, 2008 through 2014

• Compare observed to expected changes in incidence in 21-24 year olds
**Methods 1**

- Use deduplicated cases assigned to the year in which their initial diagnosis occurred.
- Determine age & age-group specific incidence rates using annual population estimates (US Census).
- Compared observed to maximum expected decrease through 2014 in 21-24 year olds.
  - 21 is youngest age for routine PAP screening.
  - 21-24 year olds in 2014 were 13-16 years old in 2006, group most likely to be HPV-infection naïve when vaccinated.

**Maximum Expected Decrease 21-24 yo, CT**

\[
\text{Max expected decrease} = \left( \text{max. } \% \text{ of CIN2+ that are vaccine-preventable} \right) \times \left( \text{est. max. percentage vaccinated in age group} \right)
\]

- % CIN2+ vaccine-preventable = \([100\% \text{ types } 16/18 + 21\% \text{ other HPV types}] = 54.3\% * + 9.6\% ** = 63.9\%*
- % vaccinated = 66\% ***

Max expected decrease = 42.2\%  

*Hariri. Cancer Epidemiol Biomarkers Prev 2015;24:393-399  
***NIS Teen 2008-2011.

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**Rates of CIN2+ in Women 21-39 y.o. CT, 2008-2014**

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate per 100,000</th>
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<tbody>
<tr>
<td>2008</td>
<td>600</td>
</tr>
<tr>
<td>2010</td>
<td>500</td>
</tr>
<tr>
<td>2012</td>
<td>400</td>
</tr>
<tr>
<td>2014</td>
<td>300</td>
</tr>
</tbody>
</table>

-21.0% decrease

**Rates of CIN2+ by Age Group Women 21-39 y.o., CT, 2008-2014**

- 21-24: -11.6% decrease
- 25-29: -57.1% decrease

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* Frequent updates or additional information needed for specific references.
**Hypotheses**

- Cross-protection for non-vaccine strains
- Under-reporting in 2014 relative to 2008
- Reduced rates of detection of CIN2+ due to changes in PAP screening recommendations in 2012
- Herd immunity

**Observed vs. Maximum Expected Decrease in CIN2+ in 21-24 year olds**

[max. % cases potentially preventable: 63.9%] x [max % vaccinated: 66%] = 42.2% (314 cases*)

Actual decrease = 57.1% (425 cases*), p=0.00004

Relative actual to expected decrease: 1.36 [95% CI 1.17-1.57]

* Using 2008 denominator and baseline 744 cases

**Conclusions**

- There has been a progressive decrease in CIN2+ diagnoses, mostly since 2011.
- Vaccination rates may be high enough in those who were 13-16 years (now 21-24) when vaccine licensed to reduce the probability of HPV exposure in the unvaccinated, leading to herd immunity.
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Limitations

• Don’t know what HPV types responsible for the changes observed – changes in behavior could account for some of the decrease.

• Percentage of CIN2+ prevented in 21-22 yo already at estimated maximum – suggests some parameters could be off.

• Estimate of % of CIN+ that are vaccine types were from EIP data collected 2008-2012 – possible underestimate of % CIN2+ preventable.
Percentages of CIN2+ in 21-24 yo unvaccinated women that are Types 16/18 and Types with Possible Cross-protection, 5 HPV IMPACT sites, 2008-11*

- 54.3% Types 16,18
- 9.6% X-protection
- Other types

Up to 63.9% preventable with bi-valent vaccine


Percentage of 21-24 y.o. vaccinated* with >1 HPV dose by age 17 years, CT

* Based on NIS Teen 2008-11

* Ages in 2014 (yrs)

Percentage

- 59% 21
- 66% 22
- 59% 23
- 59% 24
- 66% 21-24 yrs

* Point estimate  95% UL

59% 66%