The Future of Cervical Cancer Prevention

John T. Schiller, Ph.D.
National Cancer Institute, NIH

The Promise and Problems
Disclaimer

The opinions expressed are my own and don’t necessarily reflect those of the NCI.
We Have the Essential Tools

• The knowledge that virtually all cervical cancer are caused by oncogenic HPV infection.

• Vaccines for primary prevention of HPV infection.

• Screening for secondary prevention by diagnosis and treatment of precancerous lesions.

Worldwide, cervical cancer remains a leading cause of cancer deaths in women.
Vaccination and Screening Are Complementary, Targeting Different Stages in HPV Carcinogenesis

<table>
<thead>
<tr>
<th>Age</th>
<th>Rate</th>
<th>Screening Diagnoses</th>
<th>Vaccine Prevents</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 y.o.</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>30 y.o.</td>
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<td></td>
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<tr>
<td>45 y.o.</td>
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</tbody>
</table>
Performance of HPV Vaccines in Clinical Trials

Safety

• Low grade transient injection site reactions common.
• Systemic reactions mild and self-limiting.
• No pattern of serious adverse events, in trials or post-licensure that would suggest a causal relationship.

Efficacy

• Virtually 100% protection from precancer caused by incident HPV16/18 infections for Ceravirx and Garasil, and HPV31/33/45/52/58 for Gardasil-9.
• Limited protection against infections by other types.
• No effect on preexisting infections or lesions.
Effectiveness: Reduction in Cervical Precancer by Gardasil in Australia

So What’s the Problem?

Implementation and Utilization

Opportunities for:
• Advocacy
• Implementation Science – use what we have
• Translational Science – lower cost facilitate uptake
Trends in U.S. Vaccination Rates: Ages 13-17 Yrs

Abbreviations: Tdap = tetanus, diphtheria, acellular pertussis vaccine; MenACWY = meningococcal conjugate vaccine; HPV-1 = human papillomavirus vaccine, ≥1 dose; HPV-3 = human papillomavirus, ≥3 doses.

* Tdap and MenACWY vaccination recommendations were published in March and October 2006, respectively.
† HPV vaccination recommendations were published in March 2007.
Variable Uptake of HPV Vaccine
(2012 data for girls)

United States: 54%
France: 33%
United Kingdom: 33%
Australia: 33%
“HPV vaccination represents a rare opportunity to prevent many cases of cancer that is tragically underused. As national leaders in cancer research and clinical care, we are compelled to jointly issue this call to action.”
Increasing Vaccine Uptake

• Convince GPs and Pediatricians to more strongly recommend the vaccines. Monitor their vaccination rates.

• Overcome parental hesitancy. Stress cancer prevention and better response in 9-14 year olds.

• Counter misinformation campaigns by anti-vaccine groups.

• Promote vaccine distribution in pharmacies and schools.

• Support a two dose schedule for <15 year olds.
A Shift to an HPV-Based Cervical Cancer Prevention Strategy

Historically: Pap Smears/Cytology

Future?: Vaccinate

HPV DNA Test 1
HPV DNA Test 2
HPV DNA Test 3

Thanks to Mark Schiffman and Phil Castle, NCI
Cervical Cancer Screening Issues

Current Options:

• Pap: 3 yr interval in 21 yo+
• Pap/HPV DNA co-testing: 5 yr interval in 30 yo+ (2011)
• HPV DNA primary screen: at least 3 yr interval in 25 yo+.  
  FDA approved 2014, U.S. guidance published 2015

Current Issues:

• Educate women about their options.
• Assure that vaccinated women continue screened.
• Increase coverage – self sampling.
• Discouraging over screening.
Screening Accounts For Most of the Direct Costs of HPV Interventions in the U.S.

Annual direct medical cost burden of preventing and treating HPV-associated diseases

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cost- Billion $</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>8.0</td>
<td>100%</td>
</tr>
<tr>
<td>Cx Ca Screening</td>
<td>6.6</td>
<td>82.3%</td>
</tr>
<tr>
<td>Cancer Tx</td>
<td>1.0</td>
<td>12.0%</td>
</tr>
<tr>
<td>Cx Ca Tx</td>
<td>0.4</td>
<td>5.0%</td>
</tr>
<tr>
<td>Oropharyn Ca Tx</td>
<td>0.3</td>
<td>3.6%</td>
</tr>
<tr>
<td>Genital Warts</td>
<td>0.3</td>
<td>3.6%</td>
</tr>
<tr>
<td>RRP</td>
<td>0.2</td>
<td>2.1%</td>
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Prevention of Cervical Cancer: What Next?

• Will one dose of vaccine be enough for protection? Post-hoc analysis of NCI Costa Rica trial supportive.

• What is the optimal cervical cancer screen strategy for vaccinated vs unvaccinated women? Herd Immunity?

• How do we manage women diagnosed with oncogenic HPV infection? Can suitable treatments be devised?

• Cervical cancer prevention for low resource settings:
  - Lower cost vaccines and better implementation.
  - Effective point of care screening and treatment.