Primary HPV Screening – Current State of the Science - USA

Thomas C. Wright, Jr. MD
Professor Emeritus Columbia University, New York
Pathologist, Enzo Clinical Laboratories, Farmingdale, NY

Financial Disclosure: Dr. Wright is a consultant to Roche and BD Diagnostics
Disclosures

- Dr. Wright is a consultant and study pathologist for Roche and BD Diagnostics and receives payment for his services.

- Dr. Wright is a speaker for Roche and BD Diagnostics and receives payment for his services.
In April 2014 the FDA approved the use of the cobas HPV Test for primary cervical cancer screening.

Approval included a specific management algorithm.

Can begin screening with HPV at age 25 years.
Cohort of 42,209 women >25 years from US

Had gynecological exam, ThinPrep cytology test, HPV testing (and genotyping)

All HPV (+) and/or cytology (+); and a subset of hrHPV (-) / WNL underwent colposcopy

Patients with initial colposcopy were followed for 3 yrs and had exit colposcopy (n=4063)

Total of 240 CIN 2 and 347 CIN 3 lesions

Wright et al. (2015) Gynecol Oncol
ATHENA: 3 Year CIR of CIN2+ or CIN3+
Stratified by screening test result at baseline

<table>
<thead>
<tr>
<th>Test result</th>
<th>CIN2+</th>
<th>CIN3+</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Cytology</em> (-)</td>
<td>1.7 (1.2-2.2)</td>
<td>0.8 (0.5-1.1)</td>
</tr>
<tr>
<td><em>HPV</em> (-)</td>
<td>0.9 (0.5-1.5)</td>
<td>0.3 (0.1-0.7)</td>
</tr>
<tr>
<td><em>Cytology &amp; HPV</em> (-)</td>
<td>0.9 (0.4-1.4)</td>
<td>0.3 (0.1-0.6)</td>
</tr>
<tr>
<td><em>Cytology</em> (+)</td>
<td>14.0 (12.5-15.5)</td>
<td>9.2 (7.9-10.5)</td>
</tr>
<tr>
<td><em>HPV</em> (+)</td>
<td>15.5 (14.3-16.8)</td>
<td>7.5 (6.7-8.3)</td>
</tr>
</tbody>
</table>

Wright *et al.* 2015  Gynecol Oncol
Primary HPV Screening - ≥25 yrs
HPV with 16/18 Genotyping and Reflex Cytology

HPV Testing

Routine screening
HPV−

12 other hrHPV+

HPV16/18+

Cytology
NILM
≥ ASC-US

Follow up in 12 months

COLPOSCOPY

Wright et al. (2015) Gynecol Oncol
## Comparison of strategies in ≥25 years

**Tradeoffs between CIN3+ detected and colposcopy**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Screening Tests</th>
<th>CIN3+ Baseline</th>
<th>Total CIN3+</th>
<th>Colpos</th>
<th>Colpos to detect 1x CIN3+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology only</td>
<td>45,166</td>
<td>143</td>
<td>179</td>
<td>1,934</td>
<td>10.8</td>
</tr>
<tr>
<td>Hybrid Strategy*</td>
<td>82,994</td>
<td>143</td>
<td>240</td>
<td>3,097</td>
<td>12.9</td>
</tr>
<tr>
<td>HPV Primary</td>
<td>52,651</td>
<td>197</td>
<td>294</td>
<td>3,769</td>
<td>12.8</td>
</tr>
</tbody>
</table>

*Cytology for women ≤30 yrs and cotesting (without genotyping) for women 30 yrs and older

Wright, T.C. *et al.* (2015) Gyn Oncol

Crude estimates in women 25 years and older
Total # women with ≥CIN3 = 347
Key Findings:

- A negative hrHPV test provides greater reassurance of low CIN3+ risk than a negative cytology result.

- Because of equivalent or superior effectiveness, primary hrHPV screening can be considered an alternative to current US cytology-based cervical cancer screening methods.

- Based on limited data, triage of hrHPV (+) women using combination of 16/18 genotyping and reflex cytology appears reasonable.
2015 Interim Guidance - HPV Primary Screening: ASCCP and SGO

Huh, W. et al. (2015) Obst Gynecol

Diagram:
- Primary HPV Screening
  - 12 other hrHPV +
    - Type 16/18 Positive
      - Colposcopy
    - Cytology
      - ≥ASC-US
      - NILM
    - Follow up in 12 months
  - Negative
    - Routine Screening
Other Interim Guidance

- Re-screening after a negative primary hrHPV screen should occur *no sooner* than every 3 years
- Primary hrHPV screening should not be initiated before 25 years of age
- Cytology alone and cotesting remain the screening options specifically recommended in major guidelines

Key Findings:

- If screening with primary HPV testing is used, it should be performed as per the ASCCP and SGO interim guidance.
- Screening should stop at 65 yrs if negative screening history.
- Should not be used in women who no longer have a cervix.
- Cotesting is reasonable to perform at 1 yr in HPV (+) women with negative genotyping and cytology.
- Only use the FDA-approved test.
## Screening Women 25-29 Years

**Prevalence of hrHPV by age group - ATHENA**

<table>
<thead>
<tr>
<th>Age Group, years</th>
<th>Abnl Pap</th>
<th>hrHPV</th>
<th>16</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-24</td>
<td>21.5%</td>
<td>9.6%</td>
<td>5.3%</td>
<td>1.6%</td>
</tr>
<tr>
<td>25-29</td>
<td></td>
<td></td>
<td>5.3%</td>
<td>1.6%</td>
</tr>
<tr>
<td>30-39</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prevalence of CIN 3+ by Age
Results from ATHENA and PALMS

More CIN3+ disease in women aged 25 to 29 years than in women aged ≥ 40 years

Aged 25 to 29: n = 6767 (ATHENA) and 3373 (PALMS).

Why Not Cytology for Women 25 - 29 Yrs?
Results From ATHENA

More than half of the CIN3+ cases in the 25 - 29 age group had false-negative cytology.
HPV for Primary Screening
How commonly is it being used in the U.S.?

• Adoption to date has been very slow

• There are a number of possible reasons

  No one group / agency has decision-making power on how to screen and the decision is left up to individual clinicians

  Many clinicians and patients are comfortable with cytology and do not see a reason to stop using it

  HPV primary screening not yet endorsed by USPSTF – with Affordable Care Act this is very important