**Why Test for HPV?**

Human papillomavirus (HPV) is the leading cause of cervical cancer. According to the CDC, approximately 80% of people will get an HPV infection in their life.\(^1\) HPV can also cause cancers of the vagina, vulva, penis, anus, rectum and oropharynx.\(^2\) The American Cancer Society reports that more than half of the women in the United States who get cervical cancer were never screened or were rarely screened.\(^3\)

**What is the difference between HPV co-testing and HPV reflex testing?**

<table>
<thead>
<tr>
<th>Co-test</th>
<th>Reflex</th>
<th>HPV alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical cytology plus the HPV co-test are performed on the same date of service. The result of the HPV test is reported regardless if the Pap has a positive or negative result.</td>
<td>Cervical cytology with reflex HPV testing means if the result of the Pap is ASC-US, then the HPV sample is run by the laboratory. Therefore, the HPV test is dependent on the result of the Pap.</td>
<td>Not recommended in most clinical settings.</td>
</tr>
</tbody>
</table>

Definitions: ASC-US = atypical squamous cells, undetermined significance

**What are the recommendations?\(^4\)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Cervical cytology (Pap)</th>
<th>High-risk HPV testing</th>
<th>Example lab orders</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 21 years</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>N/A</td>
</tr>
</tbody>
</table>
| 21-29 years | Cervical cytology alone, every 3 years | HPV reflex OK if result is ASC-US | • Pap alone  
  • Pap, Rfx high-risk mRNA if ASC-US |
| 30-65 years | • Cervical cytology every 5 years with HPV co-testing (preferred method)  
  • Cervical cytology alone every 3 years (acceptable method) | HPV co-testing (preferred method) | • Pap and high-risk HPV mRNA  
  • HPV genotyping 16, 18/45 (when Pap is normal and HPV is detected) |
| 66+ years | Discontinue if patient has history of adequate negative results defined as 3 consecutive negative cervical cytology results, or 2 consecutive negative co-tests within last 10 years with most recent test in the last 5 years, and no history of CIN2 or higher.  
If patient has positive history of CIN2, CIN3 or adenocarcinoma in situ, continue screening for up to 20 years, even if the patient is older than 65 years of age. | | See above |

Definitions:
- CIN = Cervical intraepithelial neoplasia
- Rfx = reflex

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2. [https://www.cdc.gov/cancer/hpv](https://www.cdc.gov/cancer/hpv)
4. Screening guidelines for the general population (healthy, low-risk patients) consistent with American College of Obstetricians and Gynecologists (ACOG), American Cancer Society, American Society for Colposcopy and Cervical Pathology (ASCCP), and American Society for Clinical Pathology.

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[https://mediproviders.anthem.com/ca](https://mediproviders.anthem.com/ca)
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HPV testing is recommended regardless of prior HPV immunization status. HPV testing should only be performed to detect high-risk HPV.\(^5\)

For management of abnormal cervical cancer screening results, refer to ACOG and ASCCP guidelines.

**Benefit of HPV co-testing for ages 30 to 65**
Co-testing is shown to have better detection of adenocarcinoma of the cervix than cervical cytology alone.\(^6\) HPV co-testing is shown to have higher sensitivity to detect CIN3 compared to cervical cytology alone.\(^7\) According to ACOG, by completing co-testing every five years, evidence has shown lower rates of cancer with less screening and fewer follow-up colposcopy procedures.

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