



## NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

### SCREENING FOR CERVICAL CANCER

#### Guidelines

1. **Kaiser Permanente Care Management Institute (KPCMI).** [Cervical cancer screening guideline: October 2006](#). Oakland (CA): Kaiser Permanente Care Management Institute; 2006 Oct. 124 p. [199 references]
2. **Program in Evidence-based Care (PEBC).** [Cervical screening](#). Toronto (ON): Cancer Care Ontario (CCO); 2005 May 20. 39 p. [74 references]
3. **University of Michigan Health System (UMHS).** [Adult preventive health care: cancer screening](#). Ann Arbor (MI): University of Michigan Health System; 2004 May. 12 p. [4 references]

#### INTRODUCTION

A direct comparison of Kaiser Permanente Care Management Institute (KPCMI), Program in Evidence-based Care (PEBC), and University of Michigan Health System (UMHS) recommendations for cervical cancer screening is provided in the tables below. The PEBC guideline is broader in scope than the others. In addition to general screening recommendations, PEBC includes recommendations for screening women with special circumstances (immunocompromised or HIV positive women [KPCMI also provides recommendations for this population], pregnant women, and women who have sex with women) and for managing women with abnormal cytology. All of the guidelines consider the role of new screening technologies, such as liquid-based Pap cytology and HPV testing.

- [Table 1](#) provides a quick-view glance at the primary interventions considered by each group.
- [Table 2](#) provides a comparison of the scope of the guidelines.
- [Table 3](#) provides a more detailed comparison of the specific recommendations offered by each group for the topics under consideration in this synthesis, including:
  - [Whom to Screen](#)
  - [Screening after Hysterectomy](#)
  - [Screening Modality and Frequency](#)
  - [Patient Education/Counseling](#)
- [Table 4](#) lists the potential benefits and harms associated with the implementation of each guideline.
- [Table 5](#) presents the rating schemes used to rate the level of evidence and/or the strength of the recommendations.

Following the content comparison tables, the [areas of agreement](#) and [areas of differences](#) among the guidelines are identified.

Abbreviations used in the text and tables follow:

- ACS, American Cancer Society
- ASC-US, atypical squamous cells of uncertain significance
- ACOG, American College of Obstetricians and Gynecologists
- CIN, cervical intraepithelial neoplasia
- DES, diethylstilbestrol
- DNA, deoxyribonucleic acid
- FDA, U.S. Food and Drug Administration
- HIV, human immunodeficiency virus
- HPV, human papillomavirus
- KPCMI, Kaiser Permanente Care Management Institute
- LBP, liquid-based Pap
- NCCN, National Comprehensive Cancer Network
- Pap, Papanicolaou
- PEBC, Program in Evidence-based Care
- STD, sexually transmitted disease
- UMHS, University of Michigan Health System

<b>TABLE 1: COMPARISON OF INTERVENTIONS AND PRACTICES CONSIDERED</b> <i>("✓" indicates topic is addressed)</i>			
	<b>KPCMI (2006)</b>	<b>PEBC (2005)</b>	<b>UMHS (2004)</b>
Whom to Screen	✓	✓	✓
Screening after Hysterectomy	✓	✓	✓
Screening Modality and Frequency	✓	✓	✓
<b>Screening Tests</b>			
• Liquid-based cytology	✓	✓	✓
• Conventional smear cytology	✓	✓	✓
• HPV testing	✓	✓	✓

• Computerized rescreening	✓		✓
• Algorithm-based screening			✓
Patient Education/Counseling			✓

TABLE 2: COMPARISON OF GUIDELINE SCOPE	
Objective and Scope	
<b>KPCMI (2006)</b>	<ul style="list-style-type: none"> <li>To provide recommendations (evidence-based and consensus-based) on cervical cancer screening</li> <li>To assist primary care and specialist physicians and other health care professionals in counseling asymptomatic adolescents and adults about cervical cancer screening procedures</li> </ul>
<b>PEBC (2005)</b>	<ul style="list-style-type: none"> <li>To identify the optimal cervical screening tool (conventional cytology, liquid based cytology, or HPV DNA testing)</li> <li>To evaluate whether organized cervical screening programs with recall mechanisms reduce the incidence of and mortality due to cervical cancer compared to spontaneous cervical screening</li> <li>To identify the most appropriate time for initiation and cessation of cervical screening</li> <li>To identify the time interval at which women should be screened</li> <li>To identify whether women in special circumstances should be screened (i.e., pregnant women, women post-hysterectomy, HIV positive women, women who have sex with women)</li> <li>To identify the optimal management for women with abnormal cytology (up to but not including colposcopy/HPV management)</li> </ul>
<b>UMHS (2004)</b>	<ul style="list-style-type: none"> <li>To implement an evidenced-based strategy for cancer screening in adults</li> </ul>
Target Population	
<b>KPCMI (2006)</b>	<ul style="list-style-type: none"> <li>United States</li> <li>Asymptomatic adult women 21 years of age and older and females under age 21 who are sexually active who have had none of the following: <ul style="list-style-type: none"> <li>Hysterectomy with total removal of the cervix for a benign condition</li> </ul> </li> </ul>

	<ul style="list-style-type: none"> <li>• Hysterectomy with total removal of the cervix for a precancerous or cancerous condition of the uterus, cervix, or vagina</li> <li>• HIV infection and/or immunosuppression (due to organ transplantation or other condition)</li> <li>• A single positive HPV test</li> <li>• Persistently positive HPV tests</li> <li>• A recent abnormal cytologic result</li> <li>• Previous diagnosis of cervical cancer or CIN grade 2/3</li> </ul> <ul style="list-style-type: none"> <li>• Asymptomatic adolescent and adult females with a cytology smear of ASC-US</li> <li>• Asymptomatic adult women who have had a hysterectomy with total removal of the cervix for a benign condition of the uterus, cervix, or vagina</li> <li>• Women who are infected with HIV, are immunosuppressed (e.g., due to organ transplantation or other condition), or who have been previously diagnosed with cervical cancer or CIN grade 2/3</li> </ul>
<b>PEBC (2005)</b>	<ul style="list-style-type: none"> <li>• Women in Ontario, Canada</li> <li>• All women who are, or have ever been, sexually active</li> </ul>
<b>UMHS (2004)</b>	<b>Cervical Cancer Screening Recommendations</b> <ul style="list-style-type: none"> <li>• Women in the United States</li> <li>• Women starting within 3 years after onset of vaginal intercourse</li> <li>• Women age 21 and older</li> <li>• Women who have undergone a total hysterectomy</li> </ul>
<b>Intended Users</b>	
<b>KPCMI (2006)</b>	<p>Advanced Practice Nurses</p> <p>Allied Health Personnel</p> <p>Nurses</p> <p>Physician Assistants</p> <p>Physicians</p>
<b>PEBC (2005)</b>	Physicians
<b>UMHS (2004)</b>	Physicians

**TABLE 3: COMPARISON OF RECOMMENDATIONS FOR CERVICAL CANCER SCREENING**

<b>Whom To Screen (Including when to initiate and discontinue)</b>	
<b>KPCMI (2006)</b>	<p><b>Recommendations: Effectiveness of Cervical Cancer Primary Screening Tests in Asymptomatic, Average-Risk Women</b></p> <p>Routine cervical cancer screening is recommended for all asymptomatic, average-risk women. <b>(Evidence-based: B)</b></p> <p><b>Recommendations: Optimal Age to Begin and End Screening in Asymptomatic, Average-risk Women</b></p> <p>Initiation of cervical cancer screening is recommended approximately 3 years after first sexual intercourse or by the age of 21, whichever comes first.*‡ <b>(Consensus-based)</b></p> <p>Routine screening for cervical cancer for women older than age 65 is not recommended if they have had adequate recent screening** with normal results on their last cytology (and HPV test if applicable). <b>(Evidence-based: D)</b></p> <ul style="list-style-type: none"> <li>• <i>*The Guideline Development Team (GDT) recognizes that the age to begin screening may not adequately reflect the current The Health Plan Employer Data and Information Set (HEDIS) measures. Some regions may choose to offer screening at a younger age. The HEDIS®* cervical cancer screening rate estimates the percentage of women aged 21 to 64 that were enrolled in the health plan and who had one cytology test during measurement year or the two years prior.</i></li> <li>• <i>‡Routine cervical cancer screening continues to be recommended for women who have received the HPV vaccine. For additional information, see Kaiser Permanente (KP) National HPV Vaccine Practice Resource online at <a href="https://cl.kp.org/pkc/control/login">https://cl.kp.org/pkc/control/login</a>.</i></li> <li>• <i>**The Guideline Development Team defined adequate recent screening as older women who have had three or more documented, consecutive, technically satisfactory normal/negative cervical cytology tests, and who have had no abnormal/positive cytology tests within the last 10 years.</i></li> </ul>
<b>PEBC (2005)</b>	<p><b>Screening Initiation</b></p> <p>Cervical cytology screening should be initiated within three years of first vaginal sexual activity (i.e., vaginal intercourse, vaginal/oral,</p>

	<p>and/or vaginal/digital sexual activity) (C-III).</p> <p><b>Screening Cessation</b></p> <p>Screening may be discontinued after the age of 70 if there is an adequate negative screening history in the previous 10 years (i.e., 3 to 4 negative tests) (B-II).</p>
<b>UMHS (2004)</b>	<ul style="list-style-type: none"> <li>Initiate. Start within 3 years after onset of vaginal intercourse <b>[B]</b> or at age 21 for women who are not sexually active <b>[D]</b>.</li> <li>Terminate. Screening may be discontinued in women past age 65 or age 70 who have at least three normal or negative smears in the past 10 years and no previous history of cervical abnormality <b>[C]</b>.</li> </ul>
<b>Screening After Hysterectomy</b>	
<b>KPCMI (2006)</b>	<p><b>Recommendations: Optimal Cervical Cancer Screening Strategy for Women Who Have Had a Total Hysterectomy for a Benign Condition.</b></p> <p>Routine cytology screening is not recommended for women who have had a total hysterectomy for a benign condition unless there was a history of CIN grade 2/3. <b>(Evidence-based: D)</b></p> <p>Three consecutive negative cytology results with or without HPV testing are recommended prior to discontinuation of screening in women who have a history of CIN grade 2/3 and a subsequent hysterectomy for a benign condition. <b>(Consensus-based)</b></p>
<b>PEBC (2005)</b>	<ul style="list-style-type: none"> <li>Screening can be discontinued in women who have undergone total hysterectomy for benign causes with no history of cervical dysplasia or human papillomavirus (C-III).</li> <li>Women who have undergone subtotal hysterectomy (with an intact cervix) should continue screening according to the guidelines.</li> </ul>
<b>UMHS (2004)</b>	<ul style="list-style-type: none"> <li>Women who have undergone a total hysterectomy do not require screening unless the hysterectomy was performed because of cervical cancer or its precursors <b>[C]</b>.</li> </ul> <p><b>Clinical Background.</b> Women who have undergone a total hysterectomy (with removal of the cervix) for benign gynecologic disease do not need to undergo screening with vaginal cytology. However, a health care provider should confirm and/or document via physical exam and review of the pathology report (when available) that the cervix was completely removed. Women who have had a subtotal hysterectomy should continue cervical cancer screening as</p>

	per current guidelines.
Screening Modality and Frequency	
<b>KPCMI (2006)</b>	<p><b>Recommendations: Effectiveness of Cervical Cancer Primary Screening Tests in Asymptomatic, Average-Risk Women</b></p> <p>Either of the following tests are options for cervical cancer screening in asymptomatic, average-risk women <u>under age 30</u>.</p> <ul style="list-style-type: none"> <li>• Conventional cytology (<b>Evidence-based: B</b>)</li> <li>• Liquid-based cytology (<b>Consensus-based</b>)</li> </ul> <p>All of the following tests are acceptable options for cervical cancer screening in asymptomatic, average-risk women <u>age 30 and older</u>.</p> <ul style="list-style-type: none"> <li>• Conventional cytology (<b>Evidence-based: B</b>)</li> <li>• Conventional cytology and HPV testing*†** cytology (<b>Consensus-based</b>)</li> <li>• Liquid-based cytology (<b>Consensus-based</b>)</li> <li>• Liquid-based cytology and HPV testing*†** cytology (<b>Consensus-based</b>)</li> </ul> <p><i>*HPV testing has not been FDA approved as a standalone test for primary screening.</i></p> <p><i>†Combined cytology and HPV testing provides useful risk-stratification</i></p> <p><i>**Hybrid Capture 2 (HC2) Testing Device.</i></p> <p>No recommendation for or against routine use of computer-assisted slide evaluation or automated rescreening of cytology slides. <b>(Evidence-based: I)</b></p> <p><b>Recommendations: Cervical Cancer Screening Intervals in Asymptomatic, Average-risk Women</b></p> <p>The following screening intervals are recommended:</p> <ul style="list-style-type: none"> <li>• Cytology alone: every 3 years* (<b>Consensus-based</b>)</li> <li>• Cytology + HPV (age 30 and older): every 3 years*† (<b>Consensus-based</b>)</li> </ul> <p><i>*Screen if more than 30 months has elapsed.</i></p> <p><i>†Hybrid Capture 2 (HC2) Testing Device.</i></p> <p>No recommendation for or against routinely providing annual</p>

	<p>screening tests prior to beginning a triennial screening program. <b>(Evidence-based: I)</b></p> <p><b>Recommendations: Triage for ASC-US Results Using HPV Testing in Asymptomatic, Average-risk Women</b></p> <p>HPV testing is recommended in women of all ages for triage of cytology results indicating ASC-US. <b>(Evidence-based: B)</b></p> <p>No recommendation for or against the use of HPV testing to triage women with cytologic results higher than ASC-US. <b>(Evidence-based: I)</b></p> <p><b>Recommendations: Screening in Women at Increased Risk of Cervical Cancer</b></p> <p>Cytology and HPV testing are recommended at 6 months following treatment for CIN grade 2/3, and again at 24 months, with colposcopy for any positive result. Routine screening every 3 years can then be resumed indefinitely. <b>(Consensus-based)</b></p> <p>If HPV testing is not done, two cytology tests at 6 and 12 months after treatment are recommended, with colposcopy for a positive result, then annual cytologic screening indefinitely. <b>(Consensus-based)</b></p> <p>At least annual cytology with or without HPV testing is recommended for women who are immunosuppressed or HIV-positive. <b>(Consensus-based)</b></p> <p><b>Recommendation: Optimal Initial Management of Concurrent HPV-Positive and Cytology-Negative Cervical Screening Results</b></p> <p>HPV and cytology retesting is recommended in 12 months, rather than immediate colposcopy, for management of women with initial concurrent HPV-positive and cytology-negative screening results. <b>(Consensus-based).</b></p>
<p><b>PEBC (2005)</b></p>	<p><b>Optimal Cervical Screening Tool</b></p> <ul style="list-style-type: none"> <li>Liquid-based cytology is the preferred tool for cervical cytology screening (B-II). Conventional smear cytology remains an acceptable alternative (C-III).</li> </ul> <p><b>Screening Interval</b></p> <ul style="list-style-type: none"> <li>Screening should be done annually until there are three consecutive negative Pap tests (C-III).</li> </ul>



	<ul style="list-style-type: none"> <li>• Screening should continue every two to three years after three annual negative Pap tests (B-II). <ul style="list-style-type: none"> <li>• Screening at a three-year interval is recommended, supported by an adequate recall mechanism (B-II).</li> <li>• Women who have not been screened in more than five years should be screened annually until there are three consecutive negative Pap tests (C-III).</li> </ul> </li> </ul> <p><b>Note:</b> These recommendations do not apply to women who have had previous abnormal Pap tests. See management of abnormal cytology section in original guideline document for further information.</p> <p><b>Screening Women with Special Circumstances</b></p> <ul style="list-style-type: none"> <li>• Immunocompromised or HIV positive women should receive annual screening (C-III). <ul style="list-style-type: none"> <li>• Examples of situations where women may be immunocompromised include women who have received transplants and women who have undergone chemotherapy.</li> </ul> </li> <li>• Indications for screening frequency for pregnant women should be the same as women who are not pregnant (B-III). Manufacturer's recommendations for the use of individual screening tools in pregnancy should be taken into consideration.</li> <li>• Women who have sex with women should follow the same cervical screening regimen as women who have sex with men (B-II).</li> </ul> <p><b>Recommended Management for Women with Abnormal Cytology</b></p> <p><i>ASCUS (Atypical squamous cells of uncertain significance)</i></p> <ul style="list-style-type: none"> <li>• HPV DNA testing with cytology is recommended for women aged 30 or older with ASC-US (C-III). <ul style="list-style-type: none"> <li>• If the HPV DNA test is positive, women should be referred for colposcopy. If the HPV DNA test is negative, women should have repeat cytology in 12 months. Once a woman has had two negative cytology test results, she should return to routine screening.</li> <li>• In the absence of HPV DNA testing, a repeat Pap test in six months is acceptable. If the Pap test is abnormal, women should be referred for colposcopy. If the Pap test is negative, women should have repeat cytology in another six months. Once a woman has had two negative Pap test results, she should return to routine screening.</li> </ul> </li> </ul>
<p><b>UMHS (2004)</b></p>	<p><b>Modality</b></p> <p>Pap smear of cervical cells or liquid based cervical cytology</p>

(ThinPrep®).

### **Frequency**

- Low risk. Annually with conventional Pap smears or every two years using the ThinPrep until age 30. Starting at age 30, women who have had three consecutive technically satisfactory normal or negative cytology results may be screened every two to three years **[C]**. ("Low risk" includes women who do not have a history of in utero exposure to DES, are not immunocompromised or HIV+, and have had three consecutive normal or negative cytology results.)
- High risk. Screen annually **[D]**.

### Rationale for Recommendations

**Screening tests.** The ThinPrep® system collects more cells and leads to better quality slides. The ThinPrep system is more sensitive (76% vs. 68%) and specific (86% vs. 79%) than Pap smear.

**How often should screening be done.** Screening intervals will vary depending on the cytologic method used. After women have undergone an initial conventional cervical cancer screening with a Pap smear, the procedure should be performed annually until age 30. If the initial screening test was based on the ThinPrep system, the procedure should be performed at least every two years until age 30. At age 30 or older, a physician and patient may elect to reduce the frequency of screening to every 2 to 3 years if the woman is low-risk (e.g., does not have a history of *in utero* exposure to DES, is not immunocompromised or HIV+) and has had three consecutive normal or negative cytology results.

**New screening technology.** The United States FDA has approved a computerized device (AutoPap 300) as an adjunct to manual screening. The system is used to rescreen negative smears and approximately 10% to 20% of slides are classified as abnormal using a computerized cellular analysis. These slides are then reviewed by a pathologist.

**HPV testing.** While routine testing on all patients for human HPV has been proposed as an alternative screening test, the high prevalence of HPV in young women and low positive predictive value for higher-grade lesions limits its usefulness. At the University of Michigan, HPV testing for high risk subtypes is currently performed on the ThinPrep samples from patients with an ASC-US pap smear. Patients > age 20 years old and positive for high risk HPV subtypes should be referred for colposcopy. HPV testing is not recommended in women ≤ 20 years old. For patients ≤ 20 years old and ASC-US or low grade abnormalities, repeat pap in 1 year. Adolescent patients are extremely unlikely to develop cervical neoplasia and have a

	relatively high rate of clearing the virus. If repeat pap in 1 year is still abnormal, then patient should be referred for colposcopy. If negative for high risk HPV subtypes, the women may be followed with a repeat pap smear in one year, based on the negative predictive value, of our current HPV test, being 98%.
<b>Patient Education/Counseling</b>	
<b>KPCMI (2006)</b>	No recommendations offered
<b>PEBC (2005)</b>	No recommendations offered
<b>UMHS (2004)</b>	It is important that women who may not need a cervical cytology test obtain appropriate preventive health care, including contraception and prevention counseling, and screening and treatment of sexually transmitted diseases.

<b>TABLE 4: BENEFITS AND HARMS</b>	
<b>Benefits</b>	
<b>KPCMI (2006)</b>	<ul style="list-style-type: none"> <li>• Appropriate cervical cancer screening</li> <li>• Reduced morbidity and mortality from cervical cancer</li> </ul>
<b>PEBC (2005)</b>	<ul style="list-style-type: none"> <li>• Optimal use of cervical screening tools</li> <li>• Reduced incidence and mortality due to cervical cancer</li> <li>• Appropriate initiation, intervals, and cessation of cervical screening</li> <li>• Optimal management of women with abnormal cytology</li> </ul>
<b>UMHS (2004)</b>	<p><b>Reductions in Cancer Incidence and Mortality</b></p> <p>Correlational studies show significant declines in both the incidence of cervical cancer and cervical cancer mortality rates in North American and western Europe following the introduction of screening programs. The reduction in mortality correlated closely with the intensity of the screening. Case control studies support the correlational data and show a decrease in the incidence of invasive cancer by 60 to 90%. Increased frequency of screening is associated with a greater reduction in rate of cervical cancer.</p>
<b>Harms</b>	

<b>KPCMI (2006)</b>	<ul style="list-style-type: none"> <li>• Inconvenience, anxiety, and adverse effects of tests (e.g., discomfort, pain)</li> <li>• Unnecessary tests due to false-positive test results</li> <li>• False reassurance from false-negative test results, neglect to follow-up, progression of cancer</li> </ul>
<b>PEBC (2005)</b>	None stated
<b>UMHS (2004)</b>	None stated

**TABLE 5: EVIDENCE RATING SCHEMES AND REFERENCES**

<b>KPCMI (2006)</b>	<p>Recommendations are classified as either "evidence-based (A-D, I)" or "consensus-based."</p> <ul style="list-style-type: none"> <li>• <i>Evidence-based</i>: sufficient number of high-quality studies from which to draw a conclusion, and the recommended practice is consistent with the findings of the evidence. A recommendation can also be considered "evidence-based" if there is insufficient evidence and no practice is recommended.</li> <li>• <i>Consensus-based</i>: insufficient evidence and a practice is recommended based on the consensus or expert opinion of the Guideline Development Team (GDT).</li> </ul> <p><b>Label and Language of Recommendations*</b></p> <table> <tr> <th>Label</th><th>Evidence-Based Recommendations</th></tr> <tr> <td><b>Evidence-based (A)</b></td><td> <p><b>Language:</b> <sup>a</sup> The intervention is strongly recommended for eligible patients.</p> <p><b>Evidence:</b> The intervention improves important health outcomes, based on good evidence, and the Guideline Development Team (GDT) concludes that benefits substantially outweigh harms and costs.</p> <p><b>Evidence Grade:</b> Good.</p> </td></tr> <tr> <td><b>Evidence-based (B)</b></td><td> <p><b>Language:</b> <sup>a</sup> The intervention is recommended for eligible patients.</p> </td></tr> </table>	Label	Evidence-Based Recommendations	<b>Evidence-based (A)</b>	<p><b>Language:</b> <sup>a</sup> The intervention is strongly recommended for eligible patients.</p> <p><b>Evidence:</b> The intervention improves important health outcomes, based on good evidence, and the Guideline Development Team (GDT) concludes that benefits substantially outweigh harms and costs.</p> <p><b>Evidence Grade:</b> Good.</p>	<b>Evidence-based (B)</b>	<p><b>Language:</b> <sup>a</sup> The intervention is recommended for eligible patients.</p>
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<b>Evidence-based (B)</b>	<p><b>Language:</b> <sup>a</sup> The intervention is recommended for eligible patients.</p>						

	<p><b>Evidence:</b> The intervention improves important health outcomes, based on 1) good evidence that benefits outweigh harms and costs; or 2) fair evidence that benefits substantially outweigh harms and costs.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (C)</b>	<p><b>Language:</b> <sup>a</sup> No recommendation for or against routine provision of the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.)</p> <p><b>Evidence:</b> Evidence is sufficient to determine the benefits, harms, and costs of an intervention, and there is at least fair evidence that the intervention improves important health outcomes. But the GDT concludes that the balance of the benefits, harms, and costs is too close to justify a general recommendation.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (D)</b>	<p><b>Language:</b> <sup>a</sup> Recommendation against routinely providing the intervention to eligible patients.</p> <p><b>Evidence:</b> The GDT found at least fair evidence that the intervention is ineffective, or that harms or costs outweigh benefits.</p> <p><b>Evidence Grade:</b> Good or Fair.</p>
<b>Evidence-based (I)</b>	<p><b>Language:</b> <sup>a</sup> The evidence is insufficient to recommend for or against routinely providing the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.)</p> <p><b>Evidence:</b> Evidence that the intervention is effective is lacking, of poor quality, or conflicting and the balance of benefits, harms, and costs cannot be determined.</p> <p><b>Evidence Grade:</b> Insufficient.</p>

	<table border="1" data-bbox="418 212 1382 680"> <tr> <td data-bbox="427 222 678 669"> <b>Consensus-based</b> </td><td data-bbox="678 222 1373 669"> <p><b>Language:</b> <sup>a</sup> The language of the recommendation is at the discretion of the GDT, subject to approval by the National Guideline Directors.</p> <p><b>Evidence:</b> The level of evidence is assumed to be "Insufficient" unless otherwise stated. However, do not use the A, B, C, D, or I labels which are only intended to be used for evidence-based recommendations.</p> <p><b>Evidence Grade:</b> Insufficient, unless otherwise stated.</p> </td></tr> </table> <p data-bbox="475 699 1360 926">For the rare consensus-based recommendations which have "Good" or "Fair" evidence, the evidence must support a different recommendation, because if the evidence were good or fair, the recommendation would usually be evidence-based. In this kind of consensus-based recommendation, the evidence grade should point this out (e.g., "Evidence Grade: Good, supporting a different recommendation").</p> <p data-bbox="456 982 1170 1045"><sup>[a]</sup> All statements specify the population for which the recommendation is intended.</p> <p data-bbox="456 1087 1373 1341">*Recommendations should be labeled and given an evidence grade. The evidence grade should appear in the rationale. Evidence is graded with respect to the degree it supports the specific clinical recommendation. For example, there may be good evidence that Drugs 1 and 2 are effective for Condition A, but no evidence that Drug 1 is more effective than Drug 2. If the recommendation is to use either Drug 1 or 2, the evidence is good. If the recommendation is to use Drug 1 in preference to Drug 2, the evidence is insufficient.</p>	<b>Consensus-based</b>	<p><b>Language:</b> <sup>a</sup> The language of the recommendation is at the discretion of the GDT, subject to approval by the National Guideline Directors.</p> <p><b>Evidence:</b> The level of evidence is assumed to be "Insufficient" unless otherwise stated. However, do not use the A, B, C, D, or I labels which are only intended to be used for evidence-based recommendations.</p> <p><b>Evidence Grade:</b> Insufficient, unless otherwise stated.</p>
<b>Consensus-based</b>	<p><b>Language:</b> <sup>a</sup> The language of the recommendation is at the discretion of the GDT, subject to approval by the National Guideline Directors.</p> <p><b>Evidence:</b> The level of evidence is assumed to be "Insufficient" unless otherwise stated. However, do not use the A, B, C, D, or I labels which are only intended to be used for evidence-based recommendations.</p> <p><b>Evidence Grade:</b> Insufficient, unless otherwise stated.</p>		
<b>PEBC (2005)</b>	<p data-bbox="456 1381 743 1413"><b>Quality of Evidence</b></p> <p data-bbox="456 1451 1187 1482"><b>I:</b> Evidence from at least 1 randomized controlled trial</p> <p data-bbox="456 1520 1382 1614"><b>II:</b> Evidence from at least 1 clinical trial without randomization, from cohort or case-controlled analytic studies, or from multiple time series studies or dramatic results from uncontrolled experiments</p> <p data-bbox="456 1652 1284 1747"><b>III:</b> Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees</p> <p data-bbox="456 1785 894 1816"><b>Strength of Recommendation</b></p>		

	<p><b>A:</b> Good evidence for efficacy and substantial clinical benefit support recommendation for use.</p> <p><b>B:</b> Moderate evidence for efficacy or only limited clinical benefit support recommendation for use.</p> <p><b>C:</b> Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendations may be made on other grounds.</p> <p><b>D:</b> Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.</p> <p><b>E:</b> Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use.</p>
<b>UMHS (2004)</b>	<p>Levels of evidence reflect the best available literature in support of an intervention or test:</p> <p>A = Randomized controlled trials</p> <p>B = Controlled trials, no randomization</p> <p>C = Observational trials</p> <p>D = Opinion of expert panel</p>

## **GUIDELINE CONTENT COMPARISON**

The Kaiser Permanente Care Management Institute (KPCMI), the Program in Evidence-based Care (PEBC), and the University of Michigan Health System (UMHS) present recommendations for cervical cancer screening. All three groups rank the level of evidence for each major recommendation. All three also provide, in narrative form, the explicit reasoning behind their judgments for all major recommendations.

The guidelines differ in scope. UMHS, for instance, in addition to its cervical cancer screening recommendations, presents recommendations for breast cancer, colorectal cancer, and prostate cancer screening. PEBC provides recommendations concerning management of women with abnormal cytology. Excepting the topic of HPV testing in screened women with abnormal cytology results, these additional topics are not included in this synthesis, which focuses on primary screening for cervical cancer.

### **Areas of Agreement**

#### *When to Initiate and Discontinue Screening*

KPCMI and UMHS are in agreement concerning when to initiate cervical screening, with both groups recommending that screening be started within 3 years after the onset of vaginal intercourse, or by age 21. PEBC agrees that screening should be started within 3 years of onset of first vaginal sexual activity, but does not include an age criterion (see [Areas of Differences](#) below).

General agreement also exists among the guidelines concerning when to stop screening. All three groups recommend that screening be discontinued in older women who have had adequate recent screening (i.e., at least three normal Pap smears within the prior 10 years) and who have no risk factors for cervical cancer. The guidelines differ, however, concerning the precise age at which screening should be discontinued in older women; these differences are discussed below.

### *Screening Following Hysterectomy*

All three groups agree that screening is not necessary in women who have had a total hysterectomy for benign gynecologic disease. However, these guidelines are in general agreement regarding the need to continue screening when there is inadequate documentation of the reason for the hysterectomy and/or when risk factors for cervical cancer (such as cervical dysplasia or HPV) are present. KPCMI specifies that screening is not recommended in this population unless there was a history of CIN 2/3. They also note that three consecutive cytology results with or without HPV testing are recommended prior to discontinuation of screening in women who have a history of CIN 2/3 and a subsequent hysterectomy for a benign condition.

### *HPV DNA Testing*

All of the guidelines address use of HPV DNA testing as a primary screening tool for cervical cancer (i.e., performed on all women screened), and there is overall agreement that it is not currently appropriate as a primary screening tool. UMHS notes that while routine testing on all patients for HPV has been proposed as an alternative screening test, the high prevalence of HPV in young women and low positive predictive value for higher-grade lesions limits its usefulness. Similar to the other groups, PEBC notes that the two technology assessments (reviewed by the guideline developers) that examined HPV testing indicated that it should not be routinely recommended as a primary screening test. KPCMI notes that HPV testing has not been FDA approved as a standalone test for primary screening.

Regarding the use of HPV DNA testing combined with conventional and/or liquid-based cytology, all three groups recommend HPV testing on liquid from the Pap test for the subset of women with an ASC-US Pap smear result (PEBC specifically notes that this applies to women aged 30 or older). (**NGC note:** discussion of recommendations related to follow-up for abnormal Pap smear results are beyond the scope of this synthesis. See the original guideline documents for more information on this topic).

### *Patient Education*

UMHS recommends that women, particularly teens and young women, receive education about appropriate preventive health care, contraception, and prevention of sexually transmitted diseases. The other guidelines do not address this topic.



## **Areas of Differences**

### *Whom to Screen*

PEBC differs from the other guidelines in that it does not specify an age by which screening should be initiated; the other guidelines indicate screening should start within three years of onset of sexual activity or by age 21. The PEBC guideline developers chose not to include a specific age to initiate screening, citing lack of evidence to support a particular age over another. The guideline states that linking Pap testing to the initiation of vaginal sexual activity is also more practical than choosing a specific age. PEBC points out that Pap smear screening has evolved since the 1950's into a highly effective cancer prevention tool; this has occurred without randomized controlled trials, and the benefit of this test is so evident that trials involving withholding the test are unethical. Therefore, there is little evidence in the literature to indicate the optimal timing for the initiation and cessation of cervical screening. PEBC notes that previous cervical screening guidelines have made recommendations for the initiation and cessation of screening based on limited evidence, previous practice, and expert consensus.

The guidelines all recommend screening be initiated within 3 years of onset of sexual activity, but they differ in how sexual activity is defined. UMHS uses the term "vaginal intercourse." KPCMI uses the term "sexual intercourse." PEBC recommends that screening begin within three years of "first vaginal sexual activity," which is defined as "vaginal intercourse, vaginal/oral and/or vaginal/digital sexual activity." PEBC justifies this recommendation by pointing out that it is recognized that vaginal transmission of HPV can occur with sexual activities other than intercourse, including vaginal/oral and/or vaginal/digital activity.

### *When to Discontinue Screening*

Although all of the groups agree that screening can be discontinued in low-risk older women, the groups recommend different age cut-offs. PEBC recommends discontinuing screening at age 70, whereas KPCMI recommends stopping at age 65. UMHS recommends that, for women who have previously undergone routine screening, screening be discontinued at either age 65 or age 70. UMHS further adds that many women older than age 65 have never been screened or have been screened fewer than two times for cervical cancer and that these women would most likely benefit from continued screening efforts. Concerning this difference in opinions as to whether screening should be discontinued at age 65 or at age 70, PEBC states that the literature regarding the cessation of cervical screening is sparse and problematic. Studies have often included women who had never been screened with those who have had adequate screening histories, making an evaluation of the evidence difficult.

### *Conventional Cytology vs. Liquid-based Pap Cytology*

All three groups recommend both conventional and LBP technology. UMHS finds that the ThinPrep<sup>®</sup> LBP system collects more cells, leads to better quality slides, and is both more sensitive and specific than the Pap smear. PEBC recommends LBP cytology as the preferred tool, although conventional smear technology is an

acceptable alternative. KPCMI notes that both conventional and liquid-based cytology testing are options.

### *Screening Interval*

The organizations also differ in their recommendations concerning the screening interval for asymptomatic, low- or average-risk women. PEBC recommends screening be done annually until there are three consecutive negative Pap tests, and thereafter every 2 to 3 years (every 3 years if screening is supported by an adequate recall mechanism). For low-risk women, UMHS recommends that screening be done annually with conventional cytology or every 2 years with LBP technology until age 30. At that age, the screening interval can be lengthened to every 2 to 3 years (in women who have had three consecutive normal tests and are at low risk for cervical cancer).

In contrast, KPCMI recommends that asymptomatic, average-risk women should have cytology (either conventional or LBP cytology is appropriate) every 3 years. They also recommend an interval of 3 years for cytology and HPV testing (recommended for women aged 30 and older). In contrast to UMHS and PEBC, KPCMI makes no recommendation for or against routinely providing annual screening tests prior to beginning a triennial screening program.

The groups agree that annual cytology is recommended for high-risk women (such as women with previous abnormal Pap tests, women that are immunocompromised, HIV positive women).

### *HPV DNA Testing*

In contrast to PEBC and UMHS, both of which recommend HPV testing only in the event of ASC-US, KPCMI is the only group to recommend combined use of cytology and HPV for asymptomatic, low or average risk women. KPCMI notes that cytology (conventional or liquid-based) and HPV testing is an acceptable option for screening in asymptomatic, average-risk women age 30 and older.

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This Synthesis was prepared by ECRI on September 1, 2005. The information was verified by UMHS on October 5, 2005, and by USPSTF on October 14, 2005. This synthesis was revised March 3, 2006 to include new recommendations from the Cancer Care Ontario Program in Evidence-based Care (PEBC). The updated information was verified by PEBC on April 5, 2006. The information was updated on October 26, 2007 to remove BWH recommendations and again on November 27, 2007 to remove recommendations from ACS. This synthesis was revised on January 27, 2008 to add KPCMI recommendations. The information was verified by KPCMI on February 22, 2008. This Synthesis was updated in October 2008 to remove outdated USPSTF recommendations.

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