Cervical and Breast Cancer Screening—a primer

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What is a screening test?

* **Screening tests are used to determine whether an asymptomatic individual has an undetected disease or condition**

What is a screening test?

* **Screening is currently used in many contexts**
  * **blood pressure monitoring for hypertension, PSA for prostate cancer, colonoscopy for colorectal carcinoma, and mammography for breast cancer**

The disease should

* constitute a significant public health problem
  * common condition with significant morbidity and mortality
* a readily available treatment with a potential for cure that increases with early detection

The test for the disease

* capable of detecting a high proportion of disease in its preclinical state
* safe to administer
* reasonable in cost
* lead to demonstrated improved health outcomes
* widely available
  * as must the interventions that follow a positive result

Screening for Cervical Cancer

* **The incidence of cervical cancer in the United States has decreased more than 50% in the past 30 years**
  * **because of widespread screening with cervical cytology**
  * **1975, the rate was 14.8 per 100,000 women by 2008 it had been reduced to 6.6 per 100,000 women**

Screening for Cervical Cancer

* Mortality from the disease has undergone a similar decrease from 5.55 per 100,000 women in 1975 to 2.38 per 100,000 women in 2008
* The American Cancer Society (ACS) estimates that there will be 12,170 new cases of cervical cancer in the United States in 2012, with 4,220 deaths from the disease

Screening for Cervical Cancer

* Cervical cancer is much more common worldwide, particularly in countries without screening programs, with an estimated 530,000 new cases of the disease and 275,000 resultant deaths each year
* When cervical cancer screening programs have been introduced into communities, marked reductions in cervical cancer incidence have followed

Quick background

* Most cervical cancer occurs in women who were either never screened or were inadequately screened
* Estimates suggest that 50% of the women in whom cervical cancer is diagnosed never had cervical cytology testing, and another 10% have not been screened within the 5 years before diagnosis
  * approximately 60% of diagnoses of cervical cancer are a result of inadequate screening

Quick background

* **Additional public health measures remain critical to improving access to screening for this group of women who are often uninsured or underinsured**

Quick background

* **Although rates of cervical cancer are on the decline in women born in the United States with access to screening, *women who are immigrants to the United States, those lacking a regular source of health care, and the uninsured are at especially high risk***

Natural History of Cervical Neoplasia

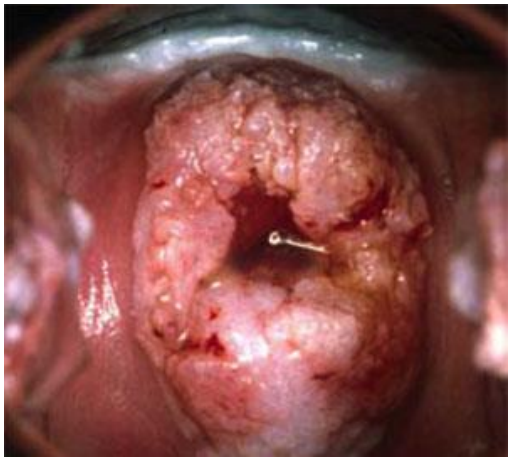
* **Human papillomavirus (HPV) is divided into two classes—1) oncogenic and 2) nononcogenic. Infection with oncogenic (or high-risk) HPV usually is a necessary but not sufficient factor for the development of squamous cervical neoplasia**
  * **Only a small fraction of women infected with HPV will develop significant cervical abnormalities and cancer**
* **The current model of cervical carcinogenesis posits that HPV infection results in either transient or persistent infection**

* Only a small fraction of women infected with HPV will develop significant cervical abnormalities and cancer

Natural History of Cervical Neoplasia

* **Most HPV infection is transient and poses little risk of progression**
* **Only a small fraction of infections are persistent**
  * **but persistent infection at 1 year and 2 years strongly predicts subsequent risk of cervical intraepithelial neoplasia (CIN) 3 or cancer regardless of age**

Persistent infection at 1 year and 2 years strongly predicts subsequent risk of cervical intraepithelial neoplasia (CIN) 3 or cancer regardless of age



Clinical Considerations and Recommendations

* ***When should screening begin?***

When should screening begin?

* **Cervical cancer screening should begin at age 21 years. Women younger than 21 years should not be screened regardless of the age of sexual initiation or the presence of other behavior-related risk factors**

When should screening begin?

* **Human papillomavirus infection is commonly acquired by young women shortly after the initiation of vaginal intercourse**
* **Nearly all cases are cleared by the immune system within 1–2 years without producing neoplastic changes**
* **Although cancer is rare in adolescents, neoplasia is not**
  * **In a report of 10,090 Pap test results in females aged 12–18 years, 422 specimens (5.7%) were reported as LSILs and only 55 specimens (0.7%) were HSILs**

When should screening begin?

* Earlier onset of screening than recommended may increase anxiety, morbidity, and expense and lead to overuse of follow-up procedures
* The emotional effect of labeling an adolescent with both a sexually transmitted infection and potential precancer must be considered because adolescence is a time of heightened concern for self-image and emerging sexuality
  * Studies have documented a significant increase in rates of premature birth among women previously treated with excisional procedures for neoplasia
  * the long-accepted association between LEEP and adverse pregnancy outcomes has been challenged.

* Initiation of reproductive health care should not be predicated on cervical cancer screening
* Important strategies for prevention of cervical cancer in women younger than 21 years include HPV vaccination and counseling about safe sex practices to limit exposure to sexually transmitted infections

Table 1. Screening Methods for Cervical Cancer: Joint Recommendations of the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology ⇦

Population	Recommended Screening Method	Comment
Women younger than 21 years	No screening	
Women aged 21–29 years	Cytology alone every 3 years	
Women aged 30–65 years	Human papillomavirus and cytology co-testing (preferred) every 5 years	Screening by HPV testing alone is not recommended
	Cytology alone (acceptable) every 3 years	
Women older than 65 years	No screening is necessary after adequate negative prior screening results	Women with a history of CIN 2, CIN 3 or adenocarcinoma in situ should continue routine age-based screening for at least 20 years
Women who underwent total hysterectomy	No screening is necessary	Applies to women without a cervix and without a history of CIN 2, CIN 3, adenocarcinoma in situ, or cancer in the past 20 years
Women vaccinated against HPV	Follow age-specific recommendations (same as unvaccinated women)	

What tests should be performed for screening?

- **Women aged 21–29 years should be tested with cervical cytology alone, and screening should be performed every 3 years**
- **Co-testing should not be performed in women younger than 30 years. For women aged 30–65 years, co-testing with cytology and HPV testing every 5 years is preferred**
- **Screening with cytology alone every 3 years is acceptable.**
  - **Both liquid-based and conventional methods of cervical cytology collection are acceptable for screening**
- ***These screening recommendations are not meant for women with cervical cancer and those who have HIV infection, are immunocompromised, or were exposed to diethylstilbestrol in utero***

What is the optimal frequency of cervical cytology screening for women aged 30–65 years?

- **In women aged 30–65 years, co-testing with cervical cytology screening and HPV testing is preferred and should be performed every 5 years**
- **If screening is performed with cervical cytology alone, it can be done with either conventional or liquid-based cytology collection methods and should be performed every 3 years**
- ***Annual screening should not be performed***

Are any alternative screening strategies recommended for specific populations?

- **Certain risk factors have been associated with CIN in observational studies**
- **Women with any of the following risk factors may require more frequent cervical cytology screening:**
  - **Women who are infected with HIV**
  - **Women who are immunocompromised (such as those who have received solid organ transplants)**
  - **Women who were exposed to diethylstilbestrol in utero**
  - **Women previously treated for CIN 2, CIN 3, or cancer**

At what age is it appropriate to discontinue screening?

* **Screening by any modality should be discontinued after age 65 years in women with evidence of adequate negative prior screening results and no history of CIN 2 or higher**
  * **Adequate negative prior screening results are defined as three consecutive negative cytology results or two consecutive negative co-test results within the previous 10 years, with the most recent test performed within the past 5 years**
* **Women with a history of CIN 2, CIN 3, or adenocarcinoma in situ should continue screening for a total of 20 years after spontaneous regression or appropriate management of CIN 2, CIN 3, or adenocarcinoma in situ, even if it extends the screening past age 65 years**

When is it appropriate to discontinue screening for women who have had a total hysterectomy?

* **Depends**
* **In women who have had a hysterectomy with removal of the cervix (total hysterectomy) and have never had CIN 2 or higher, routine cytology screening and HPV testing should be discontinued and not restarted for any reason**

Breast Cancer Screening

* Breast cancer is the most commonly diagnosed noncutaneous cancer in women in the United States, and the second leading cause of death from cancer in American women—second only to lung cancer
* Breast cancer mortality can be effectively reduced through screening

Table 1. Age-Specific Probabilities of Developing Invasive Female Breast Cancer*

If Current Age Is...	The Probability of Developing Breast Cancer in the Next 10 Years†	Or 1 in:
20	0.06%	1,760
30	0.44%	229
40	1.44%	69
50	2.39%	42
60	3.40%	29
70	3.73%	27
Lifetime risk	12.08%	8

Components of Breast Cancer Screening and Current Guidelines

* **Breast cancer screening has traditionally included three elements:**
  * **1 breast imaging (primarily mammography)**
  * **2 clinical breast examination**
  * **3 patient self-screening (breast self-examination or breast self-awareness)**
* **The relative value of each element and appropriate age of initiation, cessation, and frequency of screening remain controversial**

Breast Cancer Screening

	Mammography	Clinical Breast Examination	Breast Self-Examination Instruction	Breast Self-Awareness
American College of Obstetricians and Gynecologists	Age 40 years and older annually	Age 20–39 years every 1–3 years Age 40 years and older annually	Consider for high-risk patients	Recommended
American Cancer Society	Age 40 years and older annually	Age 20–39 years every 1–3 years Age 40 years and older annually	Optional for age 20 years and older	Recommended
National Comprehensive Cancer Network	Age 40 years and older annually	Age 20–39 years every 1–3 years Age 40 years and older annually	Recommended	Recommended
National Cancer Institute	Age 40 years and older every 1–2 years	Recommended	Not recommended	—
U.S. Preventive Services Task Force	Age 50–74 years biennially	Insufficient evidence	Not recommended	—

Rationale for Mammographic Screening

* Mammography screening could potentially identify a non-palpable mass measuring approximately 1 mm to 1 cm during its preclinical phase, 3 years before it becomes palpable
* This concept is commonly referred to as sojourn time, which is the time interval when cancer may be detected by screening before it becomes symptomatic.

Rationale for Mammographic Screening

* **The sojourn time of an individual type of cancer varies, with more biologically aggressive tumors typically having shorter sojourn times**

Rationale for Mammographic Screening

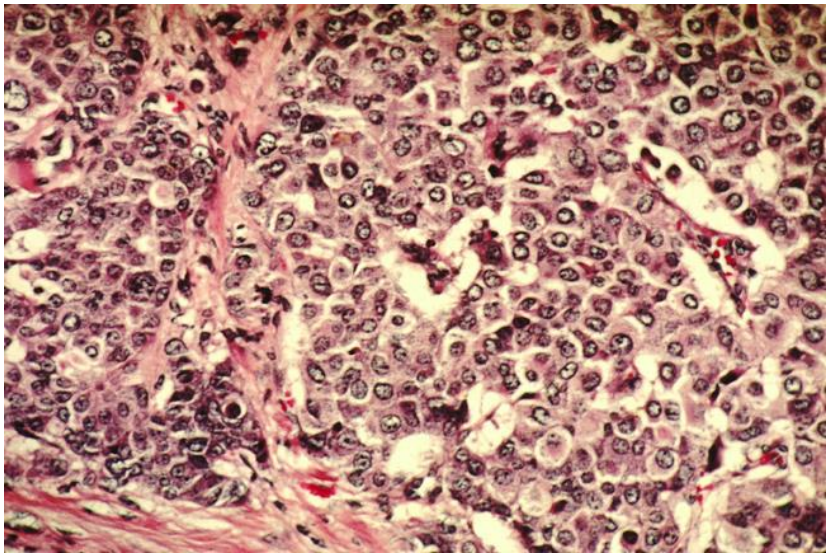
* The greatest predictor of sojourn time in breast cancer appears to be age
* Estimates of mean sojourn time for breast cancer in women increase with age
  * for ages 40–49 years, mean sojourn time is 2–2.4 years
  * 50–59 years--2.5–3.7 years;
  * 60–69 years--3.5–4.2 years
  * 70–74 years--4–4.1 years

Rationale for Mammographic Screening

* The mean sojourn time has implications for breast cancer screening because it is desirable to detect tumors during this sojourn period
* Individuals who are likely to have types of cancer with shorter sojourn times are more likely to benefit from more frequent screening when compared with those with slow-growing tumors that have a larger preclinical window

Rationale for Mammographic Screening

* **Screening strategies should be designed to maximize the likelihood of detecting the cancer during the preclinical window, when treatment options may be greater and outcomes may be improved**



Some take home points

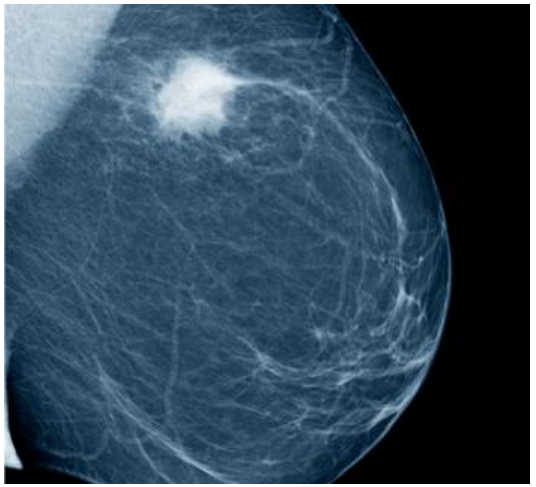
Summary of Recommendations and Conclusions

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

* **Based on the incidence of breast cancer, the sojourn time for breast cancer growth, and the potential reduction in breast cancer mortality, ACOG recommends that women aged 40 years and older be offered screening mammography annually**

The following recommendations are based primarily on consensus and expert opinion (Level C):

* **Clinical breast examination should be performed annually for women aged 40 years and older**
* **For women aged 20–39 years, clinical breast examinations are recommended every 1–3 years**



The following recommendations are based primarily on consensus and expert opinion (Level C):

* **Breast self-awareness should be encouraged and can include breast self-examination**
* **Women should report any changes in their breasts to their health care providers**

The following recommendations are based primarily on consensus and expert opinion (Level C):

* **Breast MRI is not recommended for screening women at average risk of developing breast cancer.**
* **For women who test positive for *BRCA1* and *BRCA2* mutations, enhanced screening should be recommended and risk reduction methods discussed**

Don’t perform routine annual cervical cytology screening (Pap tests) in women 30–65 years of age

* In average-risk women, annual cervical cytology screening has been shown to offer no advantage over screening performed at 3-year intervals
* However, a well-woman visit should occur annually for patients with their health care practitioner to discuss concerns and problems, and have appropriate screening with consideration of a pelvic examination

Summary of Recommendations and Conclusions

* *The following recommendations are based on good and consistent scientific evidence (Level A):*
* Cervical cancer screening should begin at age 21 years
  * Women younger than age 21 years should not be screened regardless of the age of sexual initiation or the presence of other behavior-related risk factors
* Women aged 21–29 years should be tested with cervical cytology alone, and screening should be performed every 3 years
  * Co-testing should not be performed in women younger than 30 years
* For women aged 30–65 years, co-testing with cytology and HPV testing every 5 years is preferred.

Summary of Recommendations and Conclusions

* In women aged 30–65 years, screening with cytology alone every 3 years is acceptable
  * Annual screening should not be performed
* Women who have a history of cervical cancer, have HIV infection, are immunocompromised, or were exposed to diethylstilbestrol in utero should not follow routine screening guidelines

Summary of Recommendations and Conclusions

* ***The following recommendations are based on limited and inconsistent scientific evidence (Level B):***
* **Women with ASC-US cytology and negative HPV co-testing results have a very low risk of CIN 3 and should continue with routine screening as indicated for their age**

References

* ACOG Practice Bulletin Number 131, November 2012