



The Pap test: Evidence to date

Original source:

Alliance for Cervical Cancer Prevention (ACCP)

www.alliance-cxca.org

Overview:

- Description of the Papanicolaou (Pap) smear test and how it works
- Infrastructure requirements
- What test results mean
- Test performance
- Strengths and limitations
- Program implications in low-resource settings

What does a Pap test involve?

- Performing a vaginal speculum exam during which a health care provider takes a sample of cells from a woman's cervix using a small flat spatula or brush.
- Smearing and fixing cells onto a glass slide.
- Sending the slide to a cytology laboratory where it is stained and examined under a microscope to determine cell classification.
- Transmitting the results back to the provider and then to the woman.



What infrastructure does cytology require?

- Private exam area
- Examination table
- Trained health professionals
- Sterile vaginal speculum
- Supplies and equipment for preparing and interpreting the Pap smears (e.g., spatulas, glass slides, fixative, stains, microscopes)
- Marker/pencil/glass writer/labels
- Cytology requisition forms

Continued...

What infrastructure does cytology require? (cont.)

- Record books or sheets
- Slide mailers
- Cytology laboratories with skilled personnel to interpret results
- Pathologists
- Transportation of slides to the laboratory and back
- Information systems to ensure follow-up contact with clients
- Quality assurance system to maximize accuracy

Categories for Pap test results:

■ Normal results:

- If no abnormal cells are seen, then the test result is normal.
- If only benign changes are seen, usually resulting from inflammation or irritation, then the test result is normal.

■ Abnormal results:

- Atypical cells of undetermined significance (ASCUS, AGUS).
- Low-grade squamous intraepithelial lesions (LSIL) or cervical intraepithelial neoplasia (CIN) 1. These are mild, subtle cell changes, and most go away without treatment.
- High-grade squamous intraepithelial lesions (HSIL) or CIN 2 or 3. Moderate and severe cell changes which require further testing or treatment.
- Carcinoma.

Management options if the Pap test result is abnormal:

- For women with low-grade squamous abnormalities (ASCUS or LSIL), give periodic Pap tests until the abnormality resolves, or a colposcopy referral for persistent lesions.
- Women with glandular abnormalities (AGUS) usually are referred for colposcopy.
- Women with HSIL usually are referred for colposcopy.
- Women with HSIL should be treated to remove or destroy the abnormal cells.

Test performance: Sensitivity and specificity

- Sensitivity: The proportion of all those with disease that the test correctly identifies as positive.
- Specificity: The proportion of all those without disease (normal) that the test correctly identifies as negative.

Pap test performance:

- Sensitivity = 51% for CIN I or higher
 - Range of 37% to 84%
- Specificity = 98% for CIN I or higher
 - Range of 86% to 100%
- These results are from a meta-analysis of cross-sectional studies (AHCPR 1999).
- Several ACCP studies have also found Pap test sensitivity in the range of 50% at best.

Strengths of cytology:

- Historical success in developed countries.
- High specificity, meaning women with no cervical abnormalities are correctly identified by the test with normal test results.
- A well characterized screening approach.
- May have the potential to be cost-effective in middle-income countries.

Limitations of cytology:

- Moderate to low sensitivity:
 - High rate of false-negative test results
 - Women must be screened frequently
- Rater dependent
- Requires complex infrastructure
- Results are not immediately available
- Requires multiple visits
- Likely to be less accurate among post-menopausal women

Conclusions:

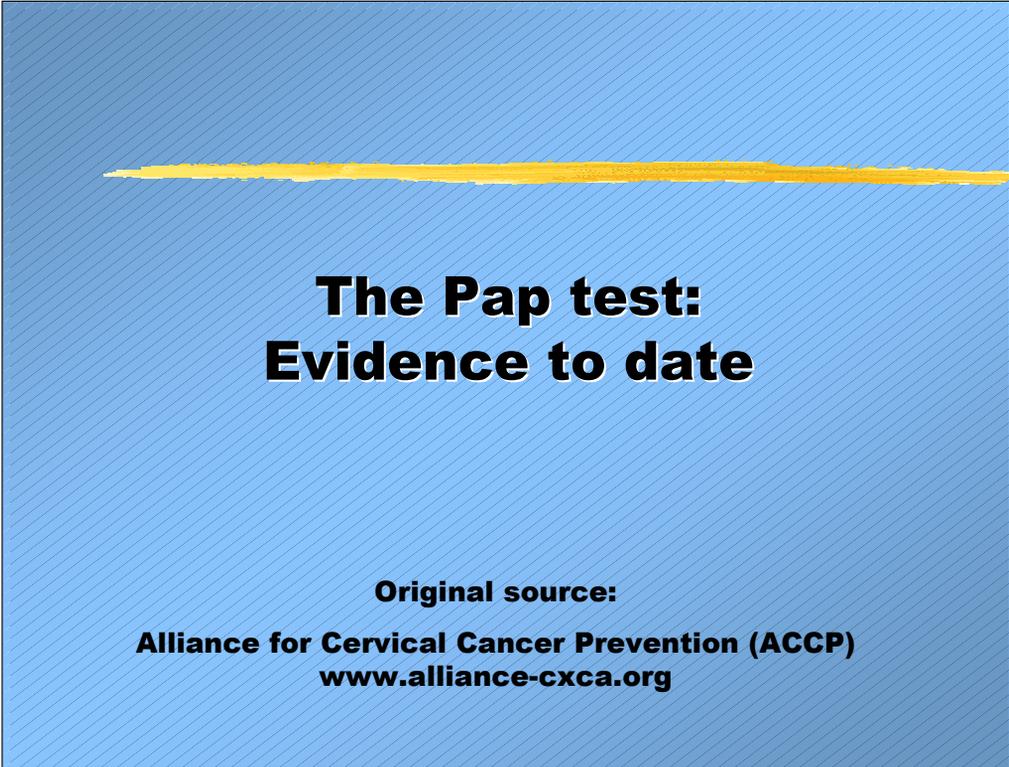
- Cytology may be an appropriate screening approach in middle-resource settings with reliable quality control mechanisms.
- Cytology infrastructural requirements generally make it an impractical approach for many low-resource settings.
- Decision makers need to carefully consider how existing Pap smear services can be strengthened or whether to explore alternative screening approaches.

References:

- ACCP. Pap smears: An important but imperfect method. Cervical Cancer Prevention Fact Sheet. (October 2002).
- Agency for Health Care Policy and Research (AHCPR). *Evaluation of Cervical Cytology*. Evidence Report/Technology Assessment, No. 5. Rockville, MD. (1999).

For more information on cervical cancer prevention:

- **The Alliance for Cervical Cancer Prevention (ACCP)**
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- **ACCP partner organizations:**
 - **EngenderHealth** www.engenderhealth.org
 - **International Agency for Research on Cancer (IARC)**
www.iarc.fr
 - **JHPIEGO** www.jhpiego.org
 - **Pan American Health Organization (PAHO)**
www.paho.org
 - **Program for Appropriate Technology in Health (PATH)** www.path.org



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Introduction: This presentation provides a summary of the Pap test as a test for the detection of cervical cancer.

Overview:

- Description of the Papanicolaou (Pap) smear test and how it works
- Infrastructure requirements
- What test results mean
- Test performance
- Strengths and limitations
- Program implications in low-resource settings

Slide overview: In this presentation we will discuss the following topics.

Note for bullet 1: The Pap smear test, or Pap test, is also called cytology, or cervical cytology.

What does a Pap test involve?

- Performing a vaginal speculum exam during which a health care provider takes a sample of cells from a woman's cervix using a small flat spatula or brush.
- Smearing and fixing cells onto a glass slide.
- Sending the slide to a cytology laboratory where it is stained and examined under a microscope to determine cell classification.
- Transmitting the results back to the provider and then to the woman.



Slide overview: The Pap test involves a number of steps that have to be done with the appropriate lab technology.

What infrastructure does cytology require?

- Private exam area
- Examination table
- Trained health professionals
- Sterile vaginal speculum
- Supplies and equipment for preparing and interpreting the Pap smears (e.g., spatulas, glass slides, fixative, stains, microscopes)
- Marker/pencil/glass writer/labels
- Cytology requisition forms

Continued...

Slide overview: Effective Pap smear screening, also called cytology, requires significant infrastructural support. The list continues on the next slide.

Note for last bullet: A cytology requisition form is used to record each woman's information and test results. This form holds very important information for contacting women about test results and possible treatment options.

What infrastructure does cytology require? (cont.)

- Record books or sheets
- Slide mailers
- Cytology laboratories with skilled personnel to interpret results
- Pathologists
- Transportation of slides to the laboratory and back
- Information systems to ensure follow-up contact with clients
- Quality assurance system to maximize accuracy

Slide overview: Cytology infrastructure requirements continued.

- *Note for bullet 5:* Transportation mechanisms are needed to send slides to the laboratory and return results to the health center in a timely manner.
- *Note for second to last bullet:* Quality control mechanisms may involve periodic refresher trainings of cytotechnicians, random checking of a subset of samples by senior cytotechnicians, or use of quality control slide panels.
- *Note for last bullet:* Elements of a quality assurance system include (but are not limited to) supervision, periodic refresher training, evaluation of on-going program activities and long-term impact, mechanisms for constructive feedback from women and health care providers, and an effective information system.

Categories for Pap test results:

■ Normal results:

- If no abnormal cells are seen, then the test result is normal.
- If only benign changes are seen, usually resulting from inflammation or irritation, then the test result is normal.

■ Abnormal results:

- Atypical cells of undetermined significance (ASCUS, AGUS).
- Low-grade squamous intraepithelial lesions (LSIL) or cervical intraepithelial neoplasia (CIN) 1. These are mild, subtle cell changes, and most go away without treatment.
- High-grade squamous intraepithelial lesions (HSIL) or CIN 2 or 3. Moderate and severe cell changes which require further testing or treatment.
- Carcinoma.

Slide overview: Pap test results are either normal or abnormal. Results are reported from the cytology laboratory to the health professional/health facility.

•*Note for bullet 2:* Pap test detects a range of cellular changes in the cervix from mildly abnormal (atypical) to malignant (cancerous).

•*Note for sub-bullets under bullet 2:* Term definitions:

- ASCUS = atypical squamous cells of undetermined significance
- AGUS = atypical glandular cells of undetermined significance
- CIN 1 = low-grade cervical intraepithelial neoplasia
- CIN 2 or 3 = high-grade cervical intraepithelial neoplasia

Management options if the Pap test result is abnormal:

- For women with low-grade squamous abnormalities (ASCUS or LSIL), give periodic Pap tests until the abnormality resolves, or a colposcopy referral for persistent lesions.
- Women with glandular abnormalities (AGUS) usually are referred for colposcopy.
- Women with HSIL usually are referred for colposcopy.
- Women with HSIL should be treated to remove or destroy the abnormal cells.

Slide overview: There are a number of steps to take when a woman's test result is abnormal. This entire process depends, however, on a country's clinical care guidelines and local resources, including the existence of a fully functioning referral system.

■ *Note for bullets 1, 2, and 3:* Colposcopy involves examining the cervix with a magnifying scope and often involves obtaining a biopsy.

■ *Note for bullet 3:* While the Pap test identifies whether abnormal cells are present in the sample, the results cannot indicate where on the cervix the lesion is located. Therefore, colposcopy is needed as a follow-up test for women with test-positive results.

Test performance: Sensitivity and specificity

- Sensitivity: The proportion of all those with disease that the test correctly identifies as positive.
- Specificity: The proportion of all those without disease (normal) that the test correctly identifies as negative.

Slide overview: The test performance of each screening method is rated by its sensitivity and specificity. Before discussing the Pap smear's test performance, it is important to understand what sensitivity and specificity mean.

Pap test performance:

- Sensitivity = 51% for CIN I or higher
 - ▮ Range of 37% to 84%
- Specificity = 98% for CIN I or higher
 - ▮ Range of 86% to 100%
- These results are from a meta-analysis of cross-sectional studies (AHCPR 1999).
- Several ACCP studies have also found Pap test sensitivity in the range of 50% at best.

Slide overview: Pap smear screening is specific, but only moderately sensitive, even when performed correctly and according to quality standards.

■ *Note for bullet 1:* Cytology is moderately sensitive, at best. That is, it often does not correctly identify true positives.

■ *Note for bullet 2:* Cytology can be specific for detecting high-grade lesions or cancer. That is, it correctly identifies as normal most true normal results.

■ *Note for bullet 3:* This meta-analysis examined 12 studies that varied widely in design and used different confirmatory reference standards.

■ *Note at the end:* It is noteworthy that one of the best screening programs in the world, in Canada where women have regular access to effective cytologic screening, Pap sensitivity from detection rates of dysplasia at subsequent screening rounds is estimated to be approximately 75% (Boyes et al., 1982).

Strengths of cytology:

- Historical success in developed countries.
- High specificity, meaning women with no cervical abnormalities are correctly identified by the test with normal test results.
- A well characterized screening approach.
- May have the potential to be cost-effective in middle-income countries.

Slide overview: There are many strengths to cytology, including its tremendous contribution to reducing cervical cancer incidence and mortality rates in developed countries.

•*Note for bullet 1:* When the Pap test was introduced in the 1940s, it was the only cervical screening test to date worldwide. Cervical cancer incidence and mortality rates have decreased in developed countries where the Pap test is used as part of well-organized screening and treatment programs.

•*Note for bullet 3:* “Well characterized” means that the Pap smear technique and the test qualities have been well studied and described.

•*Note for bullet 4:* Middle-income countries tend to have more substantial infrastructural, technical, and clinical capacities that can support the provision of effective cytology services.

Limitations of cytology:

- Moderate to low sensitivity:
 - High rate of false-negative test results
 - Women must be screened frequently
- Rater dependent
- Requires complex infrastructure
- Results are not immediately available
- Requires multiple visits
- Likely to be less accurate among post-menopausal women

Slide overview: The Pap test also has imperfections which limit its effectiveness, particularly in low-resource settings.

•*Note for bullet 1:* As defined earlier, sensitivity is the proportion of individuals with disease who are correctly identified by the test as having disease. A test with low sensitivity means that women with disease will be falsely identified as being free of disease. As many lesions go undetected, program impact is limited unless women are screened frequently. Frequent screening can be difficult in low-resource settings.

•*Note for Bullet 2:* “Rater dependent” means the test's performance depends on the abilities of the person doing the test (versus a machine, as for HPV testing). This means that even when service providers have training, test performance may vary depending on service delivery conditions and other factors.

•*Note for bullet 3:* Few low-resource countries have the resources to provide frequent and effective screening.

•*Note for bullet 5:* The fact that the Pap test requires multiple visits can lead to a great deal of loss to follow-up in many low-resource settings. Between screening, getting the results analyzed, getting a woman back in for the results, and getting her treated if confirmed abnormal, programs often are not able to follow up with women. It is noteworthy here that there is also loss to follow-up in developed countries.

Conclusions:

- | Cytology may be an appropriate screening approach in middle-resource settings with reliable quality control mechanisms.
- | Cytology infrastructural requirements generally make it an impractical approach for many low-resource settings.
- | Decision makers need to carefully consider how existing Pap smear services can be strengthened or whether to explore alternative screening approaches.

Slide overview: Pap screening can be an effective way to detect and prevent cervical cancer, however, cytology programs must be complemented by various infrastructure and program characteristics in order to be successful.

References:

- ACCP. Pap smears: An important but imperfect method. Cervical Cancer Prevention Fact Sheet. (October 2002).
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