Complete Summary

GUIDELINE TITLE

Cervical screening.

BIBLIOGRAPHIC SOURCE(S)

Ontario Cervical Screening Program, Gynecology Cancer Disease Site Group. McLachlin CM, Mai V, Murphy J, Fung Kee Fung M, Chambers A. Cervical screening. Toronto (ON): Cancer Care Ontario (CCO); 2005 May 20. 39 p. [74 references]

GUIDELINE STATUS

This is the current release of the guideline.

The Guideline will expand over time to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Cervical cancer

GUIDELINE CATEGORY

Management
Prevention

Screening
Technology Assessment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Oncology
Preventive Medicine

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To identify the optimal cervical screening tool (conventional cytology, liquid based cytology, or human papillomavirus [HPV] deoxyribonucleic acid [DNA] testing)
- 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
- To identify the most appropriate time for initiation and cessation of cervical screening
- To identify the time interval that women should be screened
- To identify if women in special circumstances should be screened (i.e., pregnant women, women post-hysterectomy, human immunodeficiency virus [HIV] positive women, women who have sex with women)
- To identify the optimal management for women with abnormal cytology (up to but not including colposcopy/human papillomavirus management)

TARGET POPULATION

All women who are, or have ever been, sexually active

INTERVENTIONS AND PRACTICES CONSIDERED

Screening

1. Liquid-based cytology (LBC)
2. Conventional smear cytology
3. Province-wide screening program with a recall mechanism
4. Biopsy of visible cervical lesion

Management of Abnormal Cytology

1. Human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing with cytology
2. Repeat Pap tests
3. Colposcopy

4. Intravaginal estrogen
5. Endocervical and endometrial sampling

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of screening tools for detecting abnormal cytology
- Rates of unsatisfactory specimens
- Safety/adverse effects of interventions
- Rates of detection of abnormal cytology and cervical cancer
- Incidence of and mortality due to cervical cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The MEDLINE (1998 to July 2004), EMBASE (1998 to July 2004), and Cochrane Library (2004, Issue 2) databases were searched for practice guidelines, technology assessments, systematic reviews, and clinical trials. Reference lists of papers and review articles were scanned for additional citations. The Canadian Medical Association Infobase, the National Guidelines Clearinghouse, and other Web sites were searched for existing evidence-based practice guidelines.

The following text words and medical subject headings (MeSH) were used: cervix, cervical, cancer, carcinoma, screening, and mass screening (as an exploded MeSH term). Search terms related to study design and publication type, used to search the MEDLINE and EMBASE databases, included clinical trial (text word and publication type), clinical trials (as an exploded MeSH term), meta-analysis (text word and publication type), and systematic review.

Inclusion Criteria

Table 1 in the original guideline document describes the details of the inclusion criteria and outcome variables for each question addressed in this practice guideline.

Exclusion Criteria

1. Abstracts, letters, and editorials were not considered.
2. Papers published in a language other than English were not considered.

NUMBER OF SOURCE DOCUMENTS

Six technology assessments, 1 systematic review, 7 retrospective studies, 7 practice guidelines, 1 in press guideline, 8 cross-sectional studies, 4 case-control

studies, 1 prospective cohort study, 3 randomized controlled trials, 1 meta-analysis, and 1 conference report were eligible for inclusion and review.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

I. Evidence from at least 1 randomized controlled trial
II. 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
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The results of the studies included in this guideline are described in the original guideline document. There were no statistical analyses performed on any of the data because there was either insufficient data to pool or meta-analyses had already been completed. The details of the meta-analyses are included in this guideline.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Cervical Screening Guidelines Development Committee met to discuss the draft guideline. The group went through the sections of guideline individually and discussed how the evidence supported the recommendations. There was general consensus regarding the recommendation to indicate that liquid-based cytology (LBC) was the preferred screening tool over conventional cytology.

In terms of the initiation of cervical screening, the group extensively discussed the optimal wording of the recommendation. The group chose not to include a specific age to initiate screening because there are women who are not sexually active by 18 or 21 (recommended ages in other guidelines), and did not want to recommend that these women be screened.

For the cessation of screening, the group spent some time discussing the potential high-risk sexual behaviours of older women. Ultimately the group decided not to

make recommendations based upon high risk behaviours in older women because the group felt it would complicate the recommendations, also there was no evidence identified to support different screening regimens for high risk older women.

There was some discussion regarding the optimal screening interval especially regarding necessary recall mechanisms for a three-year screening interval. The need for recall mechanisms either within the primary care practice or as part of the provincial registry was emphasized before a three-year interval should be considered.

Unfortunately, there is little evidence regarding cervical screening for women in special circumstances. For this reason, the group decided that it was important to clearly state throughout the guideline where there was evidence and where expert opinion was utilized.

For the recommendations regarding abnormal cytology, the group discussed simply endorsing the American Society of Colposcopy and Cervical Pathology (ASCCP) guidelines because of similarities to the Ontario setting. However, after some debate the group agreed that there are important differences in recommendations in the guideline compared to the ASCCP guidelines. It was important to the group to make the guidelines specific to the population of women in Ontario.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

A. Good evidence for efficacy and substantial clinical benefit support recommendation for use.
B. Moderate evidence for efficacy or only limited clinical benefit support recommendation for use.
C. Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendations may be made on other grounds.
D. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.
E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 180 physicians (129 family practitioners and pathologists [from supplied lists] and 51

practitioners from the Program in Evidence-based Care [PEBC] database: 30 medical oncologists, 1 radiation oncologist, 11 surgeons, and 9 gynecologists) across the province on September 15, 2004. Reminder postcards went out to the non-responders on September 29, 2004 and a second reminder (full package) was sent out on October 13, 2004. A third mailing (full package) went out on November 9, 2004.

Final approval of all practice guideline reports is obtained from the Practice Guidelines Coordinating Committee (PGCC).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The scales for the quality of evidence (I-III) and the strength of recommendations (A-E) are defined at the end of the "Major Recommendations" field.

Optimal Cervical Screening Tool

- Liquid-based cytology (LBC) is the preferred tool for cervical cytology screening (B-II). Conventional smear cytology remains an acceptable alternative (C-III).

Optimal Screening Circumstances

- Given the lower incidence and mortality associated with organized screening programs (with recall systems) elsewhere, a province-wide cervical screening program with an adequate recall mechanism is recommended (A-II).

Screening Initiation

- Cervical cytology screening should be initiated within three years of first vaginal sexual activity (i.e., vaginal intercourse, vaginal/oral, and/or vaginal/digital sexual activity) (C-III).

Screening Interval (These recommendations do not apply to women who have had previous abnormal Pap tests. Please see management of abnormal cytology section for further information).

- Screening should be done annually until there are three consecutive negative Pap tests (C-III).
- Screening should continue every two to three years after three annual negative Pap tests (B-II).
    - Screening at a three-year interval is recommended, supported by an adequate recall mechanism (B-II).
    - 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).

Screening Cessation

- 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).

Screening Women with Special Circumstances

- Immunocompromised or human immunodeficiency virus (HIV) positive women should receive annual screening (C-III).
    - Examples of situations where women may be immunocompromised include women who have received transplants and women who have undergone chemotherapy.
- 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).
    - Women who have undergone subtotal hysterectomy (with an intact cervix) should continue screening according to the guidelines.
- 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.
- Women who have sex with women should follow the same cervical screening regimen as women who have sex with men (B-II).

Recommended Management for Women with Abnormal Cytology

ASCUS (Atypical squamous cells of uncertain significance)

- Human papillomavirus (HPV) deoxyribonucleic acid (DNA) testing with cytology is recommended for women aged 30 or older with atypical squamous cells of uncertain significance (C-III).
    - 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.
    - 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.
- In women under the age of 30, a repeat Pap test in six months is recommended (C-III).
    - 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 tests results, she should return to routine screening.
- Referral to colposcopy, without HPV DNA testing or repeat cytology, is only recommended in situations where there is a high probability of patient loss to follow up, or if there are other symptoms suggesting cervical abnormality (abnormal bleeding, etc.) (A-I).

ASC-H (Atypical squamous cells: cannot exclude high grade squamous)

- Colposcopy is recommended for women with ASC-H (A-II).

LSIL (Low-grade squamous intraepithelial lesion)

- Either colposcopy or repeat cytology in six months is recommended for women with LSIL (B-II).
    - If repeat cytology is used and 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.
    - There is limited evidence to support the use of intravaginal estrogen to reverse the cytologic changes in postmenopausal women with LSIL. A course of intravaginal estrogen followed by repeat cytology approximately a week after completing the regimen is acceptable for women with LSIL who have clinical or cytological evidence of atrophy and no contraindications to using intravaginal estrogen. Referral for colposcopy is recommended if a result of atypical squamous cells of uncertain significance or greater is obtained (CIII).

HSIL (High-grade squamous intraepithelial lesion)

- Colposcopy is recommended for women with HSIL (A-II).

AGC (Atypical glandular cells)

- Colposcopy is recommended for women with AGC (A-II).
- Women with AGC should also receive endocervical and endometrial sampling, where appropriate (A-II).

<u>Definitions</u>:

Strength of Recommendations

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E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

Quality of Evidence

I. Evidence from at least 1 randomized controlled trial
II. 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

III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by technology assessments, systematic reviews, retrospective studies, practice guidelines, in press guidelines, cross-sectional studies, case-control studies, retrospective cohort studies, prospective cohort studies, randomized controlled trials, meta-analyses, and conference reports. In cases where the data did not appear conclusive, recommendations were based on the consensus opinion of the group.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Optimal use of cervical screening tools
- Reduced incidence and mortality due to cervical cancer
- Appropriate initiation, intervals, and cessation of cervical screening
- Optimal management of women with abnormal cytology

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These are minimum guidelines only. Certain clinical situations may require earlier follow-up/referral for colposcopy.
- Repeat Pap test should not be performed earlier than three months following the original.
- Pap test should not be used as the sole assessment of a visible cervical lesion. These patients require biopsy for accurate diagnosis.
- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult the practice guideline is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Ontario Cervical Screening Program, Gynecology Cancer Disease Site Group. McLachlin CM, Mai V, Murphy J, Fung Kee Fung M, Chambers A. Cervical screening. Toronto (ON): Cancer Care Ontario (CCO); 2005 May 20. 39 p. [74 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 May 20

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC), is a project supported by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Cervical Screening Guidelines Development Committee of the Ontario Cervical Screening Program

Provincial Gynecology Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Members of the Cervical Screening Guidelines Development Committee: Dr. Verna Mai (Leader- Screening Group); Dr. C. Meg McLachlin (Chair, Leader -- Screening Tool Group); Dr. Joan Murphy (Leader- Management Group); Joanne Miyazaki; Patricia Anderson; Dr. Monique Bertrand; Dr. Scott Boerner; Dr. Peter Bryson; Dr. William Chapman; Dr. Terry Colgan; Dr. Laurie Elit; Dr. Christopher Giede; Robbi Howlett; Dr. Richard Johnston; Sue Lebeau; Dr. Stan Lofsky; Leela Prasaud; Dr. Nathan Roth; Dr. R. Michael Shier; Dr. Sara Taman; Dr. Frank Thompson

For a current list of past and present members of the Gynecology Cancer Disease Site Group, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The members of the Gynecology Cancer Disease Site Group (DSG) disclosed potential conflicts of interest relating to the topic of this practice guideline. One collaborator is employed by MDS Diagnostic Services and has investments with MDS. Another collaborator is a consultant for MDS Diagnostic Services and receives honoraria from MDS for his contributions. Four collaborators are currently involved in a trial examining the results of the implementation of SurePath in Ontario, and four collaborators are involved in a trial investigating the feasibility of implementing human papillomavirus (HPV) testing in a family practice setting. Two collaborators are members of the Cytobase Data Review Committee, and another collaborator is the chair of cytology at QMP-LS. No other conflicts of interest were declared.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Cervical screening. Summary. Toronto (ON): Cancer Care Ontario (CCO). Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 11, 2005. The information was verified by the guideline developer on September 13, 2005.

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