Complete Summary

GUIDELINE TITLE

Guidance on the use of liquid-based cytology for cervical screening.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of liquid-based cytology for cervical screening. London (UK): National Institute for Clinical Excellence (NICE); 2003 Oct. 22 p. (Technology appraisal; no. 69).

GUIDELINE STATUS

This is the current release of the guideline.

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SCOPE

DISEASE/CONDITION(S)

Cervical cancer

GUIDELINE CATEGORY

Prevention
Screening
Technology Assessment

CLINICAL SPECIALTY

Family Practice
Internal Medicine

Obstetrics and Gynecology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To review and re-appraise the use of liquid-based cytology for cervical screening

TARGET POPULATION

Women at risk of cervical cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Liquid-based cytology for cervical screening

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
- Cost-effectiveness

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
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by The School of Health and Related Research (ScHARR), The University of Sheffield. (see the "Companion Documents" field).

Three types of literature search were performed:

- A clinical effectiveness search
- A cost-effectiveness search
- A modelling search

The first two concentrated on liquid-based cytology, while the modelling search addressed the wider topic of modelling studies in respect of cervical screening.

Industry submissions to NICE were included in the review.

Databases searched were:

- Medline
- Embase
- Science Citation Index
- Cochrane Library
- NHS CRD: DARE, NEED and HTA
- HealthSTAR
- National Research Register

Web pages were contacted for International Network of Agencies for Health Technology Assessment (INAHTA) members and other Health Technology Assessment (HTA) organisations to determine if HTA reports had been produced on this topic.

A citation search was carried out for studies included in the Australian Health Technology Advisory Committee report. Search strategies for the MEDLINE searches are shown in appendix 1 of the systematic review companion document.

Inclusion and Exclusion Criteria

All health technology assessment and related secondary research studies were included. Primary research studies were included if they attempted to measure an outcome of importance, such as comparison of liquid-based cytology with conventional cervical smears in respect of an assessment of sensitivity and/or specificity, categorisation of specimens, percentage of inadequate or unsatisfactory specimens and specimen interpretation times. There are also in the market place devices developed to automate the analysis and classification of images from conventional pap smears. This methodology was excluded from the update. All papers in languages other than English were excluded because of insufficient time to arrange for translation. All databases were searched from January 1999 up to October 2002.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction Strategy

All abstracts and papers were double read. For relevant articles data were extracted by one of the authors and checked by the second. Key tabulations and calculations for summary tables were checked by entering the published study data (where available) into a spreadsheet and re-calculating the relevant percentages.

Quality Assessment Strategy

Studies varied in study design quality and presentation of results. Only those with a clear tabulation of the numerical data were used in the conventional smear versus liquid-cytology assessments. Other comments on the quality of studies and study design are made later in the text in relation to specific study types. For the review update, the methodological quality of primary studies was assessed using the Cochrane model.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Summary of Costs and Cost-Effectiveness Data

Costs

The estimated annual gross cost of consumables and operating equipment associated with introducing the new technique is about 10 million pounds sterling in England.

Cost-Effectiveness

No United Kingdom (UK)-based studies providing direct evidence regarding the cost-effectiveness of liquid-based cytology screening were identified. Analyses based upon models of disease natural history, conducted in this study, show that conventional pap smear screening is extendedly dominated by liquid-based

cytology (liquid-based cytology is always more cost-effective compared to conventional pap smear testing over the same screening interval). Comparing liquid-based cytology across alternative screening intervals gives a cost-effectiveness of under 10,000 pounds sterling per life year gained when screening is undertaken every 3 years. The cost-effectiveness results are relatively stable under most conditions, though if screening outcomes such as borderline results and colposcopy are assumed to induce even small amounts of disutility then liquid based cytology screening at 5-yearly intervals may be the most cost-effective option.

See Section 4.2 of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, assessment report and the appraisal consultation document (ACD). They were also provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Trade organisations
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- It is recommended that liquid-based cytology (LBC) is used as the primary means of processing samples in the cervical screening programme in England and Wales.
- There is currently insufficient evidence to recommend one LBC product over another. The National Health Service (NHS) Cervical Screening Programme and Cervical Screening Wales may wish to consider evaluating further the different products as the method is introduced.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

There were no randomised trials using an outcome such as invasive cancer or mortality as outcome measures. A few studies attempted to compare the sensitivity and specificity of the existing technique with liquid-based cytology by using a histological examination 'gold-standard'. Most comparisons were split-sample studies comparing cytological results.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Potential advantages of the liquid-based cytology (LBC) method include an improved means of slide preparation, producing more homogeneous samples than the Pap smear (which may make slides easier to read), increased sensitivity and specificity, and improved efficiency of handling laboratory samples, resulting in increased laboratory productivity.

POTENTIAL HARMS

Because the liquid-based cytology (LBC) sample is a homogenate there is no way of verifying that a sufficient number of cervical cells have been harvested by the smear taker. The Committee considered this to be an important issue that must be addressed as part of the implementation of LBC. Poor sampling technique, resulting in the collection of too few cells, could mean that a sample might not adequately represent cells on the surface of the cervix. Consequently abnormalities may be missed, resulting in some false-negative results. However, the Committee concluded that this potential risk of false-negatives should be balanced against the likelihood of abnormalities being detected at a subsequent screen because of the regular screening frequency of the cervical screening programme, and the increased detection of high-grade lesions (severe dyskaryosis) with the LBC technique.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Limitations of the Calculations (Assumptions Made)

There are gaps in the evidence describing the underlying natural history of the disease. Similarly, the true sensitivity of the screening tests, both conventional smears and liquid-based cytology, is unobservable without subjecting women to otherwise unnecessary and relatively invasive investigations. These characteristics have thus been estimated by fitting of mathematical models of the disease and intervention to observable events such as actual incidence.

Other Important Issues Regarding Implications

It is clear that increasing the coverage of the cervical screening programme is also an important way of reducing the burden of invasive cervical cancer. In addition, a range of economic evaluations were identified in the updated systematic search (1999-2002) that assessed the economic impact of cervical screening approaches other than conventional pap smear testing and liquid-based cytology techniques, including semi-automated slide analysis, human papilloma virus (HPV) testing as an adjunct or alternative to pap smear testing, and protocols for the management of atypical screening results.

The aggregate analysis of the cost-effectiveness of potential combinations of these approaches to screening for cervical cancer are outside the scope of the current review, though it is noted that the relative cost-effectiveness of all relevant screening programme configurations should be analysed simultaneously.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

- The National Health Service Cervical Screening Programme (NHSCSP) and Cervical Cancer Screening Wales should develop implementation plans for the adoption of liquid-based cytology (LBC) as the primary means of collecting and processing samples and consult with their respective national purchasing agencies on the preparation of national procurement strategies for LBC technology. National Health Service (NHS) organisations should consult with NHSCSP and Cancer Screening Wales before making investments in LBC.
- National and local guidelines, protocols or care pathways relating to the collection and processing of a cervical specimen should be changed to reflect the change in practice following adoption of this guidance.
- The NHSCSP and Cervical Screening Wales should include measurement of the correct use of LBC as part of an ongoing quality assurance programme.
- Local clinical audits of cervical screening could include measures of the correct use of LBC and inadequate specimens.

IMPLEMENTATION TOOLS

Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). Guidance on the use of liquid-based cytology for cervical screening. London (UK): National Institute for Clinical Excellence (NICE); 2003 Oct. 22 p. (Technology appraisal; no. 69).

ADAPTATION

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

DATE RELEASED

2003 Oct

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Liquid-based cytology for cervical screening. Summary. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Oct. 2 p. (Technology appraisal 69). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Liquid-based cytology in cervical screening: an updated rapid and systematic review. Assessment report. The School of Health and Related Research (ScHARR), The University of Sheffield; 2003 Jan. 67 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N0297. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- The use of liquid-based cytology for cervical screening. Understanding NICE guidance - information for the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2003 Oct. 8 p. (Technology appraisal 69).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N0298. 11 Strand, London, WC2N 5HR.

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NGC STATUS

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