Collection devices for cervical screening

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What is a brief report?

This brief report, prepared by HSAC Reviewers, is an overview of a specific topic area identified from a systematic search strategy of electronic databases and website resources. The materials include lists of abstracts, key full text papers (where readily available from local resources), and website resources.

The report is aimed at giving the client an informed “guided tour” of the what the search strategy identifies around the topic area and outlines the contents of the report, highlights information of particular interest and relevance, summarises key articles, and comments on the stage and extent of the research base. It also makes suggestions for publications that the client may wish to have retrieved if relevant, and comments on the potential of the topic for evidence-based reviews, such as HSAC Technical Brief or Systematic Review outputs. Brief reports do not involve systematic processes for the critical appraisal of identified research, but may present data from full text articles in tables (without appraisal). Another significant limitation is that full text articles of key interest are not retrieved unless freely obtainable from local resources. As a consequence of this, comments and summaries in the brief report may be based on abstracts rather than full text papers.

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This report is not intended to be used as personal health advice. People seeking individual medical advice should contact their physician or health professional.

The views expressed in this report are those of HSAC and do not necessarily represent those of the University of Canterbury New Zealand, Health Technology Analysts Pty Ltd, Australia or the Ministry of Health.
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<th>Description</th>
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<tbody>
<tr>
<td>95% CI</td>
<td>95% Confidence Interval</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
</tr>
<tr>
<td>APNs</td>
<td>Advance Practice Nurse(s)</td>
</tr>
<tr>
<td>ASC-US</td>
<td>Atypical Squamous Cells of Undetermined Significance</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribo Nucleic Acid</td>
</tr>
<tr>
<td>FP</td>
<td>Family Physician</td>
</tr>
<tr>
<td>H-SIL</td>
<td>High-grade Squamous Intraepithelial Lesions</td>
</tr>
<tr>
<td>HPV</td>
<td>Human Papilloma Virus</td>
</tr>
<tr>
<td>LBC</td>
<td>Liquid-Based-Cytology</td>
</tr>
<tr>
<td>L-SIL</td>
<td>Low-grade Squamous Intraepithelial Lesions</td>
</tr>
<tr>
<td>NEG</td>
<td>Negative</td>
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<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
</tr>
<tr>
<td>NSU</td>
<td>National Screening Unit</td>
</tr>
<tr>
<td>OB/GYN</td>
<td>Obstetrician/Gynaecologist</td>
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<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>PB</td>
<td>Publisher</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase Chain Reaction</td>
</tr>
<tr>
<td>t-</td>
<td>Student t-test</td>
</tr>
<tr>
<td>TBS</td>
<td>The Bethesda System</td>
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Section A

Collection devices for obtaining cervical cytology samples for cervical screening

Research Question
What is the relative effectiveness of collection devices that are available currently for obtaining cervical cytology samples for cervical screening?

Background and scope of topic
This brief report will assist the Ministry of Health in planning which collection device to use for obtaining cervical cytology samples from women as part of the national screening programme for cervical cancer.

Intervention
All forms of collection devices used to obtain cervical cytology sample these may be:

- Spatula (e.g., Ayre spatula, or extended tip spatula)
- Cytobrush
- Cervexbrush

Client/population group and condition
Women undergoing cervical smear collection for cervical screening (primary care), or colposcopy following an abnormal smear or colposcopy after treatment.

Outcomes
The outcomes are based around the performance of different sampling devices for cervical smears (that is spatulas, brushes, etc). This is not the diagnostic accuracy of different cervical cell sample reading methods (i.e. not conventional pap smears versus liquid based cytology). The main outcome of interest is the number of unsatisfactory slides.

Methodology

Search strategy and methods to identify HTA reports on cervical sampling
A comprehensive search of bibliographic and review databases was conducted on 3 April 2008. The search process included review of relevant health technology assessment electronic databases and web-based resources. The searches were not limited by date and there were no language restrictions.

The following terms were used for a search of The Cochrane Library:

- (cervical near sampl*):ti,ab,kw
- “vaginal smears”:ti,ab,kw
- “cervical smears”:ti,ab,kw
- (cytological techniques):ti,ab,kw
- (uterine cervical neoplasms):ti,ab,kw AND (mass screening):ti,ab,kw
This strategy was modified and repeated for use with the Centre for Reviews and Dissemination (CRD) databases. Slight changes were required to the syntax of the search depending on the search platform used and to accommodate indexing differences in the databases. The searches were not limited by date and there were no language restrictions. However, a focus was placed on the results retrieved from the technology assessment sections.

To locate other key documents including policies, guidelines, programmes, reports and statements of authorities, a search was conducted of Web-based resources. Web sites searched and trawled as starting points included the following health technology organisations:

- Canadian Agency for Drugs and Technologies in Health (CADTH)
- Health Technology Assessment International (HTAi)
- International Network of Agencies for Health Technology Assessment (INAHTA)
- National Institute for Health and Clinical Excellence (NICE)
- National Institute for Health Research (NIHR)
- New Zealand Health Technology Assessment (NZHTA)

Additional Web sites searched were:

- Health Services/Technology Assessment Text (HSTAT)
- Scirus

Full descriptions of the databases and Web sites are presented in Section B.

**Methods**

One reviewer (RK) carefully considered the contents and identified article abstracts of the results from search strategy of this brief report. An overview of its contents was provided, highlighting information of particular interest and relevance. Full text articles of key interest, where freely obtainable from local resources, were retrieved and summarised. Characteristics and results from three fully retrieved relevant original papers and one fully retrieved systematic review are presented in details by another reviewer (WA). The report consists of four sections:

- Section A presents methodology including search strategy;
- Section B provides full description of the database and websites searched;
- Section C presents an overview of the search results; and
- Section D presents the detailed results from the systematic review and the selected original papers, as well as the presentation of conclusions.
Descriptions of Databases and Web Sites

**The Cochrane Library – Health Technology Assessment database**
Brings together details of completed and ongoing health technology assessments from around the world, being studies of medical, social, ethical and economic implications of health care interventions.

**Centre for Reviews and Dissemination databases – Health Technology Assessment database**
The HTA database brings together details of completed and ongoing health technology assessments from around the world. The abstracts in the database are descriptive rather than analytical and do not form critical appraisals of the reports. The database is produced in collaboration with the INAHTA Secretariat, based at SBU, Sweden.

**Canadian Agency for Drugs and Technologies in Health (CADTH)**
A national body that provides Canada’s federal, provincial and territorial health care decision makers with credible, impartial advice and evidence-based information about the effectiveness and efficiency of drugs and other health technologies.

**Health Technology Assessment International (HTAi)**
Mission is to support the development, communication, understanding and use of HTA around the world as a means of promoting the introduction of effective innovations and effective use of resources in health care.

**International Network of Agencies for Health Technology Assessment (INAHTA)**
Established in 1993 and has grown to 47 member agencies from 23 countries, stretching from North and Latin America to Europe, Australia, and New Zealand.

**National Institute for Health and Clinical Excellence (NICE)**
An independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health.

**National Institute for Health Research (NIHR)**
Committed to establishing the NHS as an internationally recognised centre of research excellence through supporting outstanding individuals, working in world-class facilities, conducting leading-edge research focused on the needs of patients and the public.

**New Zealand Health Technology Assessment (NZHTA)**
A clearinghouse for health outcomes and health technology assessment.

**Health Services/Technology Assessment Text (HSTAT)**
A free, Web-based resource of full-text documents that provide health information and support health care decision-making. HSTAT’s audience includes health care providers,
health service researchers, policy makers, payers, consumers and the information professionals who serve these groups.

**Scirus**
A comprehensive science-specific Internet search engine. It searches over 200 million science-specific Web pages enabling you to quickly pinpoint scientific information on the web and find the latest reports, articles, and patents.
**Section C**

**Search results**

**Search for HTA Reports on Cervical Sampling Devices**

(accessed 3 April 2008)

**The Cochrane Library (Reviews)**


http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001036/frame.html

**BACKGROUND:** The large variation in disease detection rated with cervical smears may be partly due to differences in the sampling devices and the techniques of sampling. **OBJECTIVES:** To assess whether the design of the cervical smear device affects rates of inadequate smears and the detection of disease; and whether the presence of endocervical cells in the smear affects disease detection. **SEARCH STRATEGY:** We searched the Cochrane Gynaecological Cancer Group trials register and MEDLINE up to July 1997. We also handsearched 16 journals. **SELECTION CRITERIA:** Randomised and quasi-randomised trials and non-randomised comparative studies comparing cervical smear collection devices in women attending for primary screening, colposcopy following an abnormal smear or colposcopy after treatment. **DATA COLLECTION AND ANALYSIS:** Two reviewers independently abstracted data. Study quality was assessed. **MAIN RESULTS:** Thirty-six trials and six observational comparative studies were included. The Ayre spatula was shown to be less effective compared with extended tip spatulas for collecting endocervical cells in eight trials (odds ratio 2.25, 95% confidence interval 2.06 to 2.44). Use of a spatula with the cytobrush was more effective than spatula alone at collecting endocervical cells (odds ratio 3.33, 95% confidence interval 3.05 to 3.63) and the same effect was present for adequate smear rates (odds ratio 1.51 95% confidence interval 1.19-1.92). Extended tip spatulas were also superior for the detection of dyskaryosis in seven trials (odds ratio 1.21, 95% confidence interval 1.10 to 1.33). Based on data from two trials and three observational studies, smears that contained endocervical cells were more likely to detect dyskaryosis, particularly in severe disease. The proportion of smears with endocervical cells present increased with increasing severity of the disease. **AUTHORS' CONCLUSIONS:** Extended tip spatulas of various designs appear to be better for collecting endocervical cells than the commonly used Ayre spatula. The most effective combination appears to be the cytobrush with an extended tip spatula. The rate of detection of endocervical cells appears to be a valid and convenient surrogate for the ability to detect dyskaryosis and for adequate smear rates. The ability of the extended tip spatula with the cytobrush compared with the extended tip spatula alone to detect disease, needs to be evaluated in a trial. **PLAIN LANGUAGE SUMMARY:** This review is no longer appropriate for update as liquid based cytology has superseded smear technology. Commonly used spatula not the most effective for cervical screening. Cervical screening (pap smear) is an effective way of detecting pre-cancerous abnormalities of the cervix (cervical intraepithelial neoplasia). Tests can be affected by the tester's skill and the design of the device used. Inadequate smears can produce incorrect results, causing stress and inconvenience to...
women having to undergo repeat screening. This review of trials found that the commonly used Ayre spatula is not as effective in collecting cells as the extended tip spatula. The most effective appears to be a combination of the cytobrush with an extended tip spatula. [Cochrane Library record description]

**The Cochrane Library (Technology Assessments) listed by date order (most recent first, alphabetic order second)**

**2007**

*Stephenson M, Doughty C.* Performance of commercially available HPV tests (Brief record), 2007
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20070573/frame.html [Cochrane Library record description]

**2006**

*Canadian Agency for Drugs and Technologies in Health (CADTH).* Liquid-based techniques for cervical cancer screening (project) (Brief record) 
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060375/frame.html [Cochrane Library record description]

*German Agency for Health Technology Assessment at the German Institute for Medical Documentation and Information (DAHTA) (DIMDI).* Should colposcopy be used in primary screening for cervix carcinoma? (project) (Brief record) 
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060406/frame.html [Cochrane Library record description]

*HAYES, Inc.* Human papillomavirus vaccines for prevention of cervical cancer (Brief record), 2006
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20061574/frame.html [Cochrane Library record description]

*Hulstaert F, Arbyn M, Huybrechts M, Vinck I, Puddu M, Ramaekers D.* HTA of cervical cancer screening and HPV testing (Brief record), 2006
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20061495/frame.html [or: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32006001495 ] PB (publisher): Belgian Health Care Knowledge Centre (KCE) [Cochrane Library record description]

*Norwegian Knowledge Centre for the Health Services (NOKC).* HPV-testing for cervical cancer (project) (Brief record), 2006
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20061327/frame.html [or: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32006001327 ] [Cochrane Library record description]

**2005**

*Danish Centre for Evaluation and Health Technology Assessment.* The use of liquid based cytology (LBC) and conventional pap smear (CPS) for cervical screening in Denmark: a health technology assessment (Structured abstract), 2005
Brief report - Collection devices for cervical screening

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060169/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32006000169 ]

Methods: The HTA included systematic literature-reviews on clinical effectiveness,
economic modelling, evaluations of patient-related consequences and organisational aspects
based on data collected from national registers, local investigations, and by survey.

Results: No scientific basis was found to suggest any difference in clinical or health
economic effect between LBC and conventional CPS. However, other aspects of the
screening programme, such as increase of participation, extension of the age limit,
improvement of national homogeneity and co-ordination of management, were found to be
effective approaches for achieving clinical and health economic gains.

Conclusions: Instead of spending limited resources on changing laboratory techniques,
initiatives should be taken in order to optimize the screening programme in terms of
improvement of coverage and management of the Danish screening activities - nationally and
regionally. [found at: http://www.dacehta.dk/ ] [Cochrane Library record description]

Frank W, Konta B, Peters-Engl C. PAP-test for the screening of cervical carcinoma:
impact of different examination intervals (Brief record), 2005.
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050582/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005000582 ] PB (publisher): German
Agency for Health Technology Assessment at the German Institute for Medical
Documentation and Information (DAHTA) (DIMDI) [Cochrane Library record description]

German Agency for Health Technology Assessment at the German Institute for Medical
Documentation and Information (DAHTA) (DIMDI). HPV-DNA-diagnosis for early
detection of cervical cancer (project) (Brief record).
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050861/frame.html [Cochrane
Library record description]

Institute for Clinical Systems Improvement. HPV DNA testing for the screening and
monitoring of cervical cancer (Structured abstract), 2005.
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20051208/frame.html

DESCRIPTION OF PROCEDURE

- The American Cancer Society estimates that in the year 2005 there will be 10,370
  newly diagnosed cases of cervical cancer (excluding in situ carcinomas) and 3710
  women will die of the disease. The incidence has decreased markedly in the last 50
  years in large part due to the availability of cytologic testing for early diagnosis,
treatment, and ultimately prevention of cervical cancer.

- HPV (human papillomavirus) testing is being considered as an alternative or an
  adjunctive test to cytologic testing (i.e., Pap smear). Although screening with Pap
  smears has been shown to have significantly reduced the incidence of cervical cancer,
  the false-negative rate of a single Pap test is reported to be 20%; however, the false
  negative rate of 3 or more consecutive negative annual screens may be as low as 1%.
  Such testing requires at least 3 office visits over 3 years to be confident concerning
  the absence of abnormal cytology and thus is inefficient. It has been recently
  discovered that cervical carcinomas and their precursors are directly related to the
  presence of HPV. HPV, especially a high-risk HPV type, is considered necessary, but
  not sufficient, for the development of cervical cancer or its precursors. Thus, due to
The present inaccuracies of the Pap smear, specifically the high false negative rate, HPV DNA testing has been studied as an alternative to or an adjunct to cytology in terms of primary screening and in terms of triage of patients with borderline or equivocal cytology to further testing.

COMMITTEE CONCLUSIONS

- With regard to human papillomavirus (HPV) DNA testing for the screening and monitoring of cervical cancer, the ICSI Technology Assessment Committee finds the following:

1. In women 30 years of age or older who have an ASCUS (atypical squamous cells of undetermined significance) cervical cytology result, the HPV DNA test, when performed as a reflex test (where performance of the test is contingent on an ASCUS cytology) is safe and efficacious for use in selecting women for referral to colposcopy and biopsy (positive HPV DNA test) or for monitoring at 6 months and 12 months (negative HPV DNA test). (Conclusion Grade II)

2. In women 30 years of age or older, automatic HPV DNA testing is safe and efficacious for use as an adjunct to cervical cytology to allow less frequent screening for cervical cancer. If both the HPV DNA and the cervical cytology results are negative, the woman is considered at low risk for cervical cancer. Such women may be screened at longer intervals, such as every three years. This conclusion is not applicable for women with a recent change in sexual partner. (Conclusion Grade II)

3. The evidence does not support the use of HPV DNA testing alone as a primary screening tool. Therefore, HPV DNA testing should not be used as a standalone test in this capacity.

4. There is not enough evidence to permit conclusions regarding the use of HPV DNA testing for the monitoring of treatment response or in selecting patients at high risk of relapse following treatment of CIN or cervical cancer.

5. The test procedure for HPV DNA is safe. The risk lies in what is done with the results. Failure to diagnose high-grade squamous intraepithelial lesions (HSIL) or invasive cervical cancer (false negative) or referral to colposcopy or biopsy when not needed (false positive) may result in morbidity or mortality

 [Cochrane Library record description]

Israel Center for Technology Assessment in Health Care (ICTAHC). The Appropriateness of Preliminary Conditions for Conducting Cervical Screening Tests (project) (Brief record) http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050926/frame.html [or: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005000926 ]
 [Cochrane Library record description]


The overall objective of the project was to assess the immediate effects, the wider consequences and costs, and overall cost-effectiveness and cost-utility of introducing
automated image analysis to a screening programme with characteristics similar to those currently operating in the UK
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005000187 ]
[full text available at: http://www.hta.ac.uk/execsumm/summ913.htm ]
[Cochrane Library record description]

2004
ECRI. Pap smear plus speculoscopy for cervical cancer screening (Brief record), 2004
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060553/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32006000553 ]
[Cochrane Library record description]

HAYES, Inc. Computer-assisted screening methods for detecting cervical cancer (Brief record), 2004
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050020/frame.html [Cochrane Library record description]

HAYES, Inc. Hybrid capture HPV testing for cervical cancer (Brief record), 2004
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20040455/frame.html
[Cochrane Library record description]

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20040248/frame.html
This review aims to assess the effectiveness and cost-effectiveness of liquid-based cytology (LBC) in cervical screening. It updates the original HTA rapid review of LBC (Payne et al. Health Technol Assess 2000;4(18):173) to reflect any new evidence, including the results of the pilot studies implemented as a result of the previous review.
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32004000248 ]
[full text available at: http://www.hta.ac.uk/execsumm/summ820.htm ]
[Cochrane Library record description]

L'Agence Nationale d'Accreditation d'Evaluation en Sante (ANAES). Assessment of human papilloma virus (HPV) testing in primary screening for cervical cancer in France (Structured abstract), 2004
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20040833/frame.html [Cochrane Library record description]

Medical Services Advisory Committee. The use of human papillomavirus testing to monitor effectiveness of treatment of high-grade intraepithelial abnormalities of the cervix (Structured abstract), 2004
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20051122/frame.html
This report summarises the assessment of current evidence for the use of human papillomavirus (HPV) testing by hybrid capture II (HC-II) or polymerase chain reaction (PCR) at 12 and 24 months to monitor the effectiveness of treatment of high-grade squamous intraepithelial lesions of the cervix
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005001122 ]
[Cochrane Library record description]
2003
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20031254/frame.html
[Cochrane Library record description]

ECRI. Automated thin-layer slide preparation systems for cervical cancer screening (Brief record), 2003
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060111/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32006000111 ]
[Cochrane Library record description]

German Agency for Health Technology Assessment at the German Institute for Medical Documentation and Information. Efficacy of liquid-based and computer-assisted cervical cytology - Medical Efficacy, economic efficiency (Brief record), 2003
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050571/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005000571 ]
[Cochrane Library record description]

HAYES, Inc. Thin-layer pap preparations for detecting cervical cancer (Brief record), 2003
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20040611/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32004000611 ]
[Cochrane Library record description]

Institute for Clinical Systems Improvement. Liquid-based cervical cytology (Structured abstract), 2003
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20031071/frame.html
[Cochrane Library record description]
This review aims to assess the available evidence on the effectiveness of liquid-based cervical cytology, a technique developed with the intent of improving the accuracy of Pap tests for cervical cancer screening.
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32003001071 ]
With regard to liquid-based cervical cytology (LBC), the ICSI Technology Assessment Committee finds:

1. LBC is an option to conventional Pap testing for cervical cancer screening. a. For the detection of pre-invasive cervical lesions, LBC is comparable to conventional Pap; there is no evidence of a change in the rate of cancer detection when liquid-based samples are analyzed (Conclusion Grade II). b. For minor grade lesions, there is evidence of a higher detection rate with LBC (Conclusion Grade II). As a result, LBC acts to normalize the rate of detection of atypical squamous cells of undetermined significance (ASCUS) so that pathologists can reach the 3%-5% ASCUS rate expected (Bethesda criteria) More accurate detection of ASCUS helps to better identify patients who need further testing. Inter-observer validity is higher with LBC.

2. The implementation of a liquid-based collection system has no impact on the safety of the patient during the sample collection process. The impact of the new technology may be to objectify Pap smear diagnosis and potentially reduce the number of repeat visits (and associated costs) for additional Pap testing, HPV testing (since the residual material may be used), or more invasive procedures.
3. Of 11 studies cited in this report that presented test results as either satisfactory, satisfactory but limited by, or unsatisfactory, 8 found a higher rate of satisfactory samples with LBC. Between 75.6% and 97.7% of LBC preparations were satisfactory compared with 60.5% to 97.5% with conventional Pap preparations.

4. A recent meta-analysis of 15 studies reported a sensitivity of 80% for LBC and 72% for conventional Pap testing predominantly for the detection of low grade squamous intraepithelial lesions or more severe (LSIL+) by histology and/or independent pathology review of slides with a Pap test result of LSIL+. Specificity did not differ between conventional and LBC preparations.

[full text at: http://www.icsi.org/guidelines_and_more/technology_assessment_reports/technology_assessment_reports_-_active/liquid-based_cervical_cytology.html ]
[Cochrane Library record description]

Medical Services Advisory Committee. Computer-assisted image analysis for cervical screening (Structured abstract), 2003.
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20031187/frame.html
This review aims to assess the effectiveness of computer-assisted image analysis for cervical screening cytology [from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32003001187 ] [full report available at: http://www.msaclibrary.org/Internet/msac/publishing.nsf/Content/ref12c-2 ] [Cochrane Library record description]

[Cochrane Library record description]

Medical Services Advisory Committee. Human papillomavirus testing for cervical screening (Structured abstract), 2003.
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20040015/frame.html
This report reviews the evaluation of detection of high-risk human papillomavirus (HPV) subtypes by the Hybrid Capture-II (HC-II) test for routine cervical screening either as a stand-alone test or as an adjunct to the conventional Pap or liquid-based smear [from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32004000015 ] [report at: http://www.msaclibrary.org/Internet/msac/publishing.nsf/Content/ref12d-2 ] [Cochrane Library record description]

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20031210/frame.html
The objective was to provide guidance on the use of liquid-based cytology for cervical screening. This guidance replaces Technology Appraisal Guidance No. 5 issued in June 2000 [from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32003001210 ]
- NICE has recommended that liquid-based cytology should be used as the main way of preparing samples of cervical cells for cervical screening.
- NICE has not recommended one product for liquid-based cytology over another as it says that there is currently not enough information about the advantages and disadvantages of the different products.
This guidance replaces TA5 Cervical cancer – liquid based cytology [full text available at: http://www.nice.org.uk/cat.asp?c=89850 ] [Cochrane Library record description]
NHS Quality Improvement Scotland. The use of liquid-based cytology for cervical screening (review) (Brief record), 2003
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050685/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005000685 ]
[Cochrane Library record description]

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20040008/frame.html
Aims are:
- To compare the diagnostic accuracy of liquid-based cytology (LBC) and human papillomavirus (HPV) testing with that of Papanicolaou (Pap) smears in the detection of precancerous or malignant cervical lesions.
- To evaluate the comparative cost and cost-effectiveness of LBC and HPV testing.
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32004000008
[Cochrane Library record description]

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050399/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005000399 ]
PB (publisher) : Hannover Medical School, Medizinische Hochschule Hannover (MHH) [Cochrane Library record description]

2002
Danish Centre for Evaluation and Health Technology Assessment. Chlamydia screening with home testing - a Health Technology Assessment - Primary research, Expert panel, Systematic review, Clinical guidelines (Brief record), 2002.
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20050552/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32005000552 ]
[Cochrane Library record description]

Hartmann K E, Hall S A, Nanda K, Boggess J F, Zolnoun D. Screening for cervical cancer (Structured abstract), 2002
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20031097/frame.html
To examine the evidence about benefits and harms of screening among older women (ages 65 and older) and those who have had hysterectomies, and to examine the diagnostic performance of new technologies and human papilloma virus (HPV) testing for detecting cervical lesions
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32003001097 ] [report at:
http://www.ahrq.gov/clinic/uspstf/uspserv.htm ] [full text at:
[Cochrane Library record description]

Health Technology Advisory Committee. Screening for cervical cancer: recent advances (Structured abstract), 2002
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20030449/frame.html
This report aims to assess the effectiveness of recent advances in screening for cervical cancer.
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32003000449 ] [full report at:
Medical Services Advisory Committee. Human papillomavirus testing in women with cytological prediction of low-grade abnormality (Structured abstract), 2002.
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20030102/frame.html
This systematic review of the literature aims to assess the effectiveness and cost-effectiveness of the Hybrid Capture-II human papillomavirus DNA test in women with equivocal results following routine cervical screening
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32003000102 ]
[Medical Services Advisory Committee record description]

Medical Services Advisory Committee. Liquid based cytology for cervical screening (Structured abstract), 2002.
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20030101/frame.html
This systematic review aims to assess the effectiveness and cost-effectiveness of liquid based cytology (LBC) for cervical screening [from:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32003000101 ] [report at:
http://www.msaclibrary.wiley.com/cochrane/clhta/articles/HTA-20030101/frame.html ]
[Medical Services Advisory Committee record description]

The National Coordinating Centre for Health Technology Assessment (NCCHTA). A randomised trial of human papillomavirus testing in primary cervical screening - Primary Research (project) (Brief record) http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20020187/frame.html [or: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32002000187 ]
[The National Coordinating Centre for Health Technology Assessment record description]

ECRI. Human papillomavirus DNA testing for diagnosis of cervical dysplasia and carcinoma (Brief record), 2001
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060262/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32006000262 ]
[ECRI record description]

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20020712/frame.html
This report aims to:
- Review the scientific evidence on the cervical-vaginal cytology test process, from taking the sample to reading.
- Review the quality standards established by scientific societies both for taking, fixing and transporting the sample and for its reading in the laboratory.
- Review current operating protocols relating to the performance of this test in the different health centres in the Autonomous Community of the Basque Country and determine the level of compliance by professionals to these protocols.
- Unify the type of cytology information and the way this is collected for all the health centres in the Autonomous Community of the Basque Country.
- Establish recommendations that allow an improvement in the effectiveness of the test.
[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32002000712 ]

Brief report - Collection devices for cervical screening

The prevention of gynaecologic cancer, especially breast and uterine cervix cancer, is a top priority in women's health, since death due to these processes can be, to a large extent, avoided. The objective of this study is to analyse the current situation of early detection programmes for breast and uterine neck cancer in Spain, as well as learn about the use of mammography and Papanicolaou's test in Spanish women aged 40-70.


The aim of this report is to respond to the request from the BSV regarding the decision of the Commission to reimburse ThinPrep(R)Pap Test with the condition "under evaluation", and to present a current and complete compendium of data demonstrating the efficacy and cost benefits of the ThinPrep(R)Pap Test. This document will also briefly review the training provided to cytologists and professionals using the method; educational campaigns for women, quality assurance and quality control will be other aspects considered in the evaluation of this particular technology. The submission also presents a description of this new method for cervical cancer screening and outlines the advantages of the ThinPrep(R) method of slide preparation as compared to the conventional Pap smear.

Institute for Clinical Systems Improvement. HPV DNA testing for cervical cancer (Structured abstract), 2001 http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20030556/frame.html

[found at: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=3200300117]


[Cochrane Library record description]


[Cochrane Library record description]
2000


Objectives are:

- To systematically review the international evidence for clinical effectiveness (primarily sensitivity) and cost-effectiveness of introducing automated and semi-automated devices available for cervical screening in New Zealand in place of conventional testing.
- To consider the above evidence in terms of its applicability to New Zealand’s population-based cervical screening programme.

[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32000000909 ]
[Cochrane Library record description]

**ECRI.** Automated Pap smear screening technologies: the AutoPap System (Brief record), 2000 [http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060113/frame.html](http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20060113/frame.html) [or: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32006000113 ]
[Cochrane Library record description]

**Medical Technology Unit - Swiss Federal Office of Public Health.** Alternatives to Papanicolaou test - consensus document (Brief record), 2000. [http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20020046/frame.html](http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20020046/frame.html) [or: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32002000046 ]
[Cochrane Library record description]


To summarise the current research evidence on the effectiveness of opto-electronic devices for the detection of cervical cancer

[from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32001000990 ]
[Cochrane Library record description]


- NICE has recommended that liquid-based cytology should be used as the main way of preparing samples of cervical cells for cervical screening.
- NICE has not recommended one product for liquid-based cytology over another as it says that there is currently not enough information about the advantages and disadvantages of the different products.
- This guidance replaces TA5 Cervical cancer – liquid based cytology.

[found at: http://www.nice.org.uk/cat.asp?c=89850 ]
[Cochrane Library record description]

Payne N, Chilcott J, McGoogan E. Liquid-based cytology in cervical screening: a rapid and systematic review (Structured abstract), 2000
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20000894/frame.html
To review the available evidence on the effectiveness and cost-effectiveness of liquid-based cytology in cervical screening [from:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32000000894 ] [full text available at:
http://www.hta.ac.uk/execsumm/summ418.htm ]
[Cochrane Library record description]

1999
Agency for Healthcare Research and Quality. Evaluation of cervical cytology (Structured abstract), 1999
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-20020324/frame.html
This report compares new technologies for cervical cytological screening with conventional Papanicolaou (Pap) test screening in terms of diagnostic accuracy, costs, effectiveness, and cost-effectiveness in adult women of average cervical cancer risk [from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32002000324 ] [report at:
http://www.ahrq.gov/clinic/epcsums/cervsumm.htm ]
[Cochrane Library record description]

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-999728/frame.html
Objectives:
1. To evaluate the available data concerning the role of HPV testing:
   ▪ in primary screening, either alone or as an adjunct to cytology
   ▪ To improve the management of women with low-grade cytological abnormalities
   ▪ To improve the accuracy of follow-up after treatment of preinvasive or early invasive lesions.
2. To review the methods available for HPV testing and determine their appropriateness for widespread implementation.
3. To determine what future research is required to obtain more reliable answers about its use in screening.
   [from: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=31999009728 ]
   [full text available at: http://www.hta.ac.uk/execsumm/summ314.htm ]
[Cochrane Library record description]

Healthcare Insurance Board/College voor zorgverzekeringen. Evaluation of the PAPNET-system in cervix screening - primary research (Brief record), 1999
http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-2000067/frame.html [or:
http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=3200000067]
[Cochrane Library record description]

1998

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-998111/frame.html

To evaluate the performance of a method of re-examining cervico-vaginal smears (CVS) using an automated examination system for Papnet(R) slides (NDS Inc.).

[Cochrane Library record description]

1997

Foreman J, Hader J. Cervical cancer screening (Structured abstract), 1997

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-988938/frame.html

This report examines the provision of cervical cancer screening for women in Saskatchewan.

[Cochrane Library record description]

Noorani HZ, Arratoon C, Hall A. Assessment of techniques for cervical cancer screening. -nonsystematic review (Structured abstract), 1997

http://www.mrw.interscience.wiley.com/cochrane/clhta/articles/HTA-968340/frame.html

Aims are:
- To examine the effectiveness of the Pap test.
- To consider different strategies for improving the effectiveness of the Pap test.
- To compare the cost-effectiveness of automated rescreening strategies.
- To consider emerging technologies

[Cochrane Library record description]

Centre for Reviews and Dissemination (HTA)


http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32008000108

"The objective of this report is to assess the effectiveness and cost-effectiveness of LBC versus CC for cervical cancer screening in a population of sexually active women older than 15 years of age." (executive summary)

The clinical evidence suggests no statistical differences in sensitivity and specificity between LBC and CC. LBC is estimated to be on average 6% more sensitive and 4% less specific than CC across a range of cytological thresholds. There is an 83% chance that LBC is more
Brief report - Collection devices for cervical screening

sensitive than CC and a 72% chance that it is less specific. On average, LBC classifies approximately 1% more cell abnormalities than CC at the low-grade threshold of LSIL+. At the high-grade threshold of HSIL+, LBC may classify fewer abnormalities than CC, but the difference is not statistically different. On average, LBC may have a lower rate of unsatisfactory specimens, but the estimated differences from individual studies varied.

HPV triage of ASCUS is more sensitive to detect cervical intraepithelial lesions than repeat cytology. HPV triage has a similar specificity compared to repeated cytology. Model projections suggest that, over a woman's lifetime, LBC is likely to improve health outcomes (e.g., cancer incidence and cancer death) and increases costs when compared with CC at the same screening interval. Model projections also suggest that, over a woman's lifetime, HPV triage reduces costs and improves health outcomes when paired with any cytologic screening strategy.

Direct comparison of all screening and triage strategies show that annual screening with CC or LBC is always more costly and less effective than when paired with HPV triage. HPV triage used with LBC screening at two-year intervals is preferred to CC with HPV triage at a willingness-to-pay threshold of CAD50,000 per LY gained, and CC with HPV triage every two years is preferred to LBC with HPV triage at lower willingness-to-pay thresholds. In comparison with current practice, using liquid-based cytology with HPV triage at two-year screening intervals will reduce costs, with a similar or reduced burden of disease. Thus, the health economic evidence suggests that two-year screening strategies using HPV triage, with or without LBC, represents the best use of resources for cervical cancer screening. These results will require revision given the introduction of automated screening, HPV vaccination, and organized screening programs. [full text available at: http://cadth.ca/index.php/en/hta/reports-publications/search/publication/799] [CRD record description]

NZHTA Clearing House

Health Services/Technology Assessment Text (HSTAT)

- This statement summarizes the current U.S. Preventive Services Task Force (USPSTF) recommendations on screening for cervical cancer and the supporting scientific evidence, and updates the 1996 recommendations contained in the Guide to Clinical Preventive Services, Second Edition
Canadian Agency for Drugs and Technologies in Health (CADTH)


Miscellaneous


- Each year, the American Cancer Society (ACS) publishes a summary of its recommendations for early cancer detection, including guideline updates, emerging issues that are relevant to screening for cancer, and a summary of the most current data on cancer screening rates for US adults. In 2006, there were no updates to ACS guidelines for early cancer detection. In this issue of the journal, we describe criteria for successful screening, discuss recent evidence and policy changes that have implications for cancer screening, summarize the ACS guidelines and describe guidelines reviews that are underway, and provide an update of the most recent data pertaining to participation rates in cancer screening from the Centers for Disease Control and Prevention's (CDC's) Behavioral Risk Factor Surveillance System (BRFSS) and the National Health Interview Survey (NHIS).

- contains a section titled: Screening For Cervical Cancer
Section D

Study Results

Secondary studies: characteristics and outcomes

The search identified one relevant secondary research study, which included a meta-analysis conducted as part of a Cochrane systematic review (Martin-Hirsch et al. 2000). Characteristics of the review and comparisons are described in Table 1.

The review aimed to assess the effect of the design of the cervical smear sampling collection device on the rates of inadequate smears obtained by that device and the detection of disease; and whether the presence of endocervical cells in the smear affects disease detection. Specifically the review objectives were to determine whether the presence of endocervical cells is a quality criterion in cervical cytology, and to compare the different sampling device’s ability to detect the disease (dyskaryosis) and improve smear adequacy rates.

The review included those studies that compared cervical smear collection devices in women attending for primary screening, colposcopy following an abnormal smear or colposcopy after treatment. The literature search involved the Cochrane Gynaecological Cancer Group, trials register and MEDLINE up to July 1997 as well as conducting hand searches of 16 journals.

Randomised controlled trials were analysed for:

- the method of randomisation,
- characteristics of the patients and the source of recruitment,
- the presence or absence of endocervical cells obtained by smear devices,
- blood contamination and inadequate smears and
- the presence or absence of dyskaryosis/atypia.

Observational studies examining the incidence and severity of cytological abnormality in cervical smears according to endocervical cell status were also analysed.

The review included thirty-six trials and six observational comparative studies. In all but two trials endocervical cells were used as an outcome, whereas the rate of detection of dyskaryosis was included in only 19 trials. Trial characteristics included year of publication, origin, number of patients included, number and type of collection devices, method of randomisation, source of patient recruitment and whether endocervical cell, blood contamination, inadequate smears or dyskaryosis was used as an outcome measure. Six non-randomised trials of cervical smear collection devices with respect to detection of endocervical cells and dyskaryosis were also identified.

Patients were recruited from four principal sources:

1. primary screening centres (i.e. general practice, student health centres, genitor-urinary clinics and general gynaecological clinics).
2. colposcopy clinics (patients with a recent history of abnormal cervical cytology).
3. colposcopy clinics and gynaecology clinics (after treatment of confirmed cervical dysplasia).
4. antenatal clinics.
Nineteen of the randomised controlled trials identified for review compared the ability of cervical smear collection devices to detect abnormal cervical cytology. However, the heterogeneity in classification of the different grades of dyskaryosis across the studies limited comparisons of the abilities of devices to detect different grades of abnormality. Some studies reported on cytological abnormality with all grades of dyskaryosis grouped together, in others low or high grades were distinguished while yet other studies distinguished all grades of severity (cytological atypia, mild, moderate, severe or invasive carcinoma). Nevertheless, the trial results permitted comparisons of rates of detecting dyskaryosis per se.

Thirty-six trials and six observational comparative studies were included. The Ayre spatula was shown to be less effective compared with extended tip spatulas for collecting endocervical cells in eight trials (odds ratio 2.25, 95% confidence interval 2.06 to 2.44).

Use of a spatula with the cytobrush was more effective than spatula alone at collecting endocervical cells (odds ratio 3.33, 95% confidence interval 3.05 to 3.63) and the same effect was present for adequate smear rates (odds ratio 1.51 95% confidence interval 1.19-1.92). Extended tip spatulas were also superior for the detection of dyskaryosis in seven trials (odds ratio 1.21, 95% confidence interval 1.10 to 1.33). Based on data from two trials and three observational studies, smears that contained endocervical cells were more likely to detect dyskaryosis, particularly in severe disease. The proportion of smears with endocervical cells present increased with increasing severity of the disease.

The authors of the Cochrane review concluded that the extended tip spatulas of various designs appear to be better for collecting endocervical cells than the commonly used Ayre spatula. The most effective combination appears to be the cytobrush with an extended tip spatula. The rate of detection of endocervical cells appears to be a valid and convenient surrogate for the ability to detect dyskaryosis and for adequate smear rates. The ability of the extended tip spatula with the cytobrush compared with the extended tip spatula alone to detect disease, needs to be evaluated in a trial.
<table>
<thead>
<tr>
<th>Source Level of Evidence</th>
<th>Study design and aim</th>
<th>Data sources</th>
<th>Study selection Data extraction</th>
<th>Results</th>
<th>Author's conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Martin-Hirsch et al. 2000)</td>
<td>Met-analysis of randomised controlled trials</td>
<td>MEDLINE (before July 1997) (no specific date given)</td>
<td>Inclusion criteria: Randomised controlled trials using alternative cervical smear screening devices was eligible for inclusion if dealt with the ability of a cervical smear collection device to collect endocervical cells or dyskaryosis in women attending for primary screening, colposcopy following an abnormal smear or colposcopy after treatment. Eligible studies reported outcomes including ability of a cervical smear collection device to collect endocervical cells, produce adequate smears and detect atypia or dyskaryosis in cervical smears. Study quality was assessed according to method of randomisation and allocation concealment. 36 randomised/quasi-randomised trials were included. The trials investigated the performance of 16 cervical smear collection devices.</td>
<td>Main results: The Ayre spatula was shown to be less effective compared with extended tip spatulas for collecting endocervical cells in eight trials (odd ratio 2.25, 95%CI 2.06-2.44). Use of a spatula with the cytobrush was more effective than spatula alone at collecting endocervical cells (odd ratio 3.33, 95%CI 3.05-3.63) Use of a spatula with the cytobrush was more effective than spatula alone for adequate smear rates (odd ratio 1.51, 95%CI 1.19-1.92) Based on data from two trials and three observational studies, smears that contained endocervical cells were more likely to detect dyskaryosis, particularly in severe disease. The proportion of smears with endocervical cells present increased with increasing severity of the disease.</td>
<td>Extended tip spatulas of various designs appear to be better for collecting endocervical cells than the commonly used Ayre spatula. The most effective combination appears to be the cytobrush with an extended tip spatula. The rate of detection of endocervical cells appears to be valid and convenient surrogate for the ability to detect dyskaryosis and for adequate smear rates. The ability of the extended tip spatula with the cytobrush compared with the extended tip spatula alone to detect disease, needs to be evaluated in a trial.</td>
</tr>
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</table>
Original primary studies: characteristics

The literature search identified three eligible primary research studies, which were not included in the Cochrane systematic review. Characteristics of the primary studies included in this updated report and comparisons are described in Table 2. All the studies were conducted outside New Zealand. Two recent studies were conducted after the Cochrane review, one was based in Belgium (Depuydt et al. 2006) and the other was based in the United States (Marchand et al. 2005). The third study was conducted earlier but was not identified or cited by the Cochrane review and was based in Germany and Austria (Kohlberger et al. 1999).

Depuydt et al. 2006 presented their experience of sampling with the Cervex-Brush®. The study aimed to compare the performance of Cervex-Brush® Combi (2x 360° rotations) with the performance of the Cervex-Brush® (5x 360° rotations) (current) in obtaining liquid-based Pap smears. The study also attempted to evaluate whether the Cervex-Brush® Combi is at least as good as the Cervex-Brush® when comparing cellularity (for both squamous and endocervical cells), HPV typing/quantification and disease detection. Participants were women in Flanders (Belgium) receiving opportunistic routine gynaecological health checks. The 200 slides were collected by one gynaecologist and the study assessed the performance of these devices by counting the number of sampled squamous cells, the number of sampled endocervical cells, by ability to detect lesions (low grade squamous intraepithelial lesions), and the ability of detecting atypical squamous cells of undetermined significance.

The Cervex-Brush® Combi is a new high-tech sampling device that combines the Cervex-Brush® and endocervical brush. It is easy to use and only two rotations are sufficient for sampling.

The study design was a prospective cohort (single-blinded), used a consecutive sampling method and assessed the performance of the devices for an even distribution of cells, the percentage of slide surface covered with cells and the presence and number of squamous/endocervical cells. The liquid-based cytology (LBC) leftover, was used to measure the cell pellet, the amount of DNA after DNA extraction, HPV type prevalence and oncogenic HPV viral load. All 200 samples were tested for 15 oncogenic HPV types by real-time quantitative PCR. The screening results were blinded from the HPV results. The endpoint was disease detection (i.e. abnormal cytology positive for oncogenic HPV).

In their prospective, blinded, cohort study, Marchand et al. 2005 assessed the quality of conventional Pap smears in relation to cervical sampling collection devices and sequence of collection. The study was conducted in 2 phases approved by the University of Wisconsin Institutional Review Board. The first phase was descriptive in nature involving a survey of a large prospective sample of Pap smears obtained by family physicians (FPs), obstetrician-gynaecologists (OB/GYNs), and advance practice nurses (APNs) who practice in Dane County, Wisconsin. The survey looked at smear collection techniques (including the sequence of collection), instruments used, and management strategies.

In the second phase, conventional Pap smears that were collected by participating clinicians were analysed in two cytology labs within a 1-year period. After the investigators obtained consent, the practitioner’s next 30 Pap smears were processed in the usual manner by the cytology lab and then examined prospectively. Each Pap smear was examined for quality indicators including degree of obscuring inflammation, degree of obscuring blood, presence of diagnostic cells, and presence of infectious agents.
An earlier prospective study, Kohlberger et al. (1999) examined seven cytology sampling devices that were used to obtain 800 smears and their performance was assessed for even distribution of cells, percentage of slide surface covered with cells, and presence and number of endocervical cells. Seven expert gynaecologists participated in the study using their personal favourite cell sampling collection device. Thus the sample smear experience was not controlled across the sampling collection devices. After sampling, the smears were spray fixed or fixed in 95% alcohol. At the Gynaecopathologic Unit, Department of Pathology, University of Vienna, all cervical smears were assessed for even distribution of cells, percentage of slide surface covered with cells, and presence and number of endocervical cells.

The study characteristics are presented in Table 2.
<table>
<thead>
<tr>
<th>Citation</th>
<th>Study type and Study quality</th>
<th>Population</th>
<th>Interventions / Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention Level I evidence (A systematic review of all relevant randomised controlled trials)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Martin-Hirsch et al. 2000 (UK) | Systematic review and Meta-analysis                                                           | Women attending for primary screening, colposcopy following an abnormal smear or colposcopy after treatment (UK) | Spatulas: AYRE (wood), AYLESBURY (wood), [MILEX, ACCU-PAP, ROCKET, PAPLAST, ROOLON (Plastic)], MULTISPATULA, ARMOCERVICAL, CYTOPICK)  
Endocervical sampling devices: COTTON SWAB (Q-TIP), CYTOBRUSH  
Ectocervical and Endocervical Sampling Devices: CERVEXBRUSH, BAYNEBRUSH, PROFILEBRUSH | Collecting endocervical cells, avoiding contamination by blood, adequate smears, higher proportion of endocervical cells and also detect higher incidence of dyskaryosis, |
|                      |                                                                                       | N= 36 randomised/quasi-randomised studies + 6 observational studies |                                                                                                          |                                                                          |
| Intervention Level III-2 evidence (A comparative study with concurrent controls; Non-randomised, experimental trial, Cohort study, Case-control study, Interrupted time series with a control group) |                                                                                       |                                                                           |                                                                                      |                                                                          |
| Depuydt et al. 2006 (Belgium) | Prospective, cohort, blinded study  
Between 1 June and 1 September 2005 | Opportunistic routine gynaecological health checks, Women in Flanders (Belgium), N= 200 slides by one gynaecologist | Cervex-Brush © Combi (n=100), Cervex-Brush (n=100) | Disease detection (endpoint)  
Cytology results classified according to Bethesda system 2001  
DNA extraction and HPV testing HPV viral load |                                                                          |
Table 2 Study characteristics: effectiveness of cervical screening devices (continued)

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study type</th>
<th>Study quality</th>
<th>Population</th>
<th>Interventions/Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention Level III-2 evidence</td>
<td>(A comparative study with concurrent controls; Non-randomised, experimental trial, Cohort study, Case-control study, Interrupted time series with a control group)</td>
<td>Marchand et al. 2005 (USA) Prospective, cohort, blinded study 1-year period</td>
<td>Phase I 128 clinicians who practice in Dane County Wisconsin who send their Pap smears to either of 2 study cytology labs (N=3627 slides)</td>
<td>Ectocervix/Endocervix (broom/broom) n=534, Wooden spatula (blunt endy)/Cytobrush n=240, Broom/Cytobrush n=128, plastic spatula/Cytobrush n=276, wooden spatula (curved end)/Broom n=60, wooden spatula (curved end)/cotton swab n=55, wooden spatula (curved end)/Cytobrush n=2137, wooden spatula (curved end)/Cytobrush/Cytobrush n=197</td>
<td>Quality indicators, absent endocervical cells, Limited or unsatisfactory pap smears, obscuring inflammation</td>
</tr>
</tbody>
</table>
| Kohlberger et al. 1999 (Austria) | Prospective, serial sampling Time period not specified | 400 smears from pre-menopausal women 400 smears from post-menopausal women N=800 samples | Seven collection devices (Cervex-brush n=100, Cytobrush n=100, Szalay spatula n=100, Papex spatula n=200, WrGKK spatula n=100, Cotton swab n=100, Loop n=100) | Even distribution of cells Percentage of slide surface covered with cells Number of Endocervical cells on the slide were | | Original primary studies: results

Results from the three primary studies that were conducted more recently and or was not identified by the Cochrane review by (Martin-Hirsch, et al. 2000) are presented below with more detailed data extraction tables shown in (Tables A2-4).

Results reported by Depuydt et al. 2006 showed no difference in the mean number of sampled squamous cells between the two brush types. On the contrary, the use of Cervex-Brush® Combi was associated with an increase in the number of sampled endocervical cells ($t = 4.483$, d.f.=197, $p=0.00001$) per slide (Cervex =371 versus Combi = 986 cells). In regard to DNA extraction and HPV testing, the percentage of samples positive for oncogenic HPV types increased for both brush types from NEG (Cervex-Brush® 27.4%; Cervex-Brush® Combi 19.8%) to ASC-US Cervex-Brush® 33.3%; Cervex-Brush® Combi 50.0%) to L-SIL (Cervex-Brush® 100%; Cervex-Brush® Combi 100%). The use of Cervex-Brush® Combi resulted in the detection of a higher viral load (for HPV detection of oncogenic types) than when using the Cervex-Brush®.
The authors’ concluded: “Sampling with the Cervex-Brush® Combi resulted in the collection of the same amount of squamous cells, but in a two to threefold harvest of endocervical cells. This led to the detection of a higher viral load for oncogenic HPV and an increase in the number of detected abnormal smears.”

Reported results from phase 2 by Marchand et al. 2005 indicated that the Cervex-brush™ (broom) was significantly associated with unsatisfactory or limited pap smears, excessive inflammation, and absent endocervical cells. In total, 3657 Pap smears were examined (not all clinicians completed 30 conventional Pap smears in the 1-year study period). The majority of the smears were well woman or pregnancy-related, and few were secondary to prior abnormal Pap smears. The age range of the women who had Pap smears was 14-90 years of age, with an average age of 40 years. Four percent of the women were >65 years, and 2% of the women were <18 years of age. Of all slides evaluated, 20% were limited or unsatisfactory for interpretation. For 12% of the slides, this was due to excessive inflammation; 3% had no endocervical component on the slide; and 5% had no blood obscuring the slide. An additional 0.4% had drying artefact. The collection sequence was not significantly associated with endocervical cells being absent, air drying artefact, or blood obscuring the slide. Collecting both at once with the broom, however, was significantly associated with the absence of endocervical cells (Odds Ratio 1.46, \( p<0.05 \); 95% Confidence Interval (CI) 1.09 to 1.97). Broom use was significantly related to unsatisfactory or limited pap smears (OR 1.68, \( p<0.01 \); 95% CI 1.30 to 2.17), excessive inflammation (OR 2.01, \( p<0.01 \); 95% CI 1.44 to 2.81), and absent endocervical cells (OR 3.12, \( p<0.001 \); 95% CI 1.56 to 6.23). It was not associated with blood obscuring the slide. For clinicians with high levels of absent ednocervical cells on pap smears (defined as \( \geq 3/30 \) pap smears), 47% used the broom \(( p=0.001 \). The average rate of pap smears with no endocervical component rate was 0.85/30 pap smears. The Cytobrush™ was not associated with significant degree of absent endocervical cells, inflammation, or obscuring blood. Absence of endocervical cells was negatively associated with postmenopausal status (OR 0.18, \( p<0.001 \), and positively associated with infectious agent present (OR 3.09, \( p<0.001 \)). Blood obscuring the slide was also negatively associated with postmenopausal state (OR 0.57, \( p<0.05 \)) and presence of infectious agent (OR 0.17, \( p<0.01 \)).

The authors’ concluded: “The combination of the Cytobrush™ (endocervix) and spatula (ectocervex) is superior for a quality pap smear. The sequence of collection was not important in conventional pap smears. The broom alone performs poorly. The presence of infection decreases quality.”

The study by Kohlberger et al. (1999) reported the best even distribution of cells with the WrGKK spatula. Percentage of slide surface covered with cells was best with the Cytobrush, whereas the highest ranking for presence of endocervical cells was seen with the use of the Cytobrush. Percentage of slide surface covered with evaluable cells was best with the Cytobrush as well. Cotton swabs and loop showed inferior results in all categories. There were no significant differences when comparing the results found in the premenopausal and postmenopausal groups.

The authors’ concluded: “The use of cervical cell sampling devices showing the best cytologic results improves the interpretation and validity of cervical smears. The results of this study indicate that the widely used cotton swab should not be used. Most cells remain in the cotton and are not applied to the glass slide. When using the cotton swab, it at least has to be moistened with saline solution to prevent cells from being sucked into the dry cotton.
Larger cotton swabs do not reach the transformation zone in many patients. The loop was used years ago by many gynaecologists but is not recommended for cervical cell sampling.”
Conclusions

Research base and potential for further review

Following an extensive, systematic search of published research and consideration of various website sources, it appears that there is a very small literature on the topic of the effectiveness of the design of collection devices for cervical screening that adds to the Cochrane Collaboration review published in 2000. This update has identified two recent prospective cohort studies assessing the performance of cervical smear collection devices following the publication of the comprehensive Cochrane review by Martin-Hirsch et al. (2000).

From what has been identified in this brief report, there does not appear to be sufficient evidence of reasonable quality on this topic to benefit from more extensive review and critical appraisal as an evidence-based review (either as a HSAC Technical Brief or Systematic Review).

The Cochrane review conclusions we believe are still applicable, as confirmed by the review’s author in email correspondence (Martin-Hirsch, personal communication, 2008). Hence, we believe there is no new substantial evidence published since this Cochrane review that might influence the conclusions of the review. The Cochrane review authors indicated in the section on implications for practice that the review is no longer appropriate for update as liquid based cytology has superseded smear technology (Martin-Hirsch et al. 2000).

The most important factor in taking satisfactory cervical smears is the ability of the practitioner to perform the test accurately (Cecchini 1989; Buntinx 1993). As shown by this review, the design of the cervical smear collection device also significantly influences the yield of representative cells and the detection of cytological atypia. The replacement of the Ayre spatula with extended tip spatulas should be mandatory for mass screening since this is an inexpensive way to improve sampling. In the United Kingdom the presence of endocervical cells is not routinely used to assess the adequacy of a cervical smear. The evidence from the observational studies suggests that endocervical negative smears are less likely to detect any cytological abnormality which may be present, especially if the abnormality is severe. The introduction of more stringent assessment of cervical smears based on endocervical cell status and the repetition of endocervical negative smears might not be justified in the light of the present resources. However, assessment of endocervical cells appears to be a valid method to audit an aspect of the overall quality of a cervical smear screening program and to compare different cervical sampling collection devices (Martin-Hirsch et al. 2000).

Recommendation

The studies published and identified following the Cochrane review, do not comprehensively influence the conclusions of the review. Therefore, based on the current limited evidence available from this update for the use of collection devices for cervical screening, one option for the NSU would be to contact the other agencies/jurisdictions to ascertain their cervical sampling collection device screening protocols and the evidential basis for them. This project is beyond the scope of the current review.
Appendix 1: Data extraction tables

Table A2  Data extraction table: Depuydt et al. (2006)

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of evidence *</td>
<td>III-2</td>
</tr>
<tr>
<td>Country</td>
<td>Belgium</td>
</tr>
<tr>
<td>Research question/aims</td>
<td>The objective was to analyse and to compare the Cervex-Brush® Combi with the Cervex-Brush® for the collection of squamous and endocervical cells, human papillomavirus (HPV) typing/quantification and disease detection in SurePath LBC.</td>
</tr>
<tr>
<td>Study type/design</td>
<td>Prospective, blinded, cohort, Consecutive samples</td>
</tr>
<tr>
<td>Participant</td>
<td>Opportunistic routine gynaecological health checks, Women in Flanders (Belgium), 200 slides by one gynaecologist</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>not specified</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>not specified</td>
</tr>
<tr>
<td>Subject disposition</td>
<td>used consecutive samples collected during opportunistic routine gynaecological health checks from women in Flanders (Belgium). One hundred consecutive smears were taken with each sampling device.</td>
</tr>
<tr>
<td>Cervex-Brush® Combi (Combi) arm</td>
<td>N=100 consecutive samples collected using the Cervex-Brush® Combi (Combi), mean age 41.7 years (SD 13.3 years).</td>
</tr>
<tr>
<td>Cervex-Brush® (Cervex) arm</td>
<td>N=100 consecutive samples collected using the Cervex-Brush® (Cervex), mean age 40.6 years (SD 12.6 years).</td>
</tr>
<tr>
<td>Interventions/Comparators</td>
<td>No significant differences between the two groups of patients’ ages</td>
</tr>
<tr>
<td></td>
<td>Cervex-Brush® Combi (2x 360° rotations)</td>
</tr>
<tr>
<td></td>
<td>Cervex-Brush® (5x 360° rotations) (current)</td>
</tr>
</tbody>
</table>
**Table A2  Data extraction table: Depuydt et al. (2006) continued**

| Outcome definitions | Using either Cervex-Brush® or the Cervex-Brush® Combi 100 consecutive SurePath® LBC samples collected using each brush type. All 200 slides were read by the FocalPoint™ and screened by guided screening using slide wizards. The viral load of HPV type 16 E7, 18 E7, 31 E6, 33 L1, 33 E6, 35 E4, 39 E7, 45 E7, 51 E6, 52 L1, 52 E7, 53 E6, 58 L1, 58 E6, 59 E7, 66 E6, and 68 E7 was determined using a TaqMan-based real-time quantitative PCR analysis.  

- Cytology results classified according to Bethesda system 2001:  
  Class negative (NEG) for intraepithelial lesions  
  Class ASC-US for atypical squamous cells of undetermined significance  
  Class ASC-H for atypical squamous cells of undetermined significance cannot exclude high-grade squamous intraepithelial lesions  
  Class L-SIL for low-grade squamous intraepithelial lesions  
  Class H-SIL for high-grade squamous intraepithelial lesions  

On each slide the squamous and endocervical cells counted manually (using 40x magnification) with conventional light microscope, by one of the trained cytotechnologists (who was unaware of the cytological or HPV status of the slide, or which brush type was used). For each slide, four fields (40x magnification) were counted, and the total number of cells calculated.  

- DNA extraction and HPV testing  
- HPV viral load |

| Data analyses & statistics | Analyses: comparisons of means were studied by analysis of variance (ANOVA), followed by Student-Newman-Keuls test for all pair wise comparisons. Chi-square statistics for trend was used to verify the existence of a trend across ordered groups (such as an increase in HPV positivity according to the degree of cytological abnormality). Statistical analysis was performed using MedCalc® programme (MedCalc Software, Mariakerke, Belgium).  

Sample size calculation: not reported. |

| Results (within scope of systematic review update) | Between 1 June and 1 September 2005, 200 samples were included in the study.  

Results:  
Mean number of sampled squamous cells: No difference between the two brush types (Cervex 54 963 vs Combi 45 595 cells)  
Number of sampled endocervical cells: Significant increase with the use of Combi (2 to 3 fold increase) (P<0.00001)  
Low-grade squamous intraepithelial lesions: Combi detected 3 versus 2 for Cervex of low-grade squamous intraepithelial lesions.  
Atypical squamous cells of undetermined significance: Combi detected more atypical squamous cells of undetermined significance (6 vs 3).  
Oncogenic HPV types of abnormal smears: 65% of abnormal smears were positive for oncogenic HPV types in the Cervex group as compared to 66.7% in the Combi group.  
Median HPV viral load: 0.1825 copies/cell (Combi) vs 0.0042 copies/cell (Cervex) (p=0.02). |

| Authors conclusions | Sampling with the Cervex-Brush® resulted in the collection of the same amount of squamous cells, but in a two to threefold harvest of endocervical cells. This led to the detection of a higher viral load for oncogenic HPV and an increase in the number of detected abnormal smears. |

| Reviewers notes | All samples were taken by the same gynaecologist and were sent to the same pathology laboratory |

**Abbreviations:** HPV, human papilloma virus; LBC, liquid-based cytology; ANOVA, analysis of variance; * As per NHMRC Interim Levels of Evidence (NHMRC 2005) for Evaluating Intervention Studies

**Brief report - Collection devices for cervical screening**
Table A3  Data extraction table: Marchand et al. (2005)

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of evidence *</td>
<td>III-2</td>
</tr>
<tr>
<td>Country</td>
<td>United States</td>
</tr>
<tr>
<td>Research question/aims</td>
<td>The objective was to determine the performance of collection devices currently used in obtained conventional Pap smears and whether sequence of collection is important for higher quality results.</td>
</tr>
<tr>
<td>Study type/design</td>
<td>Prospective, blinded, cohort</td>
</tr>
<tr>
<td>Patient group</td>
<td>Participants: 128 clinicians (advance practice nurses, family physicians, and obstetrician/gynaecologists).</td>
</tr>
<tr>
<td></td>
<td>Inclusion criteria: for Phase 2: practitioners who do conventional Pap smears and process at either Dane County Cytology Lab or the Wisconsin State Cytology Lab.</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria: not specified</td>
</tr>
<tr>
<td></td>
<td>Subject disposition: of total of 230 clinicians eligible and completed survey in Phase 1, 71% (n=163) agreed to participate in Phase 2. Only 128 clinicians met inclusion criteria, of these: 17% APNs, 69% FPs, and 14% OB/GYNs. After obtaining consent, the practitioner’s next 30 Pap smears processed in the usual manner by the cytology lab and then examined prospectively. In total, 3657 Pap smears (not all clinicians completed 30 conventional Pap smears in the 1-year study period).</td>
</tr>
<tr>
<td>Instruments used:</td>
<td>(Ectocervix/Endocervix) Broom/Broom (n=534), Wooden spatula (blunt end)/ Cytobrush (n=240), Broom/Cytobrush (n=128), Plastic spatula/ Cytobrush (n=276), Wooden spatula (curved end)/ Broom (n=60), Wooden spatula (curved end)/ Cotton swab (n=55), Wooden spatula (curved end)/ Cytobrush (n=2137), Wooden spatula (curved end)/ Wooden spatula (curved end) Cytobrush/Cytobrush (n=197).</td>
</tr>
<tr>
<td>Interventions/ Comparators</td>
<td>Ectocervix/Endocervix Broom/Broom, Wooden spatula (blunt end)/ Cytobrush, Broom/Cytobrush, Plastic spatula/ Cytobrush, Wooden spatula (curved end)/ Broom, Wooden spatula (curved end)/ Cotton swab, Wooden spatula (curved end)/ Cytobrush, Wooden spatula (curved end)/ Wooden spatula (curved end) Cytobrush/Cytobrush</td>
</tr>
</tbody>
</table>
Table A3  Data extraction table: Marchand et al. (2005) continued

| Outcome definitions | Each Pap smear was examined for quality indicators including degree of obscuring inflammation, degree of obscuring blood, presence of diagnostic cells, and presence of infectious agents. Senior cytologists assigned to examine all study Pap smears. Using the standards established by the Bethesda System (TBS) prior to 2001:
If 50% to 74% of the slide was obscured by blood or inflammation the slide was judged as limited for interpretation
If >75% of the slide was obscured by blood or inflammation the slide was considered unsatisfactory.
An absent endocervical cells on pap smears was defined as ≥3/30 Pap smears |
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Table A4  Data extraction table: Kohlberger *et al.* (1999)

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Level of evidence *</td>
<td>III-2</td>
</tr>
<tr>
<td>Country</td>
<td>Austria</td>
</tr>
<tr>
<td>Research question/aims</td>
<td>The objective was to compare the most commonly used cervical sampling devices and evaluate gynaecologists using their preferred cell sampling device for quality assessment of their cervical smears.</td>
</tr>
<tr>
<td>Study type/design</td>
<td>Prospective</td>
</tr>
<tr>
<td>Patient group</td>
<td>Participants: seven expert gynaecologists participated in the study using their personal favourite cell sampling device</td>
</tr>
<tr>
<td></td>
<td>Inclusion criteria: Not specified but authors mentioned that all incoming cervical smears sent for routine cervical cancer screening were included in the study as a serial sampling</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria: not specified</td>
</tr>
<tr>
<td></td>
<td><strong>Subject disposition:</strong> 400 pre-menopausal women, 400 post-menopausal women</td>
</tr>
<tr>
<td></td>
<td>Pre-menopausal women: Cervex-brush n=50, Cytobrush n=50, Szalay spatula n=50, Papex spatula n=100, WrGKK spatula n=50, Cotton swab n=50, Loop n=50</td>
</tr>
<tr>
<td></td>
<td>Post-menopausal women: Cervex-brush n=50, Cytobrush n=50, Szalay spatula n=50, Papex spatula n=100, WrGKK spatula n=50, Cotton swab n=50, Loop n=50</td>
</tr>
<tr>
<td>Intervention Comparator</td>
<td>Seven most commonly used cervical sampling devices:</td>
</tr>
<tr>
<td></td>
<td>Cervix-brush (Rovers, Oss, the Netherland),</td>
</tr>
<tr>
<td></td>
<td>Cytobrush (Medscand, Malmö, Sweden),</td>
</tr>
<tr>
<td></td>
<td>Szalay spatula (C.S.M. Graf &amp; Co., Steinach, Switzerland),</td>
</tr>
<tr>
<td></td>
<td>Papex spatula (Hengstberger, Vienna, Austria),</td>
</tr>
<tr>
<td></td>
<td>WrGKK spatula (main social security in Vienna),</td>
</tr>
<tr>
<td></td>
<td>Cotton swab, and</td>
</tr>
<tr>
<td></td>
<td>Loop</td>
</tr>
</tbody>
</table>
Table A4  Data extraction table: Kohlberger et al. (1999)  

**Outcome definitions**

<table>
<thead>
<tr>
<th>Outcome definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cervical smears were assessed for even distribution of cells, percentage of slide</td>
</tr>
<tr>
<td>surface covered with cells, and presence and number of endocervical cells.</td>
</tr>
<tr>
<td>Even distribution of cells was scored in three groups:</td>
</tr>
<tr>
<td>Evenly dispersed cells</td>
</tr>
<tr>
<td>Irregularly dispersed cells</td>
</tr>
<tr>
<td>Only cell clumps on the slide.</td>
</tr>
<tr>
<td>Percentage of slide surface covered with cells was scored in three groups:</td>
</tr>
<tr>
<td>&gt;50% of the slide was covered with evaluable cells</td>
</tr>
<tr>
<td>20-50% of the slide was covered with evaluable cells</td>
</tr>
<tr>
<td>&lt;20% of the slide was covered with evaluable cells</td>
</tr>
<tr>
<td>Endocervical cells on the slide were counted and scored in four groups:</td>
</tr>
<tr>
<td>&gt;60 cells</td>
</tr>
<tr>
<td>25-60 cells</td>
</tr>
<tr>
<td>&lt;25% cells</td>
</tr>
<tr>
<td>No endocervical cells</td>
</tr>
<tr>
<td>Cervical smears classified as:</td>
</tr>
<tr>
<td>Benign cellular changes</td>
</tr>
<tr>
<td>Within normal limits were assessed for quality features</td>
</tr>
</tbody>
</table>

**Data analyses & statistics**

<table>
<thead>
<tr>
<th>Data analyses &amp; statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analyses: descriptive frequency distribution and percentages</td>
</tr>
<tr>
<td>Sample size calculation: not reported.</td>
</tr>
</tbody>
</table>
Table A4  Data extraction table: Kohlberger et al. (1999)  
continued

| Results (within scope of systematic review update) | In total, 800 smears were assessed for even distribution of cells, percentage of slide surface covered with cells and presence and number of endocervical cells. 400 slides from pre-menopausal women and 400 from post-menopausal women. 200 smears were obtained using Papex spatula (Hengstberger, Vienna, Austria), whereas all other devices collected 100 smears equally. Devices are: Cervez-brush (Rovers, Oss, the Netherlands), Cytobrush (Medscand, Malmo, Sweden), Szalay spatula (C.S.M. Graf & Co., Steinach, Switzerland), WrGKK spatual (main social security in Vienna), cotton swab and loop. 

Even distribution of cells was best with the WrGKK spatula (92% in both pre- and post-menopausal women). 

Percentage of slide surface covered with evaluable cells was best with the Cytobrush (46% in pre-menopausal women, and 44% in post-menopausal women). 

Highest ranking for the presence of endocervical cells was found for the cytobrush. 

Cotton swabs and loop showed inferior results in all categories. |
| Authors conclusions | The use of cervical cell sampling devices showing the best cytologic results improves the interpretation and validity of cervical smears. Our results suggest that cotton swans and loops should not be used for cervical sampling. |
| Reviewers notes | Sample smear experience was not controlled across devices, as gynaecologists used their personal favourite cell sampling device. |

* As per NHMRC Interim Levels of Evidence (NHMRC 2005) for Evaluating Intervention Studies
**Table A5  NHMRC Interim Levels of Evidence (NHMRC 2005) for Evaluating Intervention Studies**

<table>
<thead>
<tr>
<th>Level</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>I *</td>
<td>A systematic review of level II studies</td>
</tr>
<tr>
<td>II</td>
<td>A randomised controlled trial</td>
</tr>
</tbody>
</table>
| III-1 | A pseudorandomised controlled trial  
(i.e. alternate allocation or some other method) |
| III-2 | A comparative study with concurrent controls:  
• Non-randomised, experimental trial †  
• Cohort study  
• Case-control study  
• Interrupted time series with a control group |
| III-3 | A comparative study without concurrent controls:  
• Historical control study  
• Two or more single arm study ‡  
• Interrupted time series without a parallel control group |
| IV    | Case series with either post-test or pre-test/post-test outcomes |

**Table notes**

* A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence.
† This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (i.e. utilise A vs B and B vs C, to determine A vs C).
‡ Comparing single arm studies i.e. case series from two studies.

Note: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question e.g. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence.
References


