Liquid-based cytology in cervical screening: an updated rapid and systematic review and economic analysis


CRD summary
This review assessed the effectiveness of liquid-based cytology (LBC) for cervical screening. The authors concluded that there was uncertainty regarding the relative effectiveness and cost-effectiveness of the two main LBC techniques. The authors’ conclusions appear appropriate but, owing to the paucity of evidence reviewed and lack of detail on the primary studies, it is difficult to assess their reliability.

Authors’ objectives
To assess the clinical-effectiveness and cost-effectiveness of liquid-based cytology (LBC) for cervical screening compared with conventional smear testing. This review updated a previous Health Technology Assessment (see Other Publications of Related Interest no.1).

Searching
Eleven electronic databases were searched from 1999 to 2002; the search terms were reported. In addition, reference lists of identified studies and sponsor submissions were handsearched, health services research-related resources were searched on the Internet, and citation searches were conducted. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
All study designs were eligible for inclusion. The majority of the included studies used the split-sample method or methods of two cohort analysis.

Specific interventions included in the review
Studies that compared LBC with conventional cervical smears were eligible for inclusion. The specific LBC products assessed in the included studies were ThinPrep and SurePath. These were compared with biopsy, histology findings, pathologist’s review of the slides, or a combination of cytology, histology and cervicography.

Reference standard test against which the new test was compared
The reference standard was conventional smear testing, such as colposcopic biopsy, histology, cytology and cervicography.

Participants included in the review
No inclusion criteria for the participants were stated. The participants were all women undergoing cervical screening. Some studies included ordinary populations and others high-risk populations.

Outcomes assessed in the review
Studies that reported the incidence, morbidity and/or mortality rates from cervical cancer, the sensitivity and/or specificity, the categorisation of specimens, percentage of inadequate or unsatisfactory specimens, or specimen interpretation times were eligible for inclusion.

How were decisions on the relevance of primary studies made?
Two reviewers assessed studies for inclusion.

Assessment of study quality
The studies were evaluated according to criteria adapted from the Cochrane model by Broadstock for the New Zealand Health Technology Assessment Review (see Other Publications of Related Interest no.2). Two reviewers assessed study
quality.

**Data extraction**
One reviewer undertook the data extraction, which was checked by a second for accuracy. Data on the sensitivity and specificity, number of inadequate specimens and specimen interpretation time were abstracted.

**Methods of synthesis**
How were the studies combined?
For the outcome of sensitivity, the studies were combined in a narrative. For the outcome of specificity, the studies were grouped by patient population (ordinary versus high risk) and combined using a random-effects meta-analysis. Publication bias was not assessed.

How were differences between studies investigated?
For the outcome of specificity, heterogeneity was assessed using chi-squared and I-squared tests.

**Results of the review**
Sixteen studies (which appeared to be diagnostic cohort studies) were included. The total number of participants was at least 5,798.

No results on study quality were reported.

Sensitivity.
Across the studies, sensitivity ranged from 34.5 to 93.6% for the conventional smear test and from 53 to 95.7% for the LBC smear test. In the majority of the studies there was no significant difference in sensitivity between conventional and LBC smear tests.

False-negative rates.
Ordinary populations (4 studies): LBC smear tests produced significantly fewer false-negative test results than conventional smear tests when low-grade squamous intraepithelial lesions (LSIL) test results or worse were defined as positive (relative risk, RR=0.55, 95% confidence interval, CI: 0.46, 0.66). There was no significant heterogeneity between the studies.

High-risk populations (10 studies): there were no significant differences for the number of false-negative test results between conventional smear tests and LBC smear tests when LSIL test results or worse were defined as positive (RR 0.90, 95% CI: 0.68, 1.17). There was significant heterogeneity between the studies.

The pooled RR was 0.76 (95% CI: 0.60, 1.17) when the results from both population groups were combined, with the sensitivity rates for conventional smear tests and LBC smear tests being 0.72 and 0.80, respectively. This indicates that LBC smear tests were associated with a 12% improvement in sensitivity compared with conventional smear tests.

**Cost information**
LBC was always more cost-effective than conventional Pap smear testing over the same screening interval. When LBC was compared across alternative screening intervals, and screening was undertaken every 3 years, the cost-effectiveness was under £10,000 per life-year gained.

**Authors' conclusions**
The updated analysis provided more certainty regarding the potential cost-effectiveness of LBC compared with conventional Pap smear testing. However, there was still uncertainty regarding the relative effectiveness and cost-effectiveness of the two main LBC techniques.
CRD commentary
The review question was defined in terms of the interventions, outcomes and study designs. A number of sources were searched for potentially relevant studies and both foreign language and unpublished studies were sought. Efforts were made to minimise reviewer bias and errors in the study selection, data extraction and quality assessment processes. The authors stated that study quality was assessed, but no results from the assessment were reported. In addition, no study details were provided. This makes it impossible for the reader to judge whether the results and conclusions are consistent with the evidence reviewed.

The studies were combined in a narrative synthesis for the outcome of test sensitivity, and this seemed appropriate given the differences between the studies. The studies were combined using a random-effects meta-analysis for the outcome of specificity. This appears to have been appropriate for the group of studies that included ordinary populations, but the validity of this approach in the subgroup of high-risk patients is questionable given the heterogeneity between the studies. Overall, the authors’ conclusions appear appropriate but, owing to the paucity of evidence reviewed and the lack of reporting of study quality and details, it is difficult to assess their reliability.

Implications of the review for practice and research
Practice: The authors stated that increasing the uptake of screening may be more effective in reducing disease at the population level, compared with increasing the sensitivity of the tests. Furthermore, as the sensitivity of the programme is related not only to the individual tests but also to the screening interval, then a balance needs to be struck between investment in more sensitive but costly tests and more frequent testing.

Research: The authors stated that research in the area of utility assessment and a full cost-effectiveness study of LBC, based on a trial of its introduction in a low-prevalence population, may be worthwhile. In addition, a randomised comparison of the two main techniques may also be useful.

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Other publications of related interest

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MeSH
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.