

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

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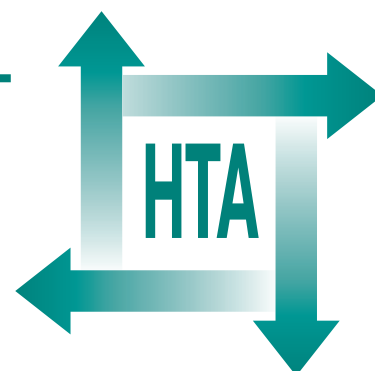
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## *Executive summary*

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## Executive summary

This report presents the results of a review of effectiveness and cost-effectiveness that updates an earlier published report with the same objectives, published in January 2000.

### Epidemiology and background

Around 4 million women per annum in England have a cervical screening test. Currently the age-standardised incidence of cervical cancer is around 9 per 100,000 per annum. The mortality rate in 1997 was 3.7 per 100,000 per annum.

Liquid-based cytology (LBC) is a new method of preparing cervical samples for cytological examination. Unlike the conventional 'smear' preparation, it involves making a suspension of cells from the sample and this is used to produce a thin layer of cells on a slide. The new intervention would thus form part of the process of population screening to reduce the incidence of invasive cervical cancer.

### Methods

This review updates the original HTA rapid review of LBC (Payne *et al.* *Health Technol Assess* 2000;4(18):1–73) to reflect any new evidence, including the results of the pilot studies implemented as a result of the previous review. The data extracted from the relevant literature searches were reviewed and assessed with respect to the quality of the evidence. Pooled estimates of the parameters of interest were derived from the original and the updated studies. Meta-analyses were undertaken where appropriate.

The mathematical model developed for the original rapid review of LBC was adapted to synthesise the updated data to estimate costs, survival and quality-adjusted survival of patients tested using LBC and using Papanicolaou (Pap) smear testing.

Cost data from published sources, if available, or derived from published or other sources of resource and cost data were incorporated into the above model to allow economic, as well as clinical,

implications of treatment to be assessed. The primary incremental cost-effectiveness ratio is the cost per life year gained (LYG), although estimates of the cost per quality-adjusted life-year (QALY) gained are also presented.

A sensitivity analysis was undertaken to identify the key parameters that determine the cost-effectiveness of the treatments, with the objective of identifying how robust the results of the economic analysis are, given the current level of evidence.

### Results

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

From the evidence available, it is likely that the LBC technique will reduce the number of false-negative test results. Modelling analyses undertaken as part of this study indicate that this would reduce the incidence of invasive cancer. There is now more evidence to support improvements emanating from the use of LBC screening in terms of a reduced number of unsatisfactory specimens and a decrease in the time needed to obtain the smear samples.

The estimated annual gross cost of consumables and operating equipment, and other one-off conversion costs associated with introducing the new technique, will be between £17 and £38 million in England and Wales, depending on the LBC system and the configuration of the service.

No UK-based studies providing direct evidence regarding the cost-effectiveness of LBC screening were identified. Analyses based on models of disease natural history, conducted in this study, showed that conventional Pap smear screening was extendedly dominated by LBC (LBC was always

more cost-effective than conventional Pap smear testing over the same screening interval). Comparing LBC across alternative screening intervals gave a cost-effectiveness of under £10,000 per LYG when screening was undertaken every 3 years. The cost-effectiveness results were relatively stable under most conditions, although if screening outcomes such as borderline results and colposcopy are assumed to induce even small amounts of disutility then LBC screening at 5-yearly intervals may be the most cost-effective option.

## Recommendations for research

The sensitivity analyses undertaken around hypothesised utility values in order to generate preliminary estimates of cost-effectiveness with respect to QALYs gained showed that such factors could influence the choice of screening programme. Therefore, further research may be worthwhile in the area of utility assessment, particularly with respect to the short-term impact of false-positive screen results.

This updated analysis provides more certainty with regard to the potential cost-effectiveness of LBC compared with conventional Pap smear testing. A full cost-effectiveness study of LBC based on a trial of its introduction in a low-prevalence population would provide more definitive information than is possible by modelling studies, although the results of the modelling analysis provide a robust argument that LBC is a cost-effective alternative to conventional cervical cancer screening, such that the large expenditure required to fund a trial is probably not justified. However, there is uncertainty regarding the relative effectiveness (and cost-effectiveness) of the two main LBC techniques, ThinPrep<sup>®</sup> and PrepStain<sup>®</sup>, and a randomised comparison of these two techniques may be worthwhile.

## Other important issues regarding implementation

It is clear that increasing coverage of the cervical screening programme is also an important way of reducing the burden of invasive cervical cancer. Given the low cost-effectiveness ratios for moving from no screening to any form of screening, it is likely that any effective intervention aimed at increasing coverage will be a cost-effective use of resources. Such interventions will also be equitable, as non-uptake of a screening programme is likely to be due to inequities in access to healthcare (whether they be defined as differences in the relative costs of screening, or through inequities in education or health information).

In addition, a range of economic evaluations was identified in the updated systematic search (1999–2002) that assessed the economic impact of cervical screening approaches other than conventional Pap smear testing and LBC techniques, including semi-automated slide analysis, human papilloma virus testing as an adjunct or alternative to Pap smear testing, and protocols for the management of atypical screening results.

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

## Publication

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# NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

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Research suggestions are carefully considered by panels of independent experts (including consumers) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or designing a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a limited time period.

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