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Rapid review

Executive summary

Liquid-based cytology in cervical screening: a rapid and systematic review

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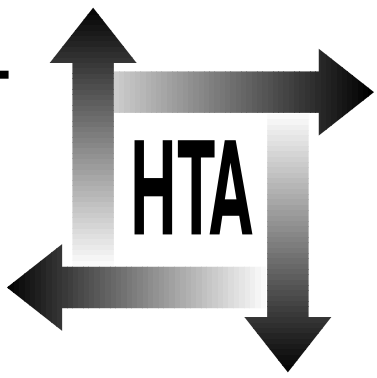

Executive summary

Background

Around 4 million women per annum in England have a cervical screening test. Currently the age-standardised incidence of cervical cancer is around 9.3 per 100,000 per annum. The mortality rate in 1997 was 3.7 per 100,000 per annum.

Liquid-based cytology 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 cervical cancer.

Methods

Data sources

Three types of literature search were performed:

- clinical effectiveness search
- cost-effectiveness search
- modelling search.

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

- MEDLINE
- EMBASE
- Science Citation Index
- Cochrane Library
- NHS CRD: DARE, NEED and HTA
- HealthSTAR
- National Research Register.

Inclusion and exclusion criteria

All health technology assessment and related secondary research studies were included. Primary research studies were included if they attempted to measure an outcome of importance, such as comparison of liquid-based cytology with conventional cervical smears in respect of an assessment of sensitivity and/or specificity, categorisation of specimens, percentage of inadequate or unsatisfactory specimens and specimen interpretation times. All databases were searched up to November 1999. Additional material identified up to February 2000 was also included.

Data extraction

Data were extracted by one of the authors. Key tabulations and calculations for summary tables were checked by entering the published study data (where available) into a spreadsheet and re-calculating the relevant percentages. Only those studies with a clear tabulation of the numerical data were used in the conventional smear versus liquid-cytology assessments.

Results

Number and quality of studies and direction of evidence

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

Effectiveness

There is some evidence that liquid-based cytological methods offer the following advantages over traditional smear techniques:

- a reduction in the proportion of inadequate specimens
- an improvement in sensitivity
- a possible reduction in specimen interpretation times.

Costs

The estimated annual gross cost of consumables and operating equipment associated with the new technique, based on a marginal cost per slide that includes capital equipment costs depreciated over a period of 6 years, is about £16 million in England.

Cost-effectiveness

There are no studies that provide direct evidence regarding the cost-effectiveness of liquid-based cytology screening. Analyses based on models of disease natural history, however, give a cost-effectiveness of under £10,000 per life-year gained, when screening is undertaken every 5 years, and under £20,000 per life-year gained at a 3-year interval, except under certain assumptions in respect of marginal costs and discount rates.

Sensitivity analyses

These results in respect of cost-effectiveness are relatively stable under most conditions. The key uncertainties are the marginal costs associated with liquid-based cytology, assumptions about improvements in sensitivity and specificity, and discounting both in terms of costs, but particularly in terms of benefits.

Limitations of the calculations (assumptions made)

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

Conclusions

From the evidence available, it is likely that the liquid-based cytology technique will reduce the number of false-negative test results, reduce the number of unsatisfactory specimens and may decrease the time needed for examination of specimens by cytologists. It is not possible to be certain whether this will reduce the incidence of invasive cancer, but modelling studies have suggested that this would occur.

In this review, it became clear that increasing the coverage of the programme, and the use of more effective cervical specimen collection devices are also important ways of reducing the burden of the invasive cervical cancer. The use of automated image analysis devices, and of other testing of the specimens (such as for human papillomavirus) have not been covered in this review.

Recommendations for research

A full cost-effectiveness study of liquid-based cytology based on a trial of its introduction in low-prevalence populations would provide more definitive information than is possible by modelling studies. However, an assessment of the uncertainties about the values and assumptions used in the economic model indicates that the key areas for further research are:

- the marginal cost per sample of the new technologies compared with conventional screening methods
- the improvement in the rate of inadequate samples and the relative specificity of the liquid-based cytology techniques.

Expiry date

It is recommended that the conclusions from this report are revisited in July 2001 or earlier if new trials and technologies emerge before then.

Publication

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NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (HTA) programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

The research reported in this monograph was commissioned by the HTA programme (project number 99/18/01) on behalf of the National Institute for Clinical Excellence (NICE). Rapid reviews are completed in a limited time to inform the appraisal and guideline development processes managed by NICE. The review brings together evidence on key aspects of the use of the technology concerned. However, appraisals and guidelines produced by NICE are informed by a wide range of sources. Any views expressed in this rapid review are therefore those of the authors and not necessarily those of the HTA programme, NICE or the Department of Health.

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