Authors' objectives
No clear objective was stated. The review evaluated the diagnostic accuracy, safety and cost-effectiveness of liquid-based cytology (LBC) for the screening of cervical cancer in non-pregnant women.

Searching
MEDLINE, Current Contents, Biological Abstracts, CINAHL, EBM Reviews and the Cochrane Library were searched from January 2000 to April 2002; the search terms were reported. Health technology assessment (HTA) databases and HTA agency websites were also searched. Non-English language studies and abstracts were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and comparative diagnostic cohorts (including case series) were eligible for inclusion. Case studies were excluded. The authors also provided a synthesis of the results of non-narrative systematic reviews and meta-analyses. The results of this synthesis were presented separately from the synthesis of the primary studies. Only the synthesis of primary studies is considered in this abstract.

Specific interventions included in the review
Studies of filter-based or centrifuge-based LBC tests were eligible for inclusion. Studies of human papillomavirus DNA diagnostic tests and of automated or semi-automated slide reading/analysing technologies were excluded. Where reported, the results of screening with the conventional (Papanicolaou, Pap) test were also included.

Reference standard test against which the new test was compared
There were no inclusion criteria relating to a reference standard. The reference standard used in the included primary studies was histology.

Participants included in the review
Studies of non-pregnant women undergoing cervical cancer screening were eligible for inclusion.

Outcomes assessed in the review
Studies reporting any outcome were eligible for inclusion. The authors stated that special reference was given to those that reported diagnostic accuracy and reliability, clinical effectiveness and cost-effectiveness.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for inclusion. Any disagreements were resolved through consensus.

Assessment of study quality
Study quality was assessed in relation to: the inclusion of an appropriate patient spectrum; blinded assessment of the reference standard and index test results; comparison of the test with a reference standard in all patients; application of the reference standard regardless of the result of the index test; test interpreted independently of clinical information; reference standard applied before commencement of treatment.

The authors did not state how the studies were assessed for quality, or how many reviewers performed the quality assessment.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data.
Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
Differences between the studies were discussed in the text.

Results of the review
Seven primary studies were included in the review (n=116,189 for LBC; n=119,831 for Pap). Of these, one was an RCT (n=997 for LBC; n=1,002 for Pap), one a non-randomised trial (n=137 for LBC; n=590 for Pap), two were diagnostic cohort studies (n=983), two used historical Pap controls (n=84,483 for LBC; n=93,119 for Pap), and one used historical and prospectively recruited Pap controls (n=29,589 for LBC; n=25,120 for Pap).

The included studies were of a poor quality. Two studies recruited an appropriate patient spectrum. Three studies blinded assessors of the reference standard and two blinded assessors of the index test; one study reported blinding to other clinical information. Two studies performed both the index test and reference standard in all patients, while another tested all participants with a positive index test with the reference standard. Two studies reported that the reference standard was performed before the index test. Two studies reported insufficient data to calculate any diagnostic measures.

None of the included studies reported safety outcomes.

Diagnostic accuracy (2 diagnostic cohort studies).

Only two studies performed both the index test and reference standard in all patients. Therefore, only these two studies were used to calculate measures of diagnostic accuracy.

LBC: the sensitivity was 82.8% (specificity 62%) in one study; in the other study, the sensitivity ranged from 41.7% (specificity 90.2%) to 82.6% (specificity 52.2%) and the specificity from 52.2% (sensitivity 81.9% or 82.6%) to 90.2% (sensitivity 41.7%), depending on which of the four definitions of positive and negative test results were used.

Pap test: the sensitivity was 89.6% (specificity 52.1%) in one study; in the other study, the sensitivity ranged from 39.4% (specificity 98.9%) to 86.8% (specificity 47.8%) and the specificity from 47.8% (sensitivity 86.8%) to 98.9% (specificity 39.4%), depending on which of the four definitions of positive and negative test results were used.

Relative true-positive rates from 5 trials varied between 0.91 (P<0.0005) and 1.52 (P<0.025). Relative-false positive rates from 3 trials varied between 0.82 (P<0.025) and 1.73 (P<0.2).

Cost information
A decision-analytic model suggested that LBC is associated with greater costs per woman than the Pap smear test, and that there is insufficient evidence to support the claim that LBC is superior to conventional cytology in detecting either high-grade lesions or invasive cancer. Currently, LBC cannot be demonstrated to be cost-effective at the proposed price ($30.50 compared with $19.00 for a Pap test).

Authors’ conclusions
There is insufficient evidence to draw meaningful conclusions about the differences in the diagnostic characteristics of LBC and the Pap test for cervical cancer screening.

CRD commentary
The question was clear in terms of the participants, intervention, outcomes and study design. There were no criteria relating to the reference standard; however, the included studies used an appropriate reference standard. The authors undertook a comprehensive search but, since they only included studies published in English, relevant studies might have been missed. In addition, abstracts were excluded and grey literature was not considered, therefore publication bias cannot be ruled out. The study selection process was conducted in duplicate, thereby reducing the potential for selection bias. It was unclear whether similar methods to reduce error and bias were employed at the data extraction and quality assessment stages. Study quality was assessed and the results for each criterion were reported for each study. However, some of the included studies were trials: not all of the criteria were relevant to trials and some relevant criteria were not assessed.

The two studies identified as recruiting an appropriate patient spectrum were stated as having compared a non-randomly selected population with historical controls; it is unclear how this population can be deemed appropriate given the potential for selection or spectrum bias. Two other studies (one recruiting a consecutive series of patients and the other a random selection of patients) were classified as inappropriate. Two studies provided no data to calculate diagnostic measures, and a further five only provided data sufficient to calculate positivity rates. The decision to combine the studies in a narrative seemed appropriate. Despite the limitations of the review, the authors’ conclusion that there is a lack of evidence appears reasonable, although the potential for missed studies in the current review must be considered.

**Implications of the review for practice and research**

**Practice:** The authors stated that, since there is currently insufficient evidence pertaining to LBC for cervical screening, they recommend that public funding should not be supported at this time for this screening test.

**Research:** The authors stated that further high-quality studies using an acceptable reference standard, such as histological confirmation of cytology results, are required to evaluate the sensitivity and specificity of LBC.

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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.