Cost-effectiveness of liquid-based cytology with or without hybrid-capture II HPV test compared with conventional Pap smears: a study by the French Society of Clinical Cytology


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Three screening tests for cervical cancer were compared. The tests examined were conventional Pap smears, liquid-based cytology (LBC) and the Hybrid-Capture II HPV test (HC II). In the HC II test two mixtures of RNA probes were used, one for low-risk human papillomavirus HPV (LR-HPV) and one for high-risk human papillomavirus HPV (HR-HPV). Further, a ‘gold’ standard reference method (colposcopy) was available and biopsies were performed whenever a lesion was detected.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised two groups of patients. Group A consisted of women with previously detected non-treated cytological lesions, whilst group B consisted of women undergoing simple screening.

Setting
The study setting was secondary care. The economic study was undertaken in France.

Dates to which data relate
The dates to which the resource use and effectiveness data referred were not reported. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively by evaluating the production costs of the conventional smear test, LBC and the HC II test in a private laboratory receiving over 100,000 smear tests per year, and also in a public-based laboratory.

Study sample
No sample size appears to have been determined in the planning phase of the study. In addition, power calculations were not performed retrospectively. Patients were recruited from both the private and public sectors by skilled gynaecologists. A total of 2,585 women were included, 828 in group A and 1,757 in group B. The mean ages in the two groups were 37.8 years (group A) and 33.3 years (group B), respectively. Four hundred and four women were excluded.
from the study because of abnormal colposcopy without biopsy, no visualised transformation zone, and thus no biopsy or representative biopsy. Thus, a total of 1,785 women (462 in group A and 1,323 in group B) were included in the study.

Study design
The study was a prospective diagnostic cohort study that was undertaken in both public and private clinics in France. In the study, conventional Pap smears, LBC, colposcopy and biopsies were all conducted at the same time. All samples were treated within one month of sampling. There was no loss to follow-up.

Analysis of effectiveness
All of the patients included in the study were accounted for in the analysis. The outcome used in the analysis was the sensitivity and specificity of each of the three diagnostic tests under investigation in comparison with the gold standard. Each sample was read twice: the first was a clinical reading, each Pap smear and LBC was read in each laboratory by two different pathologists; the second was optimised reading of anonymous slides without clinical data. In cases of disagreement, a consensus diagnosis was organised on a multiple view microscope. An independent expert was sought only if consensus could not be reached.

Effectiveness results
For lesions of Grade CIN-1 (cervical intraepithelial neoplasia) or higher in the high-risk population (group A), the sensitivity and specificity of each test were as follows:

Pap smear optimised reading, 92% (range: 90 to 94) and 80% (range: 75 to 85), respectively;
LBC optimised reading, 90% (range: 87 to 92) and 76% (range: 71 to 81), respectively;
HC II using HR-HPV, 79% (range: 74 to 83) and 77% (range: 71 to 83), respectively; and
LBC in combination with HC II using HR-HPV, 85% (range: 80 to 89) and 82% (range: 76 to 88), respectively.

For lesions of Grade CIN-1 or higher in the screening population (group B), the sensitivity and specificity of each test were as follows:

Pap smear optimised reading, 74% (range: 66 to 83) and 91% (range: 90 to 93), respectively;
LBC optimised reading, 73% (range: 65 to 82) and 90% (range: 89 to 92), respectively;
HC II using HR-HPV, 64% (range: 53 to 76) and 86% (range: 85 to 88), respectively; and
LBC in combination with HC II using HR-HPV, 67% (range: 56 to 78) and 94% (range: 92 to 95), respectively.

For lesions of grade CIN-II or higher in the high-risk population (group A), the sensitivity and specificity of each test were as follows:

Pap smear optimised reading, 85% (range: 81 to 89) and 92% (range: 89 to 94), respectively;
LBC optimised reading, 78% (range: 73 to 83) and 94% (range: 92 to 96), respectively;
HC II using HR-HPV, 80% (range: 74 to 86) and 54% (range: 49 to 60), respectively; and
LBC in combination with HC II using HR-HPV, 80% (range: 74 to 86) and 93% (range: 90 to 96), respectively.

For lesions of grade CIN-II or higher in the screening population (group B), the sensitivity and specificity of each test were as follows:
Pap smear optimised reading, 60% (range: 45 to 75) and 99% (range: 99 to 99), respectively;

LBC optimised reading, 65% (range: 50 to 80) and 98% (range: 98 to 99), respectively;

HC II using HR-HPV, 96% (range: 88 to 100) and 85% (range: 83 to 87), respectively; and

LBC in combination with HC II using HR-HPV, 76% (range: 59 to 93) and 97% (range: 97 to 98), respectively.

Clinical conclusions
The authors concluded that, compared with conventional Pap smears, LBC and HPV tests do not appear to improve the effectiveness of cervical cancer screening.

Measure of benefits used in the economic analysis
The authors did not derive a measure of health benefit. In effect, a cost-consequences analysis was performed.

Direct costs
The perspective adopted in the economic analysis was not explicitly reported, but it appears to have been that of the provider of the screening tests. The costing study evaluated the production costs of the conventional smear test, LBC and the HPV test in a private laboratory receiving over 100,000 smear tests per year. The same process was observed in a public-based hospital laboratory. The costs included in the analysis were for staff, tasks, equipment and consumables necessary for each screening technique.

Another costing study was performed in which an optimised production process was defined. This allowed the evaluation of the costs to be independent from the specificities of the observation sites, and to correspond to the maximal production capacities in view of the technical capacities of the equipment involved and the French work legislation.

The third costing estimated the cost of each of the physical quantities of materials and consumables and the salaries associated with each task.

The final study looked at the effects of variations in the annual number of examinations on the process and the costs.

The authors did not report the life expectancy of the equipment used. If the equipment used had a life span of over 2 years, the authors would ideally have had to convert these costs into net present value (i.e. discount the costs of the equipment over its lifespan). It was unclear if the authors did this. The cost results were presented in a figure. The price year was 2002.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($). The authors used the $ to Euro exchange rate for 2002.

Sensitivity analysis
The authors did not perform any sensitivity analysis.
Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The authors reported that for conventional Pap smears, irrespective of annual activity, the mean cost was lower in the public sector than in the private sector. In public laboratories, irrespective of activity, the Social Security tariff (EUR 15) covered the mean cost. This means that for a French public laboratory, there is no minimum level of annual activity required to make this activity viable. However, for private laboratories, a minimal level of 19,000 tests is required. For LBC, the estimated mean cost is never covered by the tariff (EUR 15), whatever the level of annual activity in private laboratories. In public laboratories, the annual level of activity required is about 16,500.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Liquid-based cytology and human papillomavirus (HPV) tests do not appear to have improved the effectiveness of cervical cancer screening in comparison with conventional Pap smears, but they were more expensive.

CRD COMMENTARY - Selection of comparators
The study compared three screening tests for cervical cancer (conventional Pap smears, LBC and HC II test). These three screening tests would all appear to be current practice in France. You should decide if these screening tests are current practice in your own setting.

Validity of estimate of measure of effectiveness
The study was a prospective cohort study that was undertaken in both public and private clinics in France. In the study, conventional Pap smears, LBC, colposcopy and biopsies were all conducted at the same time. The authors compared the sensitivity and specificity of the HC II test, Pap smears and LBC with colposcopy, which the authors considered to be the gold standard. Although the authors reported that their statistical analysis was based on up-to-date standards, they did not report the statistical tests used or the results of these analyses.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefit. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The authors did not report the perspective of the economic analysis. The perspective of the provider of the tests (i.e. the laboratories) appears to have been adopted, and all costs relevant to this narrow perspective were included in the analysis. However, it would have been interesting had the authors determined the wider costs of the intervention, for example the costs associated with false positives and false negatives. No statistical or sensitivity analysis of the costs was performed to account for any uncertainty in the results. The authors reported their cost results in figures, which showed the mean cost of the test depending on the annual level of activity. Although some explanation of these figures was given in the narrative, a table detailing the exact cost per level of activity would have provided more information to the reader. The authors did not report if the equipment costs were presented in net present values. The price year was reported, which will aid any possible inflation exercises.

Other issues
The authors reported that their results were in line with those from other published studies which also found that LBC
and HPV tests did not appear to improve the effectiveness of screening and were more expensive than Pap smears. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors did not report any further limitations to their study.

Implications of the study
The authors recommended that it would be most efficient to use the extra money required to perform LBC and HPV tests to screen the 40% of women who had no Pap smears in a 5-year interval, in order to decrease the incidence of cervical cancer.

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