Screening for cervical cancer in India: how much will it cost? A trial based analysis of the cost per case detected


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 strategies for the screening of cervical cancer were examined. The strategies were:

- a simple visual inspection after applying 4% acetic acid to the cervix (VIA);
- cytology; and
- human papillomavirus (HPV) testing.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women aged 30 to 59 years.

Setting
The setting was the community. The economic study was carried out in India.

Dates to which data relate
The effectiveness and resource use data were derived from a study published in 2005. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that included in the effectiveness study.

Study sample
There was limited information on the sample of women included in the analysis since the main details of the effectiveness study had already been published. Overall, 131,178 eligible women in a rural population were enrolled in February 2000. Women were allocated to the three screening arms against a control arm of no screening, with 13 clusters in each arm. The average number of eligible women was 2,836 in the VIA group, 2,707 in the cytology group.
and 2,841 in the HPV testing group.

Study design
This was a cluster, randomised controlled trial that was based at the Nargis Dutt Memorial Cancer Hospital (NDMCH) in Barshi, Maharashtra, India. It covered a catchment area of 497 rural villages grouped into 52 clusters based on primary health centres. Details on follow-up (length and loss of participants) were not reported. With VIA, screen-positive women underwent colposcopy and had biopsy samples taken during the clinic visit, and were then referred to the NDMCH if they required treatment. In the cytology and HPV arms, test samples were processed at the NDMCH laboratory and screen-positive women were then recalled for colposcopy at the NDMCH. All biopsies were processed and reported by the laboratories at the NDMCH.

Analysis of effectiveness
The main end point of the clinical trial was the impact of the screening strategies on cervical cancer incidence and mortality. However, given the short follow-up of the study, the proportion of cases detected was considered the main clinical end point for the current analysis. In particular, the proportion of detected cases of cervical intraepithelial neoplasia Grade 2/3 (CIN 2/3) or invasive cancer, or both (CIN 2/3+), was considered. The analysis of the clinical study was conducted on an intention to treat basis. No information on the baseline comparability of the study groups was provided.

Effectiveness results
The proportion of CIN Grade 2/3 cases was 0.5% (95% confidence interval, CI: 0.2 - 0.9) with VIA, 0.7% (95% CI: 0.4 - 1.1) with cytology and 0.7% (95% CI: 0.4 - 1.1) with HPV testing.

The proportion of invasive cancer cases was 0.2% (95% CI: 0 - 0.5) with VIA, 0.2% (95% CI: 0.1 - 0.4) with cytology and 0.2% (95% CI: 0 - 0.3) with HPV testing.

The proportion of CIN 2/3+ cases was 0.7% (95% CI: 0.2 - 1.2) with VIA, 1.0% (95% CI: 0.5 - 1.4) with cytology and 0.8% (95% CI: 0.5 - 1.3) with HPV testing.

Clinical conclusions
The effectiveness analysis showed that cytology detected more cancer cases than VIA and HPV testing.

Measure of benefits used in the economic analysis
The summary benefit measure used was the proportion of CIN 2/3+ cases detected with each screening option. This was derived directly from the effectiveness study. No discount rate appears to have been used.

Direct costs
The cost analysis was conducted from the perspective of the health service. Only the direct medical costs were considered. The costs were grouped as programme costs and activity costs. Programme costs included infrastructure changes, programme management, training or recruitment of staff, and data administration. Activity costs included recruitment, invitation, screening clinics, screening test laboratory (cytology/HPV testing), biopsy laboratory, transport to hospital and colposcopy in hospital. The unit costs were presented separately from the quantities of resources used for some items. The resource use data were derived from the clinical trial. The authors stated that all expenses incurred by the programme were recorded in inventories and logbooks listing all training, staff, consumables and equipment, while data on expenses incurred by the trial (e.g. vehicle maintenance costs) were recorded in and retrieved from an accountancy database. Annuity factors were based on a discount rate of 3%. The lifespan of equipment was 5 years for data management equipment and 10 years for medical and transport equipment. The costs of initial planning and infrastructure changes were amortised over a 15-year timescale and initial staff training and staff recruitment over a 5-year timescale. The costs came from local sources. The prices were adjusted to 2002 levels using the wholesale price...
index for India.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not taken into consideration.

**Currency**
US dollars ($). Indian rupees were converted into US dollars using the rate 48 rupees = $1.

**Sensitivity analysis**
Univariate sensitivity analyses were carried out to assess the impact of variations in the costs. Non-parametric bootstrapping was also used to explore the uncertainty in cost-effectiveness results used to calculate CIs.

**Estimated benefits used in the economic analysis**
In a hypothetical cohort of 1,000 women, the incremental number of CIN 2/3+ cases detected in comparison with no screening was 7.5 with VIA, 10.0 with cytology and 8.4 with HPV testing. Thus, the incremental number of CIN 2/3+ cases detected in comparison with VIA was 2.5 with cytology and 0.9 with HPV testing.

**Cost results**
In a hypothetical cohort of 1,000 women, the incremental costs in comparison with no screening were $3,917 with VIA, $6,609 with cytology and $1,799 with HPV testing. In comparison with VIA, the incremental costs were $2,691 with cytology and $7,881 with HPV testing. In comparison with cytology, the incremental costs of HPV testing were $5,190.

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio (ICER; i.e. the extra cost per CIN 2/3+ case detected) was calculated to combine the costs and benefits of the alternative screening strategies.

In comparison with no screening, the ICER was $522 with VIA, $659 with cytology and $1,397 with HPV testing. The ICER was $1,065 with cytology in comparison with VIA, while HPV testing was dominated by cytology, which was both more effective and less expensive.

The bootstrap analysis showed that the 95% CI of the ICER ranged from $429 to $652 for VIA compared with no screening, and from $713 to $2,175 for cytology compared with VIA.

The results of the sensitivity analysis did not alter the base-case conclusions.

**Authors' conclusions**
More cases of cervical intraepithelial neoplasia Grade 2/3 or invasive cancer (CIN2/3+) would be detected using cytology instead of VIA (visual inspection after acetic acid), and each additional case would cost $1,065 (95% CI: 713 - 2,175) in India. However, it is unclear whether this is an affordable cost for a low resource setting. VIA was less expensive than cytology, but was also less accurate and detected fewer cervical cancer cases. Human papillomavirus (HPV) testing was found to be much more expensive and less effective and, therefore, was not a cost-effective strategy.

**CRD COMMENTARY - Selection of comparators**
The rationale for the selection of the comparators was clear. Feasible screening strategies were examined and compared with no screening, which might represent the actual pattern of care in several low-income countries. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a published randomised trial, which was appropriate for the study question. Such a trial is usually associated with a valid and robust design. A large group of women was enrolled, which should ensure the representativeness of the patient sample. Limited information on sample selection, randomisation, follow-up, and baseline comparability of the study groups was provided. Uncertainty around the effectiveness results was investigated by means of non-parametric bootstrapping.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It is therefore not comparable with the benefits of other health care interventions. The authors acknowledged that the number of cancer cases represents an intermediate measure but, owing to the short time horizon of the analysis, a more appropriate measure of benefit (i.e. impact on mortality) could not be assessed.

Validity of estimate of costs
The economic analysis was restricted to the inclusion of the direct medical costs associated with the three screening policies. The source of the costs was reported, but details of the unit costs and quantities of resources used were not provided for all items. Only personnel costs and quantities were presented separately. Discounting was applied to annuity factors and a 3% rate was used. Statistical analyses of the costs were not carried out in the base-case. Sensitivity analyses were carried out but the results of such analyses were not reported, although the authors stated that changes in costs did not alter the main cost-effectiveness results. Since the costs were estimated from local sources, caution is required when extrapolating the results of the analysis to other settings. The price year was reported, which enhances the possibility of performing reflation exercises in other time periods.

Other issues
The authors stated that their study differed from other published economic evaluations of cervical cancer screening in that it included not only the costs of screening and diagnosis, but also the costs of implementing and running the programme. Nevertheless, the authors noted that the costs of cancer treatment were not included and this represents a limitation of the current analysis. It was also stated that the use of data from a single clinical trial limits the generalisability of the study results to other settings. Both clinical and economic data were specific to the study setting, which might limit the external validity of the analysis. The study referred to women in the general population and this was reflected in the authors’ conclusions. The results of the analysis were presented selectively since the results of the sensitivity analysis were not reported.

Implications of the study
The study results would appear to suggest that cytology was more cost-effective than VIA for the screening of cervical cancer. However, costs should decrease in order to make screening more affordable for developing countries.

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