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 cervical cytology screening were assessed. These were no screening, opportunistic screening and organised screening. Organised screening used either conventional or liquid-based cytology and was conducted at different frequencies (every 1, 2, 3, 4 or 5 years).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population comprised healthy females aged 15 years on entering the model.

Setting
The setting was primary care. The economic study was carried out in Hong Kong.

Dates to which data relate
The effectiveness and cost evidence were taken from studies published between 1993 and 2004. The costs were reported in year 2000 prices.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Modelling
A Markov model was created to simulate the natural history of cervical cancer. The model incorporated monthly transitions between the states of healthy, cervical intraepithelial neoplasia (CIN 1 and CIN 2,3), local cancer, regional cancer and distant cancer. Women may also have died from cervical cancer-related illness or other causes.

Outcomes assessed in the review
The following outcomes were assessed:

the transition probability of normal to CIN 1;
the transition probability of CIN 1 to CIN 2,3;
the transition probability of CIN 2,3 to local invasive cancer;
the transition probability of local invasive cancer to regional invasive cancer;
the transition probability of regional invasive cancer to distant invasive cancer;
the transition probability of CIN 1 to normal;
the transition probability of CIN 2,3 to normal;
the 5-year cancer survival rates with local invasive cancer, regional invasive cancer, and distant invasive cancer;
the annual probabilities of symptom detection for local invasive cancer, regional invasive cancer, and distant invasive cancer;
the sensitivity and specificity of ThinPrep cervical cytology; and
the sensitivity and specificity of conventional cervical cytology.

**Study designs and other criteria for inclusion in the review**
The authors did not report the criteria applied to studies that were used to identify model parameters, although the authors used country-specific data where possible.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Twenty-five primary studies were included in the review.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The following results (monthly probabilities unless otherwise stated) were obtained. The bracketed values indicate the ranges used for the sensitivity analysis.

The transition probabilities were:

for normal to CIN 1, 0.0007 - 0.0209 (0.0004 - 0.0418);

for CIN 1 to CIN 2,3, 0.0014 - 0.0049 (0.0007 - 0.0098);
for CIN 2,3 to local invasive cancer, 0.0040 (0.0020 - 0.0080);
for local invasive cancer to regional invasive cancer, 0.0250 (0.0100 - 0.0400);
for regional invasive cancer to distant invasive cancer, 0.0375 (0.0250 - 0.0500);
for CIN 1 to normal, 0.0068 - 0.0128 (0.0034 - 0.0256); and
for CIN 2,3 to normal, 0.0029 (0.0015 - 0.0058).

The 5-year cancer survival rate was 0.86 (0.80 - 0.93) for local invasive cancer, 0.43 (0.28 - 0.66) for regional invasive cancer, and 0.11 (0.04 - 0.33) for distant invasive cancer.

The annual probability of symptom detection was 0.19 (0.10 - 0.66) for local invasive cancer, 0.60 (0.36 - 0.84) for regional invasive cancer, and 0.90 (0.68 - 0.99) for distant invasive cancer.

The sensitivity of ThinPrep cervical cytology was 70% (50 - 100) and the specificity was 95% (90 - 100).

The sensitivity of conventional cervical cytology was 60% (50 - 100) and the specificity was 95% (90 - 100).

**Methods used to derive estimates of effectiveness**

The authors made several assumptions.

**Estimates of effectiveness and key assumptions**

To simulate opportunistic screening, the authors assumed that 45% of all women are never screened, 13% get one screen in their lifetime at age 30, and 8% get one screen at age 50. It was also assumed that 2% get screened every 3 years, 4% get screened every 2 years, and 28% get screened every year.

To simulate an organised screening programme, the authors assumed that screening starts at age 21 and occurs at regular intervals (every 1, 2, 3, 4 or 5 years) in the absence of a cytological abnormality.

The authors also made some general assumptions:

- there is no upper age limit for screening;
- colposcopy and biopsy are performed for all cytological results of either LSIL or HSIL (not defined);
- biopsy confirmed cases of CIN 2,3 or invasive cancer are treated with either loop electrosurgical excision procedure, conisation or hysterectomy;
- women who have been successfully treated for precancerous lesions return to a healthy state, but are still at risk for future disease.

**Measure of benefits used in the economic analysis**

The summary measures of health benefits were the total average life expectancy and the percentage reduction in cancer incidence. The future benefits were discounted at a rate of 3%.

**Direct costs**

The authors reported that a societal perspective was adopted for the costing analysis. The cost estimates incorporated the costs of the tests, office visits and transportation. The resource use and cost data were taken from fee schedules, regional health care organisations in Hong Kong, and the Hospital Authority. The costs of the tests were obtained from the Hong Kong Family Planning Association, the AmMed Clinic and Quality Healthcare Asia Ltd. The travel costs were...
estimated using the costs of public transport. The unit costs were reported separately from the quantities. All the costs were converted to 2000 prices. The future costs were discounted at a rate of 3%.

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

**Indirect Costs**
The costing also incorporated estimates of patients' time (lost economic productivity), which was estimated from the Cost of Labours survey completed by the Hong Kong Census and Statistics Department.

**Currency**
The costs were estimated in Hong Kong dollars (HK$) and converted into US dollars ($). The conversion rate was US$1 = HK$7.8.

**Sensitivity analysis**
Sensitivity analyses were used to assess the impact of parameter uncertainty and alternative assumptions on the results.

**Estimated benefits used in the economic analysis**
The life expectancy with no screening was 28.1678.

For conventional cytology:
- screening every 5 years gave a life expectancy of 28.3663 years and an 83.2% reduction in cancer incidence;
- screening every 4 years gave a life expectancy of 28.3770 years and an 86.8% reduction in cancer incidence;
- screening every 3 years gave a life expectancy of 28.3880 years and a 90.4% reduction in cancer incidence;
- opportunistic screening gave a life expectancy of 28.2609 years and a 37.9% reduction in cancer incidence;
- screening every 2 years gave a life expectancy of 28.3990 years and a 93.8% reduction in cancer incidence; and
- screening every year gave a life expectancy of 28.4092 year and a 96.6% reduction in cancer incidence.

For liquid-based cytology:
- screening every 5 years gave a life expectancy of 28.3795 years and an 87.3% reduction in cancer incidence;
- screening every 4 years gave a life expectancy of 28.3881 years and a 90.2% reduction in cancer incidence;
- screening every 3 years gave a life expectancy of 28.3967 years and a 92.9% reduction in cancer incidence;
- opportunistic screening gave a life expectancy of 28.2640 years and a 39.0% reduction in cancer incidence;
- screening every 2 years gave a life expectancy of 28.4047 years and a 95.3% reduction in cancer incidence; and
- screening every year gave a life expectancy of 28.4117 years and a 97.2% reduction in cancer incidence.

**Cost results**
No screening cost $207.
For conventional cytology:

screening every 5 years cost $367,

screening every 4 years cost $425,

screening every 3 years cost $525,

opportunistic screening cost $553,

screening every 2 years cost $730, and

screening every year cost $1,351.

For liquid-based cytology:

screening every 5 years cost $373,

screening every 4 years cost $435,

screening every 3 years cost $540,

opportunistic screening gave $566,

screening every 2 years gave $754, and

screening every year cost $1,400.

**Synthesis of costs and benefits**

With conventional cytology:

the cost-effectiveness of screening every 5 years compared with no screening was $800 per life-year saved (LYS);

the cost-effectiveness of screening every 4 years compared with screening every 5 years was $5,400 per LYS;

the cost-effectiveness of screening every 3 years compared with screening every 4 years was $9,000 per LYS;

opportunistic screening was a dominated strategy;

the cost-effectiveness of screening every 2 years compared with screening every 3 years was $18,600 per LYS;

The cost-effectiveness of screening every year compared with screening every 2 years was $60,800 per LYS.

With liquid based cytology:

the cost-effectiveness of screening every 5 years compared with no screening was $800 per life LYS;

the cost-effectiveness of screening every 4 years compared with screening every 5 years was $7,100 per LYS;

the cost-effectiveness of screening every 3 years compared with screening every 4 years was $12,300 per LYS;

opportunistic screening was a dominated strategy.

the cost-effectiveness of screening every 2 years compared with screening every 3 years was $26,700 per LYS;

the cost-effectiveness of screening every year compared with screening every 2 years was $92,400 per LYS.
The outcomes were most sensitive to the relative performance of the technologies and the costs of the technologies. If the threshold was $15,000 per LYS, the optimal screening frequency with liquid-based cytology would be every 3 years. If the threshold was $10,000 per LYS, the optimal screening frequency would be every 4 years. Finally, if the threshold was $1,000 per LYS, the optimal screening frequency would be every 5 years.

Authors' conclusions
The adoption of a policy of organised, mass cervical screening in Hong Kong could substantially increase benefits and reduce costs, compared with the status quo of opportunistic screening. The conclusion that, generally, “liquid-based cytology strategies had more attractive cost-effectiveness ratios than the conventional cytology strategies” was not apparent from the numerical results presented.

CRD COMMENTARY - Selection of comparators
The comparators were alternative strategies for cervical screening. Opportunistic screening represented current practice and the timeframes for organised screening were motivated by a government sponsored initiative. You should decide if these are widely used health interventions in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature was undertaken. This is not uncommon given the modelling nature of the study. The authors selected and used information from published evidence that gave information relevant to the model developed. It was unclear whether evidence from the primary sources was combined and, if so, the methods used to combine such information. The authors considered the impact of differences between the primary studies in their sensitivity analysis that assessed parameter uncertainty. The analysis would have been further improved with a thorough discussion of the sources searched to identify relevant parameter values, why particular studies were chosen, and how the authors ensured the validity of these sources.

Validity of estimate of measure of benefit
The summary health benefits were estimated using the Markov model to estimate years of life saved. The measure of benefits used is a long-term measure, thus these results can be compared with the results of other studies on cervical screening, as well as other broader studies.

Validity of estimate of costs
The authors clearly reported that a societal perspective was used for the analysis. Both direct and indirect costs were estimated in support of this perspective. The unit costs were reported separately, and the effect of omitting any potentially relevant variables was mitigated by the sensitivity analyses carried out. Resource use and the unit costs were derived from published sources, and appropriate sensitivity analyses were performed. The price year was reported, which will facilitate any future reflation exercises. Since all the costs were incurred over the lifetime of the patient, the costs were appropriately discounted.

Other issues
The authors suggested that this study was the first evidence-based study to inform a government-sponsored population-screening programme. This may explain the lack of comparison of their results with those from other studies. Although the issue of generalisability was not explicitly reported, the authors took a number of steps to improve the generalisability of the results to other settings. The authors used possible values for societies' willingness-to-pay for health improvements to postulate the optimal timings between screenings within an organised screening programme. This enables other authors to extrapolate the results to other settings where the willingness-to-pay for health outcomes may differ. Moreover, the use of a Markov model allows other authors to re-estimate the results with parameters specific to their own setting. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.
A number of limitations were presented. These focused on not including HPV DNA testing, not capturing the heterogeneous behaviour of clinicians and women, and uncertainty in the relative performance and cost of liquid-based cytology and conventional cytology.

Implications of the study
The authors clearly favoured an organised screening programme with the frequency of screening determined by societies’ willingness-to-pay for health improvements. Although no suggestions for further work were explicitly stressed, several limitations were reported which could be addressed.

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