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
The study examined cervical cancer screening in women with a prior normal Pap test. The three screening strategies considered were conventional Pap test screening every 3 years, every 2 years, or every year. Screening was considered in different sub-groups of women, which were stratified by age (under 30 years, 30 - 44 years, 45 - 59 years and 60 - 65 years) and by screening history (0, 1, 2 and 3+ consecutive prior normal Pap tests). Normal Pap tests indicated all tests defined as "normal" or "infection/reactive changes", while Pap tests were considered as "consecutive" when performed within 36 months of one another.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised the general population of women younger than 65 years.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was derived from studies published between 1999 and 2004. Dates for resource use were not explicitly stated. The price year was 2004.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' opinions.

Modelling
A published 20-state Markov model was used to simulate the natural history of cervical cancer in a hypothetical cohort of women. It was also used to assess the clinical and economic impact of the alternative screening strategies over a lifetime horizon. Yearly cycles were considered. The population of eligible women was initially distributed among different health states (well, low-grade dysplasia, high-grade dysplasia, cancer Stage I, cancer Stage II, cancer Stage III, and cancer Stage IV). Yearly, women could either remain in the same health state, progress to a more advanced disease state, or regress to a less severe disease state. Women could either die from causes other than cervical cancer or have hysterectomies for non-cancerous uterine conditions. Women were screened until age 65 and were followed-up until age 85 years or death.
Outcomes assessed in the review
The outcomes estimated from the literature were:

cancer prevalence,
the sensitivity and specificity of conventional cytology,
adherence,
the rates of disease progression, and
the utility values (used only in the sensitivity analysis).

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. Data on prevalence were derived from the National Breast and Cervical Cancer Early Detection Program and the Surveillance Epidemiology and End Results Program. Data on cytology accuracy came from large population-based studies and meta-analyses. Data on the utility weights were obtained from a sample of women diagnosed with cancer or who had a false-positive screening result.

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
Eight primary studies provided the clinical data used in the decision model.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
For women with invasive cancer found by their first programme Pap test, the distribution of prevalent cancer cases was 56% Stage I, 24% Stage II, 12% Stage III and 8% Stage IV.

For women with some history of normal cervical cytology, the distribution of prevalent cancer cases was 90% Stage I, 5% Stage II, 3% Stage III and 2% Stage IV.

The sensitivity of conventional cytology was 51% (range: 51 to 90) and the specificity was 97% (range: 85 to 97).
Forty per cent of cervical intraepithelial neoplasia (CIN) Grade 2 and 3 lesions, if untreated, would progress over 10 years to cancer.

Adherence to screening, follow-up, and treatment was 100% (range: 85 to 100).

The ranges for utility values were:

- 0.97 to 1 for false-positive cytology,
- 0 to 0.85 for cancer Stage 1,
- 0 to 1 for cancer Stage I survivors,
- 0 to 0.55 for cancer Stages II-IV, and
- 0 to 1 for cancer Stages II-IV survivors.

Utilities were applied for 5 years for those diagnosed with cancer, for a lifetime for cancer survivors who had lived longer than 5 years, and for 1 month for women with false-positive screening test results.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions that were used in the decision model.

**Estimates of effectiveness and key assumptions**
The sensitivity and specificity of colposcopy were both 100% (range: 75 to 100). Treatment of CIN was curative.

All CIN Grade 2 lesions would progress to invasion at the same rate as CIN Grade 3 lesions.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was expected survival. This was estimated using a modelling approach. An annual discount rate of 3% was applied. In a sensitivity analysis, quality-adjusted life-years (QALYs) were calculated on the basis of utility weights derived from the literature.

**Direct costs**
The analysis of the costs was carried out from the perspective of the health service payer. It included the direct costs associated with cytology (normal and abnormal Pap test) and cancer treatment, which was stage-dependent. The unit costs were not presented separately from the quantities of resources used and macro-categories of costs were reported. Resource use appears to have been based on authors’ assumptions and some published data. The costs were estimated from Medicare reimbursement rates and the Medstat MarketScan database. Discounting was relevant, as long-term costs were considered, and an annual rate of 3% was used. The costs were inflated to 2004 values using the medical care component of the Consumer Price Index.

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

**Indirect Costs**
The indirect costs were not considered.

**Currency**
Sensitivity analysis
Several sensitivity analyses were carried out to assess the robustness of cost-effectiveness ratios to variations in some clinical and economic inputs. The following alternative scenarios were considered:

- changes in the costs;
- the use of Medicare costs rather than the Medstat MarketScan database;
- CIN Grade 2 progressed like CIN Grade 1;
- the prevalence of disease was doubled;
- alternative accuracy of screening;
- changes in the adherence rate;
- the use of quality-adjustments to life expectancy (i.e. QALYs instead than life expectancy).

Alternative values were either based on the literature or set by the authors.

Estimated benefits used in the economic analysis
The discounted life expectancy decreased as the number of normal Pap tests increased. For example, in women aged less than 30 years with two prior normal Pap tests, life expectancy was 26.8618 with no further screening, 26.9079 with screening every 3 years, 26.9111 with screening every 2 years, and 26.9146 with screening every year. The same ranking was found for the other age groups and for different numbers of previous Pap tests.

Cost results
The total costs were not reported.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios (ICER; i.e. the incremental cost per life-year gained) were calculated to combine the costs and benefits of the alternative screening strategies.

In general, the ICER increased as the frequency of Pap tests increased and as age advanced. For example, in women aged less than 30 years and with no previous Pap test, the ICER was $5,648 for screening every 3 years versus no screening, $41,564 for screening every 2 years versus screening every 3 years, and $125,136 for screening every year versus every 2 years.

For women aged 45 to 59 the ICER was $76,780 for screening every 3 years versus no screening, $340,211 for screening every 2 years versus screening every 3 years, and $782,964 for screening every year versus every 2 years.

The ICER also increased as the number of previous normal Pap tests increased. For example, in women aged less than 30 years and with 3 or more previous Pap tests, the ICER was $20,265 for screening every 3 years versus no screening, $128,304 for screening every 2 years versus screening every 3 years, and $369,262 for screening every year versus every 2 years.

In synthesis, the most cost-effective strategies (ICER < $50,000) were those involving screening of younger women with no prior Pap tests or one prior Pap test at 3-year intervals.

Screening was never cost-effective in women older than 45 years of age.
The ICER associated with screening every year compared with screening every 2 years was always above $100,000.

The sensitivity analysis showed that the base-case ICERs were robust to variations in the clinical and economic assumptions. The ranking of the alternative strategies did not change. Quality-adjustments did not alter the conclusions of the analysis.

Authors' conclusions
The most cost-effective strategy to prevent cervical cancer was screening previously unscreened women younger than 30 years of age every 2 or 3 years and those aged 30 years and older every 3 years.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear and the interventions examined were consistent with the objective of the study. Each alternative was compared with the next most effective strategy. "No-screening" was also considered and a detailed sub-group analysis was performed. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence might have been derived from selectively identified studies as it was unclear whether a systematic review of the literature was performed to identify the primary studies. The characteristics of only a few primary studies were described. In general, population-based studies and national databases were used. The issue of comparability across the primary studies was not addressed. Details of the approach used to combine the clinical estimates were not reported. Some assumptions were also made on the basis of the authors' experience. Given the uncertainty surrounding some clinical estimates, an extensive sensitivity analysis was carried out.

Validity of estimate of measure of benefit
The choice of the summary benefit measure was appropriate, not only because life-years are a relevant dimension of health for patients with cancer, but also because they can be compared with the benefits of other health care interventions. The impact of the interventions on quality of life was investigated in the sensitivity analysis. Discounting was appropriately applied.

Validity of estimate of costs
The costs included were consistent with the perspective considered in the analysis. A detailed breakdown of the cost items was not given, and there was no information on the unit costs and quantities of resources used. The costs were presented as macro-categories, which limits the possibility of replicating the analysis in other settings. The cost estimates were specific to the study setting, but sensitivity analyses were performed to take their variability into account. The impact of using alternative sources of costs was investigated. No statistical analyses were carried out. The price year was reported, which enhances the possibility of performing reflation exercises in other time periods. Few details of resource consumption were provided.

Other issues
The authors stated that their findings were consistent with those published in two other studies. The issue of the generalisability of the study results to other settings was not explicitly stated, but sensitivity analyses were carried out on key model estimates, thus improving the external validity of the study. The analysis referred to the general population of women undergoing cervical cancer screening, and this was reflected in the authors' conclusions. The use of some assumptions was considered to be a potential limitation of the analysis. However, the authors pointed out that wide ranges of values were tested in the sensitivity analysis.

Implications of the study
The study results support a strategy of cervical cancer screening based on less-than-annual screening in younger women. The authors highlighted the need for cervical cancer-specific utilities in order to appropriately calculate QALYs.

**Source of funding**
Supported in part by the Institute for Health Policy Studies, University of California at San Francisco, the Centers for Disease Control and Prevention (contract number 282-98-0026), the Agency for Health Quality and Research (grant number HS07373) and the National Cancer Institute (grant number K08 CA 74973-02).

**Bibliographic details**

**PubMedID**
16449119

**DOI**
10.1097/01.AOG.0000196500.50044.ce

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Aged; Cost-Benefit Analysis; Female; Humans; Middle Aged; Quality-Adjusted Life Years; Time Factors; Vaginal Smears /economics /statistics & numerical data

**AccessionNumber**
22006006344

**Date bibliographic record published**
31/12/2006

**Date abstract record published**
31/12/2006