Costs and effectiveness of alternative strategies for cervical cancer screening in military beneficiaries

Maxwell G L, Carlson J W, Ochoa M, Krivak T, Rose G S, Myers E R

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
Several screening strategies for cervical cancer were examined:

- a conventional Papanicolaou (Pap) test every 3 years;
- liquid-based cytology (LBC) with reflex human papillomavirus (HPV) testing every 3 years;
- LBC every 3 years;
- a conventional Pap test every 2 years;
- LBC+HPV every 2 years;
- LBC every 2 years;
- a conventional Pap test every year;
- LBC+HPV every year; and
- LBC every year.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised unselected women aged 18 to 85 years, who were receiving military health care benefits.

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

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1996 and 2001. The price year was 2000.
Source of effectiveness data
The effectiveness data were derived from published studies and from the authors' assumptions.

Modelling
A published Markov model simulating the natural history of HPV infection and cervix carcinogenesis was used to assess the costs and outcomes of the screening options in a hypothetical cohort of 100,000 military health care beneficiaries. It was assumed that screening began at 18 years and the women were followed to an age of 85.

Outcomes assessed in the review
The outcomes assessed from the published studies and used as model inputs for pre-invasive disease were:
- the prevalence of HPV infection at 18 years;
- the prevalence of low-grade squamous intraepithelial lesions (SILs) at 18 years;
- the age-specific incidence of HPV infection;
- the age-specific regression rate of HPV;
- the progression rate from HPV to low-grade SIL;
- the proportion of infections progressively directed to high-grade SILs;
- the regression rate from low-grade SILs to HPV or well;
- the proportion of low-grade SILs reverting to well;
- the progression rate from low- to high-grade SILs;
- the regression rate from high- to low-grade SILs;
- the proportion of high-grade SILs reverting to well; and
- the progression rate from high-grade SILs to stage I cancer.

The outcomes assessed from the published studies and used as model inputs for invasive disease were the progression rates in unscreened patients with cancer and 5-year survival. Both depended on disease stage.

Study designs and other criteria for inclusion in the review
The authors stated that one primary study was a systematic review and another was a clinical trial. No details were provided for the remaining studies.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.
Number of primary studies included
The effectiveness evidence used in the decision model was derived from eight primary studies.

Methods of combining primary studies
The primary study outcomes were combined using narrative methods.

Investigation of differences between primary studies
Not stated.

Results of the review
For pre-invasive disease:

the prevalence of HPV infection at 18 years was 10%;

the prevalence of low-grade SIL at 18 years was 1%;

the age-specific incidence of HPV infection ranged from 0.17 at 19 years to 0.005 at 50 years and older;

the age-specific regression rate of HPV was 0.7/18 months for women aged 15 to 24 years, 0.5/18 months for those aged 25 to 29, and 0.15/18 months for those aged 30 and older;

the progression rate from HPV to low-grade SIL was 0.2/36 months;

the proportion of infections progressively directed to high-grade SILs was 0.1;

the regression rate from low-grade SILs to HPV or well was 0.65/72 months for women aged 15 to 34 years and 0.4/72 months for women older than 34 years;

the proportion of low-grade SILs reverting to well was 0.9;

the progression rate from low- to high-grade SILs was 0.1/72 months for women aged 15 to 34 years and 0.35/72 months for women older than 34 years;

the regression rate from high- to low-grade SILs was 0.35/72 months;

the proportion of high-grade SILs reverting to well was 0.5; and

the progression rate from high-grade SILs to stage I cancer was 0.4/120 months.

For invasive disease:

the progression rates in unscreened patients with cancer were 0.9/4 years for stage I-stage II, 0.9/3 years for stage II-stage III, and 0.9/2 years for stage III-stage IV;

5-year survival was 0.83 in stage I, 0.6566 in stage II, 0.3787 in stage III, and 0.1127 in stage IV.

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

Estimates of effectiveness and key assumptions
The most important assumptions in the analysis were:

- all treatments were 95% effective;
- there was perfect compliance with the follow-up of abnormal smears;
- all cervical cancer arose from HPV infections and progressed from low- to high-grade SILs to invasive cancer of different stages.

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

The benefit measure used in the economic analysis was the life-years saved. This was calculated using a Markov model. A 3% discount rate was applied to benefits occurring after the first year.

**Direct costs**

A 3% discount rate was used in the economic analysis since the lifetime costs were estimated. The unit costs were not reported separately from the quantities of resources. The health service costs included in the economic evaluation were for the screening tests and the treatment of cervical cancer (depending on disease stage). The cost of chemotherapy was estimated, but was assumed to be zero in the base-case analysis. The cost/resource boundary adopted in the study was that of the military health system. The costs and quantities were based on military estimates and were mainly derived from a published study. All of the costs were updated to 2000 (the price year) using the medical component of the consumer price index.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

The indirect costs were not included in the analysis.

**Currency**

US dollars ($).

**Sensitivity analysis**

Several sensitivity analyses were conducted to assess the impact of varying the sensitivity and specificity values of the screening tests on the estimated cost-effectiveness ratios. In addition, the costs of the tests and visits were varied and the potential cost of adjuvant chemotherapy was investigated. Univariate sensitivity analyses were conducted.

**Estimated benefits used in the economic analysis**

The life-years saved were:

- 27.6602 with no screening;
- 27.7033 with a conventional Pap test every 3 years;
- 27.7113 with LBC+HPV every 3 years;
- 27.7082 with LBC every 3 years;
- 27.7109 with a conventional Pap test every 2 years;
Cost results
The total mean costs were:

- $311.10 with no screening;
- $484.50 with a conventional Pap test every 3 years;
- $597.40 with LBC+HPV every 3 years;
- $601.30 with LBC every 3 years;
- $608.60 with a conventional Pap test every 2 years;
- $775.70 with LBC+HPV every 2 years;
- $792.50 with LBC every 2 years;
- $1,039.30 with a conventional Pap test every year;
- $1,398.50 with LBC+HPV every year; and
- $1,441.50 with LBC every year.

Synthesis of costs and benefits
An incremental analysis was conducted to combine the costs and survival of the screening strategies.

The incremental cost per life-year saved was:

- $4,017 with a conventional Pap test every 3 years over no screening;
- $14,263 with LBC+HPV every 3 years over a conventional Pap test every 3 years;
- $65,484 with LBC+HPV every 2 years over LBC+HPV every 3 years; and
- $231,270 with LBC+HPV every year over LBC+HPV every 2 years.

The remaining alternative screening options were dominated (less effective and more costly). These findings were relatively robust to variations performed in the sensitivity analyses. Only the costs and sensitivity of the tests had a relevant impact on the estimated cost-effectiveness ratios.

Authors' conclusions
Liquid-based cytology (LBC) with human papillomavirus (HPV) triage proved to be the most cost-effective screening option for cervical cancer over LBC alone and the conventional Papanicolau (Pap) test.
CRD COMMENTARY - Selection of comparators
The authors discussed the choice of the screening strategies that were compared in the analysis. Some strategies represented conventional options, while others had been recently introduced into the health care system. The option of no-screening was then used as the basic comparator. You should decide whether all the strategies are widely used in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on published studies, but a formal review of the literature was not undertaken. The primary studies were combined using narrative methods, but the authors did not state whether they took into account any differences between the studies when estimating effectiveness. Assumptions were also made in the analysis. The authors performed several sensitivity analyses to investigate uncertainty around the effectiveness estimates.

Validity of estimate of measure of benefit
Life-years were used as the benefit measure in the economic analysis. These were derived from a published decision model and were discounted appropriately. The use of life-years saved ensures the comparability with the outcomes of other screening strategies. The authors stated that quality of life adjustments were not taken into consideration, due to the lack of reliable data on the patients' preferences on the health states associated with cervical cancer prevention.

Validity of estimate of costs
The analysis of costs was performed from the perspective of the military health system. It appears that all the relevant categories of costs have been included in the analysis. Consequently, military estimates were used to estimate the costs. A complete breakdown of the costs was provided, but the unit costs were not reported separately from the quantities of resources. The price year was given, thus simplifying reflation exercises in other settings. The costs were treated deterministically in the base-case, but several sensitivity analyses were conducted to investigate the impact of variations in the baseline estimates. The costs were fairly specific to the study setting.

Other issues
The authors compared their findings with those from other studies. The issue of the generalisability of the study results to other settings was not addressed. However, several sensitivity analyses were conducted, thus improving the external validity of the analysis. The study referred to unselected women in the army and this was reflected in the conclusions of the analysis.

Implications of the study
The authors highlighted that LBC with HPV triage was the treatment of choice for the female military population. The study results also suggested that increasing the screening interval may be a feasible option to reduce the direct costs without compromising the effectiveness of the strategy. Finally, the implementation of the conversion from conventional Pap smear testing to LBC with HPV represents the first broad change in cervical cancer screening patterns in a large government organisation in the USA.

Source of funding
ERM has, in the past, received unrestricted grant funding from Digene Inc. for the evaluation of economic issues surrounding human papillomavirus testing.

Bibliographic details