The costs, clinical benefits, and cost-effectiveness of screening for cervical cancer in HIV-infected women

Goldie S J, Weinstein M C, Kuntz K M, Freedberg K A

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
Six screening strategies for cervical neoplasia and cancer in HIV-infected women were assessed. The main strategies considered were no screening, annual Papanicolaou smears, annual Papanicolaou smears after two initial smears obtained 6 months apart (the Centres for Disease Control (CDC) strategy), semi-annual Papanicolaou smears, annual colposcopy, and semiannual colposcopy.

Type of intervention
Screening.

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

Study population
HIV-infected women in 3 categories according to CD4 cell count at presentation: women with a CD4 cell count greater than 500 cells/mm^3, women with CD4 cell counts of between 200 to 500 cells/mm^3, and women with CD4 cell counts less than 200 cells/mm^3.

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

Dates to which data relate
Effectiveness data were obtained from the literature published between 1964 and 1998. Resource use data were not reported. The cost data were obtained from the literature published between 1990 and 1997. All costs were updated to 1996 prices.

Source of effectiveness data
The estimate for final outcomes was based on a synthesis of previously completed studies.

Modelling
A state-transition Markov model was used to estimate the costs and effects of alternative strategies for cervical cancer screening.

Outcomes assessed in the review
The following outcomes were assessed: The operating characteristics (sensitivity and specificity) of screening tests; the five year survival rate of early (local) invasive cancer; the five year survival rate of late (regional) invasive cancer; the
five year survival rate of late (distant) invasive cancer; the quality weights for the health states of CD4 cell counts greater or less than 200 cells/mm$^3$, women with HIV infection and regional or distant cervical cancer, women with HIV infection and local cancer.

Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
It was specified that priority was given to those studies with larger samples, well-defined control groups, and longer follow-up periods.

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

Number of primary studies included
A total of 33 studies were included in the review.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The baseline analysis took the sensitivity and specificity of Papanicolaou smears to be 70% and 90% respectively, and the sensitivity and specificity of colposcopy to be 95% and 91% respectively. The five year survival rate of early (local) invasive cancer was assumed to be 0.86; of late (regional) invasive cancer to be 0.43; and of late (distant) invasive cancer to be 0.11. The quality weights for the health states of CD4 cell counts greater or less than 200 cells/mm$^3$, women with HIV infection and regional or distant cervical cancer, women with HIV infection and local cancer were 0.94, 0.84, 0.56, and 0.65, respectively.

Measure of benefits used in the economic analysis
Life expectancy and quality-adjusted life years (QALYs) gained were the benefit measures used in the economic analysis. A Markov model was used to calculate the quality-adjusted life expectancy associated with the various screening strategies.

Direct costs
Costs were discounted. Health care costs were included in the analyses. The costs of cervical cancer screening, diagnosis and treatment protocols were estimated by applying Medicare average allowed charges to treatment algorithms outlined elsewhere in the literature. Costs of monthly HIV care were based on estimates from the AIDS Cost and Utilization Survey, which did not include the costs of current antiretroviral regimens. The perspective adopted in the cost analysis was that of society. The cost data were obtained from the literature published between 1990 and 1997.
The date to which the price data referred was 1996. The costs of highly active antiretroviral therapy was incorporated in the cost analysis in the sensitivity analysis.

**Indirect Costs**
Costs were discounted. The patient time costs covered the indirect costs of travel, waiting time, and time spent for direct care. The 1987 National Medical Expenditure Survey was used to estimate the travel and waiting times. The date to which the price data referred was 1996. Average wage rates used in the conversion of time to indirect costs were based on US mean annual earnings tables. The date to which the price data referred was 1996.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate and multivariate sensitivity analyses were conducted on almost all base-case estimates to determine the robustness of the results. Threshold analyses were also performed to identify the cut-off points with regard to the most sensitive parameters of the model.

**Estimated benefits used in the economic analysis**
For a woman with a CD4 cell count of 200 to 500 cells/mm$^3$ (the base case analysis), with no screening, quality-adjusted life expectancy (QALE) was 62.40 months; with annual Papanicolaou smear, QALE was 64.91 months; with the CDC strategy, QALE was 64.95 months; with semiannual Papanicolaou smear, QALE was 65.12 months; with annual colposcopy, QALE was 65.11 months; and with semiannual colposcopy, QALE was 65.19 months. For a woman with a CD4 count > 500 cells/mm$^3$ the respective figures were 102.92 months, 105.48 months, 106.09 months, 106.13 months, 106.32 months, 106.30 months and 106.39 months. For a woman with a CD4 cell count less than 200 cells/mm$^3$ the respective QALEs were 31.87 months, 32.70 months, 32.72 months, 32.79 months, 32.78 months and 32.82 months. The life expectancy ranged from 37.94 months to 114.59 months.

**Cost results**
In the base case analysis with no screening for a woman with a CD4 cell count of 200 to 500 cells/mm$^3$, discounted lifetime costs were $71,060; with annual Papanicolaou smear costs were $73,740; with the CDC strategy costs were $73,790; with semiannual Papanicolaou smear costs were $74,180; with annual colposcopy costs were $74,910; and with semiannual colposcopy costs were $76,350. For a woman with a CD4 count greater than 500 cells/mm$^3$ the respective figures were $70,210, $74,430, $73,080, $73,130, $73,780, $74,790 and $77,070. For a woman with a CD4 cell count less than 200 cells/mm$^3$ the figures were $75,410, $76,700, $76,750, $76,990, $77,360 and $78,160.

**Synthesis of costs and benefits**
Under the base case analysis the incremental cost per QALY for a woman with a CD4 cell count of 200 to 500 cells/mm$^3$ for the various strategies were: $12,800 for annual Papanicolaou smear, $14,800 for CDC strategy, $27,600 for semiannual Papanicolaou smear and $375,200 for semiannual colposcopy. Annual colposcopy screening was dominated. The corresponding values for a woman with a CD4 count greater than 500 cells/mm$^3$ were $10,400, $12,800, $15,800, $40,300, respectively. The respective values for a woman with a CD4 cell count less than 200 cells/mm$^3$ were $22,500, $28,700, $43,700, and $448,200. Annual colposcopy screening was dominated in all above cases. The incremental cost per life-years saved ranged from $9,300 to $484,600. Estimates of cost-effectiveness were most influenced by the prevalence of squamous intraepithelial lesions and their rate of progression to cancer.

**Authors' conclusions**
Over the broadest range of variable estimates, encompassing nearly all reported values in the literature, the screening of HIV-infected women for cervical cancer was associated with projected life expectancy benefits equal to or greater than
those provided by other preventive measures in general medicine or in HIV disease. On the basis of these results, (the authors) recommend that all HIV-infected women, regardless of their CD4 cell count, have two Papanicolaou screening smears obtained 6 months apart and then annual Papanicolaou smears thereafter.

CRD COMMENTARY - Selection of comparators
reason for the choice of the comparator is clear.

Validity of estimate of measure of benefit
limitations of the study should be taken into account when evaluating the internal validity of the estimates of benefit measures. The authors acknowledged that these limitations include the use of many small studies and uncertainty in health-related quality of life measures in HIV-infected women.

Validity of estimate of costs
ource quantities were not systematically reported separately from prices. However, adequate details of methods of cost estimation were given.

Other issues
authors' conclusions appear to be justified. The issue of generalisability to other settings or countries was addressed by performing a relatively comprehensive sensitivity analysis.

Implications of the study
The authors suggested that "a priority for future research will be to better understand the natural history of HPV in HIV-infected women and the long-term impact of highly active antiretroviral therapy on both new and established HPV-induced cervical neoplasia".

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