Cost-effectiveness of screening for anal squamous intraepithelial lesions and anal cancer in human immunodeficiency virus-negative homosexual and bisexual men

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
Screening, diagnosis and treatment of anal squamous intraepithelial lesions (ASIL) and anal cancer in HIV-negative homosexual and bisexual men.

Type of intervention
Screening and treatment.

Economic study type
Cost-utility analysis.

Study population
The study population consisted of homosexual or bisexual men who were HIV-negative.

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

Dates to which data relate
The model parameters came from studies published between 1982 and 1999. The costs were derived from studies and data sources published between 1988 to 1999. The prices were from 1997.

Source of effectiveness data
The effectiveness data came from a review of the literature.

Modelling
A Markov model was used to estimate the lifetime costs and clinical benefits of screening at intervals ranging from 6 months to 6 years.

Outcomes assessed in the review
Base case values and ranges for the model parameters were taken from the literature or estimated using data from the literature. The parameters were:

- baseline prevalence of atypical squamous cells of uncertain significance, low- and high-grade ASIL;
- annual progression rates from normal to low- and high-grade ASIL, low- to high-grade ASIL and high-grade ASIL to invasive cancer;
annual regression rates from low- and high-grade ASIL to normal;
five-year survival with invasive anal cancer;
health-related quality of life weights for anal cancer; and
sensitivity and specificity of anal cytology.

**Study designs and other criteria for inclusion in the review**
No explicit inclusion criteria were stated though most of the studies used appeared to be of homosexual men.

**Sources searched to identify primary studies**
No sources were explicitly mentioned in the review.

**Criteria used to ensure the validity of primary studies**
No criteria were mentioned in the review.

**Methods used to judge relevance and validity, and for extracting data**
No such methods were mentioned in the article.

**Number of primary studies included**
Fifteen (15) studies were used in the derivation of effectiveness parameters for the model. This included articles about two large prospective cohort studies.

**Methods of combining primary studies**
No such methods were described.

**Investigation of differences between primary studies**
The authors mentioned that there were differences between the two cohort studies but that data from both studies supported the same policy conclusions. The differences between the studies were not investigated.

**Results of the review**
The study reports the following model parameters (base case value followed by the range in parentheses):

- baseline prevalence of atypical squamous cells of uncertain significance and of low-grade ASIL, 6.9% (range: 3.5 - 10.3%); high-grade ASIL, 0.04% (range: 0.02 - 0.06%); and invasive anal cancer 0% (range: 0 - 0.0053%).
- annual progression rate of normal to low-grade ASIL, 1.90 per 100 (range: 0.96 - 3.86); normal to high-grade ASIL, 1.78 per 100 (range: 0.89 - 3.56); low-grade to high-grade ASIL, 16.50 per 100 (range: 1.78 - 26.4); and high-grade ASIL to cancer, 3.60 per 100 (range: 0.36 - 6.0).
- annual regression rate from low-grade ASIL to normal, 22.65 per 100 (range: 11.32 - 45.30); and from high-grade ASIL to normal, 11.36 per 100 (range: 5.68 - 22.72).
- five-year survival with invasive anal cancer was 56% (range: 28 - 84).
- quality of life weight for anal cancer was 0.60 (range: 0.17 - 0.79).
anal cytology had a sensitivity of 50% (range: 20% - 90%) and a specificity of 92% (range: 80% - 95%).

Measure of benefits used in the economic analysis
The main health benefit measure was the QALY. Gain in life expectancy was also used. The authors used age- and sex-adjusted health preference weights from the time-tradeoff estimates reported in the Beaver Dam Health Outcomes Study (1993) to value years of life by age ranges. A range of quality adjustment weights for anal cancer was based on quality-of-life scores reported for gastrointestinal cancer. No quality adjustment for the other health states (i.e., low- and high-grade ASIL) appear to have been used.

Direct costs
Health service costs for screening and each disease state were derived from the literature. The screening cost consisted of a brief office visit and anal cytology using a Papanicolaou smear. The low-grade ASIL cost consisted of an anoscopy and biopsies and annual follow-up. The high-grade ASIL cost consisted of a referral to a surgeon, a preoperative visit with anoscopy, two weeks of postoperative analgesia, a postoperative visit and 6 monthly follow-up. The invasive anal cancer cost included initial treatment, continuing care and terminal care based on published costs for colorectal cancer. It would appear that more details of this costing were given in previously published studies. Costs were discounted at 3% per year. Incremental costs were reported, with each screening strategy being compared with the next less costly strategy. All costs were updated to 1997 US dollars.

Statistical analysis of costs
Resource use and cost data were treated deterministically.

Indirect Costs
As this study took a societal perspective, patient time for travel, waiting and direct care were included as costs. Quantity estimates appear to have been derived from a 1991 study of a national survey in the USA. The unit cost was the average wage rate obtained from the US Bureau of Labor Statistics for 1997. A 3% discount rate was applied.

Currency
US dollars ($).

Sensitivity analysis
Several parameter values and assumptions in the model were subjected to sensitivity analysis. Parameter values were varied over a range; presumably the range mentioned above. One-way sensitivity analyses on the annual progression rate of high-grade ASIL to invasive cancer and on the effectiveness of treatment for high-grade ASIL were described. Results were said to be “minimally affected” by varying the incidence, progression and regression of ASIL; the sensitivity and specificity of the screening test; health-related quality of life; or the direct and indirect costs, although details were not provided.

Estimated benefits used in the economic analysis
A strategy of screening every 3 years generated a discounted incremental life expectancy of 1.61 months (5.46 months undiscounted) compared with no screening.

A strategy of biannual screening generated a discounted incremental life expectancy of 0.29 months (0.91 months undiscounted) compared with screening every 3 years.

A strategy of annual screening generated a discounted incremental life expectancy of 0.34 months (1.03 months undiscounted) compared with two-year screening.
Cost results
The total lifetime costs (discounted at 3% per annum) were:

- no screening, $4,130;
- 3-year screening, $5,178;
- 2-year screening, $5,583;
- and 1-year screening, $6,676.

Synthesis of costs and benefits
In the base case, screening every 3 years had an incremental cost-effectiveness (cost-utility) ratio of $7,000 per QALY compared with no screening.

- Screening every two years had an incremental cost of $15,100 per QALY compared with 3-yearly screening.
- Annual screening cost an incremental $34,800 per QALY compared with biannual screening.
- Six-monthly screening had an incremental cost-effectiveness of $143,500 per additional QALY over annual screening.

When most of the parameters were varied in sensitivity analyses, the incremental cost-effectiveness ratios for 3- and 2-year screening never exceeded $12,000 and $25,000 per QALY respectively.

Results were sensitive to the annual progression rate of high-grade ASIL to cancer where the cost-effectiveness ratio for 3-year screening approached $25,000 per QALY at a rate of 1%.

Also, the ratio of $25,000 per QALY was obtained when the effectiveness of treatment for high-grade ASIL was decreased to 20%. The justification for the selection of these lower bounds was not apparent.

Authors' conclusions
The authors concluded that a strategy of screening every 2 to 3 years appears to be as cost-effective as other preventative programmes and recommended investigating the development of such a policy for HIV-negative homosexual men.

CRD COMMENTARY - Selection of comparators
Although not stated explicitly, the comparator of no screening appears to be current practice. The choice of screening intervals ranging from 6 years to 6 months was reasonable given previous findings about cervical cytology and anal cytology for HIV-positive homosexual men.

Validity of estimate of effectiveness:
No details were given about the literature review carried out to derive the model parameters. Moreover, it was not clear how the findings of different studies were combined to yield base case values or ranges around them. Also, the justification for some assumptions (e.g., the effectiveness of treating high-grade ASIL) was unclear. The authors mentioned that the two prospective studies reviewed provided different data and suggested that both sets of data support the same policy conclusions. No details of this comparison were provided.

Validity of estimate of measure of benefit
The authors used health-related quality of life weights for gastrointestinal cancer to calculate the incremental QALY's gained by various screening strategies. The impact of using weights from a different cancer (and presumably a different patient group) was not discussed. No quality of life effects of the screening itself (e.g., the stress of being diagnosed
with possibly pre-cancerous lesions) were discussed.

**Validity of estimate of costs**
Readers are referred to another study (by the same authors) for details of the valuation of resource use for each health state. The authors did not cite any limitations pertaining to the cost analysis. You should consider the cost elements included in each disease state to decide whether the costs could apply to your own setting.

**Other issues**
The authors mentioned that the cohort studies reviewed for this model enrolled mainly white, highly educated men and that the findings may not be generalisable to other groups of men. Were a policy of regular screening to be adopted, it is likely that these same groups of men would be most inclined to present for screening. Thus, the results of this study may be a fair estimate of the cost-effectiveness of a screening programme in practice. A common limitation with studies of anal (and cervical) screening is uncertainty about the natural history of squamous intraepithelial lesions. The authors stated that their recommendations remained cost-effective over a wide range of parameters for incidence, progression and regression although it was unclear whether the sensitivity analyses were one-way or whether correlations between these parameters were considered.

**Implications of the study**
The authors suggested that screening every 2 to 3 years would be comparable in cost-effectiveness to other preventative health programmes and recommended that barriers to its development should be investigated.

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**Bibliographic details**

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Anus Neoplasms /diagnosis /economics /prevention & control; Bisexuality; Carcinoma, Squamous Cell /diagnosis /economics /prevention & control; Cost-Benefit Analysis; HIV Seronegativity; Health Care Costs; Homosexuality, Male; Humans; Life Expectancy; Male; Markov Chains; Mass Screening /economics; Middle Aged; Quality-Adjusted Life Years; United States

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