Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy

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 a screening and counselling programme for human immunodeficiency virus (HIV). Different screening intervals (i.e. one-time or recurrent screening every 5 years) were also evaluated. The testing strategy consisted of a serum enzyme-linked immunosorbent assay followed by confirmatory Western blotting.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The target population for the model was 43-year-old males or females whose HIV status was unknown.

Setting
The setting was the community and primary care. The economic study was carried out in Durham (NC), USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1988 and 2004. The resource use data were collected from two studies published in 1996 and 2004. The price year was 2004.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies, augmented by authors’ assumptions.

Modelling
A Markov model (Decision Maker software, version 2003.11.1) was used to compare the quality-adjusted life expectancy and costs of the three strategies. The cycle of the model was 1 month. A lifetime horizon was used.

The authors made several assumptions in their model:

- the benefits of testing and counselling accrued only if patients received their test results and entered care;
- the frequency with which case finding occurred was constant and high below a CD4 count of 50 cells/mm$^3$, linearly related to the CD4 count between 50 and 350 cells/mm$^3$, and not relevant with a CD4 count of more than 350 cells/mm$^3$ when patients were assumed to be asymptomatic;
- highly active antiretroviral therapy (HAART) was started when the CD4 count of an identified HIV-infected patient
was at or below 350 cells/mm³;

patients who had drug-related adverse effects switched to a new antiretroviral regimen;

if resistance developed to three successive antiretroviral regimens, only partial virologic suppression was possible; such patients continued to receive HAART and this partial suppression was sustained, reflecting the use of additional nonsuppressive regimens over time;

all patients received prophylaxis against opportunistic infections when appropriate.

**Outcomes assessed in the review**
The outcomes assessed were:

annual incidence;

the proportion of infected population who are men;

the proportion of infected men who have sex with men;

the CD4 count when infected with HIV;

the CD4 count at onset of symptoms;

adherence to the HIV-screening programme;

the sensitivity of the screening test;

the specificity of the entire sequence of screening tests;

the CD4 count triggering HAART;

the transition rate (events/100 patient-years) from HIV to acquired immune deficiency syndrome (AIDS) and from AIDS to death;

the probability of virologic suppression;

intolerance requiring discontinuation of first regimen;

the annual probability of infecting a sexual partner;

the reduction in the annual transmission rate; and

quality of life estimates.

**Study designs and other criteria for inclusion in the review**
The authors did not specify the study designs or any inclusion criteria. They reported that probability estimates were derived from high-quality published studies.

**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
Approximately 152 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
A selection of results is outlined in this abstract (the reader is referred to the original paper for more detailed results).

Annual incidence was 0.03.

The proportion of infected population who are men was 75%.

The proportion of infected men who have sex with men was 50%.

The CD4 count when infected with HIV was 900 cells/mm3.

The CD4 count at onset of symptoms was 350 cells/mm3.

Adherence to the HIV-screening programme was 100%.

The sensitivity of the screening test was 60% for the first 3 months after infection and 99.5% for established disease.

The specificity was 99.994%.

The CD4 count triggering HAART was 350 cells/mm3.

The transition rate (events/100 patient-year) from HIV to AIDS was 6, and from AIDS to death it was 3.

The probability of virologic suppression was 80% with the first regimen, 65% with the second regimen and 30% with the third regimen.

Intolerance requiring discontinuation of the first regimen was 25%.

The annual probability of infecting a sexual partner was 4% for men who have sex with men, 3% for heterosexual men and 1% for heterosexual women.

The lifetime transmissions reflected a 44% reduction in the annual transmission rate in the absence of screening, compared with the natural history of the disease, and a reduction in the annual transmission rate of approximately 21% with the use of a screening strategy, compared with the absence of screening.

Methods used to derive estimates of effectiveness
The authors made assumptions to derive estimates of effectiveness.
Estimates of effectiveness and key assumptions
The authors assumed a prevalence of unidentified HIV infection of 1%, a value consistent with the Centers for Disease Control and Prevention recommendation for screening.

The authors assumed that 80% of patients who screened positive for HIV would enter care and receive appropriate treatment.

On the basis of trials of counselling to prevent transmission of HIV by increasing condom use, the authors assumed a 20% reduction in transmission for patients with identified HIV infection.

Measure of benefits used in the economic analysis
The measures of benefits used were the number of life-days saved and the quality-adjusted life-years (QALYs) or quality-adjusted life-days gained from adopting each of the strategies examined. Quality of life estimates were derived from completed studies.

Direct costs
The costs considered were for testing and counselling, follow-up, and treatment for patients identified through screening or case finding. Costs for the care of HIV-infected patients receiving HAART were separated into drug-related and non-drug-related costs. The cost of multi-drug HAART was estimated from published wholesale costs of recommended drug regimens. The non-drug-related annual cost of treating patients varied on the basis of the CD4 count and clinical status. Discounting was appropriately carried out, owing to the long-term horizon of the study, at a rate of 3%. Estimations of the quantities and costs were derived using modelling and published studies. All the costs were adjusted to year 2004 US dollars. The authors reported the total discounted costs per patient.

Statistical analysis of costs
The costs were treated deterministically. No statistical tests were performed.

Indirect Costs
Indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Several one-way sensitivity analyses were performed on health parameters. The parameters were varied within clinically significant ranges. In addition, the impact of transmission from injection-drug users to their partners was evaluated.

Estimated benefits used in the economic analysis
Life expectancy was 21.063 years with no screening, 21.073 years with one-time screening and 21.076 years with recurrent screening.

Compared with no screening, 3.92 life-days were saved with one-time screening and 0.97 with recurrent screening.

The QALYs obtained were 18.626 with no screening, 18.634 with one-time screening and 18.636 with recurrent screening.

Compared with no screening, 2.92 QALYs were gained with one-time screening and 0.70 with recurrent screening.
Cost results
No screening had a cost of $51,517;

one-time screening cost $51,850 (incremental cost $333); and

recurrent screening cost $52,086 (incremental cost $236).

Synthesis of costs and benefits
Both screening strategies were compared with no screening.

The incremental cost-effectiveness ratios (ICERs) were expressed as $ per life-years saved (LYS) or QALYs gained.

For one-time screening, the ICER was $31,084/LYS compared with no screening. For recurrent screening, the ICER was $88,328/LYS compared with one-time screening.

For one-time screening, the ICER was $41,736/QALY gained compared with no screening. For recurrent screening, the ICER was $123,614/QALY gained compared with one-time screening.

When the costs and benefits to partners were incorporated, the ICERs were $12,919/LYS and $15,078/QALY gained for one-time screening compared with no screening, and $49,509/LYS and $57,138/QALY gained for recurrent screening compared with one-time screening.

When a 1-log decrease in viral load reduced transmission by a factor of 1.5, screening cost $24,800/QALY compared with no screening.

If counselling resulted in a reduction in risk behaviour of only 10%, screening cost $20,500/QALY.

If men who have sex with men had only 1 partner at risk and heterosexuals had only 0.5 partner at risk, screening cost $25,300/QALY compared with no screening.

If infectivity varied from a factor of 2 per 1-log decrease in viral load to no change, the cost-effectiveness ratio was $15,900/QALY. If the proportion of injection-drug users among HIV-infected patients varied from 25 to 35%, the cost-effectiveness ratio was $9,700/QALY. If the effectiveness of counselling in reducing high-risk injections varied from 25 to 50%, the cost-effectiveness ratio was $8,800/QALY.

If HAART was started at a lower CD4 count (e.g. 300 cells/mm3), screening cost $14,200/QALY.

Even if the identification of false positives took 3 years, the cost of screening would be less than $45,000/QALY gained at a prevalence of 0.1%.

Authors' conclusions
Screening for human immunodeficiency virus (HIV) infection is cost-effective relative to other commonly accepted screening programmes and medical treatments, even when the prevalence of HIV infection is substantially lower than 1% (a prevalence that the Centers for Disease Control and Prevention has used as general guidance for the initiation of routinely recommended as opposed to targeted screening). The authors suggested that in many health care settings, HIV screening will provide important health benefits for a reasonable investment in health care resources.

CRD COMMENTARY - Selection of comparators
The authors explicitly justified their choice of the comparators. No screening represents current practice in the authors’ setting. In addition, the 'no screening' strategy allows for the active value of screening to be evaluated. However, screening practices are widely implemented in developed countries and a more appropriate question should be which kind of HIV screening policy is implemented in USA: general population, high-risk individuals or/ and low-risk individuals.
Validity of estimate of measure of effectiveness
Published studies were used to obtain the input parameters. However, the authors did not state that a systematic review of the literature had been performed, nor did they report the review methodology. For example, the criteria used to ensure the validity of the primary studies and the methods used to extract the data were not stated. In addition, the impact of differences between the primary studies was not considered. The number of studies appears to have been adequate for assessing the parameters incorporated in the model. Where evidence of effectiveness was lacking, data were derived from assumptions, hence introducing the possibility of confounding bias. However, uncertainty around all outcomes was evaluated using a sensitivity analysis, which included reasonable ranges for all parameters analysed. Limitations in the reporting of the review made it difficult to ascertain whether the best available evidence had been used to populate the model.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The Markov model used for this purpose was appropriate since it enabled the estimation of long-term benefits obtained by the adoption of each of the strategies examined. It was unclear whether future benefits were discounted at the same discount rate as that used for the costs (3% per annum). QALYs were derived using utility values obtained from the literature. Those values represent a person’s preferences for a given state of health. The authors did not report that a sensitivity analysis was conducted on this parameter.

Validity of estimate of costs
The perspective of the analysis was not explicitly stated. Therefore, it is not possible to say whether all the categories of cost relevant to the perspective adopted were included. If a societal perspective had been considered, indirect costs should have been included in the analysis. The costs and the quantities were not reported separately, thus limiting the extrapolation of the results to other settings. The resources used were modelled using published studies and authors’ assumptions, but no sensitivity analysis was performed on this aspect. The unit costs were taken from published sources and, again, no sensitivity analysis was performed. This limits the interpretation of the results. The date to which the prices referred was reported, which increases the reproducibility of the results. Discounting was appropriately undertaken since the costs were incurred over a lifetime horizon.

Other issues
The authors did not compare their findings with those of other studies on HIV screening. The issue of generalisability to other settings was partially addressed in the sensitivity analysis. The authors’ conclusions reflected the scope of the study. The authors did not report any future limitations of their study.

Implications of the study
The authors suggested that their finding has potential public health implications in that screening for HIV infection is likely to be cost-effective in a much broader range of health care settings than has previously been recognised. They also highlighted the importance of the public health benefit afforded by the identification of HIV infection.

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Bibliographic details

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