Routine human immunodeficiency virus testing: an economic evaluation of current guidelines


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 for the human immunodeficiency virus (HIV) was examined. The screening of all inpatients in hospitals with an HIV prevalence of at least 1% was compared with strategies for screening all inpatients at hospitals with an HIV prevalence of 0.01, 0.1 or 10%. The baseline comparator was no HIV screening.

Type of intervention
Screening.

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

Study population
The study population comprised a hypothetical cohort of 100 million hospital inpatients over 18 years of age, with an unknown HIV status. Based on data from the Nationwide Inpatient Sample of hospitalised patients, the average age was 55.8 (+/- 11.9) years and 39% were male.

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

Dates to which data relate
The effectiveness evidence and resource use data were gathered from studies published between 1993 and 2004. The cost data were taken from published and electronic sources relating to 1996 to 2003, and were adjusted to 2001 prices.

Source of effectiveness data
The estimates for the final outcomes were derived from a synthesis of published studies.

Modelling
A decision analysis model was used to estimate the costs and benefits of each strategy. The time horizon for the model was the patient’s life course. The screening model incorporated a Markov process to simulate disease progression in HIV-positive patients. Four health states were used in the Markov process. These were acute HIV infection, chronic HIV infection, acute clinical events and death. The cycle length was unspecified.

The model made the following assumptions:

all HIV-infected patients enter the disease model, regardless of whether they have been diagnosed with HIV or not;
HIV infection may be detected by the screening programme or later when presenting with an opportunistic infection, or by HIV testing outside the hospital; patients who are detected after discharge through the latter two mechanisms have the opportunity to receive HIV-related care at a later time;

patients are only eligible for HIV-specific care in the model after they have been diagnosed as HIV positive;

patients who are HIV-infected, consent to testing and receive a positive test result, only receive care if they return for their test results and keep their HIV care appointment (linkage to care);

HIV-infected patients may die from non-HIV-related causes, opportunistic infections, or other chronic HIV related causes; and

acute cases would not be identified by enzyme immunoassay, and test results that are positive by enzyme immunoassay are confirmed with Western blot.

Further details were not provided, but the model has been described in full in other publications (Freedberg et al. 1998 and 2001, and Weinstein et al. 2001, see ‘Other Publications of Related Interest’ below for bibliographic details).

Outcomes assessed in the review
The following parameters were used in the model:

HIV prevalence;

CD4 count among those with acute infection;

CD4 count among those with chronic infection;

test offer/acceptance rate;

the rate of return/linkage to care;

antiretroviral starting criterion;

antiretroviral efficacy at viral suppression, 1st line;

antiretroviral efficacy at viral suppression, 2nd line;

antiretroviral efficacy at viral suppression, 3rd line;

antiretroviral efficacy at viral suppression, 4th line; and

the sensitivity and specificity of the enzyme immunoassay test.

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

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
The values for the parameters in the model were obtained from at least 22 published studies and reports.

Methods of combining primary studies
An explanation of how the study results were combined was not provided. For each model parameter, a base-case value and a range for use in the sensitivity analysis were presented. For some parameters only one source was cited.

Investigation of differences between primary studies
Not reported.

Results of the review
The following values were used in the model:
- HIV prevalence was 1% (range: 0.001 - 100);
- CD4 count among those with acute infection was 534 cells/mm3 (range: 400 - 600);
- CD4 count among those with chronic infection was 320 cells/mm3 (range: 50 - 500);
- the test offer/acceptance rate was 37% (range: 10 - 100);
- the rate of return/linkage to care was 88% (range: 10 - 100);
- the antiretroviral starting criterion was CD4 count of 200 cells/mm3 (range: no therapy - 350 cells/mm3);
- the antiretroviral efficacy at viral suppression, 1st line, was 70% at 48 weeks (range: 60 - 95);
- the antiretroviral efficacy at viral suppression, 2nd line, was 60% at 24 weeks (range: 50 - 80);
- the antiretroviral efficacy at viral suppression, 3rd line, was 34% at 12 weeks (range: 20 - 50);
- the antiretroviral efficacy at viral suppression, 4th line, was 22% at 12 weeks (range: 10 - 40);
- the sensitivity of the enzyme immunoassay test was 99.6% (range: 95 - 100) and the specificity was 97.5% (range: 95 - 100); and
- the specificity of Western blot was 100%.

Measure of benefits used in the economic analysis
The summary measures of health benefit used were the life expectancy and quality-adjusted life expectancy measured in quality-adjusted life-years (QALYs). These outcomes were obtained from the model. The authors did not report the method of valuation for the health states. Presumably this is detailed in the other publications (Freedberg et al. 1998 and 2001, Weinstein et al. 2001). The benefits were discounted at a rate of 3%, as recommended by the Panel on Cost-Effectiveness in Health and Medicine.

Direct costs
Only the direct costs to the health service were considered. These included initial testing costs (comprised of the HIV
test, counselling and linkage to care), antiretroviral therapy-associated costs per month (for 1st, 2nd, 3rd and 4th line
treatment), and additional tests (CD4 cell count, HIV RNA, and genotypic antiretroviral resistance testing). The costs
were obtained from six published and electronic sources. The model was used to calculate the costs over each individual
patient's life expectancy. The quantities and the cost parameters entered in the model were not reported separately.
Charges for treatment were converted to economic costs using a national cost-to-charge ratio for HIV/AIDS. Details of
this conversion were published elsewhere (AIDS Cost and Services Utilization Survey, 1994, Finkler 1982, see 'Other
Publications of Related Interest' below for bibliographic details). Discounting was appropriately performed at a rate of
3%, as recommended by the Panel on Cost-Effectiveness in Health and Medicine. The price data were either from 2001
or were adjusted to that year, although the method used was not reported. The direct costs estimated were the total costs
per thousand persons.

Statistical analysis of costs
No statistical analysis of the costs was reported.

Indirect Costs
Although the authors stated that the study was undertaken from a societal perspective, productivity losses do not appear
to have been included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was conducted to investigate variability in the data and to increase the generalisability of the
results. The methods used were not specifically described, although it appears that one-way sensitivity analyses have
been performed. A sensitivity analysis was undertaken on all the effectiveness parameters and cost parameters, with the
exception of the cost of specific tests. The ranges used for the sensitivity analyses appear to have been taken from the
reviewed studies.

Estimated benefits used in the economic analysis
For the base-case of 1% HIV prevalence, the discounted benefits gained were 17,004.83 QALY/1,000 persons for a no
screening strategy and 17,010.96 QALY/1,000 persons for a screening strategy. This resulted in an incremental benefit
of 6.13 QALY/1,000 persons screened.

At 0.01% HIV prevalence, the discounted benefits gained were 17,118.85 QALYs per 1,000 persons for a no screening
strategy, and 17,118.91 QALYs per 1,000 persons for a screening strategy.

At 0.1% HIV prevalence, the discounted benefits gained were 17,108.49 QALYs per 1,000 persons for a no screening
strategy and 17,109.10 QALYs per 1,000 persons for a screening strategy.

At 10% HIV prevalence, the discounted benefits gained were 15,968.26 QALYs per 1,000 persons for a no screening
strategy and 16,029.52 QALYs per 1,000 persons for a screening strategy.

The benefits were discounted at a rate of 3%. The duration of benefits was modelled over the lifetime of each
individual patient.

Cost results
For the base-case of 1% HIV prevalence, the discounted total costs were $1,031,400 per 1,000 persons for a no
screening strategy and $1,248,000 per 1,000 persons for a screening strategy. This resulted in an incremental cost of
$216,000 per 1,000 persons screened.
At 0.01% HIV prevalence, the discounted total costs were $10,300 per 1,000 persons for a no screening strategy and $32,100 per 1,000 persons for a screening strategy.

At 0.1% HIV prevalence, the discounted total costs were $103,100 per 1,000 persons for a no screening strategy and $142,700 per 1,000 persons for a screening strategy.

At 10% HIV prevalence, the discounted total costs were $10,313,900 per 1,000 persons for a no screening strategy and $12,301,600 per 1,000 persons for a screening strategy.

The costs were discounted at a rate of 3%. The duration of costs was modelled over the lifetime of each individual patient.

**Synthesis of costs and benefits**

The costs and benefits were combined by calculating cost-effectiveness ratios from the incremental cost per additional QALY gained by screening compared with no screening, at each HIV prevalence threshold.

For the base-case of 1% HIV prevalence, the discounted cost per QALY gained was $35,400.

At 0.01% HIV prevalence, the discounted cost per QALY gained was $356,000.

At 0.1% HIV prevalence, the discounted cost per QALY gained was $64,500.

At 10% HIV prevalence, the discounted cost per QALY gained was $32,400.

The sensitivity analysis showed that the outcomes were generally stable with cost-effectiveness ratios below $100,000 per QALY gained. Increasing the cost of testing (including counselling) from $53 to $103 per patient, at an undiagnosed HIV prevalence of 0.1%, resulted in a cost-effectiveness ratio of $94,900 per QALY gained. Higher cost-effectiveness ratios, and greater screening programme benefits, were observed when undetected HIV-infected patients had higher CD4 cell counts. The outcomes for the index of participation, lead- and length-time bias, the cost of antiretroviral therapy, and alternative CD4 counts for the initiation of antiretroviral treatment, were robust.

**Authors' conclusions**

Routine inpatient human immunodeficiency virus (HIV) screening programmes, at the recommended prevalence threshold of 1% undiagnosed HIV infection, are cost-effective. Screening programmes would be likely to remain cost-effective at the lower prevalence threshold of 0.1%. The authors implied that there was an acceptable cost-effectiveness threshold of $100,000.

**CRD COMMENTARY - Selection of comparators**

No explicit justification was provided for the comparator HIV prevalence thresholds of 0.01, 0.1 and 10%, but they would appear to be appropriate for HIV prevalence levels in the authors' setting. You should decide if the comparator thresholds are valid for the undiagnosed inpatient HIV prevalence in your own setting.

**Validity of estimate of measure of effectiveness**

A systematic review of the literature was not undertaken. Although this is common practice with models, it does not always ensure that the best data available are used in the model. The authors did not report the methods used to derive the estimates of effectiveness, nor did they consider the impact of differences between the studies when estimating effectiveness. Given the lack of detail on the methodology used, it was difficult to comment on the quality of the model inputs. A sensitivity analysis was conducted on many of the model input parameters for effectiveness. The ranges used appear to have been derived from the literature. These analyses improve both the internal validity and the generalisability of the study by demonstrating the robustness of the results to changes in the base-case estimates.
Validity of estimate of measure of benefit
The summary measure of benefit used in the analysis was the QALYs gained, which was modelled. This measure of benefit was appropriate for the type of intervention under analysis. By estimating the number of QALYs gained, the authors facilitated comparison with different screening programmes. The valuation tool used to measure QALY gains was not reported in this paper. The validity of the reported QALY gains relies on the methodology used to estimate the utility.

Validity of estimate of costs
The authors stated that the study was undertaken from a societal perspective, but productivity losses do not appear to have been included in the analysis, as is required for this perspective. In this case, the perspective would more appropriately be described as that of a hospital or a third-party payer. Categories of costs relevant to the latter perspective appear to have been included in the analysis. The quantities and the unit costs were not reported separately, thus limiting the reproducibility of the study in other settings. A sensitivity analysis was conducted on all of the model input parameters. The costs were treated deterministically, but sensitivity analyses were conducted to assess the robustness of the estimates used.

Discounting was applied, which was appropriate given the time horizon of the study. Both the costs and benefits were discounted at 3%, which was in line with recommendations of the Panel on Cost-Effectiveness in Health and Medicine. Costs, rather than charges, were reported. Charges for treatment were converted to economic costs using a national cost-to-charge ratio for HIV/AIDS. This practice is methodologically superior to reporting charges and enhances the generalisability of the study findings. The cost data were taken from electronic and published sources relating to 1996 to 2003 and were adjusted to a single price year (2001), which increases the generalisability of the results. However, the authors did not report the method used to do this.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, particularly with the cost-effectiveness of other screening programmes. They did not directly address the issue of the generalisability of the results to other settings, although they did explore the effect of disease prevalence. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported several limitations to their study. First, by not including the benefit of averting secondary infections, the study might have underestimated the benefits of the screening programme. This would extend to simplified needle-stick injury protocols for occupational health. Second, the study did not include the short-term impact of anxiety on quality of life while waiting for HIV test results. Third, implementation issues such as hospital readmission rates, HIV incidence among readmitted patients and the optimal frequency of repeat testing were not addressed. If the HIV screening programme leads to a decrease in disease incidence, as observed in screening programmes in other settings, the cost-effectiveness would increase. In addition, in reporting that the screening programmes were cost-effective at a prevalence of 1% and possibly 0.1%, the authors assumed the acceptability of a cost-effectiveness ratio of $100,000.

Implications of the study
The authors stated that current HIV counselling, testing and referral guidelines should be implemented nationwide to link patients to HIV care. The screening programmes should be frequently assessed for the number of new cases diagnosed, cost and cost-effectiveness, to confirm their continued value.

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Other publications of related interest


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