Optimal frequency of CD4 cell count and HIV RNA monitoring prior to initiation of antiretroviral therapy in HIV-infected patients

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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 use of CD4 lymphocyte counts and human immunodeficiency virus (HIV) RNA monitoring to predict the risk of opportunistic infection or death and disease progression in HIV. The optimal CD4 cell count and frequency of HIV RNA monitoring were compared in the study.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was a hypothetical cohort in the USA. The cohort had an initial median CD4 cell count of 546/mm3 and a median HIV RNA of 4.8 log10 copies/ml, the mean age was 33 years and 80% were male.

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

Dates to which data relate
The effectiveness data were taken from studies published in 1995 and 1997. All the costs were adjusted to 2001 US dollars using the medical care component of the Consumer Price Index.

Source of effectiveness data
The effectiveness data were obtained from a review of published studies.

Modelling
A computer-based simulation model of the natural history and treatment of HIV disease was developed to compare the costs, clinical benefits and cost-effectiveness of alternative frequencies of CD4 cell count and HIV RNA level monitoring strategies prior to the initiation of antiretroviral therapy.

Outcomes assessed in the review
The outcomes assessed were:

the initial probability distribution of demographic and HIV disease characteristics,
the distribution of CD4 cell count,
the distribution of initial HIV RNA, and
the mean monthly CD4 cell count decline by HIV RNA stratum.

In addition, the risk of acute events and death was determined within CD4 cell count groups of >500, 301 - 500, 201 - 300, 101 - 200, 51 - 100 and \( \leq 50 \) mm\(^3\).

**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**
Twenty-three primary 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**
Initial probabilities for demographic and HIV characteristics were reported in three published studies (Freedberg et al. 1998 and 2001, and Weinstein et al. 2001, see ‘Other Publications of Related Interest’ below for bibliographic details).

The distribution of CD4 cell count was:

- 47.6% for >500 cells/mm\(^3\),
- 23.7% for 301 - 500 cells/mm\(^3\),
- 5.9% for 201 - 300 cells/mm\(^3\),
- 3.1% for 101 - 200 cells/mm\(^3\),
- 0.3% for 51 - 100 cells/mm\(^3\), and
- 19.4% for \( \leq 50 \) cells/mm\(^3\).
The distribution of initial HIV RNA was:

- 36.2% for >100,000 copies/mL,
- 31.3% for 30,001 - 100,000 copies/mL,
- 20.7% for 10,001 - 30,000 copies/mL,
- 9.5% for 3,001 - 10,000 copies/mL,
- 2.2% for 501 - 3,000 copies/mL, and
- 0.1% for ≤500 copies/mL.

Methods used to derive estimates of effectiveness
Data on the natural history of HIV disease were derived from the Multicenter AIDS Cohort Study. CD4 cell count decline was derived using a random-effects model adjusted for age, gender and baseline CD4 cell count. The risk of acute events and death was derived using an incidence density analysis, with risk stratified by CD4 cell count and history of opportunistic infection.

Estimates of effectiveness and key assumptions
The mean monthly CD4 cell count decline (cells/mm3) was:

- 6.375 for >30,000 copies/mL,
- 5.4 for 10,001 - 30,000 copies/mL,
- 4.6 for 3,001 - 10,000 copies/mL,
- 3.733 for 501 - 3,000 copies/mL, and
- 3.025 for ≤500 copies/mL.

The key assumptions were that observed measurements from CD4 cell count and HIV RNA diagnostic tests reflect disease status. CD4 cell count and HIV RNA tests were not subject to test variance, and laboratories of equal quality evaluated the tests with equal consistency. All individuals who entered HIV care visited a health care provider at intervals defined by the frequency of CD4 cell count and HIV RNA diagnostic tests. The CD4 cell count and HIV RNA tests were administered concurrently.

Measure of benefits used in the economic analysis
The benefit measure used was the quality-adjusted life-years (QALYs). Health-related quality of life estimates were derived from the HIV Care and Services Utilisation Survey. Additional details on derivation were reported elsewhere (Freedberg et al. 1998 and 2001, Weinstein et al. 2001 and Schackman et al. 2002, see ‘Other Publications of Related Interest” below for bibliographic details).

Direct costs
It was not stated whether or not discounting was carried out. The CD4 cell count and HIV RNA test costs were obtained from the Clinical Diagnostic Laboratory component of the 2001 Medicare Fee Schedule. All other medical charges were taken from the Drug Topics Red Book 2001 and were adjusted to constant 2001 US dollars using the medical care component of the Consumer Price Index.
Statistical analysis of costs
No statistical analysis was undertaken.

Indirect Costs
The indirect costs were not used in the model.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses on baseline assumptions and parameter estimates were undertaken. The range of values used for the analysis was based on assumptions and comparisons with the John Hopkins HIV Clinic cohort.

Estimated benefits used in the economic analysis
Testing every 24 months resulted in 11.31 QALYs.
Testing every 18 months resulted in 11.44 QALYs.
Testing every 12 months resulted in 11.55 QALYs.
Testing every 6 months resulted in 11.62 QALYs.
Testing every 4 months resulted in 11.64 QALYs.
Testing every 3 months resulted in 11.64 QALYs.
Testing every 2 months resulted in 11.65 QALYs.

Cost results
The total average lifetime cost was:
$206,800 for testing every 24 months,
$211,700 for testing every 18 months,
$216,300 for testing every 12 months,
$220,700 for testing every 6 months,
$222,600 for testing every 4 months,
$223,900 for testing every 3 months, and
$225,800 for testing every 2 months.

Synthesis of costs and benefits
The costs and benefits were combined to give a cost per QALY.
The cost per QALY was:
$37,800 for testing every 18 months,
$43,600 for testing every 12 months,
$62,600 for testing every 6 months,
$86,700 for testing every 4 months, and
$303,300 for testing every 2 months.

The cost per QALY for testing every 3 months was dominated (greater cost and less clinical benefit than the 4-month strategy)

The sensitivity analysis showed that, when the patient population had a higher HIV RNA level at clinical presentation, there was faster disease progression, decreased QALYs and lower total average lifetime costs. Likewise, with a lower HIV RNA level, there was slower disease progression, increased QALYs and higher average costs. The rate of change in life expectancy, QALYs and cost was consistent, irrespective of the HIV RNA level upon clinical presentation. When the analysis was based on the John Hopkins HIV Clinic cohort, there were similar results.

Authors' conclusions
The monitoring frequency should depend on the CD4 cell count threshold at which treatment is planned. The use of adaptive testing frequencies or accelerated monitoring before a pre-specified treatment threshold results in similar or lower cost than constant testing frequencies.

CRD COMMENTARY - Selection of comparators
The rationale for the comparators was clear. US guidelines recommend testing every 2 - 6 months and the purpose of the study was to determine the optimal cell count and frequency of testing prior to the initiation of antiretroviral therapy.

Validity of estimate of measure of effectiveness
The effectiveness data were taken from published studies, in particular the Multicenter AIDS Cohort Study. The design of the model and inputs were not reported in full in the current paper, although the original paper was referenced. The authors carried out sensitivity analyses on several parameters to explore the impact of uncertainty in parameter values.

Validity of estimate of measure of benefit
The economic benefit was measured through QALYs, which were estimated using a decision model. The model considered the health states that the patients could enter and the probability of moving between states. The utility weights were taken from published literature.

Validity of estimate of costs
The authors presented results from the perspective of the health service. The source of the cost data was appropriately reported. The price year was also reported, which would assist any reflation exercises. Although the paper did not state whether the costs were discounted and at what rate, since the discount rate was varied in the sensitivity analysis it is safe to assume that the costs were discounted.

Other issues
The authors did not make any comparisons with other studies. However, in the sensitivity analysis, a cohort from an alternate study was used as the basis of the analysis. This did not affect the results. The authors acknowledged the limitations of the study, namely that assumptions were made about the variance of the CD4 cell count and HIV RNA
tests, and that the laboratories used to analyse the tests were of similar quality. The authors did not take different types of CD4 cell count and HIV RNA monitoring assays into consideration, or account for individual biological variability. Sensitivity analyses were conducted, which further increases the external validity of the analysis.

**Implications of the study**
The authors did not make any recommendations.

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**Bibliographic details**

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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