
Le Pen C, Rozenbaum W, Downs A, Lilliu H, Maurel F, Foucher F

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
Highly active antiretroviral therapy (HAART) was compared with non-HAART treatments in the treatment of human immunodeficiency virus (HIV) infection. HAART represents a new advance in HIV treatment.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The population comprised two samples of HIV-infected patients matched for age, gender and T4 cell counts. They were selected regardless of the severity of the disease.

Setting
The setting was a hospital. The economic study was carried out in France.

Dates to which data relate
The effectiveness data and the resource data related to two consecutive periods. There were between October 1994 to 1996 for the CONTROLE group and between October 1996 to 1998 for the CAS group. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient groups as those used in the effectiveness study.

Study sample
The authors did not report whether power calculations were used to determine the number of patients required to detect a statistically significant difference in the outcomes, either before the trial started or retrospectively after the data were collected. A total of 100 patients were retrospectively enrolled in the CAS group. These patients had to be treated with HAART or to start a HAART treatment between October 1996 and April 1997. Some patients may have received mono- or bi-therapy a few times after inclusion. Two patients were subsequently excluded from the initial sample because of poor data. Each patient was then matched for age, gender and T4 cell counts with a CONTROLE patient.
(n=98), for the period 1994 to 1995. Some patients may have received HAART around the end of the follow-up period. A total of 196 patients were retrospectively enrolled in the study. The two groups were comparable according to age (mean: 36.2 versus 35.9 years), gender (88.8% males) and T4 cell counts (mean: 291 versus 280 cells/mm³).

**Study design**
The study was a matched retrospective cohort study conducted in a single centre. The data were recorded retrospectively from the Rothschild Hospital. The duration of follow-up was 2 years after the first inclusion in each group. Two patients were excluded during the observation period.

**Analysis of effectiveness**
The basis of the analysis of the clinical study was intention to treat. The primary health outcome used in the analysis was the increase in the T4 cell count (immune recovery). This increase was observed through 3 criteria:

- the number of patients with an increase in T4 cell count of greater than 50 cells/mm³ (criterion 1);
- the number of patients with an initial T4 cell count below 350 cells/mm³ and final T4 cell count above 350 cells/mm³, the number of patients with an initial T4 count below 500 cells/mm³ and a final T4 count above 500 cells/mm³, or the number of patients with an initial T4 count above 500 cells/mm³ and an increase in T4 count of at least 100 cells/mm³ during the study period (criterion 2); and
- the number of days with a T4 cell count above 500 cells/mm³ (criterion 3).

The mean duration of follow-up was 504 days in the CAS group versus 385 days in the CONTROLE group. At inclusion, 4.1% of the patients in CAS group received mono-therapy versus 41% in the CONTROLE group. During the follow-up, 67% of the patients in CAS group received tri-therapy versus 14.1% in the CONTROLE group.

**Effectiveness results**
There were no significant differences in the incidence of death.

The proportion of patients with a T4 cell count of above 500 cells/mm³ increased in the CAS group (14 to 32%) and decreased in the CONTROLE group (14 to 8%), (p=0.0027).

Conversely, the proportion of patients with a T4 count below 200 cells/mm³ decreased in the CAS group (42 to 23%) and increased in the CONTROLE group (43 to 50%), (p<0.0001).

The mean T4 cell count after 2 years was higher among patients in the CAS group (344 cells/mm³) than those in the CONTROLE group (234 cells/mm³), (p<0.0001).

Fifty patients in the CAS group had an increase in T4 count of greater than 50 cells/mm³, versus 13 in the CONTROLE group (criterion 1).

Twenty-seven patients in the CAS group were ameliorated according to criterion 2, versus 5 in the CONTROLE group.

The number of days with a T4 cell count above 500 cells/mm³ were 9,986 in the CAS group and 4,053 in the CONTROLE group (criterion 3).

**Clinical conclusions**
The immune recovery at the end of the follow-up was better in the CAS group than in the CONTROLE group.

**Modelling**
A statistical model was used to compare the life expectancy between the two groups (log-rank) and to study the
statistical differences in benefits and costs between the two groups (matched Student t-test).

**Measure of benefits used in the economic analysis**
The authors did not develop a summary benefit measure. The primary health outcomes (reported earlier: criteria 1, 2 and 3) were expressed as benefits.

**Direct costs**
The costs and the quantities were not reported separately. The perspective of a health care payer was adopted in the cost analysis. No discount rate was applied, although the costs were incurred over a total of 4 years. The cost analysis covered the costs of hospitalisation (full-time and ambulatory), physician consultations and drugs. HIV treatment costs were calculated on the basis of daily treatment costs, which were derived from Mission SIDA. Other treatment costs (mainly for opportunistic infections) were based on average wholesale prices or data from the Rothschild Hospital. The cost of hospitalisation was derived from the Rothschild Hospital. The cost of physician consultation was estimated from the Health Care reimbursement system. The price data referred to 1998.

**Statistical analysis of costs**
The cost data were reported as the mean (plus or minus the standard deviation) per patient-year. Statistical analyses were performed on the costs using the matched Student t-test.

**Indirect Costs**
No indirect costs were reported.

**Currency**
French francs (Ffr).

**Sensitivity analysis**
A sensitivity analysis was not carried out.

**Estimated benefits used in the economic analysis**
The primary health outcomes were expressed as benefits. See the 'Effectiveness Results' section.

**Cost results**
The antiretroviral treatment costs were higher in the CAS group than in the CONTROLE group. The mean cost per patient-year was Ffr 35,695 (CAS) versus Ffr 13,156 (CONTROLE), p<0.0001).

Conversely, other treatment costs and hospitalisation costs were lower in the CAS group than in the CONTROLE group. The treatment costs were Ffr 16,490 (CAS) versus Ffr 43,092 (CONTROLE), (p=0.0560), while the hospitalisation costs were Ffr 32,136 (CAS) versus 42,790 (CONTROLE), (p=0.2960).

There was no significant difference in the mean medical total costs.

The authors reported the global medical costs and incremental costs. The incremental savings using HAART were Ffr 275,758 compared with other treatment regimens.

**Synthesis of costs and benefits**
The authors did not produce a summary measure that combined the costs and effectiveness, as it is likely that they...
concluded that the HAART regimen was both more effective and generated lower costs.

Authors’ conclusions
In a large human immunodeficiency virus (HIV)-infected population, the use of highly active antiretroviral therapy (HAART) may confer clinical benefits after 2 years. It may also lead to a drop in global direct costs due to hospitalisation and opportunistic infection items, although the acquisition cost of HAART is high.

CRD COMMENTARY - Selection of comparators
The comparators used were justified on the grounds that they were treatment regimens before HAART. The authors argued that the size of the study sample would have to be considerable to compare HAART with only one treatment regimen, due to the wide practice in term of HIV treatment. The choice of two consecutive periods, before and after HAART introduction, allowed the impact value of the HAART treatment to be evaluated.

Validity of estimate of measure of effectiveness
The analysis used a matched retrospective cohort study, which was appropriate for the study question, although it may be associated with bias and confounding due to the non-randomised and non-concurrent study design. However, the study sample was representative of the study population and the patient groups were shown, generally, to be comparable at analysis. The exception was the mean duration of the observation, which was 504 days in the CAS group and 385 days in the CONTROLE group. This difference may influence the final outcomes. Confounding factors, such as the length of treatment period or the existence of co-morbidities, were not taken into account.

Validity of estimate of measure of benefit
The estimate of benefits was obtained directly from the effectiveness analysis (patients with immune recovery). This choice of estimate was justified. Life expectancy would not show any significant difference because the follow-up period was less than 2 years.

Validity of estimate of costs
The authors reported that the costs were estimated from perspective of the health care payer, but the costs of home hospitalisation or stays in palliative service centres were not included. These omissions may influence the total cost of each alternative. The resource quantities were not reported separately from the prices. Statistical analyses were conducted on the mean costs per patient-year. A sensitivity analysis of the prices was not conducted. Discounting was not undertaken, even though the costs were incurred over a 4-year period. These features of the cost analysis weaken the generalisability of the results to other settings.

Other issues
The authors compared their findings with those of one American study (Bozette - see Other Publications of Related Interest). Other comparisons were likely to have been made, but were not reported. The issue of generalisability to other settings was not clearly addressed. The study enrolled patients with HIV infection, regardless of the level of severity of the disease, and this was reflected in the authors’ conclusions. The authors reported a number of further limitations to their study. These were principally the unmeasured cost variables and the short follow-up period.

Implications of the study
The findings of this study suggest that, for HIV-infected patients, HAART is associated with clinical benefits and is cost-saving after 2 years of follow-up.

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None stated.
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Other publications of related interest


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