Early antiretroviral therapy for patients with acute AIDS-related opportunistic infections: a cost-effectiveness analysis of ACTG A5164

Sax PE, Sloan CE, Schackman BR, Grant PM, Rong J, Zolopa AR, Powderly W, Losina E, Freedberg KA, Cost-Effectiveness of Preventing AIDS Complications US and AIDS Clinical Trials Group A5164 Investigators

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.

CRD summary
This study examined the cost-effectiveness of early versus late antiretroviral therapy (ART) for patients with human immunodeficiency virus (HIV) and acute opportunistic infections. The authors concluded that early initiation of ART was effective and cost-effective for these patients. The study was based on a valid cost-effectiveness framework, but the validity of the authors’ conclusions depended on some critical model parameters.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of early versus late antiretroviral therapy (ART) for patients with human immunodeficiency virus (HIV) and opportunistic infections.

Interventions
The two interventions were to initiate ART immediately after treatment of opportunistic infections (early) versus to initiate ART one month after treatment of opportunistic infections (late). No ART was considered as the background comparator.

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a published model of HIV infection, which consisted of a state-transition first-order Monte Carlo simulation. A short-term and a lifetime horizon were considered. The authors stated that a modified societal perspective was adopted.

Effectiveness data:
The clinical data came from a selection of relevant studies. Most of the evidence was from the 262 patients in the US arms of the published AIDS Clinical Trials Group (ACTG) A5164 trial, which provided data on the baseline characteristics of patients, the rates of opportunistic infection at presentation to care, and the efficacy of first-line treatment. Additional data to extend the short-term evidence to the long-term and to estimate the natural progression of disease were from other sources, including the Multicenter AIDS Cohort Study. Early versus late ART efficacy was the key clinical input for the analysis.

Monetary benefit and utility valuations:
The utility values were from a published study.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3%.

Cost data:
The economic analysis included in-patient and out-patient costs, emergency department visits, and ART regimens.
(including personnel time). The resource use data were from a cohort of patients enrolled at HIV Research Network sites (59,093 patient-months). It was assumed that the resources required for early ART were at least 5% of the annual work of a physician, a registered nurse, and a case manager. The costs were from the medical literature, the University Health System Consortium, average wholesale prices, and average annual salaries from the Bureau of Labor Statistics. All costs were in US dollars ($) and a 3% annual discount rate was applied. The price year was 2008.

Analysis of uncertainty:
Several one-way sensitivity analyses were carried out on the per-patient intervention cost, the cluster of differentiation 4 (CD4) cell count and opportunistic infection distribution at presentation to care, the rates of successful referral to and retention in out-patient care, the delay from presentation to ART initiation for patients on late ART, the efficacy of first-line ART, the incidence of immune reconstitution inflammatory syndrome (IRIS), and the assumption of no IRIS-related deaths in patients on early ART.

Results
The projected lifetime costs were $80,700 with no ART, $385,220 with late ART, and $397,500 with early ART. The QALYs were 1.69 with no ART, 10.07 with late ART, and 10.39 with early ART. The incremental cost per QALY gained was $36,300 with late ART over no ART and $38,600 with early ART over late ART.

The sensitivity analysis showed that early ART remained cost-effective at a threshold of $50,000 per QALY as long as at least four patients presented to care each year. An influential input was the rate of virologic efficacy of first-line ART for patients initiating early ART: if this decreased from 70% (base case) to 58%, early ART was dominated by late ART, as late ART was more effective and less expensive.

Authors' conclusions
The authors concluded that early initiation of ART was effective and cost-effective for patients with acute opportunistic infections.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear; the authors pointed out that the best time to initiate ART therapy had not been defined.

Effectiveness/benefits:
The selective approach used to identify the relevant sources of evidence was justified as the authors used the evidence from a recent trial investigating the efficacy of early versus late ART. More details of the methods of this trial would have been useful, but the rigour and strengths of the design of clinical trials should ensure the validity of these clinical inputs. Additional data were from other sources, which were not described, but the used of a large cohort to extrapolate the data from the short to the long-term was appropriate. No information on the derivation of the utility values was provided and the impact of variations in these inputs was not considered in the sensitivity analysis. QALYs were a valid benefit measure because the disease has a substantial impact on both survival and quality of life.

Costs:
The economic analysis appears to have included only the direct medical costs. A list of cost items was presented and the unit costs were reported for some items, while others were presented as category totals. Most of the costs were from conventional US sources. An important assumption was the resource use for personnel time for early ART and this was varied in the sensitivity analysis. Other details of the analysis, such as the price year and discounting, were clearly reported. Variations in the key cost estimates were assessed in the sensitivity analyses.

Analysis and results:
The study results were clearly presented. The projected costs and benefits were synthesised, using an appropriate incremental approach, which allowed the identification of the best strategy. The sensitivity analyses investigated the cost-effectiveness of the two strategies in several scenarios that might reflect alternative settings. The authors stated that patients with tuberculosis were excluded and these results cannot be applied to those patients. In general, the model results were dependent on the ART efficacy and high uncertainty was found in this parameter.
Concluding remarks:
The study was based on a valid cost-effectiveness framework, but the stability of the authors’ conclusions depended on some critical model parameters.

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