The cost-effectiveness of HLA-B*5701 genetic screening to guide initial antiretroviral therapy for HIV


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 evaluated the clinical and economic impact of human leukocyte antigen B*5701 screening for the selection of first-line antiretroviral therapy for human immunodeficiency virus in the USA. The authors concluded that testing was cost-effective only if the abacavir regime was as effective and cost less than the tenofovir regime. Apart from some description of the model and parameters, the methodology seems to have been appropriate and was clearly and transparently reported. The authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to study the clinical impact and cost-effectiveness of human leukocyte antigen (HLA)-B*5701 screening to guide the selection of the first line antiretroviral therapy for human immunodeficiency virus (HIV) in the USA.

Interventions
A 2008 US guideline recommended testing for HLA-B*5701 before starting abacavir-based regimes of combination antiretroviral therapy, to reduce the likelihood of severe hypersensitive reactions. Abacavir, lamivudine, and efavirenz were recommended for those who tested negative and tenofovir, emtricitabine, and efavirenz for those who tested positive.

This universal testing strategy was compared with no testing and using the abacavir combination or the tenofovir combination. For patients in the tenofovir regime, who developed nephrotoxicity, three alternatives were considered: testing for HLA-B*5701, switching all to the abacavir regime, or switching all to a zidovudine regime (zidovudine, lamivudine, and efavirenz).

Location/setting
USA/ambulatory and hospital care.

Methods
Analytical approach:
A state transition model, which simulated a cohort of patients starting HIV treatment (the Cost-Effectiveness of Preventing AIDS Complications, CEPAC, model), with a lifetime horizon, was used to synthesise the data. The perspective was not explicitly stated.

Effectiveness data:
The effectiveness data came from selected published studies. The methods used to find the studies, data sources, and criteria for selecting particular studies were not stated. The drug efficacy and regime toxicity data were mainly derived from clinical trials.

Monetary benefit and utility valuations:
Quality of life weights were derived from the literature, but no other details were given.
Measure of benefit:
The measure of benefit was the quality-adjusted life-year (QALY). Discounting for long-term effects was applied at an annual rate of 3%.

Cost data:
The cost categories were those for HLA-B allele testing, different antiretroviral therapies, and toxicity costs (hypersensitivity for abacavir and nephrotoxicity for tenofovir). Medicare and Medicaid were the main sources and 2006 US dollar ($) prices were used. Discounting for the long-term costs was performed at an annual rate of 3%.

Analysis of uncertainty:
A scenario with an ethnic mix more similar to that in the USA (with different HLA-B allele prevalences and hypersensitivity incidences) was considered. Another scenario was considered, which evaluated a population restricted to HIV patients with more than 100,000 ribonucleic acid copies per mL. One-way and two-way sensitivity analyses were conducted, including varying the drug regime efficacies, which were assumed to be equal in the base case.

Results
The discounted quality-adjusted life-months (QALMs) were 194.75 for the abacavir regime without testing, 194.71 for the tenofovir regime without testing and zidovudine if nephrotoxicity occurred, and 194.79 for each of the following strategies: universal HLA-B*5701 testing; tenofovir regime without testing and HLA-B*5701 testing if nephrotoxicity occurred; and tenofovir regime without testing and abacavir if nephrotoxicity occurred.

The discounted lifetime costs were $472,210 for abacavir, $472,290 for tenofovir then zidovudine, $472,320 for universal testing, and $472,550 for both tenofovir then testing, and tenofovir then abacavir.

The incremental cost-effectiveness ratio of universal testing compared with no testing and initiating all patients on abacavir-based therapy, was $36,700 per QALY. All the other strategies were dominated, which means that they had higher costs and equal or lower effectiveness.

Universal testing remained cost-effective only if the abacavir regime had equal efficacy and lower costs than the tenofovir regime. Other sensitive parameters were the cost of HLA-B*5701 testing and its prevalence.

Authors' conclusions
The authors concluded that testing for HLA-B*5701 was cost-effective only if the abacavir-based regime was as effective and cost less than the tenofovir-based regime.

CRD commentary
Interventions:
The relevant interventions appear to have been included and were described in adequate detail.

Effectiveness/benefits:
The authors used a well-known HIV model, which was not described in detail in this paper. The methods used to search for the data, the data sources and the criteria used to selecting particular studies were not reported. Additional information was available in an online appendix.

Costs:
Although the perspective was not stated, the authors included the “direct medical costs”. They provided an adequate description of the cost categories and their values. The price year and cost adjustment methods were reported.

Analysis and results:
The primary results and the sensitivity analyses were adequately reported. The parameter uncertainty was assessed through sensitivity analyses, but no probabilistic sensitivity analysis was reported. Issues of generalisation to non-US settings were discussed. The authors acknowledged some limitations, such as the exclusion of: newer and future regimes and sequences; potential cardiovascular toxicity of abacavir; and other tests to predict abacavir hypersensitivity. Most importantly, they assumed equal efficacy for the abacavir and tenofovir regimes, which was not proven.
Concluding remarks:
Apart from the description of some aspects of the model and parameters, the methodology seems to have been appropriate and was clearly and transparently reported. The conclusions reached by the authors appear to be appropriate.

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