

Clinical issues

in HIV/AIDS

This series of bulletins focuses on advances in therapy for HIV/AIDS, particularly developments in triple therapy employing protease inhibitors.

This bulletin looks at the cost of healthcare for those living with HIV – a cost that is constantly rising. Patients now live longer but need

continuing therapy to maintain their health.

There is also a website review which highly recommends the US-based HIV/AIDS Treatment Information Service site (HIVATIS) and its sister site the AIDS Clinical Trials Information Service (ACTIS).

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Commentary

A quick straw poll of our colleagues recently confirmed that none of us were given any formal help in dealing with the finances of healthcare provision during our medical training. This knowledge is becoming increasingly important, and is one of the skills a modern doctor should possess. Even so, we have not been able to determine whether this crucial skill is now being taught as part of the standard curriculum to our undergraduates, or even to junior colleagues. The cost of drugs is a factor in healthcare finance, but it is not the only consideration.

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Commentary continued

The following article by Mike Youle gives us some insight into this complex and important field. Its core message is that cost–utility (a measure that includes quality of life) is more important than univariate values – such as drug cost or doctor time – alone. If you weren't acquainted with, or assured of, the importance of a quality-adjusted life-year (QALY) before, then you certainly will be after reading his piece.

Cost–utility is not part of the doctor–patient conversation but is creeping into the discussions we have with our drug representative colleagues. We often feel certain about the absolute price of a drug, and it is a factor used in clinical decision-making. This approach may, however, be too simplistic.

Doctors often feel that a direct comparison of one antiretroviral or antibiotic drug with another can be made based on cost alone. But how reliable is this method of decision-making? All drugs seem to have a bewildering variety of prices depending on the supplier, the volume bought, the presentation and whether there is a 'special deal'.

The manufacturer must, of course, be assured of a reasonable return over the lifetime of a drug, if only to cover the enormous costs of research and development. While these can be built into initial costings, variables such as advertising rates and the effects of political decisions are always liable to change. The impression is that drug costs seem to fluctuate a great deal.

Even a fixed price, however, may not be all that it appears to be. Take indinavir, for example, the price of which is pegged to the Euro. Because of the significant devaluation of the Euro against the pound over the past months, this drug has effectively decreased in price.

What is more significant than the actual price, however, is affordability, and this varies from society to society. It is this, and the 'willingness to pay', often influenced by governmental and political determination to make the benefits of modern healthcare available to all, that determines whether drugs and medical treatments are denied, available, used or abused.

It is also necessary to consider a drug's side-effect profile; adverse events might result in increased hospitalisation costs, for example.

While not based solely on price, the decisions of bodies such as the National Institute for

Clinical Evidence (NICE) can have far-reaching effects. A drug or treatment that offers a poor cost–utility will not be approved. But how many times have drugs found a new use after they have been superseded in their primary indication?

In the USA health economics are considered to be so important that there is a regulatory requirement to build economic assessment into large, phase-three clinical trials.

Health economics are likely to become increasingly important as we struggle to address inadequacies in provision and to use present resources in the most effective ways. But when there are choices, such as a decision to prescribe a more expensive drug with fewer doses or an agreement about how many patients a doctor should see each hour, then the data need to be analysed carefully before a decision is made. Doctors must work actively to involve their patients in this process.

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Pharmacoeconomics of HIV

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The cost of healthcare for those infected with HIV is constantly rising. That is not to say that providing such care is not cost-effective, or that the cost is excessive compared with that for a similar quality of care for other chronic diseases. Rather, as the use of highly active antiretroviral therapy (HAART) has increased, morbidity and mortality have plummeted, resulting in patients who not only live longer and are fitter but are in need of constant therapy to maintain their health. As the adage says, 'the cheapest patient is either cured or dies'. So we have the worst of all worlds in financial terms – a rising number of patients are presenting for chronic treatment that does not cure the infection but averts or delays death, thereby potentially increasing individual lifetime costs. The use of intermittent therapy is not yet an accepted treatment modality – thus, currently, once treatment is started it is 'for life'. This may change of course.

These facts should not unduly dismay the health economist, since it is cost-effectiveness or cost-utility (which includes quality of life measures) that matters.

Economic analyses

Cost-effectiveness analysis is useful when there is one main natural dimension along which to measure changes in health outcome, such as 'years-of-life saved'. An 'intermediate' outcome measure, such as CD4 count, may be used but it may be a poor surrogate of final outcomes.

Cost-utility analyses are more sophisticated and have been designed to address the shortcomings found with cost-effectiveness analyses. They combine evidence on mortality with evidence on morbidity, and express health outcomes in terms of a single utility (preference) score such as quality-adjusted life-years (QALYs). Hence, cost-utilities incorporate the notion of health-related quality of life (QoL) and permit cost-effectiveness comparisons across different clinical settings.

The ability to obtain the best value per unit cost and to combine assessment of clinical improvement and QoL with financial considerations underpins the practice of

health-outcomes research. However, finance-driven decision-making within health services is the norm, and rising expenditure must be managed. Information must be current and accurate, and it is clear that many services lack the infrastructure and support to determine their costs adequately and thereby maximise the benefits of well-planned interventions.

HIV service costs

There is a continued paucity of real data-driven health-outcomes research in HIV.¹ Modelling of data is the first approach used to assess the potential impact of new treatments and diagnostic methods; it is a technique that can give insights into real-world scenarios.² One problem remains – the lack of up-to-date costs for hospital services. There are often discrepancies between the costs used by the service and the true costs when independently assessed. In one study of paediatric HIV services at a major UK centre, significant differences were seen between hospital estimates of price and the costs derived from specific costing exercises.³ These ranged from £364 per patient-year for HIV-negative children to £7,330 for children with AIDS. Another issue is the spectrum of cost across different healthcare settings, where limits on expenditure may be finite, as in managed healthcare compared with fee-for-service care. In the USA, Medicaid – the government-funded health programme – has shifted from the former (which favours individual choice without cost control) to the latter over the past few years in an attempt to control spiralling expenditure, which reached \$3.8 billion in 1998.⁴

Since the advent of HAART, several clinical trials and cohort studies have shown parallel benefits of this treatment approach in terms of cost as well as clinical outcomes.⁵⁻⁷ In the Swiss Cohort Study of 3,856 individuals, in an analysis limited to healthcare costs, the cost-effectiveness ratio ranged from 14,000 to 45,000 Swiss Francs (£5,380–17,300 approx) between an optimistic and a pessimistic estimate of natural disease history.⁶ When estimates of changes in productivity were included, the pessimistic

cost-effectiveness ratio improved to 11,000 Swiss Francs (£4,230). These figures are comparable to drug interventions that are routinely offered in many reimbursed healthcare services, such as statins for hyperlipidaemia.⁸ Much debate has occurred as to the usefulness of such research, but it serves to establish the economic credibility of interventions in this rapidly changing area of medicine, where short-term alterations in surrogate markers have become the benchmark for clinical efficacy of therapy.

HIV costs worldwide

The potential costs of providing antiretroviral therapy for all those affected worldwide by HIV has been estimated by a group of Canadian researchers, who note that currently the total bill would stand at approximately US\$66 billion.⁹ The cost expressed as a percentage of gross domestic product ranged widely, being higher in less developed settings – for example, sub-Saharan Africa averaged 15% of GDP compared with <1% for western European countries. Unfortunately, it is suggested that globally only approximately 7% of those who could benefit from antiretroviral therapy are currently receiving it.¹⁰ Whether, however, the treatment of HIV with antiretroviral agents is the highest priority for nations which also carry a great burden from other diseases such as malaria or tuberculosis is a subject of uncertainty and debate.

HIV prevention costs

Interventions other than drug-related ones are often not scrutinised for their economic impact. However, data exist that establish the utility and cost-effectiveness of preventive interventions in HIV, such as counselling, testing and partner notification.¹¹ In addition, modelling of preventing vertical transmission showed a cost per life-year saved of £51,258;¹² although this is greater than the cost of treating an infected individual, it must be seen in the context of avoidance of transmission.

Additional benefits

The use of effective antiretroviral therapy, which reduces illness and improves quality of life, will allow the individual to consider returning to work. This not only reduces social care costs but also increases societal benefit, raises taxes and allows carers to return to their own careers.

Conclusion

More work is needed to establish the economic consequences of action in all areas of HIV treatment and care. The growing number of publications in this field reflects its importance in the planning and execution of healthcare provision in HIV and AIDS.

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Website review

There is a wide choice of websites that offer advice on treatment options for patients with HIV/AIDS. This review describes one of the most useful as regards clinical guidelines, and gives a mention to its sister site which concerns clinical trials.

HIVATIS

For a thoroughly comprehensive and up-to-date site dealing with HIV and AIDS treatment, go to **www.hivatis.org**

This is the excellent site of the HIV/AIDS Treatment Information Service, which is sponsored in part by the National Institutes of Health and the Centers for Disease Control (CDC) and Prevention. As well as treatment guidelines, there are sections on what's new, general treatment information, a daily news update from the CDC and top quality links ranging from the NAMES Project Foundation AIDS Memorial Quilt to CDC Atlanta.

The site is regularly updated and, when I visited it, was absolutely contemporary. Its section on peer-reviewed journals is incisive, as are its opinions on the handling of sexually transmitted infection issues by the media.

It has a very 'clean' look and is really easy to use, but its biggest attraction is a library of current treatment guidelines. Almost as useful is an archive of previous treatment guidelines for comparison.

If you have Adobe Acrobat, you can download all the material as a PDF file.

The guidelines are comprehensive. They comprise adult and adolescent, paediatric,

perinatal, healthcare worker exposure and non-occupational exposure guidelines, as well as some for opportunistic infections and tuberculosis. All are regularly updated.

There are recommendations for the use of resistance testing in the management of HIV disease, which, as suggested, makes the reduction of viral load to undetectable levels more likely through selection of a new drug regimen for patients failing on current antiretroviral therapy.

There is also a section on the goals of therapy, which includes strategic thinking about restoration and/or preservation of the patient's neurological function, improvement of the quality of life and reduction of HIV-related illness and death. The tools which can help to achieve these goals are also described, with particular reference to compliance, food requirements, dosing frequency, toxicity and drug interactions.

A hypertext link can take you to detailed information about antiretroviral drugs in pregnant women.

ACTIS

The sister site of this useful resource is the ACTIS (AIDS Clinical Trials Information Service) site on **www.actis.org**

This site describes many ongoing trials, and you can even sign up to enter your patients if so minded.

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