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
People who may have been exposed to human immunodeficiency virus (HIV) infection after sexual or injection-drug use exposure were given post-exposure prophylaxis (PEP). This consisted of 4 weeks of antiretroviral drug treatment and was started within 72 hours of exposure. The patients were given a clinical assessment, risk reduction counselling and medication adherence counselling, and were tested for HIV antibodies. The patients were encouraged to bring the (infection) source partner for HIV testing and counselling. Female patients were given a pregnancy test. The patients were given a 1-week supply of medication and asked to return one week later. At the first follow-up visit (1 week), patients received the results of the HIV test, post-test counselling and an additional 21 days’ supply of medication, with strong advice on the importance of continuing with the prophylaxis. At weeks 12 and 26 the patients were re-tested for HIV antibodies and received their results at weeks 13 and 27. All the follow-up visits included brief HIV risk counselling. Additional consultations were provided to patients needing advice on the toxic effects of the treatment.

Full details of the medication were given in the original San Francisco study on PEP (see Other Publications of Related Interest), which provided much of the information used in this study. This study examined a simplified form of the San Francisco protocol.

Type of intervention
Secondary prevention and diagnosis.

Economic study type
Cost-utility analysis.

Study population
The study population comprised people who believed that they may have been exposed to HIV infection through sexual or injection-drug use exposure.

Setting
The setting was the community and primary care. The economic study was conducted in San Francisco, USA.

Dates to which data relate
The effectiveness evidence and resource evidence related to 1997 to 1999. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a single study, which also used information from other studies.

Link between effectiveness and cost data
The cost data were derived from a different study to the effectiveness data. The costing was carried out retrospectively.

**Modelling**
The reduction in infection risk by PEP was predicted by multiplying together the probability that the partner or syringe is infected with HIV (pi), the probability of HIV transmission associated with the particular exposure assuming that the partner is infected (alpha), and the effectiveness of PEP at preventing sustained infection in the face of exposure to the virus (E).

Each patient's long-term infection probability was derived (formula given) using the annual HIV incidence for the patient's exposure group (iota).

The total number of infections avoided was obtained by calculating each patient's effective risk reduction (formula given) and summing across all patients.

The estimates for pi, alpha, E and iota were obtained from the literature.

**Outcomes assessed in the review**
The effectiveness outcome assessed in the review was the percentage reduction in seroconversion risk from PEP with zidovudine.

**Study designs and other criteria for inclusion in the review**
The effectiveness measure was selected from a multinational case-control study by the Centers for Disease Control and Prevention (Cardo et al., see Other Publications of Related Interest).

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
The effective evidence was obtained from one primary study.

**Methods of combining primary studies**
Not relevant.

**Investigation of differences between primary studies**
Not relevant.

**Results of the review**
Compared with no treatment, there was an 81% reduction in seroconversion risk from PEP with zidovudine.
Methods used to derive estimates of effectiveness
The authors made some assumptions.

Estimates of effectiveness and key assumptions
The authors assumed there was no benefit from PEP with zidovudine if the patient failed to complete the course. They also assumed that patients are at risk of infection for 10 years.

Measure of benefits used in the economic analysis
The measure of benefit used in the economic evaluation was the quality-adjusted life-years (QALYs) gained. The number of QALYs gained by preventing someone from becoming infected with HIV were estimated using the estimates of Holtgrave and Pinkerton (see Other Publications of Related Interest). According to their model, a 32-year-old who becomes infected loses 9.31 QALYs. The future benefits were discounted at a rate of 3%.

Direct costs
The direct costs of the health service and patient were measured. The health service costs were for community outreach work, the development, production and distribution of promotional material, telephone hotline, clinic (clinician, staff, laboratory tests and miscellaneous supplies), antiretroviral medication and the downstream lifetime costs of HIV-related care. The intervention programme data were analysed retrospectively from the records of the study investigators, clinic records, San Francisco General Hospital pharmacy, and wholesale drug listings of the San Francisco PEP study. The lifetime cost of HIV-related care was obtained from the literature. The patient costs were for travel, time and calls to the hotline. These costs were also derived from the San Francisco PEP study, as obtained through participant questionnaires. Discounting was carried out at a rate of 3%. The costs and the quantities were not analysed separately. The price year was 2000.

Statistical analysis of costs
No statistical analysis of the costs was carried out.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out. The effectiveness of PEP for non occupational exposures to HIV (taken in the main calculation as 81%) was varied according to the 95% confidence interval (48 - 94%). The HIV treatment cost and QALYs saved, and the two together, were also varied. The discount rate was varied between 0 and 5%. The transmission probability of receptive anal intercourse (RAI) was varied in a threshold analysis. The robustness of the main study conclusions was tested using data on HIV prevalence and incidence from an alternative information source. A sensitivity analysis in which all transmission variables were set at either the lowest or highest value was also conducted.

The sensitivity of the cost results was tested using the prices obtained by the San Francisco General Hospital pharmacy, rather than the average wholesale prices listed in the Red Book of drug prices. In the original San Francisco study patients received individually tailored antiretroviral drug regimes. The cost implications of giving all patients either the most expensive regimen or the least expensive regimen were assessed. The effect of increasing the standard risk-reduction counselling from 10 to 25 minutes was assessed. One-way, multi-way and threshold analyses were carried out.
Estimated benefits used in the economic analysis
A total of 11.74 QALYs (associated with 1.26 infections) were saved when estimating the effects of the programme over 10 years. It is unclear whether the side effects of the prophylaxis treatment were considered.

Cost results
The total cost per patient (programme cost minus the saved future health care cost) was $1,125. The discount rate was 3%. The costs were estimated for 10 years. The costs of adverse effects were included in the costing.

Synthesis of costs and benefits
The cost per QALY saved was $14,449. When the PEP was only applied to men reporting RAI with other men, the PEP programme was cost-saving. For injection-drug exposures, the cost per QALY was $86,462. For male-female RAI, the cost per QALY was $165,289. For all other kind of exposure, the cost per QALY was more than $200,000. The PEP programme was cost-saving for patients who reported that their partner was HIV positive whereas, for unknown status partners, the cost per QALY was $58,025.

The threshold value for cost per QALY was taken to be $60,000. If the programme costs were increased to $2,458, or if the number of infections averted were as low as 0.58, the threshold value would not be exceeded. When the number of years that patients were estimated to be at risk was increased from 10 to 44 years, and when the infection incidence was raised to 9% in all groups, the threshold cost per QALY was not exceeded. If the PEP effectiveness parameter was lowered from 81 to 48% (the lower level of the 95% confidence interval), and if PEP completion rates were at least 29%, the threshold level of cost per QALY was not exceeded. This was also true irrespective of the percentage of partners known to be infected by HIV, or the prevalence of HIV among partners whose HIV status was unknown.

The RAI transmission probability was the most sensitive parameter. If this probability was greater than 0.033, the PEP programme would be cost-saving. Also, as long as the probability was at least 0.009, the cost per QALY would not exceed the threshold level. When all the transmission probabilities were set to their lowest levels the cost per QALY was $71,381. When the probabilities were set to their highest levels the programme became cost-saving.

Authors’ conclusions
Although there is much uncertainty about which crucial variables determine the cost-effectiveness of PEP prophylaxis, the study has shown the importance of key variables. In particular, the prevalence of patients reporting male-male receptive anal intercourse (RAI) and the per exposure transmission probability associated with RAI. The main areas of uncertainty are the effectiveness of post-exposure prophylaxis (PEP) for non occupational exposure (prior studies examined occupational exposure), the possibility that PEP might cause more risk-taking behaviour, and whether the antiretroviral agents used in PEP could induce resistance to the medications used to treat human immunodeficiency virus (HIV) infection.

The authors stated that their cost per QALY may be an overestimate since they did not account for the fact that four participants and one source partner were diagnosed with HIV, and this knowledge would have reduced the number of future HIV infections.

CRD COMMENTARY - Selection of comparators
The choice of the comparator, no prophylaxis programme, was implicitly justified by it being current practice in many areas.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single published study. The authors also made a few assumptions about effectiveness. The reader should consider whether the effectiveness source was appropriate. However, the authors did conduct appropriate sensitivity analyses around the effectiveness data.
Validity of estimate of measure of benefit
The measure of benefit (QALYs) was valid, although it was unclear whether the authors included any undesirable side effects of the prophylaxis in their QALY calculation.

Validity of estimate of costs
A societal perspective was adopted in the study. The authors did not consider the economic benefit resulting from fewer HIV infections, as more people would be economically productive. They acknowledged that this omission would overestimate the indirect costs in the study and overestimate the overall cost per QALY. The authors provided a comprehensive list of the costs that were included. Unfortunately, the costs were not reported separately from the quantities, which limits the ability to generalise the results to other settings. When the authors did obtain resource use information (which was not reported) it was taken from a single study. The price information was taken from the authors' setting and from published sources.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies. They addressed the issue of generalisability by examining the effectiveness aspect of the study, noting that the epidemiology of HIV and the sexual behaviour in San Francisco is not necessarily typical of other locations. They suggested that a PEP programme in a location where HIV is primarily spread heterosexually, or where HIV incidence is low, would obtain very different results. The authors did not present their results selectively and the authors’ conclusions reflect the scope of the analysis. The authors are aware that there are many areas of uncertainty that still need to be investigated.

Implications of the study
The authors concluded that a simplified San Francisco protocol carried out in San Francisco could definitely be justified in terms of the gain in QALYs, the cost of the gain would be socially acceptable. However, a similar programme in other locations could probably only be recommended if the sexual behaviour and HIV incidence were not dissimilar from those in San Francisco. The authors’ conclusions could be more certain if the per-exposure transmission probability associated with RAI, and the effectiveness of PEP after non occupational exposure, were known.

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Other publications of related interest


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