Cost-effectiveness of post-exposure prophylaxis following sexual exposure to HIV

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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
The use of post-exposure prophylaxis (PEP) following potential HIV exposure through sexual contact with a partner who may or may not be infected was compared to a 'no programme option'.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population was a hypothetical cohort of 10,000 patients who reported sexual intercourse with a partner of unknown HIV status.

Setting
The setting for this evaluation, in terms of primary or secondary care, was not stated. The economic study was conducted in the United States.

Dates to which data relate
The effectiveness evidence was derived from relevant literature published between 1993 and 1997. The analysis used a time horizon of 4 weeks for the administration of PEP and all costs were reported in 1996 US dollars.

Source of effectiveness data
The source of effectiveness data was a review/synthesis of the literature.

Modelling
The study used a decision-analytic model, to evaluate the cost-effectiveness of PEP.

Outcomes assessed in the review
The outcomes used as input parameters to the model were:

- probability of infection in the absence of PEP following receptive anal intercourse;
- probability of infection in the absence of PEP following receptive vaginal intercourse;
- probability of infection in the absence of PEP following insertive anal or vaginal intercourse;
probability partner is infected - receptive or insertive anal intercourse;

probability partner is infected - receptive or insertive vaginal intercourse;

effectiveness of PEP (%);

percentage of patients completing PEP;

quality adjusted life years (QALY’s) saved per prevented infection.

**Study designs and other criteria for inclusion in the review**
The study reported efficacy data from a case control study; the study designs of the other studies used in the review were not reported. The authors did not report inclusion or exclusion criteria for studies included in the synthesis of data.

**Sources searched to identify primary studies**
The authors did not report the sources searched or the search strategy used to identify studies for the synthesis of data.

**Criteria used to ensure the validity of primary studies**
The criteria used to ensure the validity of primary studies were not reported.

**Methods used to judge relevance and validity, and for extracting data**
The authors did not report the methods used to judge the relevance or validity of data or to determine which data were extracted.

**Number of primary studies included**
The authors used 8 published studies to derive the probability data for the evaluation.

**Methods of combining primary studies**
The authors did not state the method used to combine data from more than one source.

**Investigation of differences between primary studies**
The authors did not report whether there were differences in estimates of the probability of events between the studies used, or whether the reasons for these were investigated.

**Results of the review**
The authors reported the outcomes assessed in the model as follows:

- probability of infection in the absence of PEP following receptive anal intercourse = 0.02 (range: 0.008 - 0.032);
- probability of infection in the absence of PEP following receptive vaginal intercourse = 0.001 (range: 0.0005 - 0.0015);
- probability of infection in the absence of PEP following insertive anal or vaginal intercourse = 0.0006 (range: 0.0003 - 0.0009);
- probability partner is infected - receptive or insertive anal intercourse = 0.18 (range: 0.0 - 1.0);
probability partner is infected - receptive or insertive vaginal intercourse = 0.02 (range: 0.0 - 1.0);
effectiveness of PEP = 79% (range: 43% - 94%);
percentage of patients completing PEP = 69% (range: 59% - 76%);
QALY saved per prevented infection = 11.23 (range: 13.18 - 9.34).

**Measure of benefits used in the economic analysis**
The measure of benefit for the economic analysis was QALY's gained.

**Direct costs**
The authors included the following costs in the model:

- cost of PEP therapy per patient, $619 (range: $400 - $955);
- cost of incomplete therapy, as a percentage of the cost of PEP therapy per patient, 50% (range: 0% - 100%);

The costs were estimated and derived using actual data.

The authors' reported that the antiretroviral drugs used in triple combination therapy constituted the primary cost associated with PEP, this includes drug, laboratory and administration costs. The wholesale drug prices for a 4-week supply at recommended doses were reported as: $260 for ZDV (200mg thrice daily); $209 for 3TC (150mg twice daily); and $336 for indinavir (800mg thrice daily). This results in a total drug cost of approximately $469 for a 4-week regimen of ZDV and 3TC, and $805 if indinavir is added. The estimated mean cost of PEP-associated laboratory work and office visits ($150) was also included, bringing the total base-case cost of ZDV-3TC PEP to $619 or $955 for the triple combination.

The price year was 1996. Costs and the present value of benefits (savings) accrued in the future were discounted in the base-case analysis at a 3% annual rate.

**Statistical analysis of costs**
No statistical analysis of costs was reported.

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
US dollars ($). No currency conversions were reported.

**Sensitivity analysis**
One-way, multi-way and threshold sensitivity analyses were conducted. The authors did not state explicitly which parameters were tested, but appear to have included all the variables in the one way sensitivity analysis.

**Estimated benefits used in the economic analysis**
The base-case analysis for a cohort of 10,000 patients receiving PEP reported 19.62 HIV infections averted following receptive anal intercourse; 0.59 HIV infections averted following insertive anal intercourse; 0.11 HIV infections...
averted following receptive vaginal intercourse and 0.07 HIV infections averted following insertive vaginal intercourse. The authors did not report the number of QALY’s associated with PEP and no PEP.

Cost results
The gross costs for the base-case analysis of a cohort of 10,000 patients receiving PEP were: receptive anal $5,230,550, insertive anal $5,230,550, receptive vaginal $5,230,550 and insertive vaginal $5,230,550. Per infection averted the gross costs were therefore: receptive anal $266,544, insertive anal $8,884,795, receptive vaginal $47,977,894 and insertive vaginal $79,963,157.

The net costs for the base-case analysis of a cohort of 10,000 patients receiving PEP were: receptive anal $1,400,259, insertive anal $5,115,641, receptive vaginal $5,209,271 and insertive vaginal $5,217,782. Per infection averted the net costs are, therefore: receptive anal $71,356, insertive anal $8,689,607, receptive vaginal $47,782,706 and insertive vaginal $79,767,969.

Synthesis of costs and benefits
The incremental cost utility ratios for the base-case analysis for a cohort of 10,000 patients receiving PEP were as follows: receptive anal $6,354/QALY, insertive anal $773,785/QALY, receptive vaginal $4,254,916/QALY, insertive vaginal $7,103,114/QALY.

The sensitivity analyses indicated that the results for the receptive anal case were not sensitive to changes in the parameter values and were always cost-effective across a plausible range of values. Both the insertive anal and insertive vaginal were not sensitive and were not cost-effective across a plausible range of values. The receptive vaginal case was sensitive to the probability of the sexual partner of the patient being HIV infected. In this case if the probability of infection is greater than 0.73 then PEP may be cost-effective. Triple PEP therapy was unlikely to be cost-effective relative to dual combination PEP. The results did not appear to be sensitive to repeated exposure and PEP.

Authors' conclusions
The authors reported that, from a purely economic standpoint, PEP should be restricted to partners of infected persons (e.g. serodiscordant couples), to patients reporting unprotected receptive anal intercourse (including condom breakage), and possibly to cases where there was a substantial likelihood that the partner is infected. Providing PEP to all who request it does not appear to be an economically efficient use of limited HIV prevention and treatment resources.

CRD COMMENTARY - Selection of comparators
The author chose a 'no programme option' as a comparator for the drug intervention. Although no explicit justification was given for the comparator used, it would appear to represent current practise in the authors' setting. The authors did, however, report that some physicians have apparently already begun prescribing PEP for their patients who report sexual exposure to HIV. You, the user of this database should decide if the comparator, no PEP prophylaxis, represents current practice in your setting.

Validity of estimate of measure of effectiveness
The authors stated that a literature review had been undertaken, however, it is unclear if the review was conducted in a systematic way to identify relevant research and minimise bias. The authors appeared to use data from the few available studies selectively. The authors used a model to synthesise data and estimate the effectiveness endpoints of the evaluation. This model was described in detail. The authors did not report whether the model structure was validated. The authors noted a number of limitations with the data and with the assumptions used. To address these issues, the authors conducted extensive sensitivity analyses to test the effect of variability in the data.

Validity of estimate of measure of benefit
Quality adjusted life years were used as the measure of benefit. The authors used QALY estimates from published literature. The authors did not report any details about the quality and validity of the published studies used or the method used to derive the utility weights.

Validity of estimate of costs
Although the authors reported that the costs were reported from a societal perspective, indirect costs were not included. The authors did not report costs and resource use separately. The cost data were derived mainly from published studies. The authors did not report details about the quality and validity of these studies.

The authors did not indicate if the full range of costs were considered. However the analysis did not include the costs of informal care or the costs of side effects from PEP, therefore, the cost-effectiveness of the intervention therapy may have been overestimated. You, as a user of this database should decide if the omission of these costs in your setting is likely to effect the authors' conclusions.

Other issues
The authors reported a number of limitations to their study, most of which were tested in the sensitivity analysis. The authors noted that there is substantial uncertainty about the accuracy of the per contact transmission probabilities used. They noted that these can vary considerably and that this should be considered when making decisions with patients. The authors also noted that there are a number of cost-effective approaches to preventing HIV exposure, which may be a more efficient use of resources than preventing HIV infection after exposure.

Implications of the study
The authors report that PEP is only likely to be cost-effective for anal receptive sexual exposure and receptive vaginal exposure if the probability of partner infection is high. The authors suggest that the analysis supports only a limited role for PEP in the prevention of HIV infection.

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