

Non-occupational postexposure prophylaxis for HIV: a systematic review

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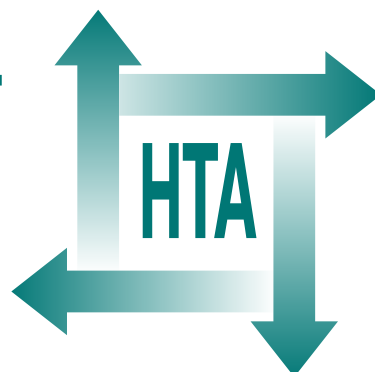
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Executive summary

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Executive summary

Background

Human immunodeficiency virus (HIV) is a sexually transmitted and bloodborne virus found primarily in the blood, semen or vaginal fluid of an infected person. It is transmitted in two main ways: by having unprotected sex (anal, vaginal or oral) with someone infected with HIV or by sharing needles and syringes with someone infected with HIV. Postexposure prophylaxis (PEP) for HIV is the prompt administration of antiretroviral therapy following known or potential exposure to HIV infection in an attempt to prevent the establishment of infection. The effectiveness of PEP in preventing seroconversion (i.e. converting from HIV negative to HIV positive, with the detection in the blood of antibodies to HIV) after non-occupational exposure to HIV is unclear.

Objectives

The main aim of this study was to review the evidence on the clinical effectiveness and cost-effectiveness of non-occupational PEP for HIV.

Methods

A systematic review of the evidence was undertaken using a priori methods.

Data sources

Eleven electronic databases were searched from inception to December 2007. Bibliographies of related papers were assessed for relevant studies and experts contacted to identify additional published references.

Study selection

Studies were included if they fulfilled the following criteria:

- Intervention: any antiretroviral drug regimen administered as non-occupational PEP for a short period (28 days) to HIV-negative people potentially exposed to HIV through unprotected sexual contact or use of a potentially contaminated needle or potentially contaminated biological fluid.

- Participants: humans with non-occupational exposure to HIV through unprotected sexual exposure (oral, vaginal, anal), either voluntary or rape, with an HIV-infected partner or partner of unknown HIV status; humans with exposure to a needle contaminated by a known or potentially infected substance in a non-occupational setting.
- Comparator: no intervention; group not receiving PEP; a different PEP regimen.
- Outcomes: HIV seroconversion frequency; adverse effects and complications of PEP; adherence to PEP; health-related quality of life; costs or some measure of cost-effectiveness.
- Design: randomised controlled trial, controlled clinical trial, cohort study or case-control study; cost-effectiveness/utility studies; economic evaluations; prospective observational studies for adverse events.

Studies identified were assessed for inclusion in two stages with titles and abstracts and full papers of retrieved studies assessed independently by two reviewers, with differences in decisions resolved through discussion or through recourse to a third independent reviewer.

Data extraction and quality assessment

Data were extracted by two reviewers using a data extraction form developed a priori. Any disagreements were resolved through discussion or through recourse to independent assessment by a third reviewer. The methodological quality of the studies included in the systematic review was assessed by means of modified quality assessment tools using individual components of methodological quality rather than relying on summary scores. The quality criteria were applied by two reviewers, with any disagreements resolved through discussion or through recourse to a third independent reviewer.

Data synthesis

Studies were synthesised using a narrative approach with full tabulation of results from all included studies.

Results

Number and quality of studies

One clinical effectiveness study meeting the inclusion criteria for the review was identified. This was a cohort study of PEP in a high-risk HIV-negative homosexual male cohort in Brazil. The methodological quality and the quality of reporting of the study were generally weak.

Four economic evaluations met the inclusion criteria of the review (three conducted in the US and one in France). The methodological quality of the studies is mixed. Each of the studies is constrained by a lack of published data on the clinical effectiveness of PEP after non-occupational exposure, with effectiveness data derived from one study of occupational PEP. Their generalisability to the UK is not clear.

Summary of clinical effectiveness

Seroincidence in the cohort as a whole (2.9 per 100 person-years) was very similar to that expected by the study authors in this population (3.1 per 100 person-years, $p > 0.97$), despite the seroconversion to HIV being 1/68 in the PEP group and 10/132 in the group not receiving PEP. The study reported that, on average, high-risk sexual activities declined over time for both PEP and non-PEP users. The study authors concluded that a public health PEP programme would not have a major impact on HIV transmission in the study population.

Summary of cost-effectiveness

Results from the included economic studies suggest that PEP following non-occupational exposure to HIV is cost saving for men who have unprotected receptive anal intercourse with men, whether the source partner is known to be HIV positive or not; heterosexuals after unprotected receptive anal intercourse; and intravenous drug users sharing needles with a known HIV-positive person.

PEP following non-occupational exposure to HIV was cost-effective for all male–male intercourse (unprotected receptive and insertive anal intercourse, unprotected receptive oral sex, and ‘other’). PEP following non-occupational exposure to HIV was possibly cost-effective for intravenous drug users and high-risk women.

Adverse events

Four additional studies (two comparative studies and two observational studies) were identified that supplied further information about adverse

events associated with PEP after non-occupational exposure to HIV. The majority of participants experienced adverse events with the most common being nausea and fatigue. Rates were generally higher in participants receiving triple therapy than in participants receiving dual therapy. Completion of PEP therapy was variable, ranging from 24% to 78% of participants depending on type of therapy. Toxicity was the main reason for discontinuation of treatment.

Conclusions

It is not possible to draw conclusions on the clinical effectiveness of non-occupational PEP for HIV because of the limited evidence in terms of quantity and quality of studies. Only one cohort study was identified that met the inclusion criteria for the systematic review. Cost-effectiveness has been assessed in four economic evaluations using evidence on effectiveness taken from the use of PEP in the occupational setting. Results are consistent across studies and suggest that non-occupational PEP may be cost-effective, especially in certain population subgroups. Although the studies have been conducted in an appropriate way and may have internal validity in terms of the structure of the model and plausible results, the assumptions and data sources mean that results should be used with caution. The generalisability to the UK of studies conducted in the US is not clear as sexual behaviour and HIV incidence may not be similar.

Suggested research priorities

The most important research need is to establish the clinical effectiveness of non-occupational PEP within the UK. Ongoing research in the form of the NONOPEP project, an MRC-funded surveillance programme of PEP for non-occupational exposure to HIV, will address aspects of clinical effectiveness in terms of seroconversion rates in people who take PEP compared with those who do not and evaluate problems associated with taking antiretroviral medications. This project is due for submission shortly. Data generated from this study can then be assessed and used to inform future economic modelling of the cost-effectiveness of non-occupational PEP in the UK.

Publication

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NIHR Health Technology Assessment Programme

The Health Technology Assessment (HTA) Programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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