

PEP study newsletter



NATIONAL CENTRE IN HIV
EPIDEMIOLOGY AND
CLINICAL RESEARCH

Non-occupational HIV Post-Exposure Prophylaxis study: issue 4

April 2003

The PEP study: four years on

The PEP study has been monitoring the implementation of guidelines recommending non-occupational post-exposure prophylaxis to HIV since late 1998. The study has been expanding and is now enrolling from NSW, ACT, Queensland and Victoria.

Australia is one of the pioneers in the world in recommending PEP for HIV in the community setting. The study provides unique data on the extent and appropriateness of non-occupational PEP utilization in a population setting. Data on clinical outcomes may guide and influence the use of non-occupational PEP worldwide.

We Value your contributions

We greatly appreciate your contributions to this study in enrolling your patients and completing the data collection forms. The study is actively continuing to enrol and follow up patients.

If you have any queries regarding the study or require more enrolment forms, please contact Wei Zheng on 02 93324648.

Focus of this issue

In this newsletter, we examine whether or not prescribing practice follows the ANCAHRD guidelines for use of non-occupational PEP

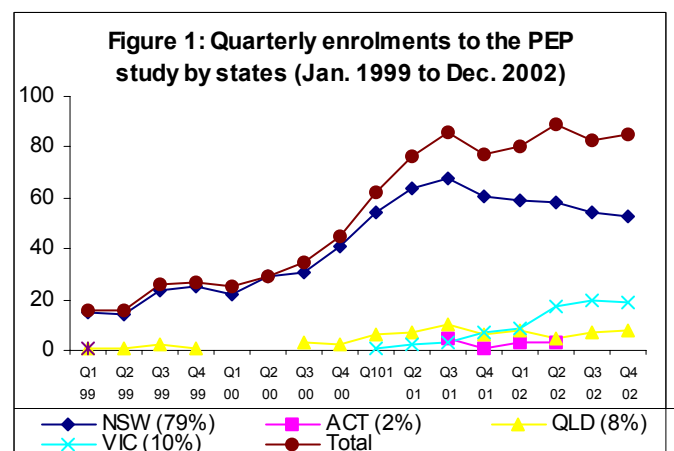
Study results

Local health authorities have utilized the data from PEP study in their local service planning and policy development.

If you would like to know more about the results of the PEP study at your local level, please feel free to contact us.

Enrolments

By the end of 2002, 857 people were enrolled, of whom 819 received PEP. Although NSW still constitutes the large majority of enrolments, there has been a rapid increase in enrolments from Victoria.



Demography

Participants were predominantly men (771, 94.1%) and the median age was 32 years ranging from 17 to 72 years. Most people (645, 76%) were from the Sydney metropolitan area and of them 242 resided in Gay Sydney (postcodes 2000, 2010-12) (38%). A small proportion of prescriptions were to repeat PEP presenters (80, 9.8%).

Baseline HIV testing

⇒ **Guideline:** According to ANCAHRD guidelines, a baseline HIV antibody test should be performed on all exposed individuals.

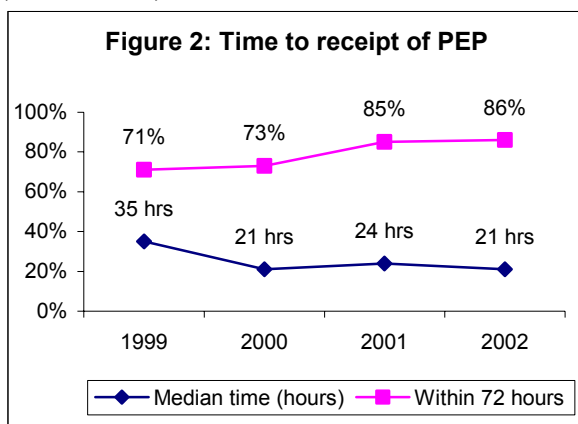
⇒ **Practice:** HIV antibody tests were obtained at baseline in 92% of cases. The importance of this test is illustrated by the fact that 4 people were diagnosed as HIV positive on the basis of a baseline test.

Risk of exposure

- ⇒ **Guideline:** PEP is recommended only after an assessment of the probability that the source was HIV positive, and the risk of the exposure.
 - ⇒ **The source** must be known to be HIV positive, or report HIV risk behavior, or be from a population in which the HIV seroprevalence is high.
 - ⇒ **The exposure** must be high risk. (Unprotected anal or vaginal intercourse, sharing needles and syringes, non-intact skin or wounds exposed to HIV positive blood; receptive oral sex with ejaculation in the presence of oral lesions with source known to be HIV positive; or mucous membranes, non-intact skin or wounds exposed to HIV positive secretions including blood-stained body fluid.)
- ⇒ **Practice:** The large majority of PEP prescriptions (779, 95.1%) were appropriate according to the ANCAHRD guidelines.

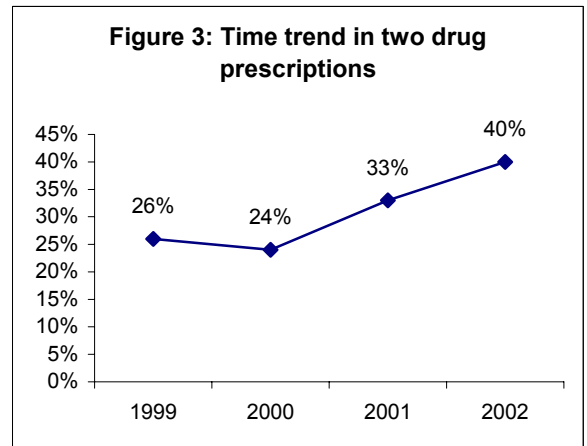
Time to receipt of PEP

- ⇒ **Guideline:** The guidelines recommend initiating PEP as soon as possible, and usually within 72 hours.
- ⇒ **Practice:** In the PEP study, information on time to receipt of PEP was reported for 87% (713) of PEP recipients. Among them, 95% commenced PEP within 72 hours. The median time to receipt of PEP was 23 hours (IQR: 12-41).



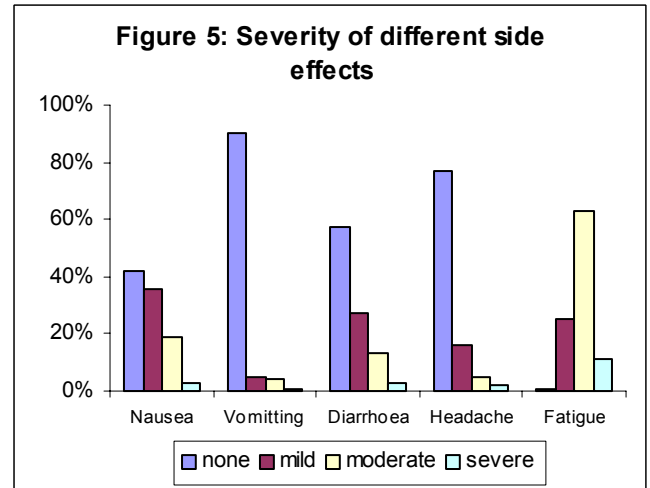
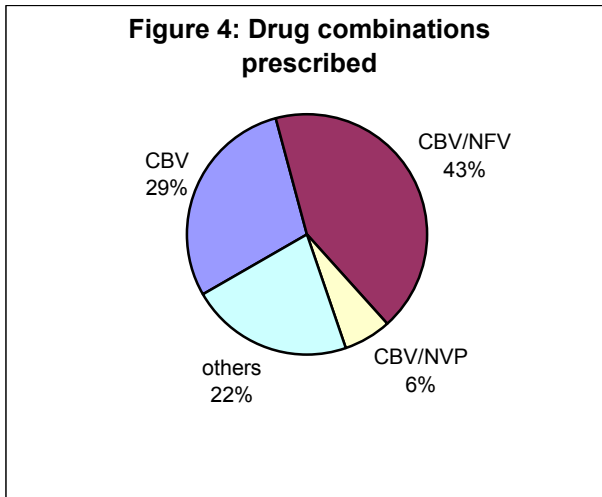
PEP regimens

- ⇒ **Guideline:** Two antiretrovirals are sufficient in most circumstances. Three drugs are recommended only when the source is known to be HIV positive, where there has been a high risk exposure, **AND** the source has advanced HIV disease, **OR** is known to have an HIV plasma viral load >10,000 copies/ml bDNA (>20,000 copies/ml RT-PCR) **OR** the source has evidence of antiretroviral drug resistance.
- ⇒ **Practice:** Overall, 66% (543) of PEP prescriptions were for three or more drugs. Three drug combinations have commonly been used, and 59% (319) of three drug prescriptions were after an exposure to a source of unknown HIV status. In cases where the source was known to be HIV positive, 78% (224) of them were prescribed three or more drugs. The use of 3 rather than two drug combinations is the main area in which practice has not followed the national guidelines.



Drug combinations

The dual combination of lamivudine and zidovudine (29%) and the three drug combinations of lamivudine and zidovudine with nelfinavir (43%) were most frequently prescribed. The use of nevirapine declined since 2001, from 35% of prescriptions in 2000 to 1% in 2002.



Compliance

792 participants were due for four-week follow-up visits by the end of 2002 and 77% (613) of them had follow-up information available. Overall, 63% (502) had been fully compliant to the regimen including 452 (57%) participants who completed the initially prescribed regimen and 50 (6%) participants who completed a modified regimen. For those who were moderately or poorly compliant to the prescribed regimen, the median days of remaining fully compliant was 10 days (IQR: 6-19 days). The adherence to the therapy did not differ among 2 drug recipients in comparison to three or more drugs recipients.

Side effects

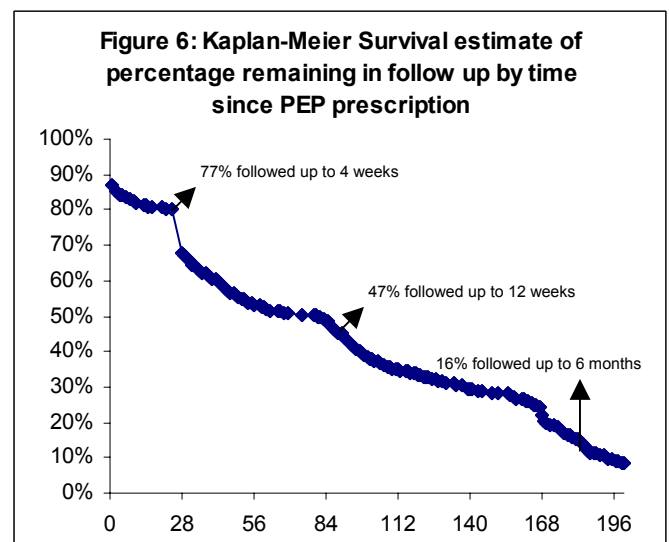
Most people (489, 80%) with known follow up information reported some side effects. Nearly all of them reported at least two side effects and the large majority rated them as mild or moderate (433, 89%). The most frequently occurring side effects include nausea in 350 (57%), diarrhoea in 252 (42%), headache in 135 (22%), and fatigue in 93 (15%). As reported in the last issue of PEP study newsletter, there were two cases of Steven-Johnson's Syndrome (CBV/NVP) and two cases of kidney pain probably related to nephrolithiasis (CBV/IDV).

Being prescribed three or more drug combinations was associated with a higher incidence of side effects ($P < 0.001$).

Follow up

⇒ **Guideline:** For an individual who has received PEP, HIV antibody testing should be repeated at 3-6 weeks, 3 months and 6 months.

⇒ **Practice:** As showed in figure 6 below, about 77% of participants completed four-week follow-up, 47% completed three months and only 16% completed six-month follow-up.



HIV seroconversion

No HIV seroconversions definitely related to treatment failure have been observed in the PEP study. Six participants were found to be HIV positive, and four of these tested HIV positive at

baseline. One participant seroconverted three months after being prescribed PEP (CBV/NFV), but he was poorly compliant, took PEP for only 7 days, and also engaged in ongoing risk behaviour. Another participant seroconverted 110 days after initiation of PEP (D4T/DDI/3TC), had been fully compliant to the regimen, but was believed by the doctor to have had other risk episodes that could have lead to the positive result.

St Vincent's Hospital in Sydney offers comprehensive counselling with the prescription of PEP. It aims to enhance the patient's compliance to the PEP regimen and minimise the potentials for future risky exposures. Our follow up data showed that the percentage of full compliance to the prescribed regimens enrolled from St Vincent's Hospital was 73%, which was significantly higher ($P < 0.001$) than those from other clinics as a whole (58%).

Number of HIV seroconversion expected without the provision of PEP

We have calculated the numbers of HIV seroconversion expected among the 857 participants who were potentially exposed to HIV in this PEP study. This was based on:

- Published risk estimates of HIV infection after a single exposure to HIV.
- When the HIV status of the source was unknown, the risk of HIV transmission was based on the estimated risk per single exposure multiplied by the probability the source was positive based on local seroprevalence data.

These calculations indicated that **two to six** HIV infections would have been expected during the study period. Although we have observed no seroconversions in participants who were compliant with therapy, loss to follow up in the study means it is not possible to definitively conclude that PEP was effective.

Completeness

Data from drug cost reimbursement records from 11 area health services in NSW showed that 52% (248) of the re-imbursed PEP prescriptions in those areas had been recruited into this study between April 2001 and March 2002. In Queensland, 52% of PEP prescriptions were enrolled into PEP study from June 2000 to Oct 2002.

Conclusions

In most respects, prescription of PEP in Australia follows the ANCAHRD guidelines. There are two areas where practice commonly departs from the guidelines:

- Prescription of two rather than three drugs;
- The length of follow up is much shorter than the recommended six months.

PEP NOW - Worldwide overview

Seven countries including six European nations and Australian have developed official HIV non-occupational PEP guidelines. In American, with the absence of national recommendation, California and New York have guidelines for non-occupational PEP for victims of sexual assault. In 2002, Rhode Island issued guidelines to help clinicians evaluate and manage patients potentially exposed to HIV as a result sexual assault or other non-occupational exposures.

Should you have any questions regarding the study or you require any clarification of information within the newsletter, please don't hesitate to contact us:

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Alternatively you may contact **Associate Professor Andrew Grulich** at NCHECR.