Adherence to HIV post-exposure prophylaxis in victims of sexual assault: a systematic review and meta-analysis
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CRD summary
This review found that adherence to prophylaxis after exposure to HIV, for victims of sexual assault, was low across a range of developed and developing countries. Some methodological flaws mean that the reliability of the authors’ conclusions is uncertain.

Authors’ objectives
To assess the rates of, and determinants of, adherence to medication to prevent HIV infection, after exposure, for victims of sexual assault.

Searching
MEDLINE, EMBASE, HMIC, PsycINFO, The Cochrane Library, POPLINE, and GHL were searched to June 2011, for relevant studies; search terms were reported. The bibliographies of all retrieved articles were checked for additional references. No language restrictions were applied.

Study selection
Observational and experimental studies that reported data on adherence to prophylaxis after exposure, by victims of sexual assault, were eligible for inclusion. Unpublished studies and non-peer-reviewed reports were excluded.

The included studies were conducted in developed countries (the USA, the UK, France, Denmark, or Canada) or developing countries (Brazil, Kenya, or South Africa). The prevalence of HIV in adults ranged from 0.20 to 0.60% in the developed countries, and from 0.45% to 17.80% in the developing countries. Where reported, prophylaxis consisted of either two drugs or three drugs. Drug adherence was poorly defined. The interventions to improve adherence were telephone counselling with written information and diaries, nurse-driven models of post-rape care integrated into hospital services, and nurse-driven follow-up visits over six months at any of four sites. All the interventions took place in South Africa.

It was not clear how many reviewers selected the studies from the search results.

Assessment of study quality
Methodological quality was assessed by the proportions of patients who were defined as "refusals", the methods of adherence measurement, the reporting of side-effects, the definition of the inclusion and exclusion criteria, the study design, sample size calculations, and statistical analyses.

The authors did not state how many reviewers assessed study quality.

Data extraction
Point estimates and 95% confidence intervals, for the proportions of patients who adhered to treatment, at various times from the offer of treatment to the final follow-up, were extracted. Patients were defined as "adherent" if they completed a 28-day course of treatment, and those who refused to start prophylaxis were defined as "refusals". Patients who agreed to prophylaxis, but did not collect their medication nor return for follow-up appointments were classified as "defaulters overall".

The authors did not state how many reviewers extracted the data.

Methods of synthesis
The results of the cohort studies were adjusted, using a Freeman-Tukey square-root transformation. Randomised controlled trials and cohort studies were analysed separately, using a DerSimonian and Laird random-effects model. Statistical heterogeneity was evaluated using $I^2$. 


Subgroup and meta-regression analyses were undertaken to examine the effects on the results of age (adults or children), drug regimen, country (developed or developing), and setting (sexual assault services or hospital).

**Results of the review**

Twenty-four studies (2,497 patients; range five to 347) were included in the review. One was a randomised controlled trial, six were prospective cohort studies, and 17 were retrospective studies, including data collection studies, or record, chart and case-note reviews. Seven studies reported the percentage of patients who refused prophylaxis; this was higher than 20% in two studies. The inclusion criteria were specified in 16 studies and the reasons for treatment discontinuation were provided in seven studies. Adjustment for potential confounders was reported in 11 studies.

In the randomised controlled trial (274 patients), telephone support was compared with no support, for adults and children, who were offered prophylaxis after sexual assault. There was a non-significant increase in adherence to prophylaxis in the intervention group (38.2%) compared with the control group (31.9%), and a statistically significant increase in use of an adherence diary (p=0.001).

One prospective cohort study found an increase of 38 percentage points in self-reported adherence and patient treatment literacy, with nurse-integrated care. One non-comparative prospective study attained a completion rate of 74% with nurse-driven follow-up visits, over six months.

In the meta-regression, adherence to prophylaxis was higher in developing countries (β-coefficient 20.3, 95% CI 6.2 to 34.3). Three studies found that adherence was associated with the side-effects of treatment, finding worse effects with three drugs than with two drugs.

**Authors' conclusions**

The rates of adherence to prophylaxis after exposure to HIV, for victims of sexual assault, were low across a range of developed and developing countries.

**CRD commentary**

The review addressed a clear question and stipulated broad criteria for the inclusion of studies. Appropriate databases were searched, without language restrictions. The restriction to published peer-reviewed studies introduced a risk of publication bias. Steps were taken to minimise reviewer errors and bias in study selection, but were not reported for the assessment of methodological quality and data extraction.

Some elements of study quality were assessed, but no information was provided on randomisation, allocation concealment, blinding and losses to follow-up, in the randomised trial, which makes it difficult to judge the reliability of its results. Overall, the quality of the included studies was low and the results of the evidence synthesis were unclear. Little information was provided on follow-up in the cohort studies. There was some variation in study design, patients and setting, across the included studies. The results of the randomised trial were analysed separately from those of the non-randomised studies, but the statistical combination of studies with a wide range of designs may not have been appropriate.

The lack of a rigorous quality assessment means the results of the review should be interpreted with caution, and the reliability of the authors' conclusions is unclear.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further research was required to standardise the care for victims of sexual assault. Consistency in the definition, measurement and reporting of adherence outcomes was required, and interventions to improve adherence to prophylaxis should be assessed.

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