Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review
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CRD summary
This review determined if highly active antiretroviral therapy (HAART) increased the risk of engaging in unprotected sex. The authors concluded that human immunodeficiency virus-positive patients receiving HAART did not show increased risky sexual behaviour. The results were not consistent among studies and the quality of the included studies was not assessed. Hence the authors' conclusion may not be reliable.

Authors' objectives
To determine if treatment with highly active antiretroviral therapy (HAART) increased the risk of engaging in unprotected sex.

The review also assessed the influence of undetectable viral load and specific beliefs about HAART on the risks of engaging in unprotected sex, but this abstract only refers to the effect of treatment with HAART.

Searching
AIDSLINE, MEDLINE, PubMed, CINAHL, PsycINFO, ERIC, EMBASE and Sociofile were searched from 1966 through August 2003 for articles, book chapters and conference abstracts; the search terms were stated. Doctoral dissertations were also eligible. The reference lists in identified studies were checked and 12 journals (published between August 2002 and August 2003) were handsearched. Authors were also contacted for details of additional studies. Only studies reported in English were eligible.

Study selection
Study designs of evaluations included in the review
The inclusion criteria for study design were not specified. All but one of the included studies was a controlled trial (no further details were given).

Specific interventions included in the review
Studies of HAART or protease inhibitors were eligible for inclusion.

Participants included in the review
Studies of human immunodeficiency virus (HIV)-positive patients were included. The included studies were in adolescents, men and/or women, heterosexuals, gay or bisexual men, and injection drug users.

Outcomes assessed in the review
Studies that assessed unprotected insertive or receptive anal intercourse or unprotected vaginal intercourse, the consistency of condom use during sexual intercourse, or the diagnosis of a new sexually transmitted infection (STI) during a specific recall period, were eligible for inclusion. The studies had to present statistical tests for the association between HAART and sexual behaviour, or report sufficient information to allow the calculation of an effect size.

Studies that only measured perceptions or intentions were excluded.

How were decisions on the relevance of primary studies made?
Three reviewers, working in pairs, independently selected the studies.

Assessment of study quality
The authors did not state that they assessed validity.
Data extraction
Pairs of reviewers independently extracted the data using a standardised spreadsheet. Agreement between the reviewers was 98%, and any disagreements were resolved with the aid of a third independent reviewer. For each study an odds ratio (OR) was calculated. For studies reporting continuous measures for outcomes, the reviewers calculated the OR from the standardised mean difference.

Authors were contacted, if required, for adequate data to enable the calculation of an effect size. Where studies reported data for independent subgroups of participants, the reviewers calculated a separate effect size for each subgroup. Where studies reported more than one measure of sexual behaviour, the reviewers calculated the effect size for the sexual behaviour with the highest risk for transmitting HIV infection. For studies reporting sexual behaviour with two or more types of partner, the reviewers extracted data for the partner type with the highest risk for transmitting HIV. For studies reporting sexual behaviour with primary and casual partners, the reviewers extracted data for casual partners. The reviewers extracted results from univariate analysis where possible.

Methods of synthesis
How were the studies combined?
The studies were combined using a random-effects meta-analysis. Pooled ORs and 95% confidence intervals (CIs) were calculated, with studies weighted using the inverse variance for each independent sample. The potential for publication bias was assessed using a funnel plot and a linear regression test.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q statistic. The influence of each study was assessed by repeating the analysis after omitting each study in turn. Pooled ORs were calculated according to participant characteristics (men who have sex with men only, mixed samples, heterosexual or injection drug user), type of sexual partner, location (USA or non-USA) and sample size (greater than 200, or 200 or fewer).

Results of the review
Sixteen studies with twenty-one independent effect sizes were included in the meta-analysis (n about 19,878).

The percentage of patients receiving HAART or protease inhibitors ranged from 18 to 78% (median 59%).

Only one study reported the duration of HAART treatment, and only four studies reported the length of time since the patients were tested as HIV positive.

There was no significant difference in the prevalence of unprotected sex between participants receiving HAART and participants not receiving HAART (OR 0.92, 95% CI: 0.65, 1.31). Statistically significant heterogeneity was detected (P<0.001). No single effect size accounted for the heterogeneity.

The results were similar for USA and non-USA studies, and for studies with large and small sample sizes.

There was no evidence of publication bias.

Authors’ conclusions
HIV-positive patients receiving HAART did not show increased risky sexual behaviour.

CRD commentary
The review question was clear in terms of the participants, intervention and outcomes; inclusion criteria for the study design were not specified. Several relevant sources were searched and the search terms were stated. Attempts were made to minimise publication bias, but not language bias. Two reviewers independently selected the studies and extracted the data, which reduces the potential for bias and errors. The authors did not appear to have undertaken any validity assessment. In particular, the comparability of patients receiving and not receiving HAART was not discussed, nor was the validity of the methods used to collect the data.
The meta-analysis was performed regardless of heterogeneity, and the forest plot showed no consistency of direction of effect. The authors explored various potential sources of heterogeneity among the studies, but heterogeneity appeared to be unexplained. In view of this unexplained variability, the conclusion about the sexual behaviour of HIV-positive patients receiving HAART may not be reliable.

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

**Practice:** The authors stated that HIV and STI patients should receive prevention messages that having an undetectable viral load does not abolish the possibility of transmitting HIV and does not mean the patient is ‘cured’. They also stated that this message should be directed at HIV-positive patients engaging in safe sex and at a broader audience, using a wide range of approaches.

**Research:** The authors stated that future research should consider the influence of disease severity beliefs in relation to other beliefs and behaviours.

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