Review Article

The impact of highly active antiretroviral therapy on high-risk behaviour of HIV-infected patients in sub-Saharan Africa

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Abstract

Introduction: High-risk sexual behaviors such as multiple sexual partners, inconsistent condom use, acquisition of sexually transmitted infection (STIs), and non-use of contraceptives persist in HIV patients undergoing care. We conducted a systematic review of studies conducted in the era of increased access to HAART (2000-2010) to assess whether wide-scale use of HAART was associated with high-risk behavior among HAART-using patients.

Methodology: We conducted a comprehensive search of databases (AIDSLINE, National Library of Medicine, MEDLINE, PubMed, CINHAL and EMBASE) from January 2002 to January 2010, reviewed conference proceedings and journals, and contacted the researchers involved. We analyzed the association of high-risk behaviors (non-disclosure of sero-status to sexual partners, inconsistent condom use, unprotected sexual intercourse, multiple sexual partners, non-use of contraceptives and acquisition of STIs) with using HAART. Information from eligible studies was abstracted using a standardized checklist. Fourteen English-language studies met the selection criteria of having high-risk behavior as an outcome in patients using HAART in sub-Saharan Africa.

Results: Of the 92 eligible articles screened, 14 met the criteria for inclusion as primary articles, 10 showed that HAART is not associated with increased high-risk behavior, two showed increase in acquisition of STIs among HAART-using patients, (which was inconsistent with other measures of high-risk behavior), and two studies showed short-term increase in high-risk behavior.

Conclusions: Persistence of high-risk behavior in HAART-using patients suggests that more effort needs to be incorporated in HIV care to reduce such behavior to reduce HIV transmission to uninfected populations.

Key words: HIV infection; HIV care; high risk behavior; sub-Saharan Africa

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Introduction

In sub-Saharan Africa, access to highly-active antiretroviral therapy (HAART) has increased markedly over the last decade (2000-2010), largely due to the international efforts in the global fight against the human immune deficiency virus (HIV) infection. HAART is effective in decreasing HIV viral loads to undetectable levels, significantly reducing the incidence of HIV related opportunistic infections, and thereby restoring a decent quality of life for a high number of HIV-infected patients [1]. By increasing life expectancy, decreasing morbidity, and with the potential to reduce vertical and sexual transmission of HIV, HAART has made HIV a manageable chronic disease, as HIV-infected individuals on therapy are anticipated to live well into (and past) their peak reproductive years [1]. In developed countries where access to HAART has become widely available, the incidence of acquired immune deficiency syndrome (AIDS) and AIDS-related mortality declined considerably in the 1990s [2,3] The reduction in viral load that occurs in individuals treated with antiretroviral therapy led to optimistic expectations about the ability of antiretroviral therapy to limit the HIV epidemic. There has been support for widespread use of HAART as a prevention strategy for HIV infection in areas of high prevalence such is in sub-Saharan Africa [1].

Meta-analysis studies conducted in developed [4] and developing countries [5] did not show a significant association between HAART and sexual behavior. A systematic review of investigations from developing

countries [5] involved only three studies [6-8], two of which were from Uganda. This review highlighted the dearth of studies on the association between HAART and sexual behavior from sub-Saharan Africa. As HIV treatment becomes more widely available in developing countries such as those in sub-Saharan Africa, assessing the effect of such treatment on sexual risk behavior in these countries becomes critical. Whether this lack of association has persisted during the course of the evolving HIV epidemic in sub-Saharan Africa and the increased access to HIV therapy remains undocumented.

The health improvement benefits of HAART highlight the importance of assessing the impact of HAART on sexual behavior among patients on therapy. Concerns have been raised worldwide that improvements in health status and quality of life of HIV-infected patients due to access to effective treatment with HAART may increase opportunities for continued high-risk behaviors [9]. In Uganda, there are several reasons to think that HAART accessibility may impact negatively on behavior: data on sexual behavior of HIV patients and its trends over time indicate that reduction in high-risk sexual behavior has been inconsistent over time and across age-groups, with some studies indicating an increase and others a reduction in high-risk behaviors [8,10-12]. Recent cross-sectional studies in Uganda [13,14] indicate that patients using HAART continue to manifest high-risk behavior, such as multiple and concurrent sexual partnerships. Since they are associated with clustering of sexual risk behaviors, multiple and concurrent sex partners are especially important in promoting HIV transmission [15,16]. High-risk sexual behavior in patients on HAART is a major social and public health problem. If HIV-positive individuals continue to have unprotected sex with HIV-negative persons or persons of unknown HIV status, such behavior may continue to spread HIV infection, even increasing risk of HIV super-infection [17,18].

The studies that showed no association between HAART and high-risk behavior [5] were conducted between 2002 and 2005 (before HAART became widely available and affordable). Since 2004, access to HAART has increased in resource-limited settings because of the increased international commitment to providing therapy, funding from the Presidential Emergency Fund for AIDS Relief (PEPFAR), and availability of generic drugs. The aim of this review was to assess the impact of initiation of HAART on high-risk behavior in sub-Saharan African settings.

Methodology

Data sources

We searched electronic databases including the U.S. National Library of Medicine's (NLM) Gateway system, AIDSLINE, National Library of Medicine (Medline) EMBASE, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) for articles published from January 2002 through January 2010. The search terms used included "Antiretroviral therapy and sexual behavior", "Antiretroviral drugs sexual behavior", "HAART and sexual behavior", "antiretroviral therapy and risk behavior", "HAART and HIV transmission", "Persons living with HIV/AIDS and risk behavior in the era of antiretroviral therapy", "medical treatment of HIV and risk behavior", "HAART, risk behaviors and HIV", " medical care and sexual behavior in the era of HAART", "medical care, risk behaviors and HIV", and "medical treatment, HIV, and risk behavior". The search was limited to "sub-Saharan Africa", and "heterosexual HIV transmission".

Search strategy

To identify published articles not obtained from electronic databases, tables of contents of the following journals were scanned: *AIDS*, *Sexually Transmitted Infections*, A*IDS and Behavior, AIDS Patient Care and Sexually Transmitted Infections*, *AIDS Care*, *AIDS Education and Prevention*, *PLOS One*, *PLOS Medicine*, *The Lancet*, *Journal of Infectious Diseases*, *Journal of Infections in Developing Countries*, and all the BioMed Central journals. Using a snowball procedure, we checked the reference lists of articles selected to further identify potential articles for inclusion, until no new articles could be obtained. The figure shows a flowchart that indicates the selection of articles for the systematic review. Initial exclusion of studies was performed by the first author of all qualitative studies, case reports, commentaries, and opinion articles, based on the article titles and abstracts. The remaining articles were then reviewed and classified into the following categories: (1) articles qualifying for inclusion in the synthesis; (2) articles providing background information; and (3) articles providing explanation of the relationship between HAART and high-risk behavior. Full texts of all the identified articles were obtained and read. Finally, only studies conducted in sub-Saharan Africa among HIV patients using antiretroviral therapy, where a longitudinal study design was employed and where behavioral outcomes were reported were included.

Data extraction

The table shows the methodological rigor scores of the studies used in the systematic review of impact of HAART on high-risk behavior. A detailed procedure was used to identify and code the objectives, study design, setting and context of each study, study location, sample population (especially gender and age distribution, sample size, sampling strategy), comparison that was performed between groups, intervention received, loss to follow-up (why and how these were minimized), data analysis process, steps taken to control for confounders, outcome measures, key findings, conclusions, and main limitations. The studies were scored according to the following criteria where each scored one mark: (1) longitudinal study design such as prospective or retrospective cohort; (2) presence of a referent or comparison group; (3) quasi-experimental design where data of pre/post intervention is available; (4) random assignment of the intervention; (5) comparability of participants on baseline characteristics; (6) comparability of participants at baseline regarding the outcome measures; (7) comparison of high-risk behavior outcomes; (8) efforts to minimize loss to follow-up. Only three studies [21,22,24] scored at least 5 on the methodological rigor, indicating that 11 studies had low rigor.

Results

The figure shows a flowchart that indicates the selection of articles for the systematic review. From database and journal searches of titles and abstracts, 190 articles were identified. Of these, 98 were excluded on the initial screening for not meeting inclusion criteria. The full-text versions of the remaining 92 articles were screened further. Of these, 50 were excluded from the systematic review (for reasons such as unclear study designs, outcomes or unclear relationship between HAART and sexual behavior variables), but used in the literature review, while 28 were entirely excluded. Finally, 14 articles [6-8,19-29] met the criteria for inclusion in this review as primary articles.

Methodological rigor

Most studies had low rigor, as only three [21,22,24] scored at least 5 on methodological rigor. Limitations found in the reviewed studies were reliance on self-report of sexual behaviors, convenience, consecutive or other non-random sampling, assessment of health facility-based populations, and failure to adjust for major confounding variables or failure to assess any interaction effects in the predictor variables. In some studies, patients had been on HAART for a short duration of less than two years. Self-reported sexual behavior is limited in reliability by both recall and social desirability bias. Social desirability bias may have been exacerbated in the study by Bunnell *et al*. [8], counselors who provided on-going risk reduction counseling also administered interviews. For all the studies, the interviewers were not the same people who provided the clinical services; however, the studies did not adjust for potential confounders. For instance, Bateganya *et al*. [7] found that HAART-using and non-HAART-using groups were not comparable on socio-demographic variables such as sex, employment, age, residence, education level and monthly income, but did not adjust for gender or employment status. In this study, the mean duration of ARV therapy was 1.6 years; HAART-using patients had a higher mean Karnofsky score compared to HAART-naïve patients (93 versus 83, $p = 0.001$). HAART-experienced patients were significantly more likely to be male (OR 1.43, 95% CI 1.04–1.95), employed (OR 1.97, 95% CI 1.36–2.85), less likely to be younger than 37 years of age (OR 0.39, 95% CI 0.29–0.54), less likely to reside in an urban area (OR 0.21, 95% CI 0.14–0.32), and less likely to have university or tertiary education (OR 0.24, 95% CI 0.17–0.35) or earn less than $50 United States dollars monthly (OR 0.29, 95% CI 0.21–0.41). In most studies only bivariate (unadjusted) comparisons are presented as multivariate analysis was not conducted.

Number of sexual partners

In the cross-sectional study from Kenya [20], patients receiving HAART were less likely to report multiple partners compared to those receiving preventive therapy for opportunistic infections ($p = 0.006$). In this study, preventive therapy included counseling on sexual behavior, provision of isoniazid chemoprophylaxis to prevent tuberculosis, and co-trimoxazole to prevent opportunistic enteric and pneumococcal infections, without any antiretroviral therapy. Most respondents reported sex with regular partners. More participants receiving HAART reported sexual intercourse with regular partners ($p = 0.044$) and fewer episodes of sexual intercourse with casual partners ($p = 0.001$) compared to those receiving preventive therapy.

Table 1. Methodological Rigor Score of the articles used in the meta-analysis of impact of HAART on sexual behavior

Author	Cohort	Control or comparison group	Pre/post intervention data	Random assignment to intervention	Random participant selection for assessment	Follow-up rate over 80%	Comparison groups equivalent on socio-demographic data	Comparison groups equivalent at baseline on outcome	Score
Moatti, 2003 [6]	No	Yes	No	No	No	n/a	No	n/a	1
Bateganya 2005 [7]	No	Yes	No	No	No	n/a	No	n/a	1
Bunnell 2006 [8]	Yes	Yes	Yes	No	No	Yes	n/a	n/a	4
Skogmar 2006 [19]	Yes	Yes	No	No	No	n/a	No	No	2
Eisele 2008 [24]	Yes	Yes	Yes	No	No	n/a	Yes	Yes	5
Luchters 2008 [21]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	6
Sarna 2008 [20]	No	Yes	No	No	No	n/a	Yes	No	2
Diabate 2008 [22]	Yes	Yes	Yes	No	No	Yes	Yes	no	5
Maier 2008 [25]	No	Yes	No	No	Yes	n/a	No	n/a	2
Homsy 2010 [26]	Yes	Yes	No	No	No	n/a	Yes	n/a	3
Peltzer 2010 [23]	Yes	Yes	No	No	No	Yes	Yes	No	4
Venkatesh 2010 [28]	Yes	Yes	No	No	No	Yes	No	n/a	3
Kaida 2010 [27]	No	Yes	No	No	No	n/a	Yes	n/a	2
Andia et al 2010 [29]	No	Yes	No	No	No	No	yes	n/a	2

n/a = data not available

Condom use

Condom use at last sexual intercourse was significantly higher among HAART users regardless of partner type. Bateganya *et al*. [7] found that condom use at last sexual intercourse with a spouse was 71% for HAART-using patients compared to 47% for non-HAART-using patients (95%CI: 1.7-4.6). In the longitudinal study by Bunnell [8], condom use at last sexual intercourse increased significantly from baseline to follow-up among participants with HIV-negative or unknown partners (59% to 82%, 95% CI: 1.7-5.8) and with HIV-positive partners (58% to 74%, 95% CI: 1.4-3.7). In this study, the episodes of unprotected sex acts with a partner whose HIV status was negative or unknown declined significantly by six months after initiating HAART, (by as much as 70%) and there was a much higher reduction (75%) in unprotected sex encounters among men (5.4 acts vs. 1.3 acts, $p = 0.02$) compared to 58% reduction for women (3.5 acts versus 1.5 acts, $p = 0.03$). Likewise, the estimated risk of HIV transmission to partners of negative or unknown status declined from 45.7 per 1,000 person years at baseline to 0.9 per 1,000 person years at follow-up, representing a 98% decrease. However, over 85% of unprotected sexual intercourse (with a partner who was HIV negative or of unknown HIV status) occurred within married couples, implying persistent risk of HIV transmission.

Sexual abstinence and frequency of sexual intercourse

In all the studies, participants often reported practicing sexual abstinence. However, higher rates of sexual abstinence, as indicated in the number of current sexual partners and frequency of sexual

intercourse, was more frequent in patients on HAART. Whereas Moatti *et al*. [6] found that HAART patients were more likely to report that the last sexual encounter was with a main sexual partner compared to non-HAART patients (95.6% vs. 86.8%, p = 0.02), Bateganya *et al*. [7] found no difference in the unadjusted percentage of HAART and non-HAART patients reporting multiple sexual partners in the last six months (34% vs. 35%, Unadjusted OR: 0.96, 95% CI: 0.60-1.52). In the Kenyan study by Sarna *et al*. [20], of the 45% of study participants who reported sexual intercourse in the reference period, there was no difference in self-reported sexual activity between participants receiving HAART and those receiving preventive therapy (44% versus 47%; $p = 0.476$). In this study, sex, education, employment, and study group (HAART-using or preventive therapy only) were not associated with sexual activity. On multivariate analysis, age and marital status were independent predictors of sexual activity, as older participants were less likely to report sexual activity compared to younger participants (OR: 0.94; 95% confidence interval [CI]: 0.91–0.97; $p = 0.001$). Likewise, married or cohabiting respondents were 8.3 times more likely to report sexual activity compared to single/divorced/widowed respondents (95% CI: 4.96–14.14; $p = 0.001$). In longitudinal studies [8,24], the percentage of patients who were sexually active as well as the number of sexual partners either did not increase or decreased significantly at follow-up when HAART users and non-HAART users were compared.

Disclosure of HIV status

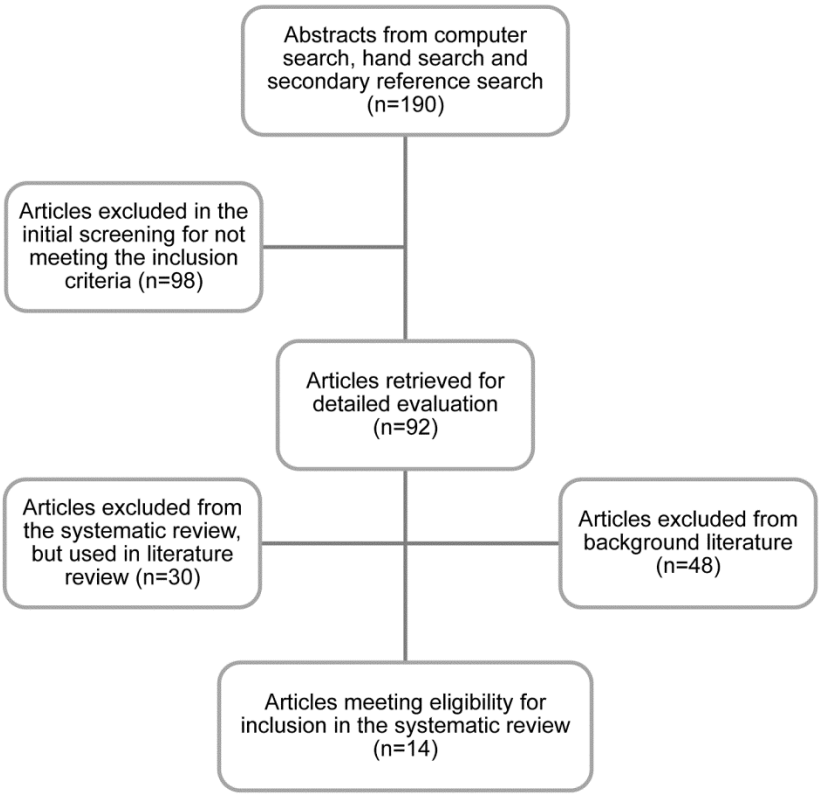
Only three studies reported in detail on sero-status disclosure among patients on HAART. In the study by Bateganya *et al*. [7], HAART-experienced using patients were significantly more likely than ARV-naïve patients to have disclosed their HIV status to their spouses (OR 1.57 95% CI 1.07–2.30). However, there was no significant difference between the two groups regarding disclosure to "other" or casual sexual partners (OR 1.56 95% CI 0.88–2.76) or in knowledge of a partner's sero-status (OR 1.12 OR 0.82–1.55). In addition, regarding awareness of their partners' status, of 348 who were sexually active, only 213 (61%) were aware of their partners' HIV sero-status. Overall, participants who knew the HIV status of their sexual partners were more likely to report sexual intercourse in the prior six months (OR 2.5 95% CI 1.8–3.4). Finally, HAART use was not significantly associated with knowledge of partner HIV sero-status (OR 1.56 95% CI 0.97–2.53). In the study by Skogmar *et al*. [19], there was no association between ARV use and disclosure. In the Kenyan study [20], more HIV-positive participants receiving HAART reported sexual intercourse with regular partners ($p = 0.044$) and fewer episodes of sexual intercourse with casual partners ($p = 0.001$) compared to those receiving preventive therapy, even though over 40% of respondents in both groups were unaware of the HIV status of their regular partners. There was no difference among groups with regard to knowledge of partner's status or disclosure of HIV-status to regular partners. In our review, we consequently concluded that there were no differences in disclosure of HIV status to primary or main sexual partners for patients on HAART and those not on HAART. There were also no statistically significant differences in disclosure by gender of respondent.

Acquisition and treatment of sexually transmitted infections (STIs)

Acquisition of new STIs indicates inconsistent condom use, having unprotected sex, and acquisition of new sexual partners. All these indicate high-risk behavior among respondents or their sexual partners. In our review, Sarna *et al*. [20] found that participants receiving preventive therapy for opportunistic infection (and not on HAART) reported more STI symptoms (OR: 1.7; 95% CI: 1.0-2.8; $p = 0.059$) when compared to patients who were on HAART, with or without preventive therapy. This observation may be explained by the fact that patients on preventive therapy for opportunistic infection (without ART) had more unprotected sexual intercourse compared to those on ART. In contrast, Bateganya *et al*. [7] found that HAART-using patients were more than twice as likely as non-HAART patients to report STI treatment in the previous six months (AOR, 2.6; 95% CI, 1.77-3.82). This finding was inconsistent with all other measures of risk behavior in this study, which found that HAART patients were less likely to engage in risky behavior. All other studies indicated decreased frequency of treatment for STDS. Bateganya *et al*. [7] suggested that their finding of more STIs in patients on HAART may have been the result of better diagnoses and treatment among individuals with more regular access to health care [7]; however, this finding may also reflect the weakness of self-reported data.

Some studies identified an increase in risky sexual behavior among persons on HAART. For instance, the study by Diabate *et al*. [22] identified an increase in risk-taking among treated patients. In this longitudinal study comparing 312 untreated and 303 HAART-

Figure 1. Flow chart showing the selection of articles for inclusion in the systematic review



initiating patients to determine whether HAART is related to sexual risk taking in Côte d'Ivoire, unprotected sex was higher among untreated patients ($p = 0.014$) at enrollment. However, during the course of the follow-up, risk taking was similar ($p = 0.484$) consequent to increase in unprotected sex among treated patients (from 20.4% to 30.1%, $p < 0.0001$). Risk taking remained stable among untreated patients (from 27.0% to 28.8%, $p = 0.301$), suggesting that HAART was associated with sexual risk taking, a fact consistent with the clinical improvements associated with HAART. This observation could also be viewed as a "normalization of sexual behavior with increasing time on ART, a phenomenon that may be associated with improvement in health in HIV-infected patients. In addition, the significant decrease in the intergroup gap (28.8% and 30.1%) over time highlighted an increasing adverse effect of HAART on sexual behavior.

Contraceptive use, pregnancy intention and fertility

Closely related to risky sexual behavior in people living with HIV/AIDS are pregnancy desires, pregnancy intentions and actual fertility in HIV-positive persons, as it is linked to non-use or inconsistent condom use, failure to abstain, and non-use of contraceptives. HIV-infected women face difficult decisions regarding childbearing for several reasons. HIV-infection compromises their immunity, reducing sexual activity, ability to conceive, and ability to sustain a pregnancy to term, in case conception occurs. In the study by Maier *et al*. [25] using HAART was associated with increased odds of fertility desire (AOR 2.99, 95% CI 1.38-6.28), but decreased odds of pregnancy (AOR 0.56, 95% CI 0.33-0.95) and live birth (AOR 0.30, 95% CI 0.13-0.66). In the study by Homsy *et al*. [26] 120 (16.9%) women experienced 140 pregnancies; pregnancy incidence increased from 3.46 per 100 women-years in the first quarter to 9.5 per 100 women years at 24 months ($p < 0.0001$). In addition, younger age (Hazard ratio 2.71 per 10-year decrease, 95% CI: 2.95-3.78) and inconsistent condom use in the previous three months (Hazard ratio 1.79, CI: 1.02-3.13) were independently associated with pregnancy. In contrast, Venkatesh *et al*. [28] found higher contraceptive use among patients on HAART with an odds ratio of 1.56 for injectables (1.27–1.92; $p < 0.0001$) and an odds

ratio for pills of 2.66 (1.70–4.15; $p < 0.0001$). Andia *et al*. [29] found that women receiving HAART were more likely to use contraceptive methods (AOR] 2.64; 95% CI1.07, 6.49), while Kaida *et al*. [27] found no association between HAART use and contraception.

Discussion

With increasing efforts to expand HIV treatment access and advocacy of HAART for secondary prevention of HIV in sub-Saharan Africa, analyzing, quantifying and comparing potential shifts in sexual behaviors over time among populations of HAART initiators is a major priority. Our analysis shows that HAART was associated with reduced sexual risk behavior. These findings are consistent with the results of a meta-analysis of literature from developed countries which found that the likelihood of engaging in unprotected sexual behavior was not higher among persons receiving HAART compared to those not receiving HAART, although they did report a wide heterogeneity of results [4]. The danger of high-risk behavior being manifested by persons with or at high-risk of HIV infection is increased by the fact that HIV infectiousness decreases but does not entirely disappear with therapy. In a study conducted in the United States to evaluate the time course and magnitude of decay in cervical and vaginal HIV-1 shedding as women initiate HAART [30], genital HIV-1 shedding decreased rapidly after HAART initiation, which is consistent with a rapid decrease in infectivity. In a study from Kenya assessing the effect of acquisition and treatment of cervical infection on genital HIV shedding in women on HAART [31], most cervical HIV-1 RNA concentrations were near the threshold for detection, which suggested that HIV infectivity remains low, and thus HAART reduces genital HIV-1 shedding. Another study [32] found a positive correlation between HIV-1 RNA levels and plasma HIV-1 RNA and a negative correlation with the CD4 cell count. In this study, use of HAART was significantly associated with below-detectable levels of HIV-1 RNA in both plasma and the genital tract, suggesting that HIV-1 RNA suppression in the genital tract may occur rapidly after initiating therapy.

Several studies have, however, reported that although genital shedding of HIV decreases after initiation of HAART, there is often incomplete viral suppression [30,33,34], especially among patients with poor adherence to antiretroviral medication [30] or with concurrent sexually transmitted infections such as herpes simplex virus type 2 infection [34]. The risk of HIV transmission is dependent on an individual's adherence to the HAART regimen, which affects viral suppression, the viral load, and subsequent development of drug resistance in case of poor adherence [35]. Indeed, widespread access to HAART may be able to reduce incident HIV infection [36,37].

The explanation for the phenomenon of increased risk behavior in HIV patients on HAART is that improvement in health and life expectancy of HIV-infected people may lead to a misconception that HIV is no longer a serious disease. Secondly, the significant viral load suppression may lead to the perception that patients on HAART are no longer infectious. Thirdly, the improvement in physical health and quality of life may enable or encourage individuals to resume sexual activity, including unsafe sexual practices (phenomena that have been referred to as treatment optimism or behavioral disinhibition). Some epidemiological studies have indicated persistent high-risk behavior, such as inconsistent condom use, multiple sexual partners, acquisition of new sexually transmitted infections, and concurrent sexual partnerships populations where HIV prevalence is high. Consequently, such high-risk behaviors create a new public health threat through ongoing transmission of the HIV virus and possible transmission of HIV viral strains that have already acquired genetic resistance to existing therapies [38].

The analysis showed no difference in disclosure of sero status between HAART users and non-users. Positive rewards resulting from disclosure include increased social support and intimacy with partners, and reaffirmation of one's sense of self [39,40]. However, negative consequences include risk of stigma and violence [41-43]. Our findings on disclosure are in agreement with the review of 17 studies by Medley *et al*. [44] which also found high rates of non-disclosure and concluded that "barriers to disclosure identified by the women included fear of accusations of infidelity, abandonment, discrimination and violence". Sethosa and Peltzer [45] found that social support was significantly related to disclosure of HIV status, while counseling context and content and counseling satisfaction were not related with HIV disclosure.

In our systematic review, most studies did not reveal statistically significant increase in high-risk behavior in HAART-taking patients compared to patients not taking HAART. Considering that many sexually active patients reported HIV-related risky sexual behaviors such as unprotected sex with persons of unknown HIV status, non-use of condoms, non-disclosure of HIV status, fertility desires and multiple

and often concurrent sexual partnerships, our findings raise several concerns. Heterosexual intercourse is the main mode of transmission of HIV in sub-Saharan Africa. The fact that HAART-taking patients may manifest high-risk behavior [22] is strengthened by the finding in this study that patients with less advanced infection reported unsafe sex more often than those with severe symptoms. In addition, observed changes in unprotected sex among treated patients were more likely to be attributable to those who became sexually active because there was adjustment for sexual abstinence at baseline. Secondly, the increase in risk taking among the treated patients was, partly, initially limited to steady sexual partners as the median number of partners did not increase during follow-up. However, this study suggests it is possible that if the positive outcomes become more evident and stable with time, treated patients could start seeking unprotected sex with casual or sero-discordant partners. Indeed, this study further suggests that more than half of treated patients reported having their last sexual intercourse with a person who was HIV negative or of unknown status. In the study by Bateganya *et al*. [7], HAART significantly enhanced the quality of life and personal sense of well-being of patients who initiated therapy, such that the Kanofsky score of HAART-using patients was higher than that of HAART-naïve patients, enabling many individuals to resume sexual activity.

Regarding fertility intentions and contraception, the HIV/AIDS epidemic remains a serious public health and social challenge, as most affected women are within childbearing age [46]. Several investigations conducted in sub-Saharan Africa have documented reduced fertility among HIV-positive women [47,48], though these studies were conducted before HAART was widely available. The impairment in fertility does not occur during early HIV infection [49] but is marked with disease progression, and reduced fertility has been documented with onset of AIDS in both males and females [50]. Though the mechanisms through which fertility impairment in advanced HIV infection are not fully understood, higher viral load and decreased CD4 counts with advanced HIV disease are possible patho-physiological mechanisms [51]. Since progression to AIDS leads to decreased general health and well-being and the possibility of genital infections, advanced HIV infection may be associated with reduced libido and sexual activity in both males and females. The use of HAART improves general health and may therefore reverse the effects of AIDS on libido and sexual activity. With increased prospects for survival, as well as the related stigma of infection, HIV infected persons may develop fertility desires and intentions, and even go ahead to conceive [25,26]. Though Kaida *et al*. [27] found significantly higher levels of contraception in HAART-using patients compared to the HIV-negative patients the association between HAART and contraception was not statistically significant when HAART users and HAART-naïve individuals were compared. In a longitudinal study from Uganda, ART was associated with increased pregnancy rates in HIV-positive women, mainly those with higher CD4 counts and good immunologic response to therapy, suggesting a need to strengthen reproductive health services for both women and their partners that could address their fertility decisions/intentions, particularly after HAART initiation [52].

The findings of the systematic review somehow contradict the findings from the re-evaluation of the HPTN 052 study findings [53] which showed that HIV treatment reduced the risk of HIV transmission to sexual partners. However, in the re-evaluation, this effect occurred only in patients who started antiretroviral therapy at a CD4 count between 350 and 550 cells/mm^3. The explanation for the findings is that in such patients, many would not have manifested AIDS symptoms, and with good adherence to therapy, the HIV-infected patients may acquire undetectable viral loads, particularly if they do not develop concurrent sexually transmitted infections. In such situations, the risk of HIV transmission through vaginal intercourse to uninfected sexual partners may be low or even negligible, especially in the short term. In this study, the median follow-up duration was only 1.7 years; therefore, it is possible that the situation may be different if treatment is continued for a longer period of time, or if patients who had CD4 counts of less than 350 cell/mm^3 were included in the analysis. It is important to note that in most programs, initiation of HAART occurs for patients whose CD4 count is less than 200 cells/mm^3. Indeed, in the evaluation, the final multivariate analysis showed that baseline viral load, which correlated with CD4 count in most cases, was the strongest predictor of transmission in both groups (hazard ratio 2.84, 95% confidence interval 1.51-5.41). Likewise, consistent condom use at baseline, which reduces risk of concomitant STIs in sero-discordant couples, was highly protective of HIV acquisition in the HIV negative partners (HR 0.33, 95% CI 0.12-0.91).

The findings of this systematic review, that HAART is rarely associated with increases in high-risk behavior among HIV-positive individuals, is limited in several ways and should be interpreted with caution. Most studies were health-facility based and employed non-random (convenience or consecutive sampling). Such patients are not representative of all HIV patients and may be a select population with appropriate health seeking behavior. Secondly, in most studies, the numbers are not large enough to analyze confounding by gender, age or duration of HIV infection. Thirdly, in most of the studies, behavior was by self-report, which makes the results subject to reporting bias. Lastly, most studies were before/after or cross-sectional in nature and of low methodological rigor. As HAART is the standard of care, it would be unethical to randomize participants into intervention groups receiving HAART and control groups not given HAART.

In addition, despite showing no statistically significant association, many studies revealed that high-risk behaviors were common among HIV-positive HAART-taking patients, and several studies mentioned this occurrence. For instance, in a study that assessed sexual behavior of HAART-taking HIV patients attending an urban HIV clinic in Kampala, unprotected sex reduced over time, but women reported unprotected sex more often than men and disclosure of HIV status was low [54]. A cross-sectional study conducted in an ART clinic in Nairobi urban slums [55] reported inconsistent condom use especially common among women and patients who had recently started HAART, at a time when infectiousness is high. Likewise, having multiple partners was common, especially among married men, with the potential of creating sexual networks and an increased risk of HIV transmission.

The success of HAART in reducing morbidity and mortality from HIV/AIDS has been widely documented worldwide. Indeed, low viral load may reduce the level of infectiousness of HIV-positive persons receiving HAART; however, negative consequences include increased prevalence of unprotected sex and increased incidence of sexually transmitted infections (STIs). HIV transmission risk in patients on HAART is low only if the following conditions are met: the HIV-infected patient is receiving HAART with excellent adherence; patients disclose their HIV status and inquire about HIV status of their sexual partners; the viral load is consistently undetectable for a long time; and no sexually transmitted infections (STIs) are present in either partners. The above conditions are not met in many sub-Saharan African settings, as many studies [56-61] report that sub-optimal adherence, high fertility intentions, and risk factors for acquisition of STI (such as multiple sexual partners, and inconsistent condom use) are common. In many settings in sub-Saharan Africa, such as eastern and southern Africa, high-risk behaviors occur in HIV patients before and after initiating HAART [62-65].

Conclusion

As HAART becomes increasingly available in many African communities, it is important to understand its effects on sexual behaviors, as this has implications for the spread and control of the HIV epidemic. While HAART has reduced mortality and morbidity from HIV infection and thus improved the well-being of many people living with HIV, the perceived threat of HIV has decreased. With increased HIV treatment optimism and beliefs that HAART eliminates the risk for HIV transmission, the concerns that some patients continue with high-risk behaviors are genuine. As patients regain health and return to their productive lives, they resume sexual activity, have multiple sexual partners, acquire new partners, fail to use contraception, or even desire to have and go on to have children. The context of HIV treatment varies widely across projects and programs in many countries, with differences among countries and often between settings in the same country, depending on differences in health system factors and differences in available support services such as counseling and laboratory support services. There are also differences in clinical guidelines followed for initiating or switching therapy. Primary and secondary prevention efforts targeting high-risk sexual behaviour among HIV-positive persons, emphasis on treatment adherence to ART, and effective and sustained counseling should be strengthened in all HIV treatment programs and guidelines so that secondary prevention messages in HIV/AIDS care and treatment settings could yield more positive results. There is also need to strengthen laboratory support services for monitoring treatment outcomes as well as adverse outcomes such as treatment failure and drug resistance

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