

**Partner Disclosure And Early CD4 Response Among HIV-Infected Adults Initiating
Antiretroviral Treatment In Nairobi, Kenya**

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Abstract

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Background: Disclosure of HIV sero-status can have significant positive implications for people living with HIV/AIDS. However, there is limited data on whether partner disclosure influences ART treatment response. **Methods:** We conducted a retrospective cohort study of recently diagnosed, ART-naïve HIV-infected adults (>18 yrs) who enrolled at the Coptic Hope Center in Nairobi, Kenya between January 1st 2009 and July 1st 2011 and initiated ART within 3 months. Analysis was restricted to adults who had a partner/spouse and reported to either disclose or not disclose HIV status to a partner/spouse. CD4 counts were analyzed at baseline, 6 and 12 months after ART initiation. **Results:** Seventy six percent of adults reported they had disclosed their HIV-status to a partner/spouse. Those who disclosed were significantly younger and more likely to be married/cohabitating. At baseline, there was no statistically significant difference in median CD4 count between disclosure groups. At 6 months following ART, those who disclosed experienced significantly higher CD4 counts than those who did not, after adjusting for age, gender, baseline CD4 count, and married/cohabitating status ($B = 19$, 95% CI 0.3 to 38 $p=0.046$). **Conclusion:** Our results suggest that partner disclosure is associated with CD4 recovery following ART initiation.

Background

Disclosure of HIV serostatus can have significant positive implications for people living with HIV/AIDS (PLWHA). Disclosure to one's social support network has been associated with decreased anxiety, depression, stigma and increased feeling of acceptance and a sense of strengthened relationships [WHO 2004, Kalichman 2003, Pryzbyla 2013]. In the era of effective combination anti-retroviral therapy (ART), disclosing HIV status to one's support network has been linked to increase ART use [Waddel EN 2006], retention in care [Halperin 2013] and uptake of important services such as prevention of mother to child transmission (PMTCT) [Sendo 2013, Farquhar 2004]. Disclosure to sexual partners has the added public health benefit of allowing informed choices that lead to risk behavior reduction [Bachanas 2013 Crepaz 2003] and other efforts to prevent transmission to partners such as pre-exposure prophylaxis [Brooks 2011]. In sub-Saharan Africa where the global burden of HIV is the greatest and where approximately two thirds of overall HIV incidence is estimated to occur in steady couples [Chemaitelly 2014], partner disclosure continues to be a major point of emphasis in HIV testing and counseling programs [WHO 2004].

With the advent of ART, long-term outcomes for PLWHA have vastly improved through sustained viral suppression and effective immune recovery. An adequate CD4 response to ART is defined as an increase in the range of 50 to 150 cells/ μ L per year. Subsequent increases in those with good virologic control average approximately 50 to 100 cells/ μ L per year until a steady state level is reached. Factors including low pre-treatment CD4 count, older age, and male gender may attenuate CD4 response following ART [AIDS info 2013] [Corbeau 2011] [Kelley 2009]. Rates of CD4 response have direct clinical implications since immunosuppression increases risk for opportunistic infections.

HIV-infected persons who disclose their status to their social support network, specifically partners, may find support that motivates ART adherence. Those who disclose to their partners can gain social and emotional support as well as practical support in the form of assistance with care appointments and treatment reminders. In steady partnerships, partner disclosure can provide an open home environment where pill taking does not need to be concealed. Furthermore, knowledge that ART adherence prevents partner transmission may provide added motivation[Cohen2012]. In these ways, partner disclosure can promote improved ART adherence and improve clinical outcomes.

Despite the benefits of disclosure, there is limited data on whether partner disclosure influences ART treatment response. In a recent study involving a small US cohort (n=36) , patients who disclosed to their support network had a trend towards higher mean CD4 counts at baseline and 2 years after ART than those who did not [Halperin 2013]. There have been no published studies to our knowledge evaluating influence of partner disclosure on CD4 recovery following ART.

In this study, we compared immunologic response to ART in HIV-infected individuals who report disclosing their HIV status to their steady partner (disclosers) versus those who do not (non-disclosers) at the Coptic Hope Center for Infectious Diseases in Nairobi, Kenya.

Methods

We conducted a retrospective cohort study using data obtained from the Coptic Hope Center for Infectious Disease in Nairobi, Kenya. The Hope Center has provided free ART to HIV-positive individuals since 2004. The Hope Center is funded by the President's Emergency Plan for AIDS Relief (PEPFAR) and administered by the Coptic Orthodox Mission with support

from the University of Washington, and has enrolled over 20,000 clients and provided over 15,000 clients with free ART. ART is routinely initiated for patients with WHO stage I or II if $CD4 \leq 350$ cells/ul, WHO stage III or IV irrespective of CD4 count, and any HIV-infected patient co-infected with either Tuberculosis (TB), Hepatitis B with evidence of liver disease, and any patient with HIV associated nephropathy. First-line therapy consists of two nucleoside reverse transcriptase inhibitors (NRTI) [i.e. tenofovir (TDF), lamivudine (3TC), zidovudine (AZT) and stavudine (d4T)] and one non-nucleoside reverse transcriptase inhibitor (NNRTI) [i.e. efavirenz (EFV) or nevirapine (NVP)]. Prior to ART initiation, clients undergo two weekly counseling sessions on adherence, as well as evaluation by clinical officers and nutritionists.

Hope Center adult clients (>18 years of age) who enrolled as new patients between January 1st 2009 and July 1st 2011 were eligible for this analysis. We included adults who at enrollment were recently diagnosed with HIV (i.e. having their first confirmatory test within 3 months), were ART-naïve, initiated ART within 3 months of enrollment, identified themselves as having a spouse or a steady partner, had a partner disclosure status documented on enrollment interview. At enrollment, all clients were interviewed using standard forms to capture basic demographic information such as age, gender, educational level and employment status.

Information regarding steady partner/spousal relationship status and serostatus disclosure is obtained during pre-ART counseling sessions from trained counselors and are recorded on standardized forms. Using a standardized questionnaire, the client is asked, “how many spouse(s) or steady partner(s) do you have?”. In reference to disclosure, the client is asked, “have you revealed your status to” the separate categories of “spouse(s) or steady partner(s)”, “casual or non-casual partner(s)”, “parents”, “siblings” “children”, “friends” and “others (specify)”. The answer is recorded as “all” “some” “none” or “has no partner / spouse / parents /

siblings / children / friends”. Any client with “00” to the steady partner questionnaire, or answered, “has no partner” to the disclosure questionnaire, was determined not to have a steady partner and was excluded from analysis. A client was determined to have disclosed to their partner, if they had answered “all” or “some” to the “spouse(s) or steady partner(s)” category of the disclosure questionnaire. Partner non-disclosure was determined if the client had answered “none” to the “spouse(s) or steady partner(s)” category of the disclosure questionnaire. Clients with unrecorded answers to the steady partner or disclosure questionnaire were excluded. Any client with discordant or inconsistent answers between the steady partner and disclosure questionnaires (e.g. “01” to the steady partner questionnaire, and “ has no partner” to the disclosure questionnaire) was also excluded from analysis.

As part of routine care for clients on treatment, clients are evaluated every 3 months and CD4 counts [BD FACSCalibur, San Jose, California] are measured at baseline and approximately every 6 months. CD4 measurements were taken before ART initiation and at 6 and 12 months after initiation within a 60-day time window. For follow up immune recovery analysis, we included clients who had CD4 measurements at both 6 and 12 months following ART initiation. Those who were missing both 6 and 12 month CD4 count were excluded. Those who were missing CD4 count at either 6 or 12 months were also excluded.

Chi square statistics were used to measure differences between categorical baseline characteristics (gender, married/cohabitating status, secondary education or higher, employment). A two-sample t-test was used to measure differences between normally distributed continuous baseline variables (i.e. age, time to ART initiation). Wilcoxon-Mann-Whitney test was used to determine significant differences between baseline CD4 measurement, 1st CD4 measurement post-ART (6 month) and 2nd CD4 measurement post-ART (12 month).

Multivariate linear regression was used to determine differences in CD4 response from baseline to 6 months and from baseline to 12 months, adjusting for age, gender, baseline CD4 count and other significant baseline differences identified between the exposure groups. All analyses were performed using Stata/SE 11.2 software (StataCorp).

Results

Between January 2009 and July 2011, 3414 adults were enrolled at the Hope Center and were available for review (Figure 1). Of these, 246 (7%) were not diagnosed within 3 months of enrollment, 286 (8%) were ART-experienced and 1262 (37%) did not initiate ART within 3 months of enrollment. Seven hundred and two (21%) were excluded because they did not have a spouse or steady partner, 100 (3%) had incomplete data regarding disclosure or partner status, and 203 (6%) did not have CD4 measurements at either month 6 or month 12, or both.. At 6 months, 675 (20%) were retained in follow-up and had CD4 data. At 12- months, there were 615 (18%) HIV-infected adults who were retained in follow up and had CD4 data for analysis.

Baseline characteristics at enrollment Among 615 adults in the analysis cohort, 52% were men (Table 1). The mean age was 38.3 years [95% Confidence Interval (CI) 37.6-39.0), and most individuals were married or cohabitating (90%), had a secondary education or higher (73%) and were employed (78%). Most (76%) reported that they had disclosed their sero-status to a partner/spouse. At baseline, disclosers were significantly younger than non-disclosers (37.8 years of age, versus 40.0, $p < 0.016$) and more likely to be married or cohabitating (93% versus 80%, $p < 0.001$) (Table 1). There was no difference in the median time to initiate ART from enrollment between both groups (30.2 v 29.3 day $p = 0.53$). At baseline, the median CD4 count

was not significantly different between disclosers (134 cells/ μL) and non-disclosers (119 cells/ μL ; $p=0.15$) [Table 2]

Follow-up immune recovery on ART Overall, at 6 months CD4 increased by a median of 100 cells/ μL [Interquartile Range (IQR) 48 - 172]. At 6 months after ART initiation, disclosers had a significantly higher median CD4 count compared to non-disclosers (227 cells/ μL v 212 cells/ μL ; $p< 0.03$) [Figure 2]. . At 12 months, there was a trend for higher median CD4 count among disclosers than non-disclosers (256 cells/ μL versus (228 cells/ μL , $p=0.08$). In multivariate analysis, the baseline characteristics that were significantly associated with CD4 response at 6 months were pre-treatment CD4 count ($B=0.96$, 95%CI 0.84 to 1.1, $p<0.001$) and age ($B=-1.3$, -2.4 to -0.18 $p=0.023$). Gender and marital/cohabitation status were not significantly associated with CD4 response at 6 months (data not shown). Multivariate linear regression for age, gender, married/cohabitating status and baseline CD4, demonstrated significantly higher CD4 counts among disclosers after adjustment for these covariates at 6 months on ART ($B = 19$, 95% CI 0.3 to 38 $p=0.046$), but not at 12 months ($B = 8.8$, 95% CI - 12.9 to 30, $p=0.43$)

Discussion

In our retrospective cohort of new enrollees initiating ART who had follow up at 6 and 12 months following ART, we found that the majority (76%) had disclosed their HIV serostatus to their partners. At baseline, disclosers were younger and more likely to be married or cohabitating with their partners compared to non-disclosers. At 6 months after ART initiation, disclosers were found to have a significantly higher CD4 count compared to non-disclosers. At 12-months post ART there was also a trend for higher CD4 in this group.

The low prevalence of partner non-disclosure (24%) that we observed is similar to that observed in other studies in sub-Saharan Africa. Vu and colleagues surveyed 958 individuals (on or preparing for ART) from multiple sites in Capetown, South Africa and found a 20% prevalence of partner non-disclosure [Vu 2012]. A study at two hospital-based clinics in Johannesburg observed a non-disclosure prevalence of 21% [Skogmar 2006]. Similar to our study, both of these studies also observed a higher prevalence of non-disclosure among older clients and those not living with their spouse or partner. Observational studies in both resource rich and limited settings have shown that HIV-infected older adults are less likely to disclose to partners, friends and family [Emler 2006] [Shacham 2012]. [Medley 2004, Farquhar 2000]. This may be related to an increased sense of stigma as well as stigmatizing beliefs related to HIV [CDC 2000]. Though our study was not designed to assess stigma, multiple studies set in sub-Saharan Africa have shown a significant negative association between stigma and disclosure [Tsai 2013] [Vu 2012].

Our study found a significantly higher proportion of disclosure among partners who were married or cohabitating with their partner. In their South African cohort, Vu and colleagues showed that the odds of disclosure were 1.7 times higher among clients living with their partner [Vu 2012]. Cohabitation not only reflects a lack of spatial privacy, which would make concealing ART and HIV sero-status challenging, but may also suggest a higher degree of emotional intimacy between partners, which may translate into a greater sense of shared responsibility. In one US based study, HIV-positive individuals reported a greater sense of responsibility to disclose to partners with whom there was a shared emotional relationship and this sense of responsibility was lower or absent for non-primary partners [Larkin 2005].

We found that disclosers had a significantly higher CD4 count at 6 months after ART initiation than non-disclosers. This CD4 difference at 6 months after ART initiation likely reflects early ART-adherence patterns following treatment initiation between the two groups. In contrast to self-reported adherence measures, biologic measures such as CD4 and viral levels are not prone to the challenges of reporting bias and measurement options in adherence measurement [Kagee 2012]. Our study provides important complementary evidence regarding the potential benefits of disclosure. It is well known that suboptimal adherence predisposes to suboptimal treatment response [DHHS 2012]. The relationship between disclosure and treatment adherence has also been well studied [Katz 2014]. In a cross-sectional study in rural Zambia, partner disclosure and knowledge of partner status was associated with improved adherence [Birbeck 2009]. Similarly, in a US-based cross-sectional study assessing ART adherence tracked by bottle cap devices, and self-reported disclosure, there was higher adherence among those with HIV disclosure [Stirratt 2006]. Conversely, non-disclosure may limit the number of potential support persons that can assist with HIV care appointments and treatment reminders. Qualitative research in South Africa has suggested that a treatment supporter (i.e. clinic buddy) is a valuable aid in promoting adherence, especially among partners [Nachega 2007]. Non-disclosure may inhibit individuals from taking ART openly, thus increasing omission of doses. Disclosure-related reasons for missing ART doses as “I didn’t want others to notice me taking medication” and “ I was with people who didn’t know I were HIV+” were noted in a South African study [Stirratt 2006]. The authors found that those who were non-adherent for disclosure-related reasons had lower rates of adherence motivation and higher rates of depression.

When assessing immune response at 12 months, disclosers tended to have higher CD4 counts but not at the significant levels noted at 6 months. Our study population was restricted to patients who had been retained in care to the extent that they had CD4 follow up measurements at both 6 and 12 months on ART. This restriction likely excluded patients with significant difficulties engaging and retaining in care i.e. those most severely affected by stigma and thus most reluctant to disclose status. Our population restriction may have biased any immunologic differences between disclosers and non-disclosers towards the null. Our ascertainment of disclosure was limited to the enrollment visit and non-disclosers may have subsequently disclosed and this could have attenuated differences detected between disclosers and non-disclosers due to misclassification. Qualitative studies have shown that disclosure is a dynamic multidimensional process that occurs over time. In a large cohort HIV-infected pregnant women in Tanzania, prevalence of disclosure was 22% within 2 months to 40% nearly 4 years after diagnosis [Antelmann 2001]. In another study from Tanzania, while more than a quarter of PWLA disclosed within a period of 1 month after diagnosis, about 18% disclosed between a period of 1 to 6 months, 5% between 6 months and one year, and 4% after more than a year [Lugalla 2012]. It is possible that subjects in our study who did not disclose at enrollment could have disclosed during their time in care. Increased time in care would have increased exposure to clinicians and counselors promoting disclosure and self-efficacy.

There are several additional limitations to our study. This was a single-site study in an urban setting in Kenya using retrospective data. We did not have data on adherence and thus could not analyze its potential role as a mediator between disclosure and CD4 response. Our study was restricted to subjects who were retained in care for at least 12 months. We did not control for active co-morbid diseases that can affect CD4 measurements independent of ART.

We restricted disclosure definition to steady partners and excluded disclosure to friends, family, or other social support persons. We assumed that steady partner/spouses represented a significant source of support our subjects. However, there is growing evidence to suggest that disclosure to a partner/spouse is a distinct process from disclosure to close friends, family and the larger community [Dima 2014] and that those who chose to disclose between partners, family and friends may differ [Shacham 2012]. Any association between clinical outcome and disclosure may be more linked to disclosure recipients identified as social supporters independent of their identities as partners. More research is needed to study the effect of type and recipient of disclosure, especially between support persons identified as partners and non-partners, on objective clinical measures.

In conclusion, our study is the first to analyze the association between early CD4 response and partner disclosure among ART-naïve patients initiating treatment. Our results suggest that partner disclosure is associated with CD4 recovery. Our findings support the need for more research to study the dynamics of disclosure and to further investigate the mechanisms of how disclosure effect objective clinical outcomes for HIV-infected patients initiating ART.

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Figure 1: Flow Diagram of Cohort Inclusion

Adults (> 18 years) Enrolled at the Hope Center January 2009 - July 2011

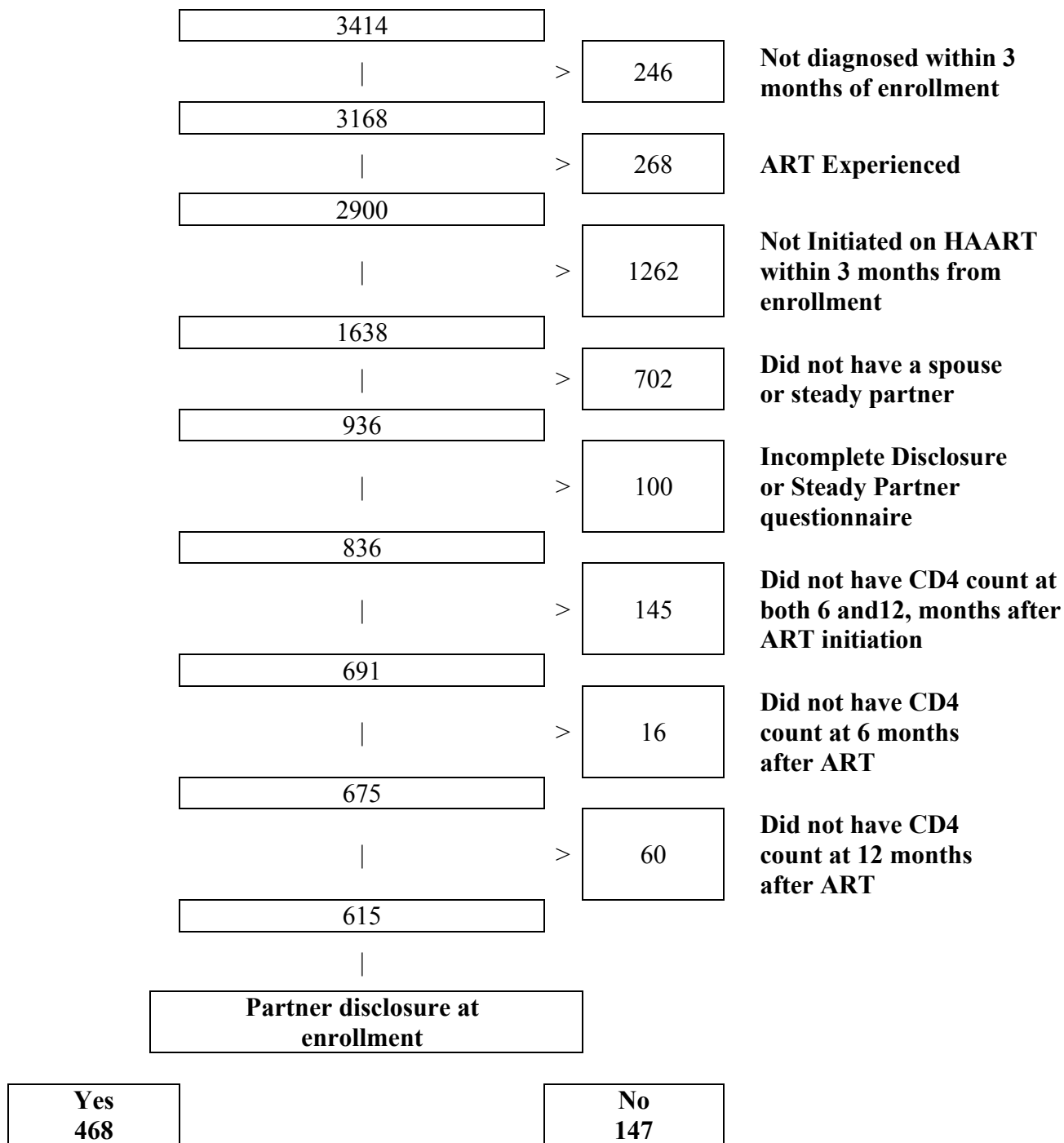


Table 1: Characteristics of adults with steady partners (n=615) initiating ART, by disclosure status at enrollment

	Partner Disclosure at Enrollment			p value
	Total 615	Yes 468	No 147	
Female, n(%)	296 (48%)	227 (49%)	69 (47%)	0.74
Male, n(%)	319 (52%)	241 (51%)	78 (53%)	
Married/cohabitating, n (%)	551 (90%)	434 (93%)	117 (80%)	<0.001
Secondary Education or higher, n (%)	449 (73%)	347 (74%)	102 (69%)	0.26
Unemployed, n (%)	136 (22%)	111 (24%)	25 (17%)	0.09
Age, mean years (95% CI)	38.3 (37.6-39.0)	37.8 (37.0-38.6)	40.0 (38.3-41.3)	0.016
Enrollment to ART initiation, median days (IQR)	30.0 (28.8-31.2)	30.2 (28.8-31.6)	29.3(26.7-31.8)	0.53

Table 2: CD4 measurements of adults with steady partners (n=615) initiating HAART, by disclosure status at enrollment

Time at CD4 measurement	Partner disclosure at enrollment		p value
	Yes (468) Median CD4 cells/ μ L (IQR)	No (147) Median CD4 cells/ μ L (IQR)	
Baseline	125 (51-214)	109 (48-173)	0.15
6 months	227 (141-371)	212 (122-313)	0.03
12 months	256 (164-373)	228 (151-340)	0.08

Figure 2: Median CD4 Count (Interquartile Range) following ART initiation by disclosure at enrollment

