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# HIV Disease Severity and Employment Outcomes in Affected Households in Zambia

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**Abstract**

The relationship between immune status and employment outcomes in HIV-infected patients on long-term antiretroviral therapy (ART) in sub-Saharan Africa and their HIV-affected households is not well understood. We assessed the relationship between CD4+ T-cell counts of ART-treated adults at public-sector clinics in Lusaka, Zambia (median treatment duration 973 days) and labour force participation in the HIV-affected households using clinical and survey data. In multivariable models, patients with a CD4+ count ≥350 cells/µl were 22 percentage points more likely to be engaged in labour (95% CI: 0.02, 0.42) and worked approximately 6 more days per month compared to patients with a CD4+ count <350 cells/µl. A similar relationship between patient CD4+ count and labour participation was observed for other adult family members in the HIV-affected household, but it was not statistically significant. These findings suggest interventions that promote and maintain robust immune recovery on ART may confer economic benefits.

**Keywords**: HIV, Africa, CD4 count, employment, household

## Introduction

In addition to a profound toll in morbidity and mortality, the HIV epidemic in sub-Saharan Africa has had severe economic consequences for HIV-infected individuals, their families, and national economies (1-3). Progressive debilitation from untreated HIV disease reduces the capacity for labour force participation and economic productivity among working-age adults, which negatively impacts the household through reduced income and the burden of caring for chronically ill family members (2, 4-6). However, with the rapid scale up of access to antiretroviral therapy (ART) in sub-Saharan Africa over the past decade, patients are now surviving far longer on treatment. Prior studies found increased labour force participation, income, and other economic benefits among HIV-infected individuals starting ART, but the relationship between the immune status of patients on long-term ART and individual and household economic outcomes are not well described (7-11).

A recent analysis of CD4+ T-cell counts and employment outcomes in 168 HIV-infected Ugandan adults (37% on ART) found that patients with a CD4+ T-cell count over 350 cells/µl worked an average of 6 more days per month than patients with a CD4+ count under 200 cells/µl, and those with a CD4+ count over 500 cells/µl worked 44% more hours per week compared to those under 200 cells/µl (11). A second study in 505 HIV-infected Ugandan adults not yet on ART found lower labour force participation among those with a CD4+ count less than 200 cells/µl compared to patients above that value (9). However, after one year of ART those who started below 200 cells/µl had reached parity with those starting at a higher CD4+ count, and both groups maintained similar trajectories in labour participation going forward.

To date, most studies have assessed the relationship between CD4+ T-cell count and patient employment outcomes prior to or shortly after ART initiation, but there has not been an adequate assessment of how the immune status of patients on long-term ART impacts both patient labour participation and other adult

family members in the HIV-affected household. Using clinical and economic data collected from HIV-infected patients on long-term ART and their households, we assessed whether patient CD4+ T-cell counts were associated with aspects of labour force participation in HIV-affected households in Lusaka, Zambia. We hypothesised that a more robust immune recovery on ART would result in increased labour force participation by the patient, and a reduced care burden would permit other family members to seek employment.

## Methods

*Participant recruitment*

We randomly sampled 179 patients receiving ART at four clinics located in the Bauleni, Chipata, Matero, and Chilenje neighbourhoods of Lusaka. All patients were 18 years of age or older and constituted 7% of the active ART patient population at the clinics. The collection of clinical and economic data for this analysis was performed as part of an impact assessment for a World Food Program-Zambia (WFP) program to provide food baskets to HIV-affected individuals and households in Lusaka, Zambia (12). The patients in this analysis comprise the control cohort at clinics not involved in the food distribution program.

*Data collection*

All participants completed a household survey questionnaire in August 2009. The questionnaire was refined through pre-testing at the Bauleni and Chawama clinics. The survey captured information on household demographics, employment outcomes, household expenditures, income sources, dwelling conditions, and productive and durable assets owned. Clinical data on duration of ART treatment and CD4+ T-cell counts were obtained from the SmartCare electronic database of the Zambian national HIV treatment program. The window period for CD4+ T-cell counts was pre-specified as the value closest to August 1, 2009 within 60 days before or after this date; an approach used by previous similar studies (7, 13). Only 112 of the 179 (63%) patients had CD4+ cell count information within the window period and

formed the analytical sample.

*Key variables*

The survey had a module to capture information on formal or informal income generating work performed by household members over age 18. Examples included farm work, owning a business of any size, and salaried work. Three variables were used to measure employment outcomes. Two were continuous variables; number of hours worked in the previous week and the number of days worked during the previous month. One variable was binary and it measured participation in any income generating work at the time of the survey (coded as 1-yes and 0-no).

*Statistical analyses*

The key independent variable in this study is CD4+ T-cell count. We used a binary classification of CD4≥350 cells/µl and CD4<350, which was based on the 2010 and 2013 WHO recommendations for ART treatment initiation (14, 15), clinical trials and observational studies showing worse health outcomes among patients with a CD4+ T-cell count <350 cells/µl at ART initiation (16-18), and to permit comparisons with prior studies of economic outcomes (11).

Three types of regressions were performed. Ordinary least squares regressions were used to determine the association between the CD4+ T-cell count of ART-treated adult patients and the continuous outcome variables (number of hours worked in previous week and number of days worked in previous month). A probit model was used to examine the association between the CD4+ T-cell count of ART-treated adult patients and the binary outcome variable (i.e., whether the patient participates in any income generating work). A probit regression was utilised to express the effect size in percentage points or marginal effects, which provides a more straightforward interpretation of labour force participation rates, as opposed to odds ratios. All regression models were adjusted for age, sex, an interaction between age and sex, duration of ART and education attainment (i.e. some formal education versus

none). We utilised the same models to assess the relationship between the ART-patient's CD4+ T-cell count and employment outcomes among non-patient adult members in the HIV-affected household.

The regression models were also used to obtain the predicted values of the employment outcomes. Non-parametric regression (kernel-weighted local polynomial regression with a zero degree polynomial) examined the association between the duration of ART and the predicted values of the three employment outcomes by comparing individuals with CD4≥350 and CD4<350. These analyses assessed whether the duration of ART mediates the influence of CD4+ T-cell count on employment. All statistical analyses were performed using Stata/SE 13.1 (StataCorp, College Station, Texas, USA).

*Ethical approval*

Ethical approval was obtained from the University of Zambia Research Ethics Committee and the Ministry of Health of the Republic of Zambia. All participants provided written informed consent.

## Results

The analytical sample is composed of 311 individuals, comprising 112 adult patients receiving ART and 199 non-patient adults. **Table 1** describes the socio-demographic characteristics of the cohort. About 70% of the patients were female compared to nearly 47% of the non-patient adults. On average, patients were older than non-patients by 10 years. The marriage and educational attainment rates of the patients and non-patients are similar. Among the patients receiving ART, the median CD4+ T-cell count was 349 cells/µl (IQR: 245– 481) and the median duration of ART was 973 days (IQR: 523-1434).

*Descriptive statistics of employment outcomes*

**Table 2** shows the means of each employment outcome for patients and non-patients. About 47% of patients with CD4≥350 participated in income generating work compared to around 32% of patients with

CD4<350. The mean number of days worked in the past months were higher for patients with CD4≥350 (16.4 days) compared to those with CD4<350 (12.0 days). For patients with CD4≥350 and CD4<350, the mean number of hours worked in the past week were 18.0 and 13.0 hours respectively.

In households of ART-treated patients with CD4≥350 (high) and CD4<350 (low), the mean number of days worked in the previous month by non-patient adults were 12.2 days and 10.8 days respectively, and the mean hours worked in the previous week were 10.2 and 12.2 hours respectively. Participation in work rates for non-patient adults were lower in households of patients with CD4<350 (30%) than in households of patients with CD4≥350 (38%).

*Association between CD4+ T-cell count and employment outcomes of HIV patients and adult family members*

The adjusted regression estimates in **Table 3** show that ART-treated patients with CD4≥350 were 22 percentage points more likely to be in the labour force than those with CD4<350 (95% confidence interval [CI]: 0.02, 0.42, p<0.05). Patients with CD4≥350 worked 5.97 more days in the previous month than those with CD4<350 (CI: 0.47, 11.47, p<0.05). On average, patients with CD4≥350 worked 9.06 more hours in the past week than those with CD4<350 (CI: -0.02, 18.14, p=0.05).

**Table 4** presents the results for the non-patient adult members living in the households with ART-treated adult patients. The results show that living with a patient with CD4≥350 was associated with a greater likelihood of labour force participation, nearly one more day worked in the previous month, but a two hour decrease in hours worked in the previous week. However these effects were not statistically significant. In results not reported here, we estimated additional models for both patients and non-patient adults which included dummy variables for the residential community for the households, to control for any unobserved location specific confounders. However, the results for both patients and non-patients did

not change.

After estimating the association between CD4≥350 and employment outcomes, we obtained the predicted values of the employment outcomes for the HIV-infected patients receiving ART. Non-parametric regressions (kernel-weighted local polynomial regression with zero degree polynomials) were used to examine whether the association between a high CD4+ T-cell count and predicted employment outcomes varies by the length of time on ART. Comparing individuals with high CD4+ T-cell count (≥350) to those with low CD4+ count (<350) the non-parametric regressions estimated the association between predicted values of the employment outcomes and duration of ART (**Figure 1**). At all points along the distribution of days receiving ART, patients with CD4≥350 consistently had higher probabilities (above 50%) of labour force participation, more days and hours worked than those with CD4<350. The gap between patients with CD4≥350 and those with CD4<350 is largely similar at both the low and high end of the distribution of ART duration, suggesting time-on-treatment was not a major confounder.

**Supplementary Table 1** presents the results for sensitivity analyses assessing the effects of a change in the CD4+ T-cell count threshold to 500 cells/µl, and the addition of the patient's medication possession ratio (MPR) at the time of the survey to the multivariable models. The MPR is a measure of adherence based on pharmacy refill data which is shown to correlate with the risk of virologic failure (19, 20). ART-treated patients with CD4≥500 were 26 percentage points more likely to be in the labour force than those with CD4<500 (CI: 0.02, 0.51, p<0.05). Patients with CD4≥500 worked 5.66 more days in the previous month than those with CD4<500 (CI: 0.47, 11.47, p=0.1). On average, ART-treated patients with CD4≥500 worked 13.23 more hours in the past week than those with CD4<500 (CI: 2.45, 24.02, p<0.05). The results also show that non-patient adults living with a patient with CD4≥500 were also 26 percentage points more likely to be in the labour force than those with living with a patient with CD4<500 (CI: 0.06, 0.46, p<0.05). They also worked 4.7 more days in the previous month, and about 0.62 more hours in the

previous week. However these effects were not statistically significant. When MPR was included in the models assessing a CD4≥350 versus CD4<350 the results were similar to those from the primary analysis in Tables 3 and 4.

**Discussion**

In this analysis of HIV-infected, working-age adults on long-term ART in urban Lusaka, Zambia, we found that a higher CD4+ T-cell count was associated with improved employment outcomes. After accounting for the duration of ART treatment and other factors, we found that ART-treated patients with CD4+ T-cell counts above 350 cells/µl were 22 percentage points more likely to be in the labour force, and they worked approximately 6 more days per month, and 9 more hours per week, than patients with a CD4+ T-cell count below this threshold. A sensitivity analyses showed a CD4+ count over 500 cells/µl was also associated with similar work participation rates for the patients. To our knowledge, this is the first study to assess the effect of CD4+ T-cell counts on labour force participation among patients on long-term ART. Our findings are similar to a recent study by Thirumurthy et al.(2013) of CD4+ T-cell counts and labour force participation among HIV-infected adults in Uganda, the majority of whom (63%) had not yet started ART (11). In that analysis, HIV patients with a CD4+ T-cell count over 350 cells/µl were found to work 6 more days per month than patients with a CD4+ count under 200 cells/µl, while those with a CD4+ count over 500 cells/µl worked 44% more hours per week compared to those with less than 200 cells/µl.

In contrast to prior studies, we also assessed the relationship between the CD4+ T-cell count of ART-treated patients and the employment outcomes of non-patient adults in the same household. We hypothesised that a more robust immune recovery for individuals on ART would result in a reduced care burden and provide greater opportunity for other family members to seek employment. Among non-patient adults in the households of ART-treated patients, we observed a similar directionality in the relationship between the HIV-infected family member's CD4+ T-cell count and labour force

participation, but the results were not statistically significant. However, a sensitivity analysis showed that living with a patient with a CD4+ T-cell count over 500 cells/µl, rather than over 350 cells/µl, was associated with higher and statistically significant labour force participation for non-patient adults in the household. This finding may indicate that more opportunities to work become available as the HIV-infected family member's immune status improves.

We found that patients with a CD4+ T-cell count ≥350 cells/µl had consistently greater labour force participation than those with <350 at differing levels of time spent on ART, suggesting our findings were not primarily due to a longer treatment duration. This area deserves further investigation, as plasma HIV-1 RNA measurements were not a routine component of care in Zambia at the time of the study and we were unable to ascertain whether poor CD4+ T-cell recovery despite a relatively long duration of ART was due to immunologic non-response or inadequate viral suppression. Poor immune recovery and persistent immune activation despite virologic suppression are associated with functional impairment and frailty in HIV-infected adults, though the directionality of this relationship is unclear (21, 22). Future studies should assess whether measurements of virologic suppression and functional capacity after ART initiation (e.g., grip strength or lean mass recovery) can predict patient and household employment outcomes better than CD4+T-cell count (23).

Current guidelines for the initiation of ART in Zambia are a CD4+ T-cell count <350 cells/µl or Stage 3 or 4 HIV disease. However, most HIV-infected individuals present for care in Zambia with CD4+ counts below this level, and up to a third have malnutrition and/or advanced immunosuppression at ART initiation (24, 25). Our finding that ART-treated patients with CD4+ T-cell counts above the Zambian ART-initiation threshold had better employment outcomes suggest that earlier diagnosis and ART initiation may have important individual and household economic effects. Prior studies of untreated HIV infection found debilitation and reduced labour force participation accelerated in the last 2 years before an employee stopped working due to advanced disease or AIDS (2, 4). At the household level, the presence

of a family member with advanced HIV reduced yearly income by 30-35% in one study (6), and resulted in markedly lower agricultural output in farming families (26, 27). At the community level, a high prevalence of untreated HIV disease compounds famine severity (28), while the illness or death of a primary earner increases high-risk sexual behaviours among remaining family members (29, 30) and increases the number of abandoned and orphaned children (31). While we cannot conclude from our study that initiating ART at a CD4+ T-cell count greater than 350 cells/µl (the current guidelines in Zambia) would have beneficial economic effects, our results do suggest that the treatment of HIV prior to advanced immunosuppression confers an economic benefit.

Poverty and food insecurity are associated with reduced clinic attendance, and our results may reflect an effect of a higher pre-treatment economic and employment position on the ability of patients to attend clinic visits, and consequently maintain ART adherence, achieve viral suppression, and promote immunologic recovery (32, 33). Our sensitivity analysis adjusted for MPR rates at the time of the assessment, a measure of adherence shown to correlate with the risk of virologic failure in prior studies (19, 20). The results were very similar to the results of our main models. However, we could not assess prior MPR values or ascertain the presence of antiretroviral resistance mutations contributing to persistent viremia despite a high MPR.

Our study had several limitations. The cross-sectional design precluded the assessment of causal relationships between CD4+ T-cell count and labour force participation. We were also unable to assess the relationships between pre-treatment CD4+ T-cell count, the rate of CD4+ recovery on ART, and economic outcomes. Furthermore, the association between current CD4+ T-cell count and labour force participation may be confounded, in part, by a patient's economic status prior to ART initiation. Patients with greater resources may be more likely to receive HIV testing, seek earlier medical care, and have the resources to attend clinic appointments, maintain adherence, and purchase sufficient food to recover from any HIV-related nutritional deficits. While CD4+ T-cell count is a reliable measure of immune recovery,

future studies should also include measurements of functional status and frailty, particularly in those patients who initiated ART with advanced disease. Additionally, our survey data did not capture other potential confounders of immune recovery such as robust social networks and mental health, which could influence disease severity at treatment initiation, continuity of care, and adherence (34, 35). Among non-patient adults living in the HIV-affected household, we did not assess HIV status due to concerns regarding privacy, response bias, and the potential for undiagnosed HIV infections in our setting, and we were unable to assess the functional capacity of the non-patients. It is also possible that there is a bidirectional association between employment and immune status, a confounding effect that is better assessed with longitudinal data. Lastly, our study cohort was primarily female and drawn from an urban population in Zambia, and the results may not be representative of men, rural populations, or other countries in the region.

In conclusion, we observed a strong association between a CD4+ T-cell count above 350 cells/μl and the labour force participation of patients on long-term ART in Zambia, and a similar directional relationship for adults living in the HIV-affected household that did not reach statistical significance. These findings have implications for testing and linkage to care of HIV-infected persons in sub-Saharan Africa. Treatment initiation at higher CD4+ T-cell counts likely has economic benefits at the household level. Future longitudinal studies are warranted to understand relationships between HIV disease severity and economic status from HIV diagnosis through ART initiation and long-term treatment, with more comprehensive assessments of socioeconomic outcomes such as asset wealth, household food security, and child health and education.

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**Table 1 Description of the participant cohort**

| *Characteristic* | Adult patients on ART (n=112) | Non-patient adults in the same household (n=199) |
|---|---|---|
| | | |
| Female, % | 70.54 | 46.97 |
| No education, % | 15.18 | 15.08 |
| Married, % | 45.54 | 45.73 |
| Age, mean | 40.92 | 30.59 |
| CD4 count, cell/mm3 | | |
| *≥350, %* | 49% | NA |
| *Mean (SD)* | 373 (190) | |
| *Median (IQR)* | 349 (245-481) | |
| Duration of ART, days | | |
| *Mean (SD)* | 978 (505) | NA |
| *Median (IQR)* | 973 (523-1434) | |

Notes: Abbreviations. IQR: interquartile range. ART: antiretroviral therapy

**Table 2: Comparison of household demographics and employment outcomes according to HIV-infected patient CD4+ T-cell counts**

| Households | | | |
|---|---|---|---|
| *Variable* | CD4≥350 n=55 | CD4<350 n=57 | p-value |
| *Female, %* | | | |
| Patients | 84 | 58 | <0.001 |
| Adults living in same household | 45 | 49 | 0.54 |
| *No education, %* | | | |
| Patients | 9 | 18 | 0.19 |
| Adults living in same household | 11 | 21 | 0.05 |
| *Married, %* | | | |
| Patients | 42 | 49 | 0.44 |
| Adults living in same household | 38 | 56 | 0.05 |
| *Age, mean years* | | | |
| Patients | 40.9 | 41.0 | 0.94 |
| Adults living in same household | 31.5 | 29.4 | 0.24 |
| *Participated in income generating work, %* | | | |
| Patients | 47.3 | 31.6 | 0.09 |
| Adults living in same household | 38.4 | 29.9 | 0.21 |
| *Days worked in previous month (mean)* | | | |
| Patients | 16.4 | 12.0 | 0.09 |
| Adults living in same household | 12.2 | 10.8 | 0.59 |
| *Hours worked in previous week (mean)* | | | |
| Patients | 18.0 | 13.0 | 0.26 |
| Adults living in same household | 10.2 | 12.2 | 0.51 |

**Table 3 Association between CD4 count and the employment outcomes of patients**

| | (1) | | (2) | | (3) | |
|---|---|---|---|---|---|---|
| Outcome | Labour force participation ME | | Days worked in previous month | | Hours worked in previous week | |
| CD4 ≥350 cells/µl | 0.22** | [0.02,0.42] | 5.97** | [0.47,11.47] | 9.06* | [-0.02,18.14] |
| Age, per year | -0.012 | [-0.03,0.01] | -0.67** | [-1.24,-0.10] | -0.75 | [-1.71,0.22] |
| Female | -0.71** | [-1.34,-0.08] | -38.7*** | [-67.86,-9.46] | -56.8** | [-105.98,-7.61] |
| Female *x* age | 0.02 | [-0.01,0.04] | 0.82** | [0.15,1.49] | 0.95* | [-0.17,2.08] |
| Days on ART | 2.44E-06 | [-0.0002,0.0002] | 0.001 | [-0.004,0.01] | 0.003 | [-0.01,0.01] |
| No education | -0.19 | [-0.42,0.04] | -4.33 | [-11.26,2.60] | -3.59 | [-15.17,8.00] |
| | | | | | | |
| Observations | 112 | | 106 | | 112 | |

Notes: ME denotes that marginal effects are reported in column 1 (probit regression); patients on ART with CD4≥350 were 22 percentage points more likely to be engaged in economic activity. Regression coefficient shown in columns 2 and 3 represent absolute days and hours, respectively; 95% confidence intervals are in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. No education refers to whether individual was never formally educated. Female *x* age is an interaction of female and age.

**Table 4 Association between HIV-patient CD4 count and the employment outcomes of non-patient adults in the same household**

| Outcome | (1) Labour force participation | | (2) Days worked in previous month | | (3) Hours worked in previous week | |
|---|---|---|---|---|---|---|
| CD4 ≥350 cells/µl in HIV-infected family member | 0.04 | [-0.12,0.20] | 0.91 | [-5.00,6.81] | -2.00 | [-8.96,4.97] |
| Age | 0.01** | [0.00,0.02] | 0.18 | [-0.12,0.49] | 0.43** | [0.07,0.79] |
| Female | -0.23 | [-0.58,0.13] | 0.75 | [-13.09,14.59] | 0.33 | [-16.04,16.69] |
| Female *x* age | -0.001 | [-0.01,0.01] | -0.15 | [-0.57,0.27] | -0.23 | [-0.73,0.27] |
| Days on ART | -0.00003 | [-0.0002,0.0001] | -0.002 | [-0.01,0.003] | -0.01 | [-0.01,0.002] |
| No education | -0.17** | [-0.33,-0.01] | -6.14* | [-13.28,0.99] | -1.60 | [-9.86,6.65] |
| | | | | | | |
| Observations | 185 | | 171 | | 185 | |

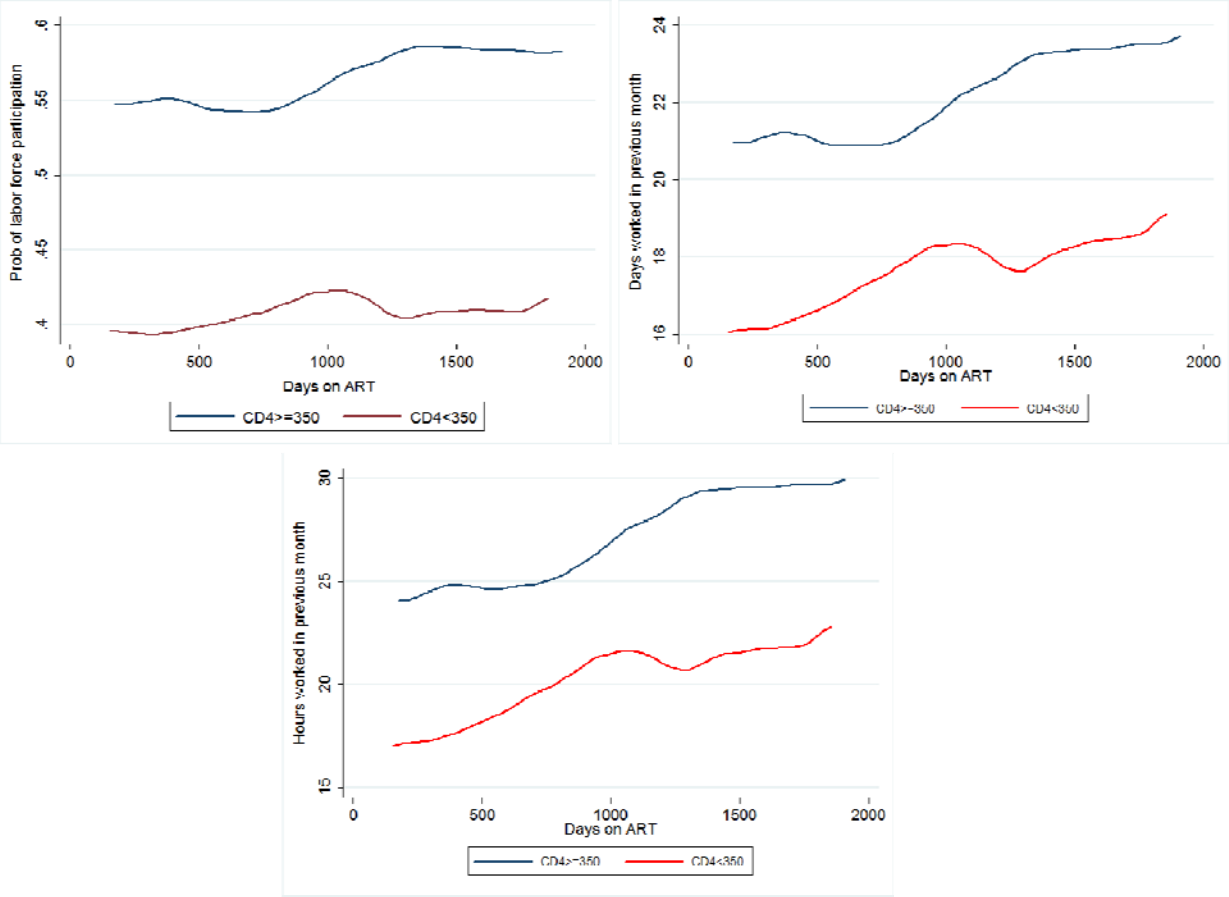
Notes: Marginal effects in column 1 (probit regression). Regression coefficients are shown in columns 2 and 3; 95% confidence intervals are in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. No education refers to whether individual was never formally educated. Female x age is an interaction of female and age.

**Supplementary Table 1: Sensitivity analyses for the relationship CD4 count and the employment outcomes of patients and non-patient adults in the same household**

| | (1) | | (2) | | (3) | |
|---|---|---|---|---|---|---|
| *Patients* | Labour force participation ME | | Days worked in previous month | | Hours worked in previous week | |
| CD4 ≥500 cells/µl | 0.26** | [0.02,0.51] | 5.66 | [-1.11,12.43] | 13.23** | [2.45,24.02] |
| CD4 ≥350 cells/µl (adjusted for MPR) | 0.22** | 0.010.42] | 5.79** | [0.24,11.34] | 8.53* | [-0.59,17.64] |
| Observations | 112 | | 106 | | 112 | |
| *Non-patient adults* | | | | | | |
| CD4≥500 | 0.26** | [0.06,0.46] | 4.70 | [-2.18,11.57] | 0.62 | [-7.50,8.74] |
| CD4≥350 (adjusted for MPR) | 0.04 | [-0.12,0.20] | 0.77 | [-5.17,6.71] | -2.33 | -9.29,4.64] |
| | | | | | | |
| Observations | 185 | | 171 | | 185 | |

Notes: All models adjusted for age, sex, duration of ART and education. ME denotes that marginal effects are reported in column 1 (probit regression). Regression coefficients are shown in columns 2 and 3; 95% confidence intervals are in parentheses. * $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$. The first sensitivity analysis compares the outcomes among ART-treated patients with a CD4+ T-cell count over 500 cells/µl versus those below that leve1. The second analysis adjusts for the medication possession ratio (a measurement of adherence based on pharmacy refill data). No education refers to whether individual was never formally educated. Female *x* age is an interaction of female and age.

**Figure 1 Role of the duration of ART on patient employment**




Notes: Nonparametric regression estimates of the association between duration of ART and predicted values of employment outcomes for patients. Results from kernel-weighted local polynomial regressions (zero degree polynomial) with width of 200 days around each point and estimated locally at 50 points. Regressions compare patients high CD4 count (CD4≥350=1) and those with low CD4 count (CD4<350=1). Abbreviation: Prob; probability.

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