Early HIV treatment and labour outcomes: A case study of mining workers in South Africa

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Abstract

This study examines whether labour outcomes of HIV-infected workers treated with antiretrovirals are associated with the stage of the disease when commencing therapy. We use data on employment separation and absenteeism from the workplace health programme of South Africa's largest coal mining company over the period January 2009 to March 2017 in a Cox proportional hazards model. When treatment was initiated at a CD4+ T cell count above 350 cells/µl, the risk of separating from the company was 37 per cent lower and the risk of absence was 20 per cent lower than initiating at a CD4 count below 200 cells/µl and these differences persist over time. Also, we find that workers initiating ART at CD4≥350 have a 8 per cent lower risk of absence prior to treatment. While many companies and the South African government have adopted universal test-and-treat policies aiming to initiate all HIV-infected people as early as possible, most HIV patients still start treatment late in the disease course when their CD4 counts have fallen to low levels. Our results indicate early HIV detection and treatment could have large productivity gains.

Keywords: HIV/AIDS, Antiretroviral therapy

1. Introduction

In 2016, 25.6 million people primarily of working age were living with HIV infection in Africa and Africa now accounts for two-thirds of all new infections globally (WHO, 2017). In South Africa where our study took place, the prevalence of HIV among those aged 15-49 is currently 20.6 per cent (SABSSM, 2018). Among the most important economic consequences of the disease is the impact of HIV-related sickness and deaths on the workforce (WHO, 2008). Although studies have shown treatment with antiretroviral therapy (ART) can eliminate much of the adverse impact, there is currently very little known on the degree to which labour outcomes depend on how sick workers are when they commence therapy (Thirumurthy et al., 2013; Tirivayi and Koethe, 2016). While many companies and the South African government have adopted universal test-and-treat policies aiming to initiate all HIV-infected people as early as possible, most HIV patients still start treatment late in the disease course when the symptom burden is higher.

In this paper, we investigate whether the timing of ART is associated with labour outcomes among workers in South Africa's largest coal mining company. Our study is the first to longitudinally examine the effect of disease stage at treatment start on employment separation and on the more responsive labour outcome of absenteeism. These labour outcome measures are important. Loss of work can have severe economic and social consequences for the worker (Hoffman, 1997). From the perspective of the firm, a lost worker implies the transaction costs of hiring and training a new worker and absenteeism reduces the productivity of the existing workforce (Rosen et al., 2004). Our study is also the first to examine differences in absenteeism by timing of ART initiation in the period before treatment has started. This first evidence is important in order to have a complete picture of the economic losses due to late ART initiation. The non-experimental design of our study precludes strong causal conclusions, because we cannot rule out endogenous selection into disease stage at ART initiation. However, we condition on a number of potentially important sources of endogenous selection allowing causal inferences that are stronger than those based on unconditional associations.

A person infected with HIV may initially experience mild flu-like symptoms as the virus replicates progressing to a prolonged latent phase where HIV symptoms gradually appear and infection-fighting CD4+ T cells of the immune system steadily decline with time. Employment and productivity can be negatively affected as symptoms of physical and cognitive impairment often appear episodically and opportunistic infections and comorbidities develop such as tuberculosis, hepatitis C, arthritis or mental health problems (Groß et al., 2016; O'Brien et al., 2014) and Beard et al. (2009) highlight higher levels of absenteeism among infected co-workers. Worthington et al. (2012) report that people living with HIV/AIDS prefer to work but often struggle to maintain paid employment due to the sequelae of HIV, time demands and side effects of some ART treatments as well as stigmatization in the workplace. Separation is therefore not only a negative outcome for the employer but also generally for the employee.

Progression of HIV disease can be halted and reversed through the use of ART and this treatment has been shown to lead to increased productivity (Larson et al., 2008), employ-

ment recovery (Bor et al., 2012) and a reduction in absenteeism (Habyarimana et al., 2010) to pre-disease levels. Initially, treatment guidelines in most countries in Africa recommended ART treatment when the patient's CD4 cell count had fallen below 200 cells/µl but countries have followed the World Health Organization (WHO) in revising its recommendations on the timing of ART initiation to higher CD4 counts. The rationale for these changes in recommendations is the strong evidence that earlier initiation reduces morbidity, mortality and HIV transmission (Cohen et al., 2011; Insight Start Study Group, 2015).

Disease stage at ART initiation can plausibly affect labour market outcomes through a number of mechanisms. First, patients who initiate ART late will take longer to recover their immunity and physical strength than patients who initiate ART earlier and will thus suffer higher rates of absenteeism and employment separation. Second, even in the long run, immunity and physical strength may not return to normal levels in some of the patients who initiate ART late leading to higher rates of HIV-related diseases and poorer work performance. Third, it is also possible that patients who initiate ART late will face stigma and workplace discrimination because they have entered disease stages associated with physical manifestations clearly visible to others. However, to date only one longitudinal study has examined how labour outcomes vary by the stage of the disease at ART initiation finding that differences in the likelihood of working between those initiated on ART at CD4<200 and CD4>200 disappear within one year (Venkataramani et al., 2014).

2. Data and Methods

2.1. Data

Anonymised data from the workplace health programme of a South African coal mining company were collected over the period January 2009 to March 2017 for all employees. At this time, this company was the largest coal producer in South Africa owning and operating eight mines.

When the programme began, WHO guidance was that patients with HIV should commence ART if their CD4 count dropped below 200 cells/µl. WHO raised the threshold for

ART treatment of HIV-infected patients from CD4<350 in 2010 to CD4<500 in 2013 and finally to all HIV patients at any CD4 count in 2015 (Maina et al., 2015). However, medical officers for the health programme in our study did not closely adhere to these guidelines. The Chief Medical Officer's guidance over this period was that ART should be initiated when a patient with HIV was fully counselled; understood the diagnosis and treatment options; and was willing to voluntarily consent and commit to lifelong treatment. In practice, both patients and medical practitioners would have been aware of changing guidelines which would have influenced their joint decision on when to commence treatment.

All workers with HIV were treated at a company health service hospital outpatients department except those at two outlying sites where they attended ambulatory health centres. Access to treatment should not have been an issue for any of the employees at Anglo American Coal. All health services including ART treatment were provided free of charge to employees. Transport to and from the hospital or health centre was arranged by the mines and was also free.

Our data includes HIV status, the date of ART initiation as well as some demographics (age, marital status and gender). A number of human resources variables also included in this dataset record the dates of engagement and termination of employment, if applicable, as well as occupation and worksite. This dataset was then merged with data extracted from a separate system recording dates of each day absent through sickness and linked to our dataset using a unique employee identification number. Across 12035 workers, absenteeism was typically 0.7 days per month and tenure was 9.81 years while 16 per cent of workers were HIV positive, 81 per cent were HIV negative and the HIV status for the remaining 2 per cent was unknown (Table 1).

From January 2009 to March 2017, 885 workers commenced ART and 775 of these had a recorded CD4 test within one month of ART initiation. We categorize these 775 workers according to whether their initial CD4 cell count was below 200 cells/µl, 200 to 349 cells/µl or 350 cells/µl and over. These categories were chosen to reflect the various ART initiation thresholds recommended by WHO or prevailing in South Africa (Maina et al., 2015; RSA Health, 2010, 2013, 2015) and used in comparable studies in Uganda (Thirumurthy et al.,

2013; Venkataramani et al., 2014). A separate category of CD4≥500 was too small to support robust analysis (63 workers). Descriptive statistics for these three categories are compared in Table 1). We see that absenteeism and tuberculosis (TB) prevalence are highest among those initiating at CD4<200 and that this category contains the lowest proportion of females. Of the category initiating at CD4≥350, a relatively high proportion initiated ART following the 2015 revision of WHO guidelines recommending ART for everyone living with HIV (19 per cent) but also a significant percentage initiated ART before 2010 when WHO guidelines recommended therapy at CD4<200 (15 per cent).

2.2. Statistical analysis

We first consider the variation in employment separation of those workers on ART within the company by initial CD4 count. The dependent variable in our model is the hazard rate or conditional probability that the worker will terminate her employment in a particular time period given that she was still working up till then. More formally, the hazard rate can be considered as the probability

$$h(t) = \frac{f(t)}{N(t)} \tag{1}$$

where $f(t)$ is the number of separations between t and $t+1$ and $N(t)$ is the number employed at time t. The proportion of workers remaining in the workforce until time t or 'survival rate' provides another way of describing variations in employment separation and is given by

$$S(t_j) = S(t_{j-1})\big(1 - h(t_j)\big) \tag{2}$$

We use the Cox proportional hazards model to explain how the hazard of separation for a worker on ART varies by CD4 count (Cox, 1992). In this model, the hazard rate is

$$h(t) = h_0(t)e^{\boldsymbol{\beta}'\mathbf{x}} \tag{3}$$

where $h_0(t)$ is the baseline hazard and the vector $\mathbf{x}$ includes the CD4 count at ART initiation and a number of control variables. The effect of a unit change in $x_i \in \mathbf{x}$ is

expressed as a hazard ratio e^{β_i} and this is assumed to be constant across time. If β_i is time-varying then (3) can be modified by the inclusion of an interaction term $\beta_i + \gamma_i t$.

To model the variation in absenteeism among workers receiving ART by initial CD4 count we use a generalisation of the Cox model which accounts for intra-individual correlation in absence hazard rates due to unobserved heterogeneity. These 'shared frailty models' are preferred as other methods commonly used to analyse sickness absences underestimate true effect sizes and have lower statistical power (Christensen et al., 2007).[1] In this model, the hazard rate for the jth absence of individual i is given as

$$h_{ij}(t) = h_0(t)e^{\boldsymbol{\beta}'\mathbf{x}_{ij}+\nu_i} \tag{4}$$

where ν_i are the individual-level log frailties.

Our controls include age, sex, marital status, tenure, job grade, diagnosis of TB and year employment commenced. We also include indicators for the year ART was initiated in the analysis to capture secular improvements in the toxicity, efficacy and ease of dosing of treatment (Lee et al., 2014; Laskey and Siliciano, 2014) as well as time-varying macroeconomic conditions. We have included additional dummies for the two outlying sites to reflect any systematic differences in doctors' advice and preferences although doctors at these sites would have been subject to the same company-wide guidance and practices. ART initiation and subsequent treatment would not generally have been subject to idiosyncratic doctor's preferences within treatment site as all those enrolled in the HIV Wellness programme were reviewed at quarterly appointments where the worker was seen by any available medical officer on duty. To capture the disutility of travelling to treatment, we have constructed a variable capturing the round-trip journey time from mine to treatment based on travel time computed from Google Maps. This variable has been used to construct additional dummies for sites close to treatment (<30 mins round trip travel time) and sites far from treatment (30-90 mins and >90 mins). We also include absenteeism in the month preceding ART

[1] Also, other approaches ignore many of the special properties of sickness absence data - time dependence, skewed distributions and clumping at zero values - leading to misguided inferences (Steensma, 2011).

initiation as an independent variable to capture unobserved factors affecting selection into treatment. For example, less motivated workers might be expected to have more absences and delay treatment. However, this variable may also control out variation in health associated with delaying treatment that we would like to capture. Estimates including this variable should therefore be regarded as overly conservative.

3. Results

The effect of the rising thresholds for ART therapy can be seen clearly in Figure 1 where the distribution of CD4 counts at ART initiation have shifted to the right over time. In 2009, some of those treated lie above the prevailing WHO threshold of 200 cells/µl while in 2016, by which time WHO advocated universal eligibility, large proportions of HIV+ employees were still commencing treatment at relatively low CD4 counts.

Figure 2 shows how CD4 counts recover following ART initiation. On average, those who initiate ART at a count less than 200 cells/µl take four years to reach an immune system strength reflective of the lowest 3 per cent of counts in a sub-Saharan HIV negative population (given as 350 cells/µl in Crampin et al. (2011)). We would therefore expect labour outcomes in this grouping to be persistently worse than in the other categories on ART especially given the physically demanding nature of mining. On the other hand, those who initiate ART with a CD4 count between 200 and 350 cells/µl have average counts within one year reflective of a HIV negative population albeit still lower than the relatively healthy group who initiate ART on a count of over 350 cells/µl.

3.1. Employment separation

In the years following ART initiation, 170 out of the 775 workers on ART in our dataset separated from the firm. Our data is therefore right censored for the remainder where date of eventual separation is not known.

It is not clear *a priori* that survival in the workforce for those initiating ART at low CD4 counts should be lower than for those initiating at higher counts as sicker workers will have less alternative employment options. We examine how the initial CD4 count

affects employment separation by plotting survival rates for workers on ART (Figure 3). We estimate that, four years after commencing ART, 77 per cent of workers with an initial CD4 count less than 200 will remain in the workforce. Survival rates are higher for the other two categories at all time periods following ART initiation and after four years the estimated survival rates are 82 per cent and 83 per cent for CD4 250-349 and CD4≥350 respectively. Although the data is noisy, there is some visual evidence to suggest that survival rates diverge over time.

The differences between the three groups are seen to be more pronounced when we adjust for possible confounders using the Cox proportional hazards model of time to separation in Table 2. We see that starting ART at CD4 200-349 leads to a 22 per cent lower risk of separation relative to starting ART at the reference level of CD4<200 although this is not statistically significant (hazards ratio [HR] = 0.778, p=0.153). The risk of separation is even lower when ART is initiated at CD4≥350 at 37 per cent below the risk of separation for the CD4<200 category (HR = 0.628, p=0.039). In the second set of estimates, we control for endogenous selection into disease stage at ART initiation by including baseline absenteeism. Results are seen to be largely unchanged.

Venkataramani et al. (2014) find that differences in labour outcomes by CD4 count disappear within one year implying the effect of initial CD4 count on risk of separation varies over time thus violating the proportional hazards assumption. We therefore test for evidence that the initial CD4 coefficients are time-varying. The initial CD4 count is interacted with time in the third set of estimates but these coefficients are seen to be statistically insignificant (CD4 200-349 : HR = 1.028, p=0.766 and CD4≥350 : HR = 1.016, p=0.897) and the null hypothesis for the exclusion of these two interaction terms is accepted by a likelihood ratio test ($\chi^2(2) = 0.09$, p= 0.686). Also, a plot of scaled Schoenfeld residuals with survival time shows no correlation for each of the initial CD4 categories confirming that the proportional hazards assumption is satisfied (figure A1 in appendix) and formal statistical tests do not reject the null hypothesis that the slope is equal to zero for each category (CD4 200-349 : $\chi^2(1) = 0.08$, p= 0.783 and CD4≥350 : $\chi^2(1) = 0.16$, p= 0.923). Therefore, there is no evidence to suggest that the differences in risk of separation by initial CD4 count dissipate

over time. In table A1 in the appendix, we also included interaction terms to check whether effect sizes varied over time. These interaction terms are jointly statistically insignificant ($\chi^2(2) = 1.96, p = 0.375$).

3.2. Absenteeism

Following ART initiation, the 775 workers on ART in our dataset had a total of 51364 sickness absences. The mean number of sickness absences was 68 (1.6 per month), the median was 37 absences, 33 persons had no absences and one person had 785 absences over 97 months. Our sickness absence data is right censored as before.

In Figure 4, we plot cumulative monthly absenteeism by CD4 count at ART initiation. Sickness absences accumulate rapidly in the first months after commencing ART especially for those with the lowest CD4 counts. The plots continue to diverge over time giving a cumulated difference of 44 days of sickness absence between those with an initial count of <200 cells/µl and those with an initial count of ≥350 cells/µl after four years.

These relationships are reflected in estimates from the Cox model with shared frailty. Table 3 demonstrates a strong graded relationship between initial CD4 count and sickness absence. Those initiating ART at CD4 200-349 had a 14 per cent lower risk of absence relative to starting ART at the reference level of CD4<200 (HR = 0.856, p=0.000) while the risk for those initiating ART at CD4≥350 was lower again at 20 per cent relative to the reference level (HR = 0.796, p=0.000). Adding baseline absences to capture endoegnous selction results but initiating ART early is still clearly associated with lower absenteeism (HR = 0.903 (p=0.001) for CD4 200-349 and HR = 0.882 (p=0.001) for CD4≥350). As explained earlier, we regard estimates including this variable as being overly conservative. We then interact the initial CD4 count with time on ART. The CD4<200 interaction term is statistically insignificant while the hazard ratio for the CD4≥350 interaction term is statistically different to one (HR = 0.9999, p=0.000). This would imply that the differences in risk of absence by initial CD4 count do not dissipate over time and actually increase marginally for CD4≥350. As a test of the robustness of these findings, time on ART was also entered in the model in a number of non-linear forms to capture the spike in absences

around ART initiation observed in Habyarimana et al. (2010) i.e. e^{-t} and an indicator function $\mathbb{1}_{t>1}$ where t is time since ART initiation (in years). Results are similar (table A2) and we therefore conclude that there is no evidence to suggest that the differences in risk of absence by initial CD4 count are lower in the long-run.

It is clear from Figure 2 that HIV-infected workers initiating ART at CD4<200 are at an advanced stage of immunosuppression for some time before treatment. Therefore the hazard rate of absenteeism would be expected to be lower in the pre-ART period for those initiating at higher CD4 counts relative to those initiating at CD4<200. This is indeed what we find in the final set of estimates in Table 3 where we consider only those absences occurring in the two years pre-ART. The effect sizes are slightly smaller than in the post-ART period with those initiating ART at CD4 200-349 at a 8 per cent lower risk of absence (HR = 0.908, p=0.011) and those initiating ART at CD4>350 also at a 8 per cent lower risk of absence (HR = 0.885, p=0.002).

4. Discussion

The aim of this study was to determine whether the timing of ART is associated with labour outcomes among workers in South Africa's largest coal mining company. From an employer perspective, both absenteeism and separation have clear negative economic effects. From the employee's perspective, workers may separate on improved terms although in our sample of mostly unskilled workers and high blue-collar unemployment in South Africa this seems unlikely. We would therefore argue that these labour outcomes are negative for the employee also. Our analysis produced several original findings.

We find that employment separation and absenteeism differ between those initiating ART earlier in the disease course when CD4 counts are still high and those initiating later when their CD4 counts have already sunk to low levels. When ART was initiated at CD4≥350, the risk of separating from the company was 37 per cent lower and the risk of absence was 20 per cent lower than initiating at CD4<200. While studies to date have reported the positive effects of ART on productivity, labour force participation and employment, very few have examined how labour outcomes vary by the timing of treatment initiation.

The most important previous study examining the association between disease stage at ART initiation and labour market outcomes is by Venkataramani et al. (2014). Our study contributes substantially to the literature because we examine for the first time the association between disease stage and labour outcomes from the perspective of a private-sector company (while Venkataramani et al. look at this association from the perspective of patients enrolled in a public-sector HIV treatment programme). We investigate the labour outcome absenteeism, which is much more responsive to health than either employment or wealth, the outcomes reported in their study. Our data is further directly extracted from the mining company's human resources data rather than self-reported. Methodologically, the detailed event data that we have access to through this source - dates of absenteeism and employment separation - allow us to conduct survival analysis (rather than the binary choice approach taken in their work.). Overall, our study is similar in causal strength to their study i.e. both studies are non-experimental rather than (quasi-)experimental and use explicit co-variate control to reduce the threat of endogenous selection.

Our second finding is that these differences persist over time. Statistical tests indicated an absence of evidence to contradict the proportionality assumption leading us to conclude that the risk of separating from the company and the risk of absence are lower for those initiating ART at higher thresholds for all times examined post-ART. Venkataramani et al. (2014) report labour force participation significantly differs between those initiating ART at CD4$\geq$200 and those below this threshold but that these differences quickly disappear. In our study, we similarly find no statistical difference in the risk of separation above and below this threshold but find a large significant and persistent difference when contrasting those with initial CD4$\geq$350 and those with initial CD4$<$200. Additionally, large significant and persistent differences in absences are observed above and below the 200 cells/µl threshold.

Many studies have reported that ART leads to full employment recovery and productivity levels comparable to uninfected workers (Razzano et al., 2006; Morineau et al., 2009; Habyarimana et al., 2010; Rosen et al., 2010; Bor et al., 2012) but other studies record persistently lower employment despite recovery of work ability (Thirumurthy et al., 2008; Wagner et al., 2009; Booysen and Geldenhuys, 2016). This may be due to non-adherence

to the treatment regimen (Coetzee et al., 2011); the effects of HIV-related stigma on social support and mental health (Tsai et al., 2011) or household disruption due to the disease (Wagner et al., 2011). These factors are likely to be more severe in the later stages of disease when the HIV symptom burden is higher (Tsai et al., 2013). The persistently worse labour outcomes that we observe in those treated at the lowest threshold may be due to these factors. Alternatively, continued immunosuppression after treatment and resultant debility would be expected to lead to worse labour outcomes especially given the physically demanding nature of mining.

Our third original finding is that ART initiation at a higher CD4 count mitigates the decline in labour outcomes prior to treatment observed when treatment begins at late disease stages. In a sample of Kenyan tea-estate workers, Larson et al. (2008) find that days worked started to decrease nine months before treatment initiation. Bor et al. (2012) link clinical data with seven waves of longitudinal socio-economic data to demonstrate a deterioration in employment pre-ART and recovery post-ART where the CD4 cell eligibility threshold for treatment was 200 cells/µl. Our contribution is to show how declines in labour outcomes vary by the level of immunosuppression at treatment start. We find that those initiating ART at CD4$\geq$350 had a 8 per cent lower risk of absence in the two years pre-ART than those initiating ART at CD4$<$200. Such differences have been suggested in prior studies (e.g Thirumurthy et al. (2013)) but have not been well documented as both clinic-based longitudinal studies and community health interventions do not routinely capture socio-economic outcomes pre-initiation.

At the start of the study period, the standard first-line ART regimen within the mining company consisted of two nucleoside reverse transcriptase inhibitors (zidovudine and lamivudine) in a fixed dose combination and one nonnucleoside reverse transcriptase inhibitor (efavirenz). When the improved fixed dose single pill combination of emtricitabine, tenofovir disoproxil fumarate and efavirenz became available in South Africa in 2013, this soon became the standard treatment. These changes in drug regimens could have affected the labour effects of ART. It is somewhat less likely that these changes would have affected the labour effects of initiating ART at different HIV disease stages, which is what we are

measuring here as the improved drug regimen should benefit people initiating ART in all disease stages. To ensure that the associations between disease stage at ART initiation and labour outcomes are not confounded by changing drug regimens and thus changing effectiveness, side effects and toxicities over time, we control for calendar year in all of our main analyses. When we additionally interact calendar time with disease stage at ART initiation, we find no evidence of either significant or substantive heterogeneity of our observed associations.

Our findings indicating the positive effects of earlier treatment on labour outcomes suggest a sound economic rationale for increasing investments in HIV testing and interventions to accelerate treatment uptake among people living with HIV. Many firms and governments in sub-Saharan Africa have adopted universal test-and-treat policies, aiming to initiate people living with HIV as soon as possible following HIV infection. However, the majority of people living with HIV still initiates in late stages of disease when their CD4 counts have already fallen to relatively low levels – as we also show in this study. Approaches to remedy this situation require additional investment in HIV interventions. Examples of potential approaches include social marketing to promote HIV testing and treatment uptake (Wei et al., 2011), HIV self-test kit distribution to allow people to test wherever and whenever they desire (Chanda et al., 2017; Ortblad et al., 2017), and financial incentives or gifts to increase HIV testing and linkage to treatment programmes (McGovern et al., 2016). The cost-benefit calculations for such supporting interventions should include the impact of earlier treatment on labour market outcomes, which are likely to at least partially offset costs.

Our findings may also have implications for social marketing content for HIV testing and treatment. One of the plausible reasons why men living with HIV are less likely to test and seek treatment than women living with HIV is that help- and care-seeking does not conform with ideas of male gender roles and conceptions of masculinity (Greig et al., 2008; Choko et al., 2017). It is plausible that social marketing messages emphasizing the effect of HIV treatment on continued employment and work performance can increase the appeal of HIV testing and treatment for men.

There is generally a paucity of research on the timing of ART initiation and labour

outcomes. We have used a unique dataset from a workplace health programme with detailed information on employment details, absences and ART. Our study has several strengths. For one, the sample size of employees on ART used here is much larger than sample sizes available in previous studies leading to relatively precise effect size estimates. Moreover, using human resource records allows us to avoid social desirability and interviewer biases that often come with self-reported measures. Finally, our data has been recorded at daily intervals which reduces errors resulting from data collection in larger intervals such as during annual survey visits.

Our study also has several limitations due to the non-experimental design of our study and potential endogenous selection into disease stage at ART initiation. Pre-2015, workers receiving treatment at higher CD4 counts are more likely to have had stage 3 or 4 HIV infection with symptoms such as severe bacterial infection, wasting, pneumonia and TB. Therefore, in our analysis, the categories of those initiating ART at higher CD4 counts would not reflect the CD4<200 category counterfactually treated before disease progression. As these categories will be sicker than in the counterfactual, any differences in labour outcomes between these workers and the CD4<200 category will be biased downwards. The effect sizes we report may then be underestimated.The group of those on ART at the lowest CD4 level will also include workers in later years who were eligible at the higher thresholds but lacked motivation to take-up treatment. Such individual characteristics may be correlated with future job attachment and hence labour outcome differences between these workers and those who initiate at higher CD4 counts may be overestimated.

It unlikely that the research question we are posing here will ever be answered with a randomized controlled trial and the causal strength of this type of study will thus always be limited. Two quasi-experimental approaches have previously been used in the literature to answer similar research questions: regression discontinuity (Patenaude et al., 2018) and individual fixed-effects analysis (Bor et al., 2012; Thirumurthy et al., 2013; Zivin et al., 2009) although these come with well-known limitations - regression discontinuity effect sizes are only causally strong in a small neighbourhood around the discontinuity and the fact that individual fixed-effects analysis only allows inference among those who have changed their

treatment status over the observation period. Neither approach is feasible given our data for this study and the precise research question that we are posing. Regression discontinuity is not possible as unlike in public-sector HIV treatment programmes CD4 count threshold rules for ART eligibility did not apply in the workplace health programme of the mining company whose data we are using here. Instead the programme advice was that ART should be initiated when a patient with HIV had full information and the physician judged that treatment was appropriate. Individual fixed-effects analysis is also not possible, because our exposure of interest – disease stage at the time of ART initiation – is only determined once in a patient's life. While our analysis is thus necessarily neither experimental nor quasi-experimental, it does have a few inferential strengths. First, the data is longitudinal, ruling out reverse causal effects. Second, to control for endogenous selection into disease stage at ART initiation we include a number of variables in our survival analysis that are likely strong predictors of labour outcomes (sex, age, calendar time, job tenure, occupation, tuberculosis, access, worksite, marital status). Importantly, we also add pre-ART values of one of our two outcome variables, absenteeism, to our regressions. In the regressions with absenteeism as our outcome, these baseline values control for all past sources of endogenous selection into disease stage at ART initiation. In the regressions with employment separation as outcome variable, these baseline values capture those past sources for endogenous selection that are correlated with absenteeism. In the two regressions controlling for baseline absenteeism values, our results remain essentially the same, strengthening our belief that the observed conditional associations are indeed causal.

5. Conclusion

In sum, we use routine employment records linked to patient data from a workplace ART programme in South Africa's largest mining company to estimate the differences in the timing of treatment on employment separation and absenteeism. We find that employment separation and absenteeism differ between those initiating ART earlier in the disease course when CD4 counts are still high and those initiating later when their CD4 counts have already sunk to low levels. When ART was initiated at CD4$\geq$350, the risk of separating from the

company was 37 per cent lower and the risk of absence was 20 per cent lower than initiating at CD4<200. We cannot be sure that these effects are completely casual due to the non-experimental design of our study and potential endogenous selection into disease stage at ART initiation although our additional analyses suggest our findings are robust. Our results support the case for increased investment in early HIV testing and treatment.

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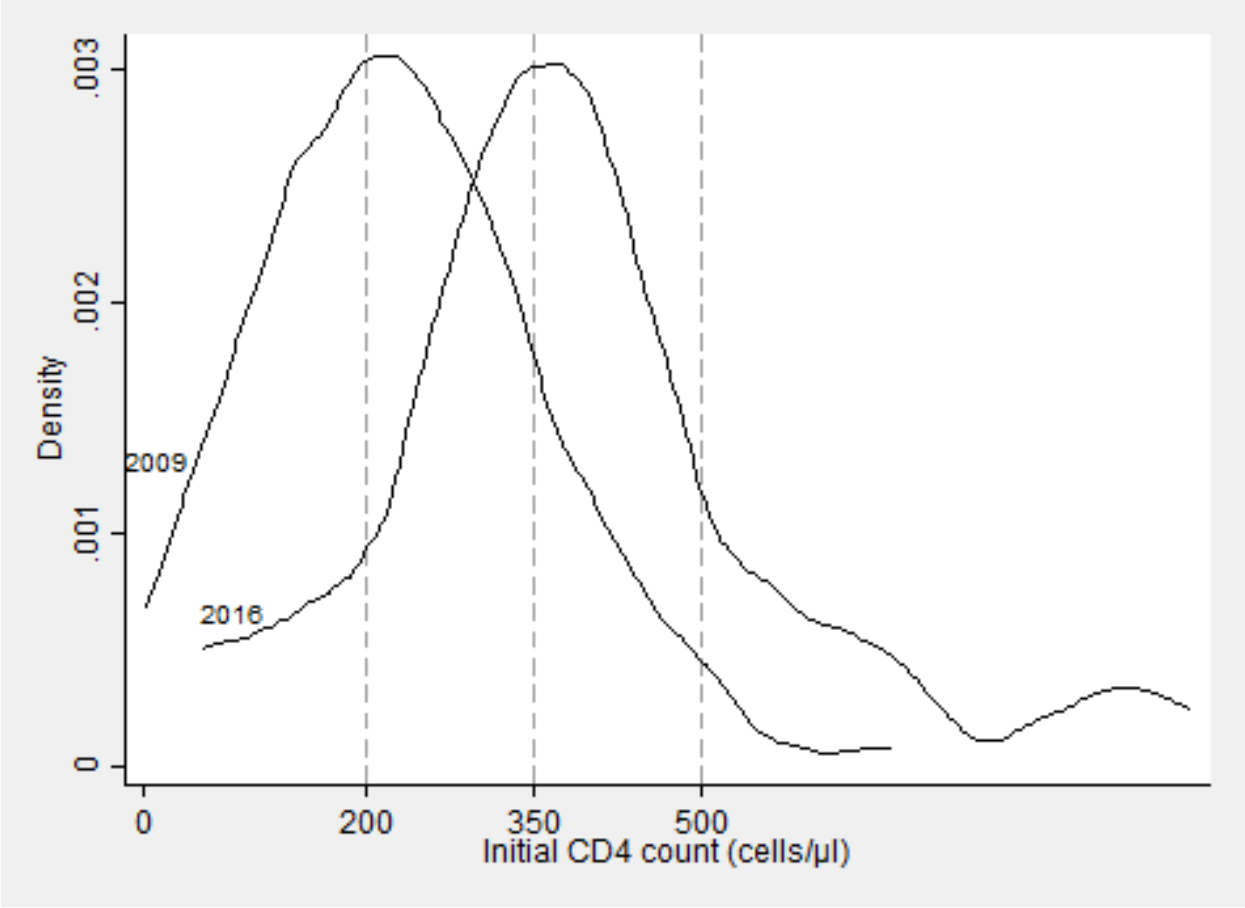
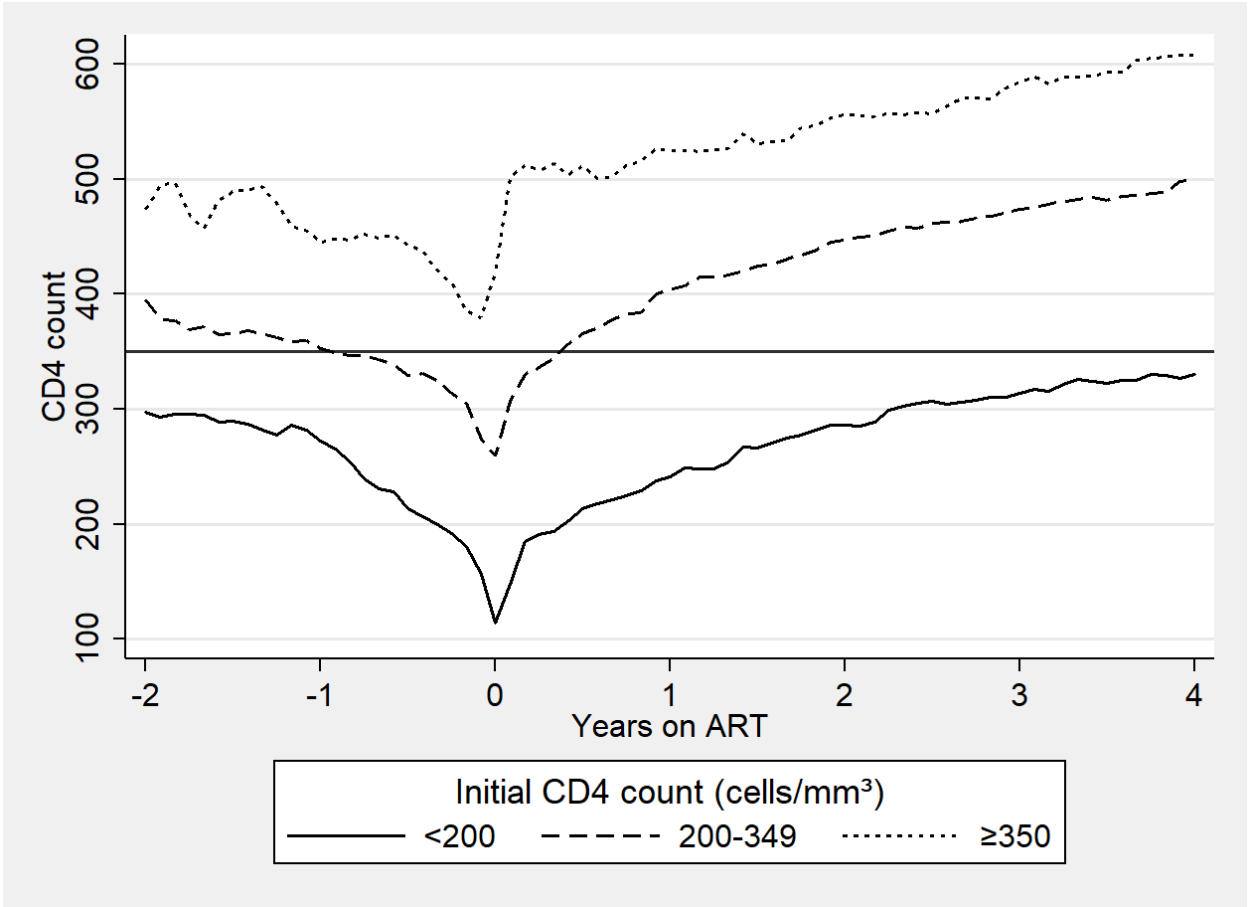
Figure 1: CD4 count for selected years of ART initiation



Notes : Years selected represent the first and last full years when workers initiated ART in our sample. Intervening years have been suppressed for clarity. Vertical lines are WHO ART treatment thresholds pre-2010 (CD4<200), 2010-2013 (CD4<350) and 2013-2015 (CD4<500). WHO recommended ART treatment for all HIV patients in 2015.

Figure 2: Average CD4 count pre and post-ART by CD4 count at ART initiation



Notes : CD4 cell count testing was provided every 3 months to HIV+ employees in the wellness programme. Averages are given for most recent CD4 counts at each month before and after commencing ART (Year 0) for those workers still employed.

Figure 3: Estimates for survival in workforce by CD4 count at ART initiation

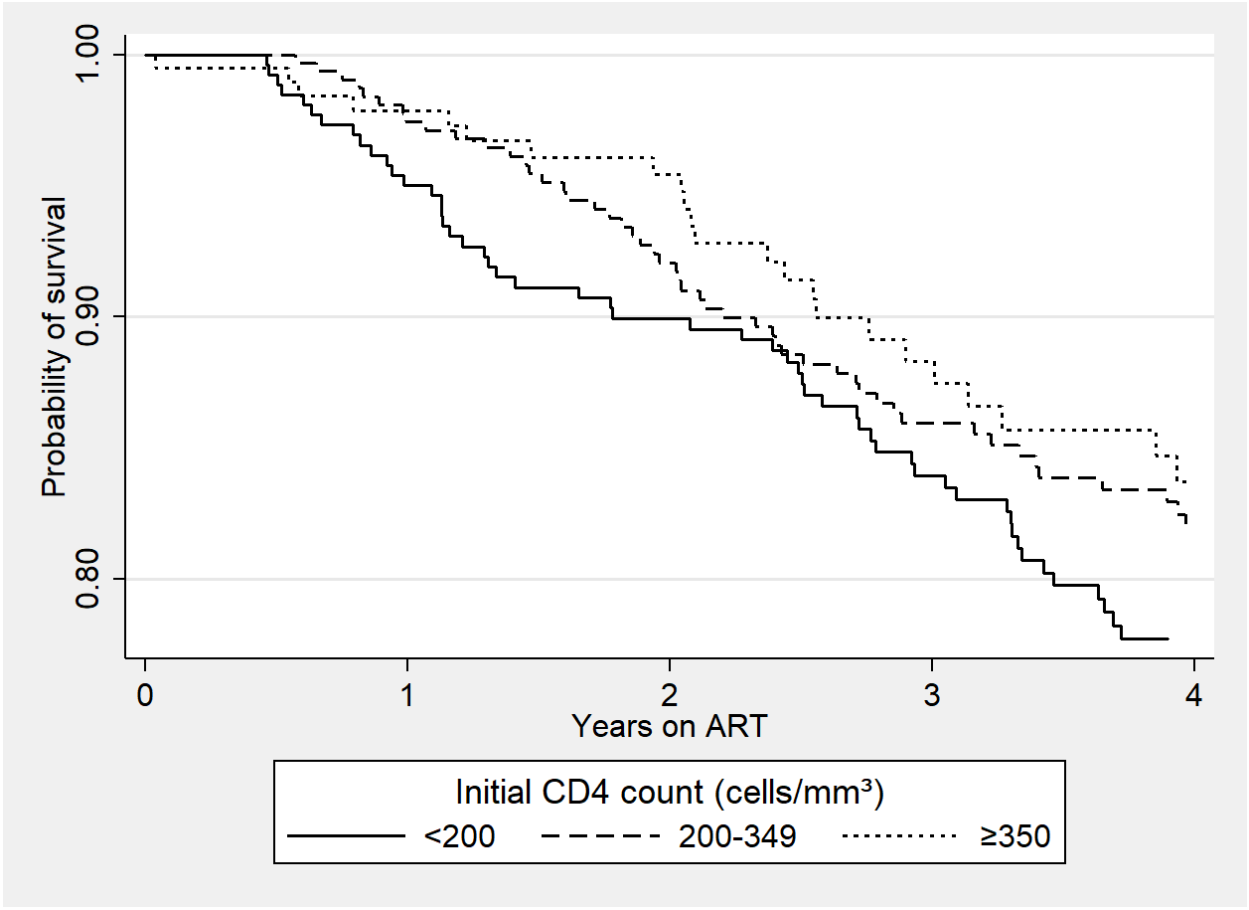
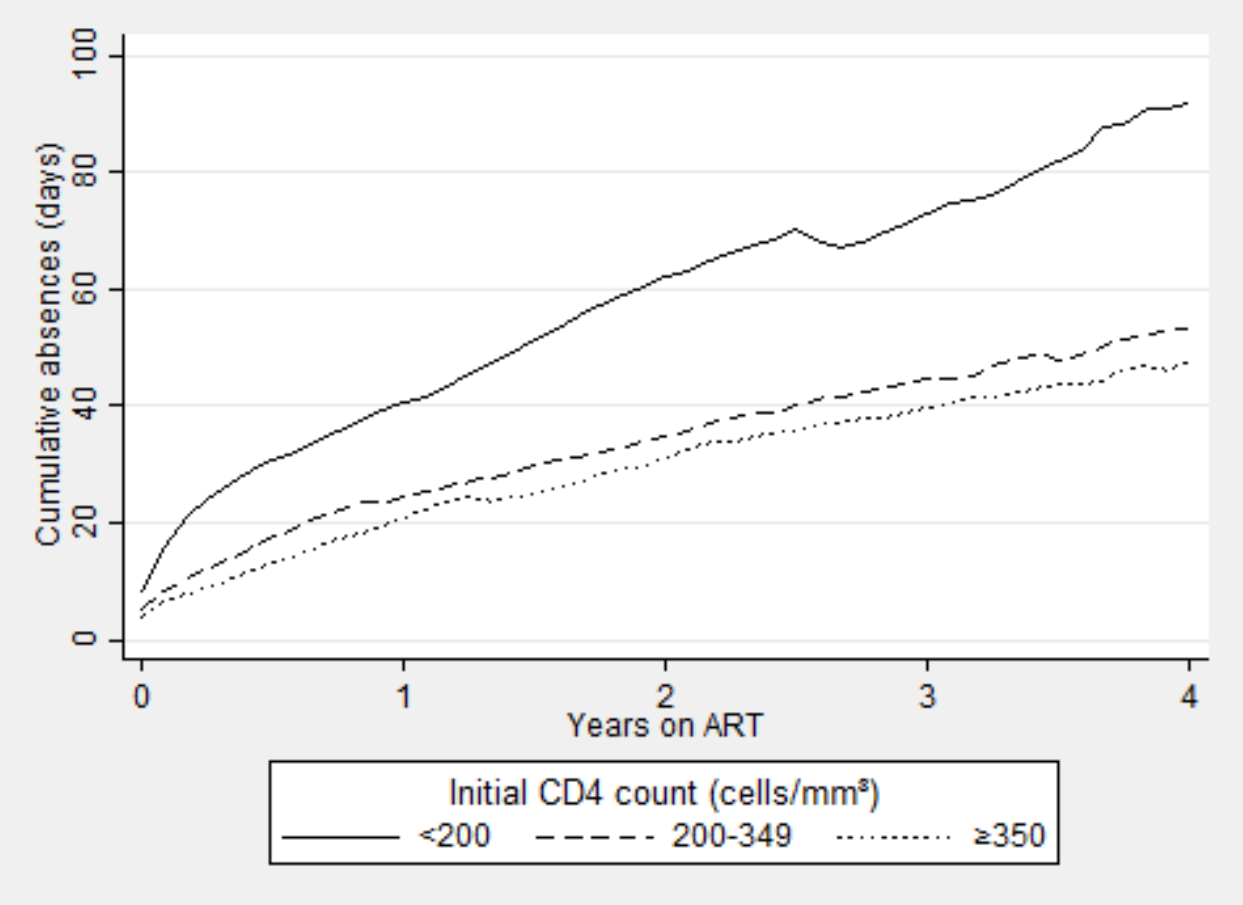


Figure 4: Cumulative monthly absenteeism by CD4 count at ART initiation



Notes : Averages are given for cumulative monthly absenteeism at each month after commencing ART for those workers still employed.

Table 1: Descriptive statistics

	All	Initial CD4 count		
		<200	200-349	≥350
Female	0.19	0.15	0.16	0.30
Married	0.63	0.68	0.64	0.60
Age	42.38	42.74	42.86	40.71
Tenure (years)	9.81	8.58	9.60	7.97
Absenteeism (days per month)	0.70	2.22	1.26	1.16
Job unskilled	0.69	0.90	0.87	0.90
Job semi-skilled	0.03	0.00	0.01	0.01
Job skilled	0.18	0.09	0.11	0.08
Job management	0.11	0.00	0.02	0.01
TB	0.02	0.15	0.07	0.11
Job start <1990	0.09	0.14	0.18	0.12
Job start 1990-1999	0.07	0.12	0.08	0.03
Job start 2000-2004	0.08	0.06	0.09	0.09
Job start 2005-2009	0.53	0.56	0.50	0.51
Job start ≥2010	0.22	0.13	0.14	0.25
HIV+	0.16	1.00	1.00	1.00
HIV-	0.81	-	-	-
HIV status unknown	0.02	-	-	-
ART start <2010	-	0.25	0.22	0.15
ART start 2010-2012	-	0.48	0.46	0.37
ART start 2013-2014	-	0.23	0.25	0.29
ART start 2015-2017	-	0.03	0.07	0.19
N	12035	262	319	194

Notes : All workers employed between Jan2009 and Mar2017. Initial CD4 count given for all those initiating ART between Jan2009 and Mar2017. Absenteeism given over duration of ART. All other variables given at ART initiation.

Table 2: Cox proportional hazards model of time to separation

	Hazard ratio	Std. err.	Hazard ratio	Std err.	Hazard ratio	Std. err.
Female	0.411*	0.145	0.411*	0.145	0.411*	0.145
Age	0.665**	0.057	0.665**	0.058	0.665**	0.057
Age squared	1.006**	0.001	1.006**	0.001	1.006**	0.001
Tenure	0.978	0.038	0.978	0.038	0.978	0.038
Initial CD4 200-349	0.778	0.137	0.777	0.137	0.717	0.234
Initial CD4 $\geq$ 350	0.628*	0.142	0.627*	0.143	0.599	0.248
Job semi-skilled	2.396	1.757	2.395	1.756	2.432	1.790
Job skilled	0.598	0.194	0.597	0.196	0.598	0.194
Job management	4.179*	2.581	4.171*	2.584	4.170*	2.577
TB	0.890	0.274	0.893	0.290	0.889	0.275
Baseline absences	-	-	1.000	0.011	-	-
Initial CD4 200-349 $\times$ time	-	-	-	-	1.028	0.095
Initial CD4 $\geq$ 350 $\times$ time	-	-	-	-	1.016	0.125
Log likelihood	-882.1		-882.1		-882.1	
No. of separations	170		170		170	
N	775		775		775	

Notes : All workers on ART at some point between Jan2009 and Mar2017. Origin is date initiated ART. The models also include controls for year employment commenced (<1990, 1990-1999, 2000-2004, 2005-2009, 2010-2017), year ART initiated (<2010, 2010-2012, 2013-2014, 2015-2017), marital status, treatment site, round trip travel time to treatment (<30 mins, 30-90 mins, $\geq$90 mins). *Baseline absences* are absences in month preceding treatment. * $p < 0.05$, ** $p < 0.01$

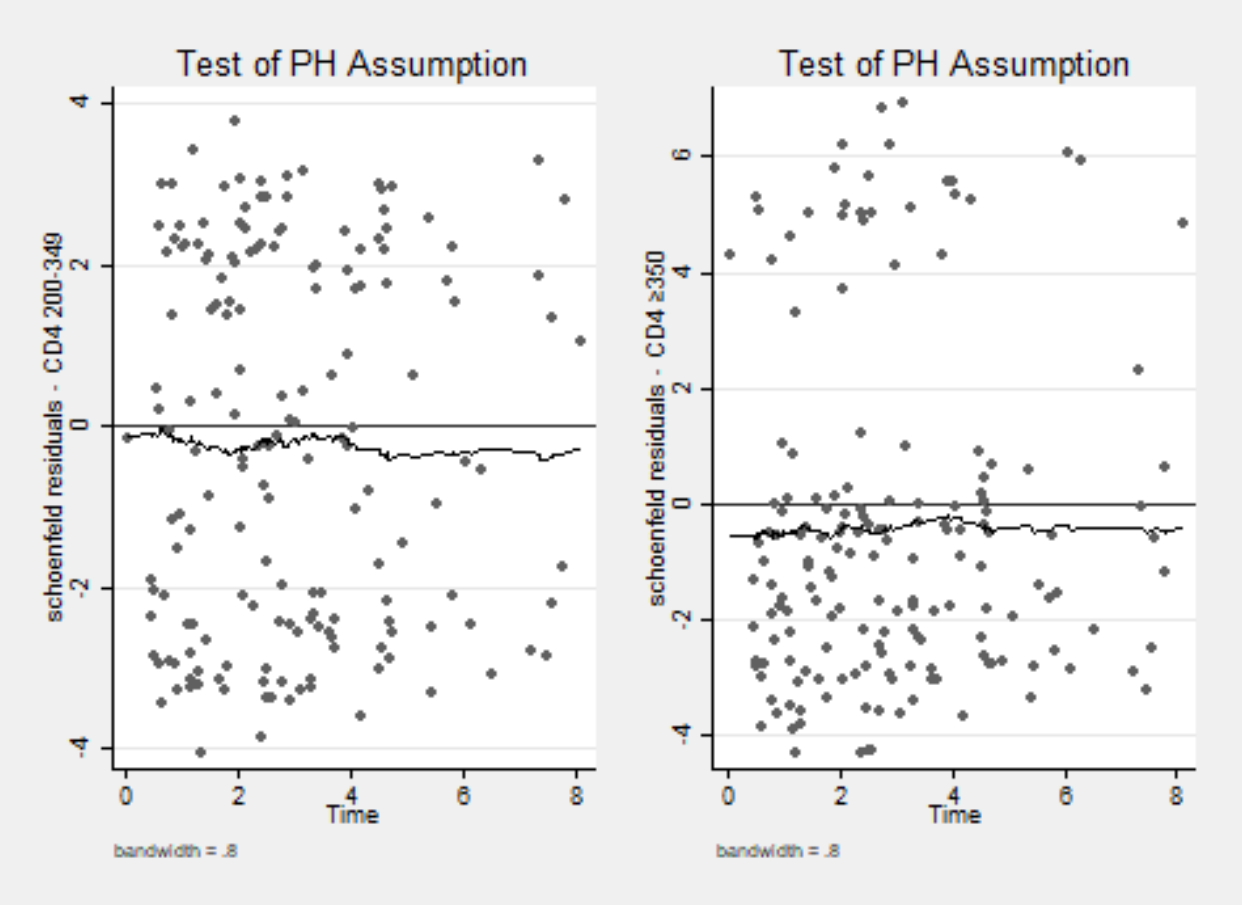
Table 3: Cox proportional hazards model with shared frailty of time to sickness absence

	Post-ART						Pre-ART	
	Hazard ratio	Std. err.	Hazard ratio	Std. err.	Hazard ratio	Std. err.	Hazard ratio	Std. err.
Female	1.108*	0.044	1.127**	0.042	1.113**	0.044	1.069	0.034
Age	1.061**	0.012	1.056**	0.011	1.063**	0.012	0.996	0.011
Age squared	0.999**	0.000	0.999**	0.000	0.999**	0.000	1.000	0.000
Tenure	1.033**	0.007	1.027**	0.006	1.033**	0.007	1.009	0.005
Initial CD4 200-349	0.856**	0.028	0.903**	0.027	0.869**	0.030	0.920**	0.025
Initial CD4 $\geq$350	0.796**	0.031	0.882**	0.033	0.844**	0.035	0.920**	0.026
Job semi-skilled	1.067	0.171	0.849	0.131	1.067	0.170	1.132	0.111
Job skilled	0.983	0.046	1.022	0.045	0.985	0.046	1.023	0.040
Job management	0.686*	0.111	0.737*	0.113	0.686*	0.111	0.879	0.113
TB	1.084*	0.039	0.987	0.036	1.087*	0.039	1.392**	0.038
Time on ART	1.000**	0.000	1.000**	0.000	1.000**	0.000	-	-
Baseline absences	-	-	1.019**	0.002	-	-	-	-
Initial CD4 200-349 $\times$ time on ART	-	-	-	-	1.000	0.000	-	-
Initial CD4 $\geq$ 350 $\times$ time on ART	-	-	-	-	1.000**	0.000	-	-
Log likelihood	-517684.3		-517626.47		-517677.5		-164486.0	
No. of individuals	775		775		775		775	
No. of absences	51364		51364		51364		17978	

Notes : All workers on ART at some point between Jan2009 and Mar2017. Origin is date initiated ART in first two sets of estimates. In the third set, the origin is two years before ART initiation and the data is right censored at ART initiation. The models also include controls for year employment commenced (<1990, 1990-1999, 2000-2004, 2005-2009, 2010-2017), year ART initiated (<2010, 2010-2012, 2013-2014, 2015-2017), marital status, treatment site, round trip travel time to treatment (<30 mins, 30-90 mins, $\geq$90 mins). *Baseline absences* are absences in month preceding treatment.* $p < 0.05$, ** $p < 0.01$

Appendix

Figure A1: Schoenfeld residuals over survival time for Cox proportional hazards model of time to separation



Notes : Under the proportional hazards assumption Schoenfeld residuals should be centred around zero.

Table A1: Alternative specifications of separation

	Cox proportional hazards model		Probit	
	Hazard ratio	Std. err.	Coeff.	Std. err.
Female	0.413*	0.146	-0.209	0.361
Age	0.657**	0.057	-0.304**	0.107
Age squared	1.006**	0.001	0.004**	0.011
Tenure	0.978	0.038	-0.064	0.059
Initial CD4 200-349	0.758	0.141	-0.305	0.239
Initial CD4 ≥350	0.543*	0.138	-0.670*	0.326
Job semi-skilled	2.441	1.792	-	-
Job skilled	0.594	0.194	-0.158	0.443
Job management	4.030*	2.491	-	-
TB	0.901	0.276	0.461	0.330
Initial CD4 200-349 × ART begin 2013-2017	1.212	0.664	-	-
Initial CD4 ≥350 × ART begin 2013-2017	2.276	1.343	-	-
Log likelihood	-881.2		-742.7	
Pseudo R^2	-		0.206	
No. of separations	170		25	
No. of absences	775		701	
LR χ^2 test	1.96		-	

Notes : All workers on ART at some point between Jan2009 and Mar2017. (Cox) Model of time to separation. Origin is date initiated ART. Null hypothesis for likelihood ratio (LR) test is exclusion of terms added to base model (first set of estimates in Table 2). (Probit) Model of 12-month out job termination probability. The models also include controls for year employment commenced (<1990, 1990-1999, 2000-2004, 2005-2009, 2010-2017), year ART initiated (<2010, 2010-2012, 2013-2014, 2015-2017), marital status, treatment site, round trip travel time to treatment (<30 mins, 30-90 mins, ≥90 mins). * $p < 0.05$, ** $p < 0.01$

Table A2: Cox proportional hazards model with shared frailty of time to sickness absence - alternative specifications for time on ART

Time on ART =	$\mathbb{1}_{t>1}$		e^{-t}	
	Hazard ratio	Std. err.	Hazard ratio	Std. err.
Female	1.086*	0.044	1.081	0.046
Age	1.056**	0.012	1.052**	0.012
Age squared	0.999**	0.000	0.999**	0.000
Tenure	0.977**	0.004	0.954**	0.003
Initial CD4 200-349	0.860**	0.031	0.849**	0.029
Initial CD4 ≥350	0.820**	0.035	0.797**	0.033
Job semi-skilled	1.141	0.184	1.147	0.193
Job skilled	0.978	0.046	0.970	0.048
Job management	0.625**	0.104	0.592**	0.103
TB	1.042	0.038	1.070	0.040
Time on ART	0.860**	0.016	1.027	0.080
Initial CD4 200-349 × time on ART	0.978	0.024	0.970	0.107
Initial CD4 ≥ 350 × time on ART	0.960	0.029	0.947	0.127
Log likelihood	-517713.4		-517721.3	
No. of individuals	775		722	
No. of absences	51364		51364	

Notes : All workers on ART at some point between Jan2009 and Mar2017. Origin is date initiated ART. *Time on ART* is specified as e^{-t} and an indicator function $\mathbb{1}_{t>1}$ where t is time since ART initiation in years. The models also include controls for year employment commenced (<1990, 1990-1999, 2000-2004, 2005-2009, 2010-2017), year ART initiated (<2010, 2010-2012, 2013-2014, 2015-2017), marital status, treatment site, round trip travel time to treatment (<30 mins, 30-90 mins, ≥90 mins).* $p < 0.05$, ** $p < 0.01$

Table A3: Alternative specifications of sickness absence (post-ART)

	Cox proportional hazards model		Regression	
	Hazard ratio	Std. err.	Coeff.	Std. err.
Female	1.109**	0.044	14.973**	4.166
Age	1.061**	0.012	3.284*	1.477
Age squared	0.999**	0.000	-0.037*	0.017
Tenure	1.033**	0.007	-0.050	0.634
Initial CD4 200-349	0.865**	0.033	-9.212**	3.281
Initial CD4 $\geq$350	0.783**	0.038	-16.499**	3.946
Job semi-skilled	1.063	0.170	-21.364	17.445
Job skilled	0.984	0.046	-5.219	4.840
Job management	0.685*	0.110	-21.472	17.228
TB	1.083*	0.039	32.986**	4.859
Time on ART	1.000**	0.000	-	-
Initial CD4 200-349 $\times$ ART begin 2013-2017	0.962	0.069	-	-
Initial CD4 $\geq$350 $\times$ ART begin 2013-2017	1.031	0.083	-	-
Log likelihood	-517683.9		-	
R^2	-		0.23	
No. of individuals	775		722	
No. of absences	51364		44147	
LR χ^2 test	0.88		-	

Notes : All workers on ART at some point between Jan2009 and Mar2017. (Cox) Origin is date initiated ART. (Regression) Dependent variable is total number of absences in 12 months following ART initiation. The models also include controls for year employment commenced (<1990, 1990-1999, 2000-2004, 2005-2009, 2010-2017), year ART initiated (<2010, 2010-2012, 2013-2014, 2015-2017), marital status, treatment site, round trip travel time to treatment (<30 mins, 30-90 mins, $\geq$90 mins).* $p < 0.05$, ** $p < 0.01$