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Survival Analysis of Patients Receiving HIV Antiretroviral Treatment in Kenya

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Abstract:
HIV infections and AIDS constitute a major cause of premature death and impose a significant disease burden in Kenya. An estimated 1.6 million people are infected with human immunodeficiency virus (HIV), while 1.5 million have died since the virus was first detected in Kenya in 1984. There is a limited understanding of the impacts of socioeconomic factors on the survival rates of HIV positive persons who have been enrolled and are on treatment follow-up.
The aim of this study was to enhance understanding of the determinants and survival rates of HIV positive patients on treatment follow up in Kenya. To achieve this objective, data were collected from two hospitals in Kenya – Mbagathi District Hospital in Nairobi and Moi Teaching and Referral Hospital in Eldoret. The study used stratified Cox Proportional Hazard model to estimate the survival rate of the patients on and those not on antiretroviral therapy from the two hospitals after controlling for potential confounders.
It was established in the study that the patients who were on ARVs and were employed at the time of treatment debut had a lower risk of dying from HIV and AIDS-related illnesses compared to the patients who were on ARVs but were unemployed at the time of enrolment. The study confirmed that ARVs were increasingly more beneficial the lower the CD4 counts were. Furthermore, the study found that condom use reduced the mortality risk for patients on treatment follow up. Finally, the study found that men who were on treatment follow up had a higher risk of dying than the women.
The study findings showed that ART increased the survival rates thereby supporting the policy of universal access to treatment for HIV positive patients that the government is currently implementing. However, for this policy to achieve the desired results, the government not only needs to increase employment opportunities for HIV positive persons but, also ensure that employees were not retrenched based on their HIV positive status.

1. Introduction

Human immunodeficiency virus (HIV) and the concomitant development of the acquired immune deficiency syndrome (AIDS) with infections has posed the greatest global public health challenges over the last quarter century (Strauss & Thomas, 2008). Although global commitment to control the HIV and AIDS pandemic has increased significantly in recent years, some evidence suggest that the virus continues to spread and much remains to be done to reverse these trends(Bertozzi, et al., 2006). By the end of 2015, an estimated 36.7 million people worldwide were living with HIV with close to 2.1 million new HIV infections including 390,000 among children aged under 14 and 1.1 million AIDS-related deaths occurred (UNAIDS, 2016). The unavailability of an imminent vaccine or cure means that many more deaths are inevitable (WHO, 2001) Eastern and Southern Africa Region (ESAR) remains the region most affected by HIV and AIDS; however, the virus appears to be spreading rapidly in other parts of the developing world including Eastern Europe, Asia and The Central Asia and in the newly emerging economies (Bertozzi, et al., 2006; UNAIDS, 2016). The ESAR accounted for 60% of all HIV infections worldwide and 42.7% of all AIDS-related deaths in 2015 (UNAIDS, 2016). In addition, ESAR also accounted for 45.7% of new HIV infections in 2015. This makes AIDS the leading cause of mortality lives, productivity and hardship in sub-Sahara Africa (Kumaranayake & Watts, 2001; Maathers, Lopez, & Murray, 2006). However, a total of 2.5 million deaths have been averted in low- and middle-income countries since 1995 due to introduction of antiretroviral therapy (ART) as observed by (UNAIDS , 2011).Kenya still bears the burden of a relatively high HIV prevalence, approximately 1.6 million people are infected with HIV, while 1.5 million have died since the HIV was first detected in Kenya in 1984 (NASCOP, 2008). However, the annual national HIV prevalence rate among adults has declined to about6% from approximately 15% in the 1990s(KNBS and ICF Macro, 2014). This reduction has been attributed to greater awareness and the resulting behaviour change, a lower incidence, antiretroviral therapy and higher death rates (RoK, 2016).

To scale upprevention and reduce morbidity and mortality due to HIV and AIDS, highly active antiretroviral therapy (HAART) had been adopted. HAART is effective in reducing viral load to almost undetectable levels and partially enabling immune restoration, thereby preventing the onset and recurrence of opportunistic infections while significantly reducing the probability of infection to others (Montaner, et al., 2006). Clinical studies in Kenya have shown that continuous use of ART results to clinical and immunologic improvement and hence increased survival rate for people living with HIV (Wools-Kaloustiana, et al., 2006; Song, 2007).

Whereas epidemiologically there has been an increasing ART coverage, controlled durational analysis studies looking at survival rates are scarce. In addition, no studies have been done that compare the economic impact of ART and no ART scenarios. Based on these information gaps, this study carried out a durational regression analysis using health care utilization, patient outcome and socioeconomic data to provide a better understanding of the impact of ART versus no ART management scenarios. In addition, the study also carried out a comparative analysis of patient treatment outcomes in AMPATH and MDH hospitals with different treatment models for people living with HIV.

1.1. Statement of Research Problems

HIV and AIDS have caused major economic and negative health impacts in Kenya. To address these challenges several interventions has been put in place including comprehensive care and treatment in which eligible patients are put of ARVs and treatment of opportunistic infections only without ART use. Although, there have been various clinical studies on the impact of ART use in Kenya, economic studies assessing the socioeconomic factors determining the survival for the people living with HIV who are using ARVs are not available. Studies addressing these issues will significantly contribute towards strengthening both policy framework and programmatic implementation of the ART programme. This research sought to determine the factors impacting on the survival of HIV positive adults on ART and those not on ART in these two hospitals with different patients' care models.

1.2. The Study Objectives

1.2.1. General Objectives

The general objective of this study was to determine factors influencing survival of people living with HIV on ARV treatment and those not on ARV using data from Mbagathi District Hospital and AMPATH treatment centre.

1.2.2. Specific Objectives

i. To compute the survival rate of people living with HIV in the two hospitals in Kenya
ii. To determine the factors influencing survival of HIV positive patients on treatment follow up.

1.3. Site and Patient Selection Criteria

This study was conducted in two hospitals in Kenya. The Academic Model for the Prevention and Treatment of HIV and AIDS (AMPATH) which is based in Moi Teaching and Referral Hospital (MTRH), Eldoret and Mbagathi District Hospital (MDH), Nairobi. AMPATH has a strong referral system starting from the grassroots level to the tertiary hospital. Mbagathi District Hospital is a public hospital located in Nairobi City on the outskirts of the Kibera informal settlement and has been considered as a hospital of the poor (Owiti, 2013).

MDH and AMPATH were the first hospitals to provide HIV and AIDS treatment in Kenya. Furthermore, they had the largest number of patients on ART in Kenya. At the time of data collection, MDH and AMPATH had been providing care and treatment for PLWHIV in Kenya for at least 10 and 7 years respectively. The sites met the criteria in terms of data availability and for have been providing ARVs adult patients for at least 4years. Detailed description of study site and data can be found in Owiti (2013). The population of study were HIV positive adult who were at least 18years at the time of treatment enrolled, had initiated their treatment in any of the two hospitals and not transferred. Random sampling was used to identify eligible patients

2. Literature Review

Yiannoutsos, (2009) used Weibull parametric models with change points to estimate the survival among HIV-infected patients who were initiating antiretroviral therapy in a care and treatment programme in sub-Saharan Africa. The study found that there was an early change in risk of death at three months, followed by an intermediate risk period lasting up to 10 months after therapy. The concluded that the existence of a high early risk of death after initiation of ART and the determination of its duration had direct implications for the optimal management of patients initiating therapy in this setting.

3. Methodology

This study's the outcome variable of interest is time to death for the HIV positive patients after enrolment to HIV treatment. We used survival analysis to establish the association between various treatments or demographic characteristics and survival rates the patients. This duration analysis data is generally positively skewed and are censored making it difficult to use ordinary least square (OLS) regression analysis (Collett, 1993) (Hosmer, Lameshow, & May, 2008) (Hosmer & Lemeshow, 1999) (Marubini & Valsecchi, 2004). We used Kaplan-Meier and univariate Cox regression model for descriptive analysis, however to control for covariates and stratification of hospitals, the study used stratified Cox regression model for the multivariate analysis (Owiti, 2013).

3.1. Cox Regression Model

Cox proportional hazards (PH) model shows the hazard at time t of an individual given the covariates. According to Hosmer and Lemeshow, (1999), the Cox Proportional Hazard model is given by;

$$h(t, \boldsymbol{X}, \boldsymbol{\beta}) = h_0(t) \exp[\beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_n x_n] \quad (1)$$

Where $h(t, \boldsymbol{X}, \boldsymbol{\beta})$is the hazard function at time$t$ for a subject with covariate values$x_1, \ldots x_n$and the estimated coefficients of the covariates of $\beta_1, \ldots \beta_n$. $h_0(t)$is the baseline hazard function, which is the hazard function for an individual for whom all the variables

included in the model are zero,$\boldsymbol{X} = (x_1, x_2, \ldots\ldots, x_n)$is the value of the vectors of the explanatory/predictor variables for a particular individual, $\boldsymbol{\beta} = (\beta_1, \beta_2, \ldots\ldots, \beta_n)$ is a vector of the estimated coefficients of explanatory/predictor variables and exp is the exponential function $exp(x) = e^x$. The Cox model is usually stratified to correct for violation of the proportional hazard assumption. The stratified estimator of the hazard at time t for a subject in group g is assumed to be

$$h(t, \boldsymbol{X}, \boldsymbol{\beta}) = h_{0g}(t) \exp \exp[\beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_n x_n] \quad (2)$$

To fit the Cox proportional hazards model, we used the partial likelihood approach as proposed by Cox (1972) to estimate $h_0(t)$ and β. This study carried our various Cox proportional hazard model diagnostics to assess the validity of the model, test the functional forms of the variables and assess the proportional hazard assumptions and evaluate the model fit.

3.2. The Data

This study used secondary data collected from the electronic medical records and the patient charts of HIV positive patients enrolled on treatment in Mbagathi and Moi Referral hospitals. A total of 701 patients were randomly sampled, 301 were from MDH while 400 were from AMPATH (see Owiti, 2013 for more details). We calculated survival time from the date the patients were enrolled in the HIV and AIDS clinics to the date of death or, if alive, at the time of data collection. That is between 2001 and March 2010 for Mbagathi hospital and 2003 to and June 2010 for Moi Referral hospital. Cox stratified model was used in the regression analysis.

3.3. Variable Selection Method: Purposeful Covariate Selection

In selecting the covariates for analysis, several statistical procedures were carried out including descriptive, univariate, and multivariate analysis. The Kaplan-Meier curves were plotted to evaluate whether categorical variables were proportional or not. Then rank test and univariate Cox proportional hazard regression were carried out to test equality across the strata. In addition, we used purposeful covariate selection method proposed by Hosmer and Lemeshow, (1999) recommending that all variables that were tested to be significant at $P \leq 0.25$ in univariate analyses or which were predetermined to be clinically significant be included in the initial model.*P*-values were two-sided and those ≤0.05 were considered to be statistically significant. We also allowed for interaction of the covariates to capture the interaction effects of the variable. ART use and CD4 count values, ARV use and employment state, CD4 strata and income and finally, income and education level were found to be significant and maintained in the final model for analysis. Data from both Mbagathi District Hospital and AMPATH were pooled for these analyses. The primary exposure variable is ARV use, the duration of interest was time to death measured in terms of 91 days cycles and other control variables included relevant clinical indicators, and socio-demographic characteristics of patients. Table 1 shows the description of all the variables included in the study.

Variable	**Description**	**Code/Values**
_id	Patient identification code	1-700
Age	Age at enrolment	Years
Alcohol	Drinking alcohol during enrolment	0 = No and 1 = Yes
BMI	Body Mass Index	10.60 – 35.26
Censor	Death	0 = No and 1 = Yes
CD4 strata	CD4 strata at enrolment	0 = 0-50
		1 = 51-249
Cd4 value	CD4 value at enrolment	1 - 250
Condom	Condoms use at enrolment	0 = No and 1 = Yes
Cycle	Length of follow-up – 91 days	91 days
Dependants	Number of dependants	0 - 13
Education	Highest level of education	1 = None
		2 = Primary
		3 = Secondary & above
Employment	If the patient was employed at enrolment	0 = No and 1 = Yes
ARV use	If the patient is on ARVs or not	0 = No and 1 = Yes
Income level	Patient's level of income at enrolment	1 = 0 – 2,500
		2 = 2,501-10,000
		3 = 10,001-50,000
Married	If married or not	0 = No and 1 = Yes
Piped water	If piped water is available in the house	0 = No and 1 = Yes
Sex	Sex of patient	0 = Female and 1 = Male
Hospital	Treatment Hospital	0 = Mbagathi and 1=AMPATH

Table 1: Description of variables

3.4. Cox PH Model Diagnostics Results

Model-based inferences depend completely on the fitted statistical model and for these inferences to be "valid", the model fitted must provide adequate summary of the data upon which it is based (Hosmer and Lemeshow, 1999 (Hosmer, Lameshow, & May, 2008)).

The following diagnostic tests were carried out to test the scale of the continuous variables, identify leverage and outliers, test for the PH assumption and model fit.
The fractional polynomials method, Martingale and deviance residuals were used to assess the scale of age, CD4 count values and number of dependants. All the tests results showed that an assumption of linearity in the log hazard was reasonable for these three continuous variables. In assessing model adequacy, the studyusedscore residuals and found that no variable had undue influenceon the inferences made the basis of the Cox PH regression model. The time interactions, Schoenfeld and scaled Schoenfeld residuals tests were used to assess the proportional hazard assumption of the Cox regression model. Both individual predictor and global tests shows that the Cox PH model does not violate the PH assumption.

	rho*	**chi2**	**df**	**Prob>chi2**
ARV use	-0.010	0.02	1	0.885
Age	0.007	0.01	1	0.919
CD4 strata	0.066	0.81	1	0.369
CD4 count value	-0.014	0.04	1	0.851
Condom use	0.111	2.23	1	0.135
Number of dependants	-0.055	0.55	1	0.460
Employment state	-0.033	0.21	1	0.648
Piped water	0.050	0.41	1	0.524
Sex	0.026	0.12	1	0.725
Income2	0.107	2.04	1	0.154
Income3	0.043	0.33	1	0.564
Marital status	-0.025	0.13	1	0.722
Education level	-0.046	0.37	1	0.541
Primary	-0.048	0.44	1	0.507
Secondary and above	0.010	0.02	1	0.887
ARV use and CD count value	-0.014	0.04	1	0.850
cd4strinco~3	-0.038	0.27	1	0.605
income3_ed~3	-0.012	0.03	1	0.874
Global test		9.79	18	**0.9387**

Table 2: Test of proportional hazard assumptions

Time: Rank(t)
*rho is correlation between residuals and time.

The study used Cox–Snell residual to examine the overall fit of the model. There was some evidence of a systematic deviation from the straight line, which gives us some concern about the adequacy of the fitted Cox PH model. We evaluated the predictive power of the CoxModel by computing the Harrell's C concordance statistic. This statistic is defined as the proportion of all usable subjects' pairs in which predictions and outcomes are concordant and measures the agreement of predictions with observed failure order(Cleves, Gould, & Gutierrez, 2010).

Number of subjects (N)	701
Number of comparison pairs (P)	87103
Number of orderings as expected (E)	62228
Number of tied predictions (T)	0.0000
Harrell's C = (E + T/2) / P	0.7144
Somers' D	0.4288

Table 3: Harrell's C concordance statistic

The value of C ranges between 0 and 1, and is 0.714 indicating that by using all the predictors in the model, we correctly identify the order of the survival times of pairs of patients 71.4% of the time. Since the value of Somers' D is greater than zero, it also confirms that the Cox model has predictive powers.

3.5. Ethical Approval
The study of received ethical approval from Moi Treatment and Referral and Moi University Ethical Committee. In addition, we also received approval from the Medical Superintendent of Mbagathi District Hospital and Ministry of Higher Education, Science and Technology.

4. Results

4.1. Univariate Analysis Results

The study sample size was 701 patients out of whom 688 were on ARVs while 33 were not on ARVs. It's important to note that there was constraint in accessing data of patients who were only on opportunistic infection and prophylactic treatment. The imbalance is therefore due to data constraints. Table 4: Demographic and clinical information of HIV patients (n = 701) summarizes the demographic characteristics of the cohort studied. Of all the patients sampled, 57% were from Moi Referral and Teaching Hospital (AMPATH) while the remaining 43% were from Mbagathi District Hospital (MDH). The median age of patients at the start of the treatment was 37 years (range 18–69). In both hospitals, the majority of the patients were women 57.1% and 64.2%, of the patients were female in MDH and AMPATH respectively. In each of the hospitals, slightly over 30% of the patients had CD4 count 50 and below at the treatment onset while 35% and 26% of the patients in MDH and AMPATH were using condoms respectively.

Demographic variable	**Mbagathi District Hospital N=301(43%)**	**AMPATH N=400 (57%)**	***P*-value**
Sex			
Male	129 (42.9%)	143 (35.8%)	
Female	172 (57.1%)	257 (64.2%)	0.124*
Dead			
Yes	106 (35.2%)	74 (18.5%)	
No	195 (64.8%)	326 (81.5%)	
Baseline CD4 strata			
0-50	100 (33.2%)	124 (31%)	
51-250	201 (66.8%)	276 (69%)	0.000*
Condom use			
Yes	105 (34.9%)	105 (26.2%)	
No	196 (65.1%)	295 (73.8%)	0.000*
Income Level (KSh)			
0-2,500	131 (43.5%)	309 (77.2%)	
2,501-10,000	126 (41.9%)	36 (9.0%)	
>=10,001	44 (14.6%)	55(13.8%)	0.544*
Highest level of educational			
None	6 (2%)	29 (7.3%)	
Primary	126 (41.9%)	207 (51.7%)	
Secondary or above	169 (56.1%)	164 (41.0%)	0.247*
Employment state			
Yes	157 (52.2%)	152 (38%)	
No	144 (47.8%)	248 (62%)	0.054*
Marital status			
Married	143 (47.5%)	233 (58.3%)	
Not Married	158 (52.5%)	167 (41.7%)	0.292*
Mean baseline CD4 counts value	98.8	108.1	0.004**
Number of dependants	3	4	0.004**
Piped water			
Yes	223 (74.1%)	144 (36%)	
No	78 (25.9%)	256 (64%)	0.075*
Age -Median age (years)	37.6	36.8	0.032**
Total time at risk (quarters)	4350	5048	
Median follow up duration (months)	15	11	
ARV use			
Yes	280 (93%)	388 (97%)	
No	21 (7%)	12 (3%)	0.000*

Table 4: Demographic and clinical information of HIV patients (n = 701)
*Note * Logrank **Univariate Cox regression*

4.2. Univariate Analysis: Kaplan-Meier Survival Curves

The survival durations were measured in 3 monthly interval. The Kaplan-Meier curve is shown in Figure 1 window 1 by the dark line, the grey around the estimated Kaplan-Meier curve represent 95% confidence interval. The estimeted survival curve declines slowly overtime. At the end of the 26 spells that is 78 months (6.5 years), the survival probability is above 50% indicating that some of the patients were still a live at the time of data collection. In Figure 1window 2 we plot the survival function by ARV use, that is whether the patients on treatment follow up were ever put on ARVs or not. As expected, the curve shows that the patients on ARVs were likely to survive longer than the patients who were not put on ARVs. In Figure 1 window 4 we plot the survival function by sex, that is whether the patients on treatment follow up were male or female. The curves shows that the female patients were likely to survive

longer than their male counterparts. The survival curve for marital status in Figure 1 window 3 shows that married patients on treatment follow up are likely to live longer than those not married.

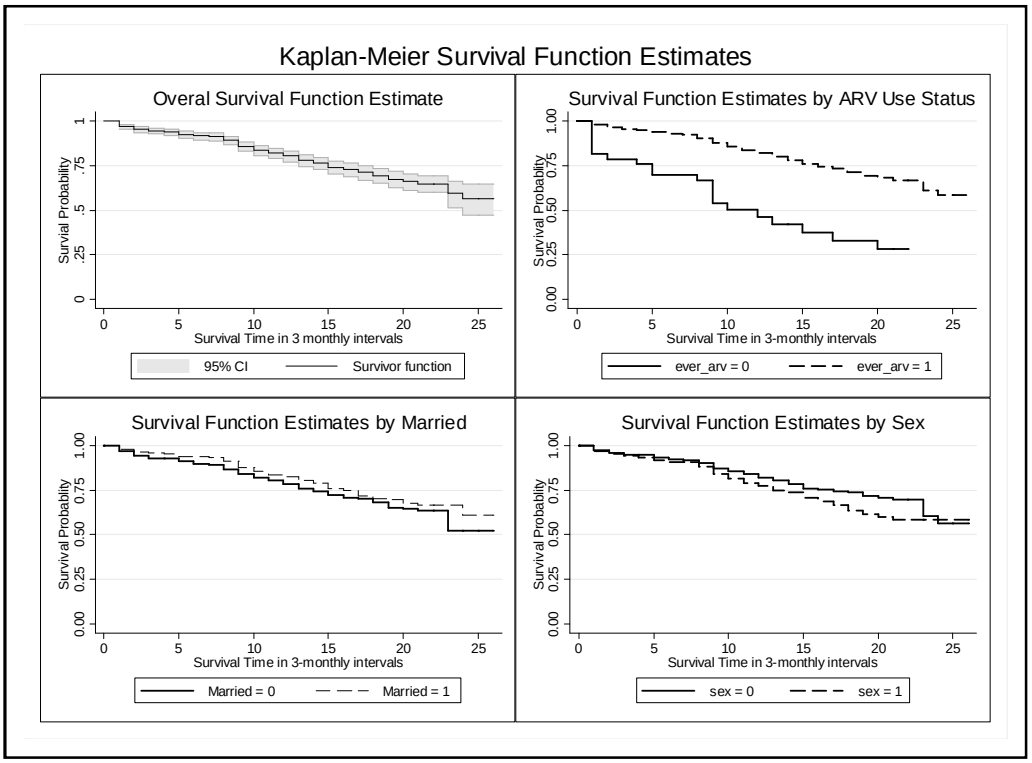

Figure 1: Survival duration: Kaplan-Meier estimate of Survival function – overall, by ARV use, by marital status and by sex

4.3. Multivariate Analysis Results: Stratified Cox PH Regression Model

The results for stratified Cox PH model are presented and discussed in this section. The model is stratified based on hospital type since the dummy variable for treatment site violated the proportional hazard assumption. The stratified Cox model controls for the hospital type by stratification while all the other variables are controlled for by inclusion in the model. However, since the hospital type variable is excluded from the model, we are unable to estimate its hazard ratio controlled for the covariates. This is the limitation of stratification on the hospital type. Stratification allows the baseline for Mbagathi hospital and Moi referral hospital to vary while the coefficients for the covariates are the same for the two hospitals. The results of this analysis are presented Table 5.

_t	Coeff.	Hazard ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
ARV use	-2.136		0.520	-4.11	0.000	-3.154	-1.117
Age	0.022		0.011	2.01	0.045	0.001	0.043
CD4 strata	0.064		0.260	0.25	0.805	-0.446	0.575
CD4 count value	-0.008		0.003	-2.59	0.010	-0.015	-0.002
Condom use	-0.754		0.195	-3.86	0.000	-1.137	-0.372
Number of dependants	-0.068		0.037	-1.84	0.066	-0.140	0.004
Employment state	0.984		0.484	2.03	0.042	0.036	1.932
Piped water	0.400		0.179	2.23	0.026	0.049	0.751
Sex	0.654		0.175	3.74	0.000	0.311	0.997
Income2	-0.432		0.226	-1.91	0.056	-0.875	0.011
Income3	-3.628		1.208	-3.00	0.003	-5.994	-1.261
Marital status	-0.180		0.164	-1.10	0.273	-0.500	0.141
Education level							
Primary	-0.174		0.344	-0.51	0.612	-0.848	0.499
Secondary and above	-0.678		0.359	-1.89	0.059	-1.381	0.025
ARV use and CD count value	0.007		0.004	1.99	0.047	0.000	0.014
ARV use and employment status	-1.297		0.490	-2.65	0.008	-2.257	-0.337
cd4strinco~3	2.736		1.043	2.62	0.009	0.692	4.780
income3_ed~3	1.484		0.656	2.26	0.024	0.199	2.769

Table 5: Stratified Cox PH analysis results (n = 701)

Log likelihood= -909.987

The stratified Cox PH model reports no intercept since it is subsumed into the baseline hazard $h_0(t)$and is unidentifiable from thedata. The primary variable of interest in this study is ARV use. Our major objective is to compare survival of patients on ARV drugs and those not on ARV drugs, adjusting for possible confounding or interaction effects of other covariates such as age, CD4 count values, CD4 strata, condom use etc. Since the CD4 count value variable and ART use variables interact, the hazard ratio for effect of ARV use is $\widehat{HR} = e^{\hat{\beta}_E + \sum_{0=j}^{J} \hat{\delta}_j W_j}$. $\hat{\beta}_E$ is the estimated coefficient of the exposure variable E (ARV use)and E is a dummy variable taking value of 1 (if the patient is on ARVs) or 0 (otherwise). $\hat{\beta}_{Ever_{ARV}} = -2.1357$. $\hat{\delta}_j$is the estimated coefficient of the interaction terms, $(\hat{\delta}_1)$ the coefficient of interaction between ARV use and CD4 value and $(\hat{\delta}_2)$ the coefficient of interaction between ARV use and employment status at treatment debut. The value of $\hat{\delta}_1 = 0.0069$ and $\hat{\delta}_2 = -1.2969$. $W_j$is the covariates interacting with exposure variable; and $j = 1, 2$. W_1 are the CD4 count values at enrolment for treatment and takes values 1, 2, …, 250. W_2 is the patient's state of employment at enrolment to treatment and it takes the value 1 (if patient is employed) or zero. The estimated hazard ratio for patients on ARV and on employment at treatment debut is exp (-2.136 -1.297+(0.007*CD4 count value)), since the CD4 count value varies; we estimated the magnitude of the hazard ratio for patients with specific CD4 countvalues as shown in Table 6.

CD4 count value	Hazard Ratio	95% Conf. Interval	
10	0.035	0.007	0.178
50	0.046	0.008	0.269
100	0.065	0.009	0.467
250	0.182	0.012	2.881

Table 6: Estimated hazard ratio and 95% CI for patients on ARV and employed at treatment debut

The estimated hazard ratios in Table 6 are all less than one and increase with the size of CD4 count values, indicating that for the patients employed, being on ARVs, is beneficial or reduces the rate of death and its increasingly beneficial the lower the value of CD4 count values. The confidence intervals support significant effects of ARV treatment for patients with CD4 counts 10, 50 and 100. Table 6 shows that for patients with CD4 count value of 10 and are employed, the estimated hazard ratio is 0.035, this implies that, being on ARVs reduces their rate of death by 96.5% compared to patients with same CD4 count value who are not on ARVs. At the same time, the patient with CD4 count value of 250 have an estimated hazard ratio of 0.182, indicating that being on ARVs for those employed reduces the risk of death by 81.8% compared to those not on ARVs.

The estimated hazard ratios for patient on ARVs who were unemployed at treatment initiation is given byexp (-2.136 + (0.007*CD4 count value)), since $W_2 = 0$ and are shown in Table 7.

CD4 count value	Hazard Ratio	95% Conf. Interval	
10	0.127	0.044	0.365
50	0.167	0.048	0.587
100	0.236	0.051	1.096
250	0.667	0.057	7.820

Table 7: Estimated hazard ratio and 95% CI for patients on ARVs and unemployed at treatment debut

These ratios are also less than one and significantly increase with increase in CD4 count values, showing that being on ARV when unemployed decreases the rate of death and its more beneficial for patients with very low values of CD4. The confidence interval for patients with CD4 counts 10 and 50 supports the significance effect of ARV treatment. The hazard ratio for the unemployed patients with CD4 counts of 10 is 0.127, indicating that, being on ARV reduces their death rate by 87.3% compared to those not on ARVs. Comparing this percentage to those of the same category for patients who were employed, we see that employment reduces the rate of death by close to 10% for patients on ARVs. The estimated hazard ratio for patients not on ARVs and were employed at treatment enrolment is given by $\widehat{HR} = e^{\hat{a}_1 W_1 + \hat{a}_2 W_2}$ since $\hat{a}_E = 0$.

CD4 count value	Hazard Ratio	95% Conf. Interval	
10	1.072	0.081	1.059
50	1.414	0.090	1.651
100	1.998	0.100	2.988
250	5.644	0.118	20.099

Table 8: Estimated hazard ratio and 95% CI for patients not on ARVs and employed at treatment enrolment

Note: Care needs to be taken when interpreting these results as the sample with no ARVs was very small and inference may result into errors

The hazard ratio for condom use of 0.472 = exp (-0.008) implies that patients using condoms face 52.8% lower risk of death compared to patients not using condoms. The 95% confidence interval suggests that the rate could be as much as 68% lower to 31% lower. The p-value is equal to 0 and the confidence interval excludes the null of 1, hence, condom use is a significant predictor of better survival.

The partial likelihood ratio test for the overall significance of the educational level coefficients is 4.31 and the p-value computed using a chi-square distribution with two degrees of freedom is 0.116, suggesting that neither secondary school leavers nor people with more than secondary school education have a hazard rate that is significantly different from people with no education. The p-value of the individual Wald statistics indicates that the hazard rate in each of the two groups is not significantly different from that of reference group.

The estimated hazard ratio comparing primary education to no education is 0.815 = exp (-0.204). And that comparing secondary or above level of education to no education is 0.5 = exp (-0.694). These hazard ratios imply that, HIV positive patients on follow up with primary levels of education and those with secondary or higher levels of education are dying at a rate that is 18% and 50% lower than patients with no education on treatment. The p-values and the confidence intervals show that the education coefficients are not significant determinants of survival.

The hazard ratio for sex is 1.903 = exp (0.643), implying that holding all other factors constant, men on HIV treatment follow up die at 90.3% rate higher than women on follow-up. The estimated *p*-value = 0.00 and the confidence interval excludes the null of one both showing that sex has a significant impact on survival.

The hazard ratio of age is 1.017 = exp (0.017); this means that holding all other factors constant, for each year's increase in age, there is 1.7% increase in the patient risk of death, 95% CI (0% increase to 4% increase). As shown by the p-value and 95% confidence interval age is not a significant determinant of survival.

The hazard ratio of dependants is 0.935 = exp (-0.067) implying that an increase in number of dependants by one reduces the patient risk of death by 6.5%. The hazard ratio for marriage is 0.832 = exp (-0.184), this means that, holding all other factors constant, those who are married and on HIV treatment follow up die at a lower rate than those not married. However, married is not a significant determinant of survival.

The hazard ratio for piped water is 1.485 = exp (-0.395), implying that, holding all the other variables constant, patients with piped water within their households, die at 48.5% rate higher than those without piped water. Piped water is a significant determinant of survival.

5. Discussion

As expected, the survival analysis findings show that the risk of mortality for patients on ART is less than for the patients who are not on ART. The survival rate is also found to be higher for the female than for male on treatment follow up. The lower survival rate of men may be partly explained by the health care seeking behaviour of men. Generally, men tend to seek care late and have difficulty with follow up, especially given the need to visit hospitals on a regular basis. Secondly for most families, the men are bread winners and they may not have freedom to miss work frequently to go to hospital. Given the long-term follow up in ART treatment, these challenges may contribute to increase in treatment default and hence increased mortality risk for men.

On the other hand, the females seek health care more frequently than men and are generally more willing to seek additional support like counselling, nutritional support and health education. The women also have more avenues for accessing ART care than their male counterparts. For example, during clinic visit for prevention of mother to child transmission, when the women take their sick and sometime HIV positive children to hospital, they too are likely to seek care. These opportunities are likely to increase women's access and adherence to treatment and hence increased survival rate.

The study also found out that condom use not only prevents HIV infection but also determines the survival of the people using ART. The risk of mortality for the patients on ART and using condoms were found to be lower than their counterparts who were on ART but not using condoms. Condom use proved to be a significant determinant of survival. This finding confirms the epidemiological studies that have been done and show that condom use reduces the chances of HIV positive people to acquire new and sometimes more resistant strains of HIV that recuses the effectiveness of ART and hence increased the risk of mortality for PLWHI and even for those on ART.In addition, employment significantly increases survival for the people living with HIV on treatment follow up. Employment, age, marital status, dependants were also found to influences the survival rate of those using ART.

5.1. Study Limitations

This study was not able to control for some of the important determinants of patient survival including the body mass index (BMI) and adherence to medication for the patients on treatment although clinically, these are key indicators to patient survival. This was due to data constraints as the patient weights were missing for several patients and adherence indicator was not captured at all in Mbagathi hospital patient record. In addition, the socioeconomic and demographic data were only capture at treatment debut and hence in was not possible to capture impact of long term ART use of employment, income etc.

5.2. Conclusion

HIV and AIDS is a major cause of premature death and has resulted into a large demographic as well as economic loss in the country. There has been both local and global response to not only prevent the new infections but also to provide treatment, care and support the population that are already infected with the HIV virus. ART treatment has been introduced to treat eligible patients.

The finding that unemployment lowers the survival rate of HIV positive patients on ARVs by 10% is a unique contribution. To achieve the HIV prevention and treatment goals, the government needs to not only focus on treatment provision but also address macroeconomic stability issues that have a bearing on employment creation, inflation control and poverty reduction. Furthermore, the government and other players in HIV and AIDS care need to emphasize the need for consistent and appropriate condom use even couples living with HIV and on ART in order to increase their length of life.

Although the education level had a positive impact on individual survival rate, this impact was not statistically significant. Hence treatment education received by the patients in the two hospitals may have been more relevant for their survival than general of education. The public and private health sector players should develop patient centred treatment approaches in which treatment education, early detection, treatment adherence and follow up are emphasized. Furthermore, the institutions for higher learning in Kenya and other developing countries should modify their curriculum especially on health care workers attitude towards patients and communication in order to encourage patient centred treatment approaches for both communicable and non-communicable diseases. Finally, these findings emphasize the need for universal ART access and gender mainstreaming of HIV treatment, as well as addressing socio-economic issues in order to improve rates of survival people living with HIV.

6. References

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