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Application of Invariant Analyses to Study Survival Trends of Patients on Antiretroviral Therapy (ART) and TB Treatment in Kenya

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ABSTRACT

Kenya is one of the countries, globally, with a high burden of human immunodeficiency virus and tuberculosis. The co-infection between tuberculosis and human immunodeficiency virus/acquired immunodeficiency syndrome makes the management of the infection more complicated and reduces the chances of survival. The current study evaluates the trends in the survival of individuals with ART and TB management, especially in relation to various Counties in the country. The specific objective was to establish the survival trends of patients on Antiretroviral Therapy (ART) and TB treatment in Kenya using Kaplan Meier function. The study used a retrospective cohort study design. The target population included patients on co-therapy TB and ART management who attended the health facilities between 1st January 2015 and 31st December 2019. The sample of the study was obtained from all the available HIV-TB co-infected patients' records in National AIDS & STIs Control Program (NASCOP) database (secondary data) from the selected counties in Kenya. Kaplan Meier estimator was used in the estimation of the survival function. Analysis was done using STATA v14.2 and Bayes' v3.0.2. The study also found that HIV-TB patients' death rates for the period between 2015 and 2019 varied from one County to another. The study also established that the distribution of TB and HIV deaths in the 47 Counties varied across the five years. In the year 2015, the total number of TB and HIV deaths in the 47 Countries was 1077, which decreased to 921 TB and HIV deaths in 2016 before decreasing to 391 in 2017, 106 in 2018 and 60 in 2019. The study found that the main factors significantly influencing HIV-TB confections include gender, marital status, WHO clinical stage, age, weight and facility levels.

Key words: Antiretroviral, Prevalence, Tuberculosis, Therapy.

1.0 INTRODUCTION

Human Immunodeficiency Virus (HIV) has over the years been a considerable challenge in the control of tuberculosis (TB), according to the World Health Organization (WHO), (2019) report, Since HIV struck in early 80s, and Tuberculosis has been the leading causes of death among individuals living with HIV. In 2019, about 10 million people developed active TB, and 9% of them were living with HIV and One-third of the 36.9 million people living with HIV and AIDS worldwide are co-infected with TB [4]. In addition, TB was responsible for about one third of all AIDS related deaths in the year 2018.

The World Health Organization (2019), developed HIV/TB collaborative activities to strengthen the mechanisms for delivering integrated TB and HIV services so as to reduce the burden of TB in people living with HIV by initiating early antiretroviral therapy (ART), diagnosing TB and start treatment.

Although the government of Kenya as well as non-governmental organizations have put up several strategies in place to reduce HIV/AIDs and TB incidence, the two diseases still account for a considerable number of deaths in the country [8].

It has been realized from research by Dhungana, G. P [3] that early initiation of ART during the treatment of TB leads to an improvement in survival of patients and hence a reduction in the prevalence of HIV/TB co-infection. This is the target population that the research will endeavor to establish the survival trends of those patients.

1.1 Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) Co infections.

HIV is a viral infection which compromises the immunity systems of the body. The impairment of the immunity system gives way to other opportunistic infections to the body due to compromised body immunity. So far there is no known cure for acquired immune deficiency syndrome (AIDS) which is a terminal condition of an HIV infected patient. Some of the opportunistic infections are Tuberculosis and other dermatological diseases such as Acne. On The other hand, Tuberculosis (TB) is a bacterial disease that affects the lungs that is treatable and preventable. In this regard, a co-infection is a case where HIV patient is infected by TB as an opportunistic infection after compromised body immunity. Individuals who are HIV positive are 20 to 30 times more likely to develop an active TB than the HIV negative (World Health Organization -2019 report). Among HIV positive individuals, diagnosis of an active TB is a sign of HIV progression to AIDs.

1.2 Spatial Temporal Patterns

Spatial patterns are observations and description of diseases (HIV-TB co-infection in this case) and their geographical variation and distribution [11]. The geographical factors to be considered like environmental, demographic, genetic and socio-economic will help the study relate how or whether they affect survival trends after the co-infection, application of ART and TB management and treatment. Temporal distribution is the distribution of the disease (HIV-TB co-infection) or other events such as death over specific duration of time and seasons. Spatial-temporal analysis of HIV-TB co- infection therefore enables the estimation of events including disease and death across both space and time in a particular location and period of time. Spatial Pattern of Deaths of People Infected With both TB and HIV

In Iran, [14] studied spatial distribution of TB and HIV coinfection in South of Iran. The aim was to describe the spatial distribution of TB/HIV co-infection using GIS and Exploratory Spatial Data Analysis (ESDA) and to identify district of Hormozgan province (south of Iran) with significant disease clustering. The data was collected from health centers in Hormozgan province. Moran global and local indicators of spatial associations (LISA) were used to test the evidence of global and local spatial clustering via ArcGIS 9.3 software. The spatial distribution of TB/HIV cases was non-random and clustered. Spatial clustering suggested that six districts could be grouped as "hot spots". These districts also have high population density. [10] assessed the temporal trend of mortality due to tuberculosis in Northeast Brazil. Prais-Winsten's regression was used to analyze the temporal trend in the TB mortality coefficients. The Kernel density technique was used to analyze the spatial distribution of TB mortality. TB deaths were clustered in the East, West and North health districts, and the tuberculosis mortality coefficient remained stable throughout the study period. Temporal trend in mortality revealed that certain areas have higher TB mortality rates, and should therefore be prioritized in public health interventions targeting the disease. [9] examined spatial patterns of co-infection and Tuberculosis/HIV in Ceara, Brazil. The population was composed by tuberculosis cases in Patients older than 15 years, between the years of 2005 and 2014, that lived in Ceará. The data collection was made in the SINAN and in the Mortality Information System (SIM), being informed the diagnoses and deaths Caused by tuberculosis between 2005 and 2014. The spatial analysis Showed the concentration of Municipalities with high risk for tuberculosis in the Health Regions of Sobral, Fortaleza, Caucaia, Maracanaú, Cascavel and Itapipoca. In the spatial autocorrelation two clusters of high risk for tuberculosis Were identified. The concentration of municipalities with high risks for tuberculosis/HIV coinfection are described in the Macro regions of Health and Sobral Fortaleza, and in the municipalities of Tauá acid, and Orós Jaguaribe had a spatial correlation of two clusters identified in the mentioned macro regions. [1] examined spatial patterns of tuberculosis and HIV co-infection in Ethiopia. The study used TB and HIV data reported from all regions of Ethiopia through the national Health Management Information System (HMIS), between June 2015 and June 2017. Spatial clustering was assessed using Moran's I statistic and Getis-Ord statistic. Spatial binomial regression models were constructed separately for the prevalence of TB among people living with HIV and for the prevalence of HIV among TB patients, with and without spatial components using a Bayesian approach. The results indicated that the prevalence of HIV among TB patients was 7.34%; hotspots were observed in districts located in Amhara, Afar, and Gambela regions, and cold spots were observed in Oromiya and Southern Nations, Nationalities, and People (SNNP) regions. The prevalence of TB among people living with HIV varied from 0.7% in Oromia region to 14.5% in Afar region. Hotspots of TB prevalence among people living with HIV were observed in districts located in Gambela, Afar, Somali, and Oromiya regions; whereas the cold spots were observed in districts located in Amhara and Tigray regions. The ecological-level factors associated with the prevalence of TB among people living with HIV were low wealth index, low adult literacy rate, and distance to an international border.

Aturinde, A et. al., [2] conducted a spatial analysis of HIVTB co-clustering in Uganda. The study used global Moran's index, spatial scan statistics and bivariate global and local Moran's indices to investigate the geographical clustering patterns of both diseases, as individuals and as combined. The data used are TB and HIV case data for 2015, 2016 and 2017 obtained from the District Health Information Software 2 system, housed and maintained by the Ministry of Health, Uganda. The results showed that while TB and HIV diseases are highly correlated (55–76%), they exhibit relatively different spatial clustering patterns across Uganda. The joint TB/HIV prevalence shows consistent hotspot clusters around districts surrounding Lake Victoria as well as

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northern Uganda. These two clusters could be linked to the presence of high HIV prevalence among the fishing communities of Lake Victoria and the presence of refugees and internally displaced people camps, respectively. The consistent cold spot observed in eastern Uganda and around Kasese could be explained by low HIV prevalence in communities with circumcision tradition.

In South Africa, [6] studied the contribution of spatial analysis to understanding HIV/TB mortality in children. The study used cross-sectional data in the rural areas of South Africa, Agincourt sub-district. South Africa accounts for more than a sixth of the global population of people infected with HIV and TB, ranking her highest in HIV/TB co-infection worldwide. Remote areas often bear the greatest burden of morbidity and mortality, yet there are spatial differences within rural settings. Modelling used multiple logit regression models with and without spatial household random effects. Spatial models disclosed that the areas which experienced the greatest child HIV/TB mortality were those without any health facility. [7] examined Bayesian modeling of spatiotemporal patterns of TB-HIV co-infection risk in Kenya. The study analyzed the TB and TB-HIV case notification data from the Kenya national TB control program aggregated for forty-seven counties over a seven-year period (2012-2018). Using spatiotemporal poisson regression models within the Integrated Nested Laplace Approach (INLA) paradygm, the study modeled the risk of TB-HIV co-infection. Six competing models with varying space-time formulations were compared to determine the best fit model. The study assessed the geographic patterns and temporal trends of co-infection risk by mapping the posterior marginal from the best fit model. Based on the Bayesian Defiance Information (DIC) and the effective number of parameters (pD) comparisons, the spatiotemporal model allowing space-time interaction was the best in explaining the geographical variations in TB-HIV co-infection. [13] carried out a spatiotemporal analysis of HIV associated mortality in rural western Kenya 2011–2015. The study used the Optimized Hot Spot Analysis to examine whether HIV-associated deaths would form statistically significant local aggregation in the 5-year period. The results indicated that the hotspot analysis showed that 20.0% of the study area (72 km2) was detected as hotspots and 4.2% of the study area as cold spots (15 km2).

According to [12] Poisson distribution expresses the probability of a given number of events occurring in a fixed interval of time or space if these events occur with a known constant mean rate and independently of the time since the last event. There are four conditions of using Poisson distribution. The first condition is that an event can occur any number of times during a time period. Secondly events occur independently. In other words, if an event occurs, it does not affect the probability of another event occurring in the same time period. Thirdly, the probability of an event occurring is proportional to the length of the time period. The Poisson distribution is also used for the number of events in other specified intervals such as distance, area or volume. The study assumes that the count data follows the Poisson distribution where the log of the relative risks will be the focus of modeling. For Instance, a study on joint spatiotemporal risk patterns for Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) in Kenya, [8] used Bayesian hierarchical modeling.

2.0 Methodology

2.1 Data

This study used Secondary data which was obtained from NASCOP programs data base. The Ministry of Health in Kenya has a routine case-based monitoring and reporting regulations for HIV and TB through NASCOP and NLTP, respectively. NASCOP has an Integrated Electronic Medical Records (EMR) Data Warehouse (IDWH) that stores HIV/AIDs related data for health facilities in Kenya. Health facilities in Kenya are required to update their EMR databases in IDWH on a monthly basis. NLTP hosts the Tuberculosis Information from Basic Unit (TIBU), which is a centrally located case-based surveillance system that allows for real-time reporting. Since its establishment in the year

2012, TIBU has made TB patients' notifications instant and very timely, allowing for easy report generation. All health facilities, both private and public, in Kenya are required to enter data regarding Tuberculosis cases into the TIBU system. Both the NLTP and NASCOP programs use WHO data recording and reporting standards in health facilities in every county (47 Counties in Kenya) and in the national surveillance system. This study used individual data for each patient per County for a period of five years (1st January 2015 and 31st December 2019). The study used a data extraction tool to obtain secondary NASCOP databases.

Treatment adherence was assessed by measure of the patient intake of the prescribed drugs in appropriate prescribed time and in the right dose. checking on the data of patients' attendance to ART clinics and TB 'sub clinics'. The principal investigator also checked on the monitored data of risk of progression from latent to active TB. Treatment outcome data also measured the adherence level.

If there were missing data the researcher used both multiple and regression imputation to solve the missing data problem.

2.2 Inclusion and exclusion Criteria

This study considered all adult patients who were co-infected with both HIV and TB with at least 15year of age. The patients should be attending their therapies and medications within the counties. Patients must have been on treatment between 1st January

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2015 and 31st December 2019. Patients who transferred to health facilities outside the considered counties after initiation of ART and TB medication was excluded from the study because it was difficult to obtain full information about them. Those patients under study whose date of death was missing was handled as censored data, all this was confirmed by looking at patients documents.

2.3 Data abstraction

The data to be obtained was de-identified and assigned unique ART and TB treatment random numbers before sharing to the researcher to enhance the study subject's privacy and confidentiality.

2.4 Variable for the Study

The outcome variable that was considered in this study is survival time, which is the time to death measured from time of co-infection to death in months. Nonetheless, the time of death was censored for co-infected patients who were lost during follow-ups and did not die at 31st December 2019. The independent covariates that were considered for the separate survival, spatial and space-time modeling as as shown in Table 1.

Table 1: List of covariates used in the study

Variable name	Values of the variable	Type
Age	Years (baseline)	Continuous
Sex	Female, male	Categorical
CD4	CD4 counts	Continuous
Still on care	Alive, dead, default, stopped and transferred out	Categorical
Weight	Weight (baseline)	Continuous
Status of patient	Alive, dead	Categorical
Marital status	Single, married, divorced and widowed	Categorical
Function	Ambulatory, working and bedridden	Categorical
WHO clinical stage	Stage I, II, II, IV	Categorical
Facility level	Clinic, health center and hospital	Categorical

WHO Clinical Stage which is classified into four; I, II, III and IV; where Stage I indicates asymptomatic disease, Stage II indicates mild disease, Stage III indicates advanced disease and Stage IV indicates severe disease. Hence disease severity increases from Stage I to Stage IV. Functional Status of the patients is also categorical covariate with three categories: Working, Ambulatory and Bedridden. Working patients are those patients who are able to work day to day while ambulatory patients are those patients who are able to work some time but bedridden patients cannot able to work due to the infectious disease.

2.5 Survivor Function

Survivor function S(t) is the probability that an individual survives for a time, t, greater than or equal, t. Collection of any sample of survival data can take into account absence or presence of censoring depending on the interest of the study. For instance, in a given single sample of survival times where censoring was absent, survivor function estimate is given by,

(t) = Number of individuals with survival times $\geq t$/Number of individuals in the data set.

$S(t) = 1 - F(t)$

Where;

S(t) is the probability that an individual survives for a time equal to or greater than t.

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F(t) is the ratio of the total number of individuals alive at time t to the total number of individuals in the study. Let t be the time until an event of interest occurs, and T be the whole time period that the experiment is supposed to take, such that the survival time of an individual can take any values, which can be written as; t< ***T*** and can take different values of the random variable T forming a probability distribution.

If we suppose that the random variable T has a probability distribution with a density function f(t) then the distribution function of T is given by;

$F(t)$ = P($T < t$) = $\int_0^t$ f(u)du .This is the probability that the survival time is less than some value t, hence we can now define survivor function s(t) as the probability that an individual survival time is greater than or equal to t and is given by;

S(t) = P($T \geq t$) = 1 −F (t) .Where survivor time is the probability an individual survives from the time the study started to sometime beyond t .

2.6 Censoring

Censoring is said to be present when we have information about subject's event time, but we don't know the exact event time. Survival time of a participant in a study is said to have been censored when the end point of interest has not been observed. It can be either left, interval or right censoring.

Assuming an individual enters the study at a time, t, denoted by ,t_0, and the event of interest is observed at unknown time, t, then the survival time, t, of that individual was;

$t_0 + t$

If the individual survived up to sometime, c, after entering the study, say $t_0 + c$ and maybe disappeared before time, $t_0 + t$, when the event of interest is observed then we say time ,c, as censored survival time.

If we let T represent failure time and C represent censoring time, then;

Left censoring is when an individual experiences the event of interest before the start of the study. That is actual survival time of an individual is less than that observed. Mathematically we present it as; T ∈ (0, c_1) and it is known that only the failure time T is less than observed censoring time cl but its exact value is unobservable.

Right censoring is a case where an individual may experience the event of interest after a given time t, we only know that the individual is alive (not failed) up to the time when the study stops. Mathematically it is presented as; T∈ (c_r,∞) and it is known only that the failure time T is greater than the observed censoring time Cr but exact value of failure time cannot be observed.

Interval censoring; is a situation where the only information known is that a given event occurred within some interval of time. Mathematically T∈ (c_i,c_r) and it is known only that the failure time is less than the observed right censoring time c_r and greater than the observed left censoring ,c_i but the exact value cannot be observed.

2.7 Hazard Function

This is the probability that an individual alive at time t experiences death in the next period., in other words it is the instantaneous death rate for an individual surviving up to time t.

If we let a random variable T lie between (t≤ $T < t + \delta t$) and T being greater or equal t , then the probability of the random variable of an individual s survival time is

P(t ≤ $T < T + \delta T | T \geq t$)

Then the hazard function therefore was the limiting value of this probability as δt tends to zero and divide the interval by δt, implying;

h(t) = $\lim_{\delta t \to 0}$ { P($t \leq T < T + \delta T | T \geq t$)/$\delta t$}

Using this hazard function definition, we can derive a relationship with survival function as;

Using the conditional probability theory that an event A occurs on condition that event B has occurred and the above hazard function we can derive a relationship with survival function and obtain accumulative hazard function H(t);

Conditional probability; P(A\B)=P(AB)/P(B) where p(AB) is the probability of the joint occurrence of A and B .

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Given that h(t)=$\lim_{\delta\to 0}[p(t \le T < t+\delta t \backslash T \ge t/\delta t]$

and F(t) = p(T < t) = $\int_0^t$ f(u)du (distribution function of T) and S(t) = p(T ≥ t) = 1 − $F(t)$ (survivor function) combining the above definitions gave us;

p(t ≤ $T < t + \delta t)/p(T \ge t)$

= F(t + δt) − $F(t)/s(t)$

Where F(t) is the distribution function of T,

Then h(t)=$\lim_{\delta\to 0} \frac{F(t+\delta t)-F(t)}{\delta t} * \frac{1}{s(t)}$

$$h(t) = \lim_{\delta t\to 0} \frac{F(t+\delta t)-F(t)}{\delta t}$$

finding the derivative of F(t) with respect to t we get f(t).

hence

$h(t) = \frac{f(t)}{s(t)}$

it then follows

$$h(t) = -\frac{d}{dt}(\log\{s(t)\}\ ,$$

and so

$S(t) = exp\{-H(t)\}$

Where H(t)=$\int_1^1 h(u)du$ (cumulative hazard)

2.8 Multivariable Survival Model

The K-M curves and the log-rank test described above provide univariate analyses useful in assessing whether a covariate affects survival and are most suitable for descriptive purposes. They are particularly handy when the predictor variables are categorical and do not work easily with continuous predictors. However, they do not allow us to see how survival of a group is affected with the influence of other covariates included in the model. The Cox Proportional Hazard model is commonly employed in analyzing survival data in a multivariate way, allowing the effects of a set of covariates on survival time to be assessed [14]. The Cox Proportional Hazard model also handles censored data, categorical and continuous variables as well as variables that change over time, all of which may influence survival [5]. The Cox Proportional Hazard model also allows for frailty to be included at various levels. The study also fitted the competing risk model, as there were outcome events that were competing with the event of interest.

2.9 Research ethics

This study involves the utilization of non-identifiable secondary data collected as part of routine programs monitoring. Ethical permission to utilize the data was obtained from both National Tuberculosis Leprosy & Lung Disease Program (NTLD-P) and National AIDS & STIs Control Program (NASCOP). The study was subjected to Institutional Research Ethics Committee (IREC), which is a body constituted jointly by Moi University College of Health Sciences (MU/CHS) and Moi Teaching and Referral Hospital (MT&RH). Extracted data from NLTP and NASCOP programs was not included the identity of patients and it was kept in locked computer for privacy and confidentiality.

2.10 Data analysis

There are three stages of analysis that were considered in this study. The first stage involved preliminary descriptive analysis relating to variables to be considered using Kaplan Meier test. The second stage involved investigation of spatial correlation structure of mortality. The last stage of analysis involved fitting models to determine how particular independent variable contributes to explaining the dependent variable, as well as mapping the risk of mortality. Multivariate analysis was employed by fitting Cox Proportion Hazard Model to estimate survival trends of subjects as well as to estimate the effects of covariates on survival and a Bayesian model also also fitted to show spatial and temporal variations in mortality hazard by Counties in Kenya. Analysis was done using STATA v14.2 and BayesX v3.0.2.

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3.0 RESULTS AND DISCUSSIONS

3.1 Socio Demographic Information

The demographic information of the participants covered their gender, marital status, WHO Clinical Stage, weight at the start of the study period and age. As shown in Table 4.1, the results show that majority of the people infected with both TB and HIV (54.4%) were female. In addition, the average age of the people infected with both TB and HIV in Kenya was 31.065± 13.0765 yrs. Further, the average weight of the people infected with both TB and HIV was 66.2114± 20.99349 kgs. The findings also show that majority of the participants (42.3%) were single followed by married monogamous at 22.9% and widowed at 19.1%. Further, majority of the people infected with both TB and HIV (44.2%) were in stage one of the WHO clinical stage and 33.7% were in stage two of the WHO clinical stage.

Table 2 : Socio Demographic Information

	Frequency (n=32281)	**Percent**
Gender		
Male	14724	45.6
Female	17557	54.4
Age		
Mean ± SD	31.065 ± 13.0765	
Minimum; Maximum	1.0,80.0	
Weight		
Mean ± SD	66.2114 ± 20.99349	
Minimum; Maximum	3.00,130.00	
Marital Status	**Frequency**	**Percent**
Cohabiting	41	.1
Divorced	1208	3.7
Married Monogamous	7396	22.9
Married Polygamous	1216	3.8
Minor	2413	7.5
Separated	162	.5
Single	13665	42.3
Widowed	6180	19.1
WHO stage	**Frequency**	**Percent**
Stage One	14272	44.2
Stage Two	10894	33.7
Stage Three	4918	15.2
Stage Four	2197	6.8

3.2 Survival Trends of Patients on ART and TB Treatment

The first objective of the study was to establish the survival trends of patients on Antiretroviral Therapy (ART) and TB treatment in Kenya. Kaplan- Meier Estimate of the survivor function was used in establishing survival trends of patients on Antiretroviral Therapy (ART) and TB treatment in Kenya. A total of 2,555 (7.9%) of the people infected with both TB and HIV in Kenya were reported dead in the 5-year period after initiation of ART. The mean survival time for the event (dead) cases was 1420.328 (range 1399.206-1441.450) indicating that the average period of event occurrence (death) was 1420 days for the group with both art and TB treatment. In addition, the median survival time for the event (dead) cases was 1617 days indicating that the majority of the deaths occurred before 1617 days of treatment. In addition, among individuals with ART treatment only, the mean survival time for the event (dead) cases was 1560.704 (range 1700-1799) indicating that the average period of event occurrence (death) was 1560 days. Further, the median survival time for the event (dead) cases was 1750 days indicating that the majority of the deaths occurred before 1617 days of treatment.

Table 3: Means and Medians for Survival Time

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ART and TB treatment	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
ART and TB treatment	1420.328	10.777	1399.206	1441.450	1617.000	18.454	1580.829	1653.171
ART Treatment Only	1560.704	15.606	1530.116	1591.291	1750.000	25.427	1700.163	1799.837
Overall	1458.906	8.975	1441.314	1476.498	1646.000	17.469	1611.760	1680.240

a. Estimation is limited to the largest survival time if it is censored.

The log rank test was used in calculating the chi-square (X^2) for each event time for each group and sums the results. The rule of the thumb is that if the p-value is less than .05, then there is a statistically significant difference in time-to-event between the independent groups. However, if the p-value is more than .05, then there is not a significant difference in time-to-event between the independent groups. The log rank test in this study showed that the two curves were statistically significantly different. This is shown the p-value of 0.000, which was less than the significance level. This implies that the use of both ART and TB treatment statistically influences the survival of HIV and TB co-infected patients.

Table 4: The Log-rank test

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	22.022	1	.000

Test of equality of survival distributions for the different levels of ART and TB treatment.

The Kaplan-Meier Curve in Figure 1 shows that that people infected with both TB and HIV who received both ART and TB treatment had higher survival time than people infected with both TB and HIV who received ART only up to around 750th day. After that, the individuals receiving ART only had better survival time that those receiving both ART and TB treatment. According to the World Health Organization, active TB disease can be treated with a combination of antibacterial medications for a period of six to 12 months. The most common treatment for active TB is isoniazid INH in combination with three other drugs—rifampin, pyrazinamide and ethambutol. However, drug-resistant TB treatment takes much longer, 20 to 30 months to complete, which is approximately 900 days. This shows that all the people infected with both TB and HIV complete their TB treatment within 900 days. As such, after this period none of the patients is under TB treatment.

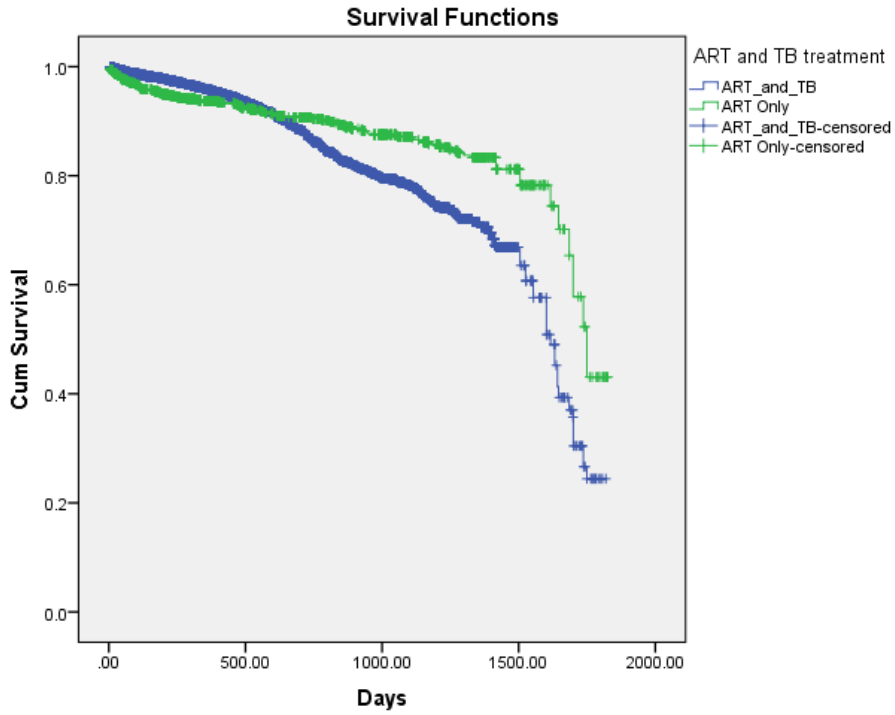

Figure 1: Kaplan- Meier Curve for Treatment and Outcome

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In Figure 2, the Kaplan- Meier curve for marital status and outcome shows that throughout the period the separated and married polygamous had low survival rates. The minors had moderate survival rates and single and married monogamous had high survival rates. The cohabiting individuals had high survival rates during the first one and a half years, which afterwards begins to decline.

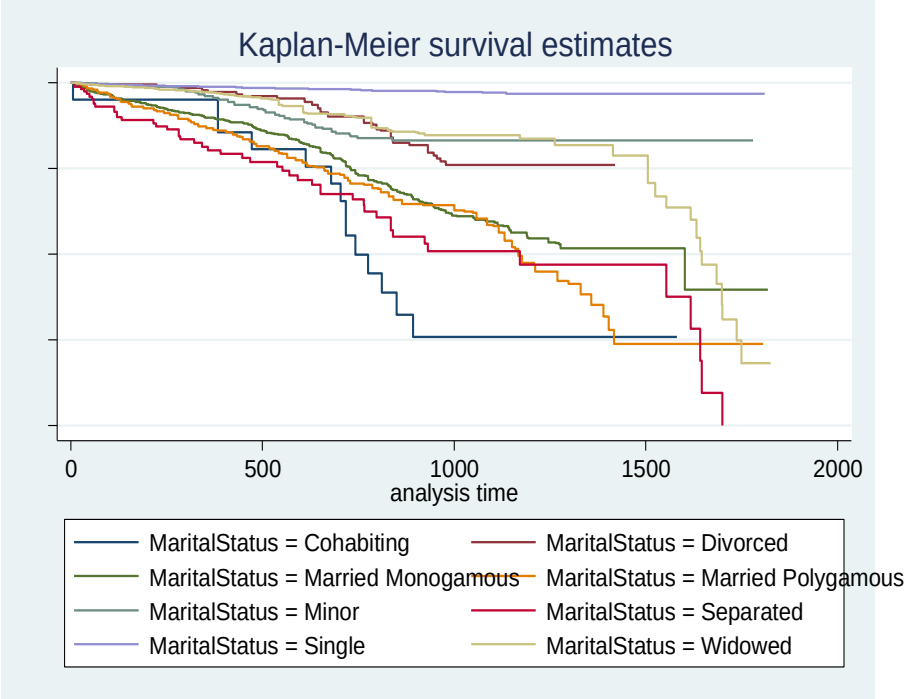

Figure 2: Kaplan- Meier Curve for Marital Status and Outcome

As shown in Figure 3, the survival rates was high among people in WHO clinical stage one, followed by those in stage two and stage three. Individuals in stage four of the WHO clinical stage had the lowest survival rates.

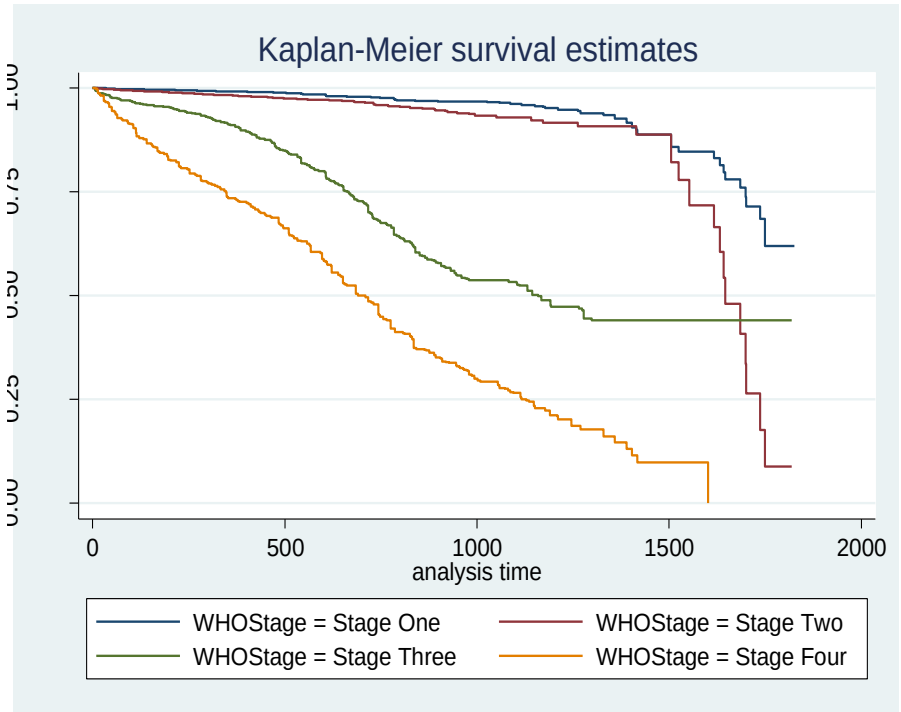

Figure 3: Kaplan- Meier Curve for WHO Stage and Outcome

The results, as shown in Figure 4. show that individuals in level 3 facilities had the lowest survival rates, followed by individuals in level 2 facilities, and level 5 facilities. Level 4 facilities had the lowest survival rates among people with HIV-TB co-infections.

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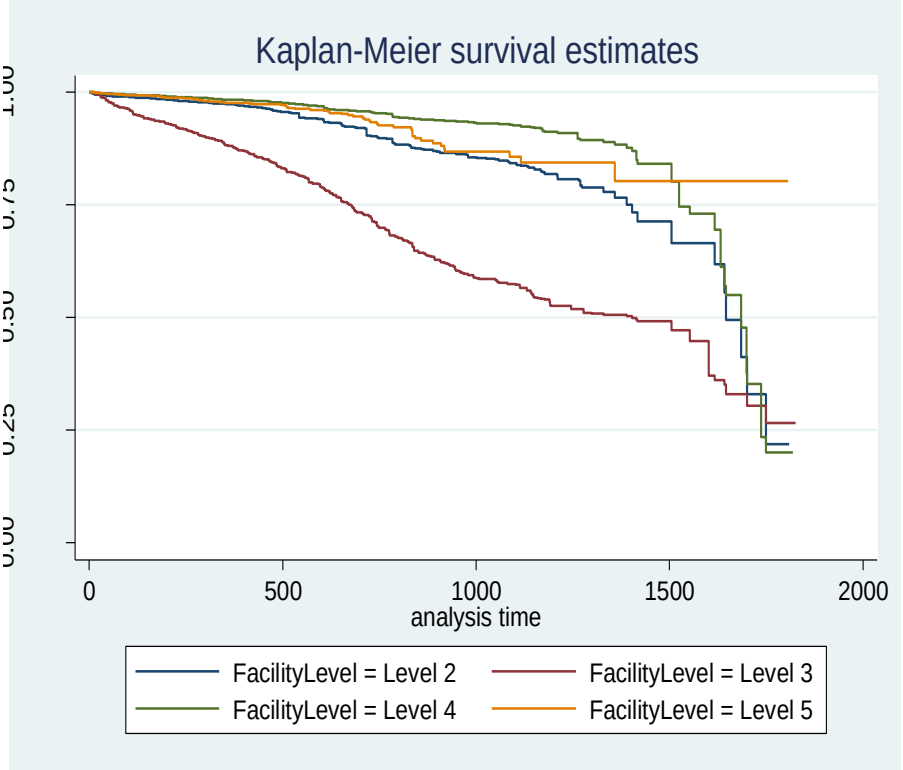

Figure 4: Kaplan- Meier Curve for Facility Level and Outcome

In the first two years, there was no much difference in the survival rates among HIV and TB co-infected patients. However, this changes in the third year, where Nairobi region is seen to have the lowest survival rate, followed by central region and coast region. However, Eastern region had the highest survival rate followed by the North Easter region.

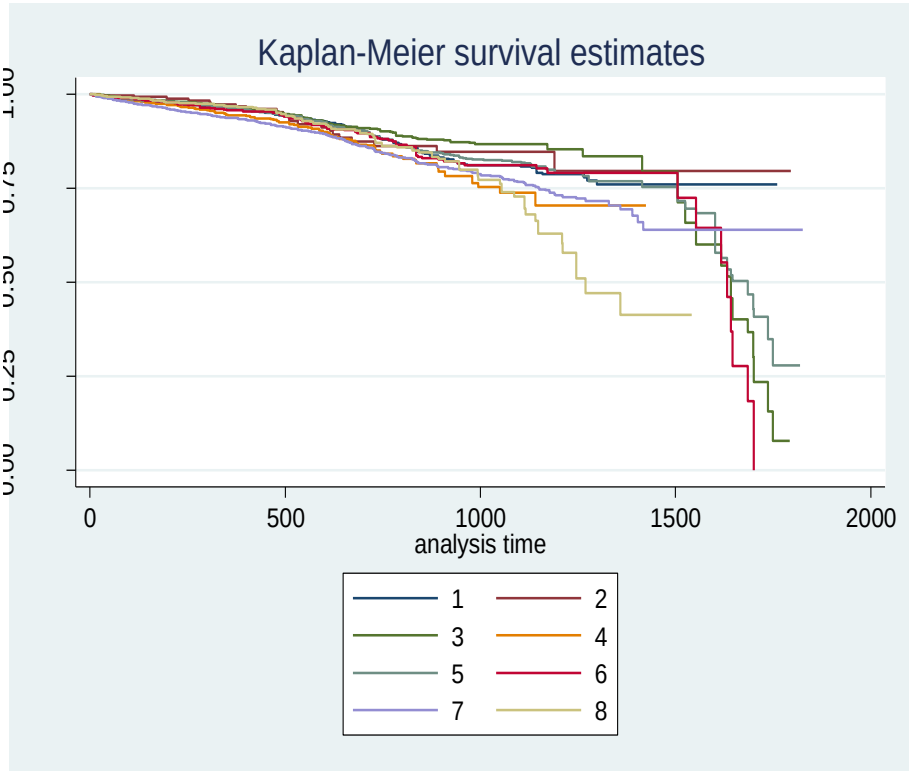

Figure 5: Kaplan- Meier Curve for County and Outcome

4.0 CONCLUSIONS AND RECOMMENDATIONS

4.1 Conclusions

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The study concludes that the use of both ART and TB treatment statistically influences the survival of HIV and TB co-infected patients. People infected with both TB and HIV who received both ART and TB treatment had higher survival time than people infected with both TB and HIV who received ART only up to around 750th day. After that, the individuals receiving ART only had better survival time that those receiving both ART and TB treatment. TB treatment normally takes a maximum of 900 days and hence after this period they do not use TB medication.

The study concludes that HIV-TB patients' death rates for the period between 2015 and 2019 varied from one County to another. TB and HIV in the study area did not uniformly occur in different geographic settings, and revealed a non-random distribution. Kisii County had the highest HIV-TB patients' death rates with 14.29% of all the people with HIV-TB confections experiencing death during the 5 year period, followed by Migori County with a HIV-TB patients' death rate of 13.85 percent, Homa Bay County with a HIV-TB patients' death rate of 13.47% and Kajiado County with a HIV-TB patients' death rate of 12.97%. Mandera County had the lowest number of HIV-TB patients' deaths (6), followed Wajir County (7), Garissa County (8), Marsabit County (10) and Bungoma County (23).

The study concludes that the distribution of TB and HIV deaths in the 47 Counties varied across the five years. In the year 2015, the total number of TB and HIV deaths in the 47 Countries was 1077, which decreased to 921 TB and HIV deaths in 2016 before decreasing to 391 in 2017, 106 in 2018 and 60 in 2019.
The study found that the main factors significantly influencing HIV-TB confections include gender, marital status, WHO clinical stage, age, facility levels. The female gender is more likely to experience the event (HIV-TB confections) than the male gender. In addition, married polygamous, minors, separated, singles and widowed were more likely to experience HIV-TB confections as compared to the cohabiting, divorced, married monogamous and married polygamous. Also, individuals who were in stage four were more likely to experience HIV-TB confections as compared to those in WHO stage three, WHO stage two and WHO stage one. This implies that the deterioration of WHO clinical stage increases the probability of the occurrence of HIV-TB confections. Further, the Individuals in level four facilities were more likely to experience the HIV-TB confections as compared to other facilities. This was followed by level five facilities and level two facilities. The results indicated that age had a significant influence on HIV-TB confections. Also, the findings indicated that weight had a significant influence on HIV-TB confections.

4.2 Recommendations

The study also recommends that the Ministry of Health through National AIDS & STIs Control Program (NASCOP) and National Tuberculosis Leprosy & Lung Disease Program should will continue giving a special focus on the co-infection of TB and HIV. Mortality of TB and HIV in this study was significant and some areas were found to be hot spots including Kisii, Homa Bay and Migori. Therefore, there is a need to have targeted intervention among these Areas to ensure that there is a reduction in the mortality of TB among HIV patients.

The study also proposes a sensitization of the ART nurses and health care workers at the facility so as to ensure a turnaround in the way we view tuberculosis among HIV patients and vice versa, hence optimize the testing of HIV in all TB patients and TB among all HIV patients.

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