Disparities in HIV/AIDS Progression among Children

A Case of Uganda

Ssebiryo Francis Exavious[1,2]

[1]Center of Nutrition Education and Technology (CeNET) Uganda

Plot 87 Bukoto Street, Kampala, Uganda.

[2]KMF Consult, Kampala- Uganda

fexavious@yahoo.com

Abstract

Background: The chronic nature of HIV/AIDS requires many resources in its management, yet knowledge on the rates of HIV infection transition from one stage to another is scanty. To shed light on this, we used a lifecourse theoretical perspective to appraise the chronological effect of demographic and socioeconomic factors on the lifecourse of HIV-AIDS progression among children. *Methods*: A 136 months retrospective follow-up of 59 children aged 0-15 for survival analysis. *Results*: Children contributed 5,108 person months on HIV infection lifecourse of which 55% is lived with asymptomatic stage. The duration of exposure to HIV infection contributed in each stage decreases with progressive amplification in the infection. Age at initiation of treatment, caregivers, father's survival and religious affiliation causes disparities in HIV infection progression. *Conclusion*: To optimize HIV infection survival time, HIV/AIDS care and treatment should strive to maintain HIV infection within asymptomatic levels yet initiating treatment on the earliest time possible.

Keywords: HIV/AIDS Survival-time, HIV-infection-progression, HIV-infection stages, HIV/AIDS-lifecourse, ART, Disparities

Introduction:

Uganda has seen improved access to Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) care and treatment in the recent past especially through a corroborative effort between the government and civil society organizations, though there are still constraints to universal access (61%) in the society (MoH, 2009). In the same way, more efforts goes to improving population health indicators in regards to the UN millennium commitments such as, delivering an effective HIV prevention, treatment, care and support needed to curb the global HIV/AIDS epidemic by 2015. Indeed, the number of adolescents who acquired HIV infection through perinatal transmission is now increasing (NIH, 2010), indicating a delayed HIV progression, that is the transition from HIV infection to AIDS or WHO stage IV (WHO, 2007) due to the improvement in HIV care and treatment. However, HIV/AIDS continue to grapple Sub-Saharan Africa in general and Uganda in particular, with an estimated 22.5 million adult and children living with HIV/AIDS (CLWH) in 2009, and 1.3 million adult and children having died of AIDS-related causes in Sub-Saharan Africa (AVERT, 2011). In Uganda, 1.2 million people (150,000 children <15) were seropositive and 64,000 persons died of HIV/AIDS and related causes in 2009 yet access to ART is limited to 39% of those in need (UNAIDS, 2010).

With Antiretroviral Therapy (ART), there is improved survival and health among both children and adults living with HIV/AIDS (NIH, 2010). Thus with advent of ART and HIV/AIDS care and treatment among children and adults, there is advances in improved health living, reduced morbidity. People on ART and HIV/AIDS care and treatment progresses through HIV infection slowly but this differ from individual to individual (Zwahlen & Egger, 2006). Indeed, Blanche (1997) indicates higher mortality among infants living with HIV/AIDS than those aged 1- 6 years of age but the study was limited to pediatric HIV. This makes information on children as a whole and the effect of social economic factors on HIV progression in children scanty. The NIH (2010) indicates that, infants may have faster progression of HIV than do other childhood ages (1-5 years), and have recommended infants to start antiretroviral treatment regardless of their clinical status, CD4 percentage, or viral load. In addition, only a few studies considered health disparities and socioeconomic characteristic (Hall et al., 2004), but have not paid much attention on disparities in

HIV/AIDS progression among population subgroups. Social groups witness different patterns of morbidity and mortality based on socioeconomic status, and access to care. Indeed persons in low social economic status experience poorer health than their counterparts in more advantaged socioeconomic status (AHRQ, 2001).

Literature Review

HIV causes chronic infection that requires life-long treatment once one starts the therapy. With HIV/AIDS care and treatment, HIV-related mortality and morbidity are reduced, and the general quality of life of People Living with HIV/AIDS (PLWH) is improved (USAID, 2010; Schneider et al., 2005). However, how much this differ by individuals' socio-demographic factors along the lifecourse of HIV-AIDS, and the estimates of how many will develop AIDS and when is barely unknown (CDC, 2006). In addition, while studies have reported on rapid HIV progression without Antiretroviral (ARV) treatment (Abrams et al., 2003), hardly a study has examined this scenario in the face of HIV care or ARV-treatment. Many a times, people of lesser socioeconomic status are highly vulnerable to deaths from certain causes such as malnutrition, yet they are preventable. Indeed, studies in the United States (US) have revealed higher burden of disease in minority population groups (AHRQ, 2001). However, there is dearth of information on how socioeconomic inequalities as factors documented for differences in cause-specific mortality (Bos et al., 2004) may affect HIV/AIDS transition rates among children. Furthermore, there is considerable evidence of disparities in life expectancy, morbidity, risk factors, and quality of life among segments of the population, defined by, sex, education, income, location, among other aspects (AHRQ, 2001; CDC, 2011). Thus, with incessant HIV/AIDS care and treatment among PLWH, there is need to examine how different, a cohort features along the HIV/AIDS lifecourse. Certainly, we cannot claim overall progress in the fight against HIV/AIDS morbidity if there are certain populations that are disadvantaged along the course of treatment. While some studies have found rapid HIV virus progression among infants (Newell et al., 2004), there is need to establish the transition rate of these CLWH from one stage of HIV to another. Furthermore, understanding population-health issues require a multidisciplinary approach that examines health determinants, disease and intervention at each stage of health transition, with critical emphasis on morbidity and mortality (Niessen, 2002).

In the same way, more efforts goes to improving population health indicators as regards the UN millennium commitments such as, delivering an effective HIV prevention, treatment, care and support needed to curb the global HIV/AIDS epidemic by 2015. Indeed, the number of adolescents who acquired HIV infection through perinatal transmission is now increasing (NIH, 2010), indicating a delayed HIV progression, that is the transition from HIV infection to AIDS or WHO stage IV (WHO, 2007) due to the improvement in HIV care and treatment. However, HIV/AIDS continue to grapple Sub-Saharan Africa in general and Uganda in particular, with an estimated 22.5 million adult and children living with HIV/AIDS (CLWH) in 2009, and 1.3 million adult and children having died of AIDS-related causes in Sub-Saharan Africa (AVERT, 2011). In Uganda, 1.2 million people (150,000 children <15) were seropositive and 64,000 persons died of HIV/AIDS and related causes in 2009 yet access to ART is limited to 39% of those in need (UNAIDS, 2010).

Theoretical Framework: This study adopts the Lifecourse Theory, which examines how chronological demographic and socioeconomic factors shape people's lives from birth to death (Hutchison, 2007). This framework is relevant in studying the causal effects of chronic disease and infectious disease (Ben-Shlomo & Kuh, 2002; Hall et al., 2002). The lifecourse theory enables the understanding of individuals by construction of an event history (series of different events and transitions) from birth to death and examines how people transit through different life periods.

In addition, the lifecourse perspective reflects how society and social institutions shape the pattern of a person's life (Elder 1985). With lifecourse perspective, the interplay of human lives and historical time provide an understanding of how people in a given cohort feature differently with their life experience (Elder, 1998). There is wealth of evidence that early experiences affect later morbidity and mortality (Halfon et al., 2005) especially with chronic diseases. Therefore, while studying differences in HIV/AIDS progression in children, the factors that influence HIV infection progression embeds within the key principles of the lifecourse perspective. In addition, the study models some parental background characteristics such as survival status, education attainment to measure their effect on child survival. The four stages of HIV/AIDS lifecourse are immunologically, clinically determined depending on certain health symptoms a PLWH attains (CDC, 1994; NIH, 2010; WHO, 2007), and Death is the definitive stage. The model thus, indicates that PLWH can stay or progress from the initial stage or state (N) to the next health state (A, B, C) or may die (D).

Furthermore, lifecourse perspective observe

health as a function of multiple factors that interplay in a genetic, biological, behavioural and socioeconomic context, health changes as experience changes (Halfon et al., 2005; Merete, 2006), and because each person has a unique lifecourse trajectory, research on irregularities in timing of life events can help in developing plausible interventions (Brent, 2004). The pace or rate of transition and the length of time a person spends in a given state are other aspects of interest in the study of lifecourse. Henceforth, considering the six principles of lifecourse perspectives (Elder, 1994, 1998), we operationalised different factors to examine the HIV/AIDS progression (lifecourse) as follows.

Socio-historical and geographical location- that is human life is understood in a historical context and the places they live in, this is exemplified by the place of residence of the child, and to whom he/she is living with.

Timing of lives- the intrinsic impact of life events that are dependent on time/ age at which they occur in one's life. Here, age of the children is an important biological and social factor that influences vulnerability to disease. Time the basic measure while denoting transitions (Elder, 1998) is synonymous to age; moreover, timing of a transition is a vital input in estimating expectation of life or transition rates.

Linked lives- assume that social and historical influences are expresses through a network of shared relationships. This is associated with factors that relate to parental survival, counselling, religion, and these represent interactions of shared relationships (Elder, 1998) as they affect self-esteem and wellbeing.

Human agency in making choices- this relate to lifecourse as determined by individual's choices and constraints in life and social circumstances. This study does not discuss this principle due to data constraint making it implausible to identify makers of decision-making and choices.

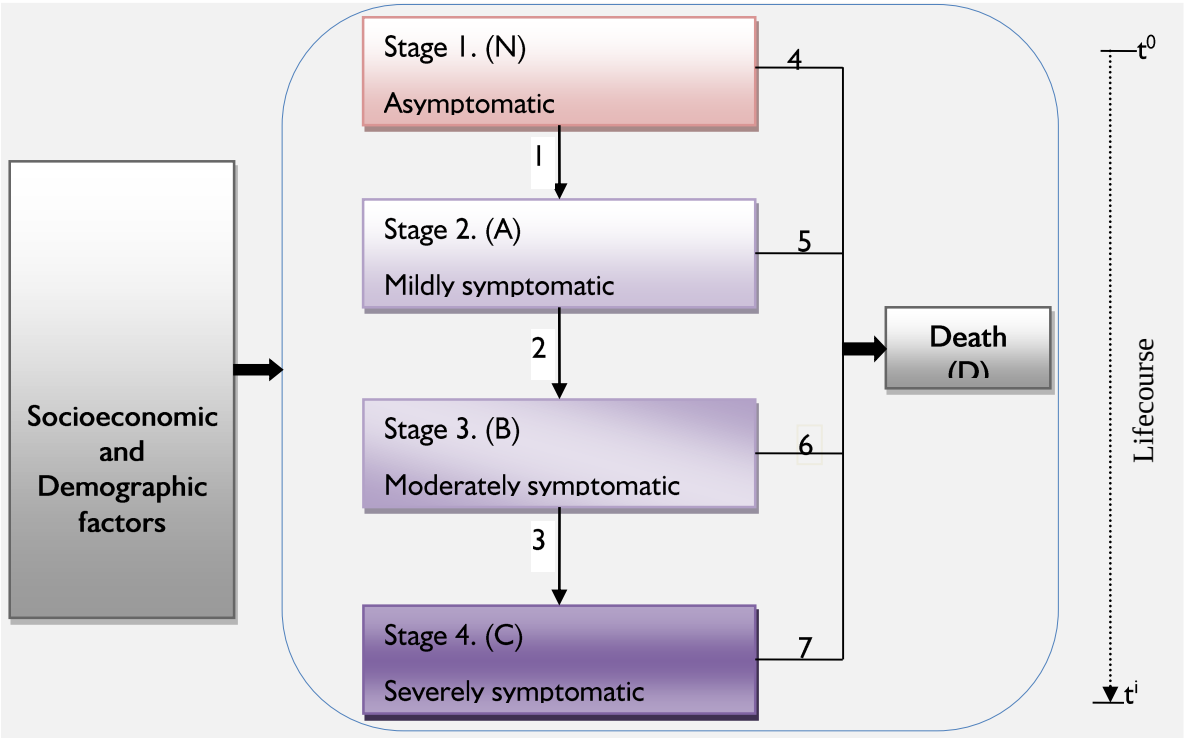
Diversity in life course trajectories- assumes that differences in life course transitions are due to differences in background traits; social economic status, religion, gender, sex, among others. These factors influence disparities in HIV/AIDS progression in the cohort (Blanche, 1997; Klimas et al., 2008; Morgan et al., 1997).

Impact of the past to the future- describes the impact prior experiences in life transition have on subsequent transitions and events, indeed factors such as mode and time of infection, start of treatment, caretakers in early years of life, among others, in this perspective may influence HIV infection progression. These themes will provide a basis of selecting input to the conceptual model and describing covariates during the analysis. Therefore, while studying differences in HIV/AIDS progression in children, the factors that influence HIV infection progression embeds within the key principles of the lifecourse perspective. In addition, the study models some parental background characteristics such as survival status, education attainment to measure their effect on child survival. Figure 1 summarises this linkage henceforth, factors affect the transition rate from one stage of HIV/AIDS to another. This is concurs with Omran's (1998) observation that health transitions are influenced by demographic and socioeconomic factors.

Conceptual Model for HIV/AIDS Progression

People living with HIV (PLWH) develop AIDS condition in a gradual process with distinct clinical stages, developing opportunistic infections and eventually die. From the analysis of the life course theory described above, we developed the conceptual model below (Figure 1) that illustrates the stages of HIV/AIDS progression among patients and death as a terminal state; the progression from stage to another is dependent on demographic and socioeconomic factors that characterize a patient's lifecourse. The author derives the study's conceptual model (Figure 1.) basing on the four immunologically and clinically determined stages of HIV/AIDS lifecourse (CDC, 1994; NIH, 2010; WHO, 2007).

Figure 1. Conceptual Model for the Study of HIV/AIDS Progression



Note: 1-7 Transition possibilities; Death is the End state (absorbing state). State space: N, A, B & C are transient states and describe HIV progression rate. 4-7- mortality rates from each HIV infection stage. (Model derived by the author)

The four stages of HIV/AIDS lifecourse are immunologically, clinically determined depending on certain health symptoms a PLWH attains (CDC, 1994; NIH, 2010; WHO, 2007), and Death is the definitive stage. The model thus, indicates that PLWH can stay or progress from the initial stage or state (N) to the next health state (A, B, C) or may die (D).

The HIV infections consists of four distinct stages, which are immunologically and clinically, determined (WHO, 2007). These stages are what we refer to as *states*, that is, the state of being HIV/AIDS stage N, A, B, C, or dead at a given age (Figure 1. and Table 1.). Thus, 'state' here describes a specific attribute of an individual's (Mamun, 2003) being in a given HIV stage of infection.

An individual can attain a given HIV infection stage at a time. Attaining another stage involves a *transition*, which is the movement through a set of discrete states in a given time interval (Blossfeld & Rohwer, 2002). Transition only takes place when an individual experiences an event that sparks a change of state. On the other hand, *event* denotes the change of an attribute/state (Mamun, 2003). It is a vital incident or occurrence constituting sudden change that may produce serious and lasting effect (Hutchison, 2007). That is the change from a prior HIV/AIDS state to another or death for the case of this study.

The occurrence of events is time dependent, thus the number of individual who are exposed to an event at the beginning of an interval experience the event at certain intensity. This transition or hazard rate (Blossfeld & Rohwer, 2002) is the probability per time unit that an individual that has survived to the beginning of a given interval fails within the interval. Thus, transition rate denotes the number of failures per time in the interval to the average number of survivors in the interval (StatSoft, Inc., 2011). The series of HIV infection transition from the first stage (Asymptomatic) to the fourth stage (severely asymptomatic) and or death constitute what is referred to as *HIV/AIDS infection progression*. These stages of HIV infections: asymptomatic, mildly asymptomatic, moderately asymptomatic and severely asymptomatic are Clinical and immunologically determined WHO (2007), NIH (2010), CDC (1994) as indicated in Table 1.

Table 1. WHO Immunological Classification for Established HIV Infection (WHO, 2007)

	Age Related CD4+ count per mm^3 of blood			
HIV- Associated immunodeficiency	<11 months (%CD4+)	12 -35 months (%CD4+)	36 - 59 months (%CD4+)	>5 years (absolute number or (%CD4+)
1. None/ Not significant	>35	>30	>25	>500
2. Mild	30-35	25-30	20-25	350-499
3. Advanced	25-29	20-24	15-19	200-349
4. Severe	<25	<20	<15	<200 or <15%

Source: World Health Organization (2007a)

Table 1 shows the four immunological stages of HIV infection progression, their cut-off points by age of persons. The Immunologic categories based on age-specific CD4+ T-lymphocyte counts and percent of total lymphocytes (CDC, 1994). Not all individual in a given state make transitions, thus, the retention of a prior state at a specified period constitute a *survival*. Survival describes the probability that the episode duration of a given HIV state is equal to the initial state of observation. The individuals who fail to make transitions are the *survivors*. That is, the number of cohort members who survive all causes of decrement before the end of a certain age interval.

It is important to make clear and correct definition of states to enable proper model specification (Blossfeld & Rohwer, 2002). The collection of all possible states yields *state spaces*. For the case of this study, there are five (5) state spaces (N, A, B, C and D) as indicated in Figure 1. Henceforth, the change of states or transition between states is subject to chance probability. The probability that is associated with the different state transitions is the *transition possibilities* in event history analysis.

The probability to make transition is influenced by a number of factors which may be biodemographic and socioeconomic. *Demographic and socioeconomic factors* relate to stratification in society based on, age, gender, social class, educational attainment, literacy, occupational status, and residence type, time of initial therapy, counselling and therapy adherence status. These population-specific differences in the presence of disease and health outcomes represent *health disparity* (Carter-Pokras & Baquet 2002). Differences in transition rates, morbidity, mortality rates and expectation of life is the basis for examining health disparity in this study.

Morbidity denotes the incidence or the prevalence of disease (ill health) in a population (Weeks, 2005). That is, the frequency of transition at a given point in time/ age to a higher HIV/AIDS infection stage/state. On the other hand, *mortality* is the pattern or the occurrence of death in a population (Weeks, 2005). In this study mortality is represented by the transitions from any given HIV/AIDS infection state to death (N, A, B or C to D), or the incidence of transition to death (Mamun, 2003).

The average expected number of years of life remaining at a given age constitutes *life expectancy* (expectation of life). The ratio of the person years spent or expected to be lived in each HIV infection state to number of survivors at each specific age interval (Mamun, 2003). The sum total of life expectancy from each HIV infection stage arises to *total life expectancy* on the lifecourse of HIV infection. Hence, the ratio of stage specific life expectancy to total life expectancy derives us to what is termed as the *proportion of remaining lifetime*, in other words, the proportion of expectation of life in a given HIV/AIDS state.

Summarizing the whole individual's HIV infection event history up to and into a single measure (life expectancy) constitutes *HIV/AIDS lifecourse*. For this study, a series of different HIV/AIDS infection events, transitions, life expectancy and cofactors describes the HIV/AIDS lifecourse.

Data Sources and Methods: The study used data from Mildmay Uganda an HIV clinical care center. The study population comprised of children under age 15 years that is a "cohort" of children of known HIV/AIDS status within an age range of 0- 14 years on HIV/AIDS care and treatment. The data enabled examining their HIV/AIDS disease life history from the time of identification to age 15 years or death. The year 2000 was the base year for recruiting the study subjects. Henceforth, the study followed the HIV/AIDS life history of these children in a retrospective manner between the periods January 2000 to December 2010. The study **design** was a retrospective cohort design, using quantitative statistical measures to estimate and describe the expectation of life in each HIV stage and establish the demographic and socioeconomic factors that contribute to differences in transition rates from one stage to another. The **analysis** involved event-history analysis procedures: Kaplan Meier and the Cox proportional hazard model to estimate exposure

time, transition probabilities and the relative risk to event respectively.

The specified Kaplan Meier survival functions helped to describe event failure against event time/ age that is, the survival function and the hazard. In addition, the specified Cox proportional hazard models helped to analyze multiple covariates for their effect on survival in a given state using the basic Cox regression model specification (Blossfeld & Rohwer, 2002):

$$h(t) = h_0(t)e^{\beta_1 x_1}$$

Where, h(t) is the dependent variable, $h_0(t)$ is the baseline hazard function and β_1, β_2,…β_i are unknown regression coefficients, and the X_1, X_2… X_i, are the covariates. The study specified four models for the hierarchical survival and survival to death. As input into the Cox regression model, the framework posits that demographic and socioeconomic factors as embedded in the five theme of the life course theory influences the rate of HIV/AIDS progression. The study considers; age, sex, education attainment, among others (covariates) as demographic and socioeconomic proxy indicators that influence HIV infection progression. Thus, the differences in demographic and socioeconomic factors constitute disparities in HIV/AIDS state transitions in CLWH.

Ethical Considerations

The study received ethical and scientific approval from Mildmay Uganda Research and Ethics Committee (MUREC) and Uganda National Council for Science and Technology (UNCST) respectively. Results reveals no personal identifiers, and the presentation all results from the study constitutes: aggregates of demographic and socioeconomic characteristics of subjects, duration of stay in each HIV infection stage, transitional probabilities, Survival functions and Cox proportional hazard model estimates.

Data Limitations

Data quality is an important aspect of research as it enhances its credibility, potential use to inform policy and reliability of conclusion thereof. The data had a lot of missing cases primarily resulting from poor record keeping procedures and coordination system. The fact that 80% of the subjects registered in care in the year 2000 missed clinical records, resulted in an insufficient sample to implement the Multi State Lifetable (MSLT) analysis technique, which could provide more analytical insights. Besides, the progressive clinical data, which was available for the 20% subjects, also was incomplete, having had missing records. As a result, it was impossible to estimate the effect of some factors thereby making a number of assumptions in order to impute the missing cases.

Study Results

The description of study subject by demographic and social characteristics to gain an overview of what the subjects constitutes, thereby easing explanation of estimates in subsequent subsections.

Table 2. Background Characteristics to Children under HIV/AIDS Care and Treatment (n=59)

Characteristics		Frequency	Percent
Sex	Male	29	49.2
	Female	30	50.8
Age at registration	0- 4	21	35.6
	5- 8	26	44.1
	9-12	12	20.3
Caregiver	Aunts	21	35.6
	Grand Parent	8	13.6
	Mother/Father	16	27.1
	Others Relatives	14	23.7
Religion Affiliation	Catholic	30	50.8
	Protestant/Pentecostal	24	40.7
	Muslim	5	8.5
Birth Weight	Low (<=3 kg)	21	35.6
	Normal (>3 kg)	38	64.4
Mother's Survival	Alive	40	67.8
	Dead	19	32.2
Father's Survival	Alive	48	81.4

	Dead	11	18.6
Schooling	Not schooling	16	27.1
	Schooling	43	72.9

The descriptive characteristics of the study subjects (Table 2) indicate that 51% were female children, and the age distribution of children at registration ranged from 1- 12 years, where ages 5 -8 had the highest frequency (44%). Age at registration denotes the age at which a child was tested and confirmed to be HIV positive, and then a10 year and 4 months retrospective follow-up period data collection.

Aunts were the main (36%) caregivers to children in care at Mildmay Uganda, and the care from grandparents was evident (14%). In addition, the care given to children living with HIV (CLWH) from persons of distant relation was substantially (24%) availed. These included charity organizations, orphanage homes and individual philanthropies. Religious affiliation among persons living with HIV/AIDS as regards inculcates hope and comfort among them. It is indicated that, 51% of the children or their caregivers were affiliated to Catholic belief, followed by Protestants or Pentecostal belief (41%) and 8% affiliated to Muslim belief.

Furthermore, birth weight is a vital indicator of child health risks and development (Mosley & Chen, 1984) child born with low birth weight have a high risk of childhood mortality. It is indicated that majority (64%) of the children were born with normal birth weight. Results indicate that 32% and 19% of the children had lost their biological mother and father respectively. Over 72% of the children had started schooling at the time of registration for HIV/AIDS care and treatment at Mildmay Uganda.

Duration Lived with HIV Infection in each HIV Stage

The duration of observation denotes that period between the time of registration for care and treatment at Mildmay Uganda and closer of observation April 2011. The study assumed that all subjected under study to occupy HIV infection stage I (Asymptomatic) at the time of registration. This led to specification of the event as the transition from Asymptomatic to Mildly asymptomatic or HIV infection stage II as the first transition.

Table 3 Duration of Exposure and Proportion of Remaining Lifetime in each Infection Stage

Estimates	Stage I	Stage II	Stage III	Stage IV
No. of Children	59	46	30	20
Person Months	3523	788	435	362
Exp Duration (months)	60	17	15	18
Exp Duration (years)	5.0	1.4	1.2	1.5
Prop of remaining lifetime	0.69	0.15	0.09	0.07

Table 3 summarizes the duration or exposure time of HIV infection for children under study at each HIV infection stage. The study constituted 59 children and these contributed 3,523 person months (5 years on average) in HIV infection stage I (Asymptomatic). At the time of the study 46 children were observed to have managed to transit to HIV infection stage II (Mildly asymptomatic). This means 13 children died or censored before transiting to mildly asymptomatic stage. The 46 children in stage II contributed 788 person months of exposure time to HIV infection.

Consequently, as the number of children progressing to a high HIV infection stage reduces, the total exposure time also reduces. The duration of stay in HIV infection stage III (Moderately asymptomatic) totals to 435 person months (1.2 years), a 6% less duration in stage II. The estimate of the duration of exposure to severely asymptomatic stage is 362 person months (1.5 years). The data thus, indicates a total 87 months (7.2 years) of a life history of HIV infection among children in the study. A sum of 5 years is the expectation of life with Asymptomatic HIV infection stage before transiting to mildly asymptomatic stage. On the other hand, children are expects to live for one and half years with severely asymptomatic HIV infection.

Furthermore, the proportion of the remaining lifetime expectation at a given HIV infection stage indicates an inverse relationship with HIV infection stage. That is, the proportion of remaining lifetime to be lived at each stage of HIV infection decreases drastically with progressive amplification of the infection. Much (69%) of the expected lifetime on the lifecourse of HIV infection is gained with Asymptomatic HIV infection. On the other hand, only

a third of the total HIV infection lifetime is in the expectation of life with mildly asymptomatic, moderately asymptomatic and severely asymptomatic HIV infection stages all together. This indicates an increasingly short expectation of life and great probability of HIV infection progression once a child progresses from asymptomatic stage.

Transition Probabilities from each HIV Infection Stage

The numbers of subjects present in a given HIV infection stages are at risk of making a transition at each point in time (month), these subjects constitute a risk set. That is, the number of children observed before the time in question and up to and after this the particular observation time. This also includes all those who have experienced the event or censored exactly at this particular time point. Thus, the risk set is the total number of children exposed to risk of HIV infection transition, and those children who survives a transition at a given point in time builds up a survivor function. Therefore, computation of transition probabilities as the residue of the survivor functions from one.

Figure 2. Transition Probabilities from each HIV Infection Stage

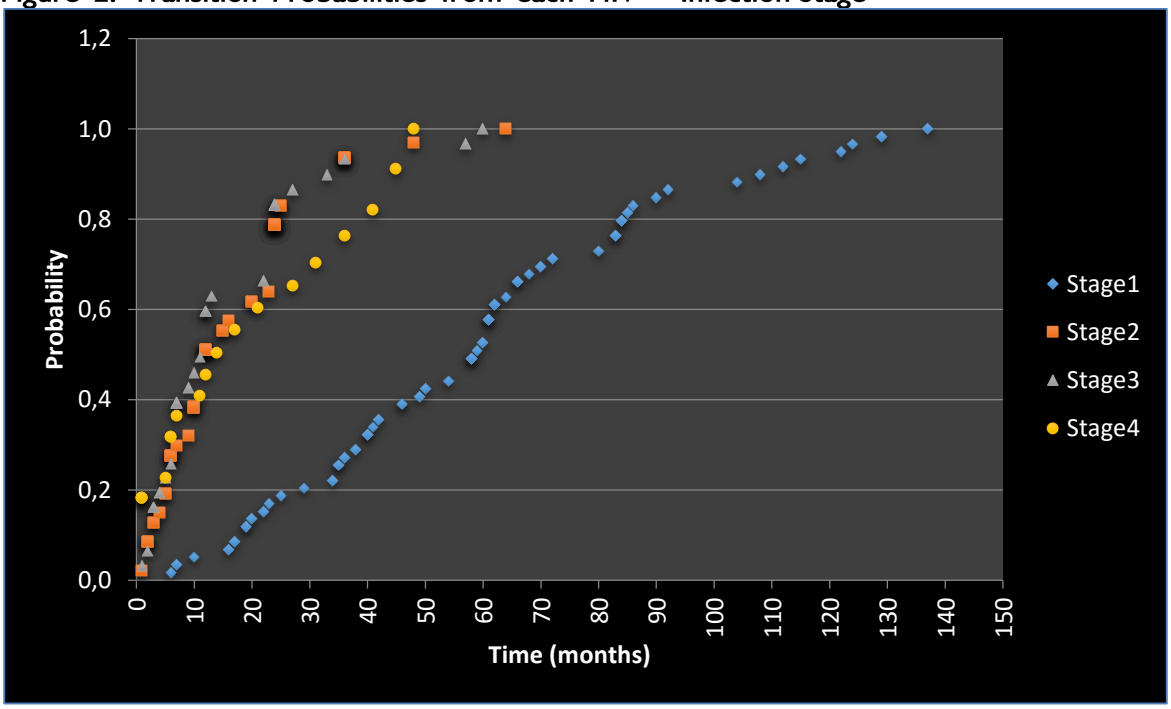


Figure 2 summarizes the transition probabilities of the four HIV infection stages for the period of 140 months of observation window. It can be seen that the transition probabilities in Asymptomatic HIV infection (Stage I) are markedly distinct from the other three stages. That is, the probabilities for children living with HIV infection stage I to progress to a higher HIV infection stage are lower at all times than those of higher HIV infection stages. For example, at a duration of 60 months, the transition probability for HIV infection stage I is half that of stage II and III. In addition, there is no distinct pattern in transition probabilities in stages II (mildly asymptomatic) and stage III (moderately asymptomatic).

Survival Function for HIV Infection Stages

Survival function depicts the probability that a subject will survive beyond a specified time. It represents the cumulative proportion of subjects surviving (not progressing) up to a specified point in time. Figure 3 depicts the cumulative survival function for children in HIV/AIDS infection stage I. The curve suggests a relatively slow transition rate at all ages but at 59 months of living with HIV infection stage I, half of the children transit to a higher HIV infection stage II (Mildly asymptomatic).

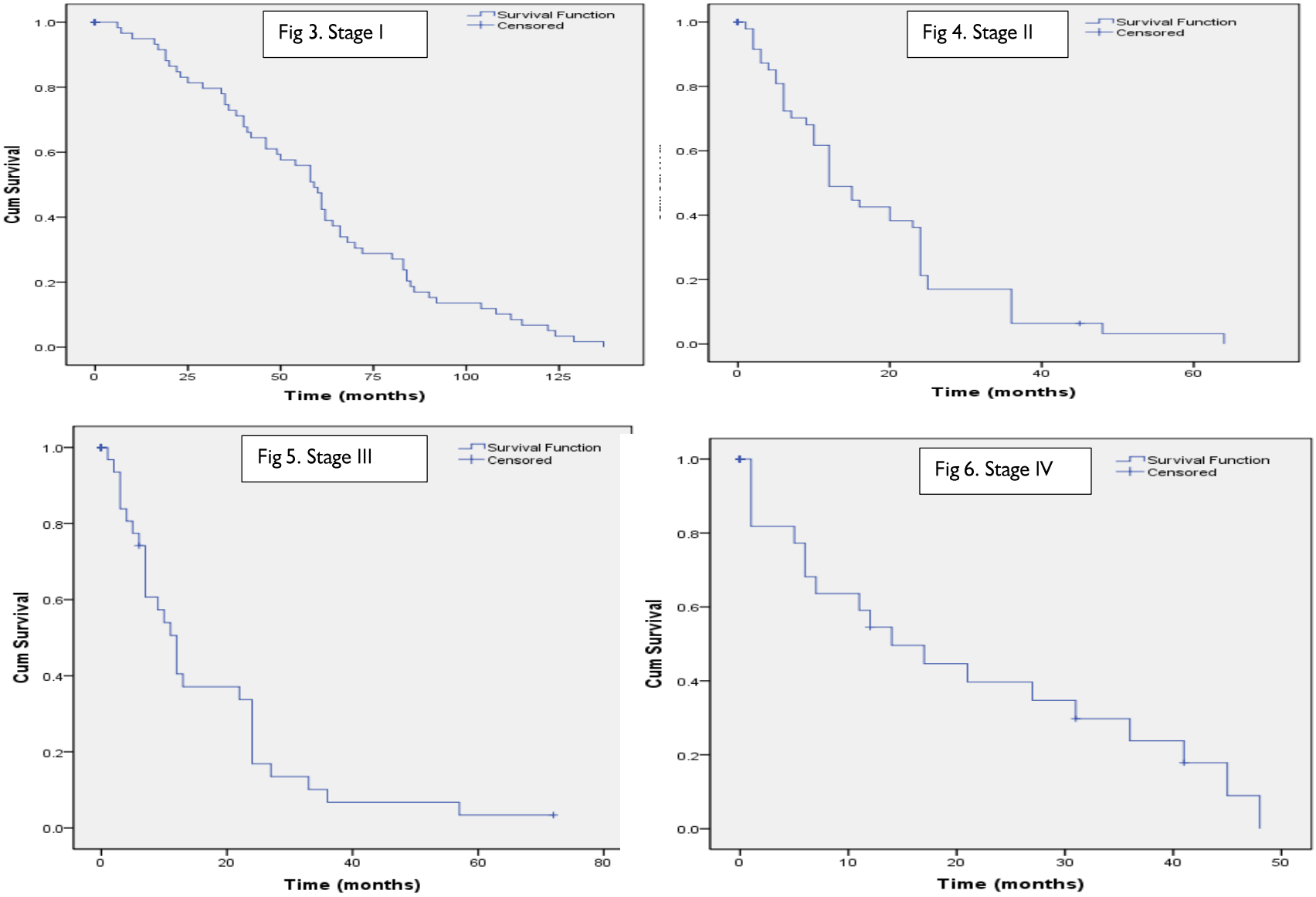
For stage II (Mildly asymptomatic), the cumulative survival function describes a fast transition rate (Figure 4), there is quick exit from stage II after the period of 21 months. In this stage, there was one death observed after a period of 42 months. Furthermore, half of children progressed to the next HIV infection stage III or death after 12 months as also indicated in the mean survival time estimate (Table 4).

Survival probability with moderately asymptomatic HIV infection (Figure 5) indicates that there is a faster progression to a higher HIV infection stage in the first 18 months than in the months there

after.

At the fifth and 72nd month of this stage, two children are censored or dead. After 12 months of observation in HIV infection stage III, half of the children progresses to another HIV infection stage or dies. On the other hand, Figure 6 presents the cumulative survival function for children surviving with severely asymptomatic HIV/AIDS infection and describes a steeper survival rate. A few subjects were censored, meaning that more of the children were right censured by the study date. Nevertheless, after 14 months living with severely asymptomatic HIV infection 50% of the children make a transition to death.

Figure 3A-D: Survival Functions through the four HIV Infection Stages respectively



Mean and Median Survival Time with HIV/AIDS Infection

The mean and median survival time describes the survival of children on the lifecourse of HIV/AIDS infection. That is, survival with Asymptomatic HIV infection (stage I) up through severely asymptomatic HIV infection (stage IV). That is person months for children living with HIV infection stage I to stage IV of HIV infection with standard errors and their confidence intervals at 95%.

Table 4 Means and Medians Survival Time (months) in each of the four HIV Infection Stages

	Mean				Median			
			95% C.I				95% C.I	
Stages	Estimate	Std. Error	Lower	Upper	Estimate	Std. Error	Lower	Upper
Stage I	59.7	4.3	51.4	68.1	59.0	3.4	52.4	65.6
Stage II	18.0	2.1	13.8	22.1	12.0	2.1	7.8	16.2
Stage III	16.9	2.9	11.1	22.6	12.0	1.6	8.9	15.1
Stage IV	20.7	3.8	13.3	28.0	14.0	4.5	5.3	22.7

The estimate of the median time of survival in Asymptomatic is 59 person months, indicating that after 59 months half of the children experience changes in HIV infection to mildly asymptomatic. Table 4 further shows that children living with HIV on average spend 60 person months in asymptomatic stage.

For mildly asymptomatic HIV infection stage, the median survival time is 12 person months. That is, after 12 months of living with mildly asymptomatic HIV infection, 50% of the children progressed to a higher HIV infection stage (Moderately asymptomatic stage). In addition, a period of 18 months on average is lived with mildly asymptomatic HIV infection stage.

With moderately asymptomatic HIV infection stage, children survive with the infection (Moderately Asymptomatic) for 12 person months before progressing to a higher HIV infection rate. Hence, at 12 months of living with moderately asymptomatic HIV infection, half of the children change their HIV infection stage to a higher one. However, estimates shows that children on average survive moderately asymptomatic HIV infection stage for 17 months.

The median survival time with severely asymptomatic HIV infection stage indicates that 50% of children survive the infection for 14 person months. On average, children survive severely asymptomatic HIV/AIDS infection stage for 21 person months before transiting to an absorbing state.

Survival Function Comparisons by Children's Characteristics

Estimates of survival functions employed Kaplan Meier procedure to compare all independent variables. However, the analysis in this study is limited to the variables presented in Table 1 background characteristics of the children under study.

Table 5 Comparison of Survival Curves by Children Characteristics

		Asymp. Sig. (2-sided) Pearson Chi^2			
Variables	df	Stage I	Stage II	Stage III	Stage IV
Sex [Male, Female]	1	0.991	0.960	0.256	0.551
Age group [0-4, 5-8, 9-12]	2	0.037	0.183	0.520	0.642
Caregiver [Aunts, Grand Parent, Parents, Others Relatives]	3	0.064	0.150	0.056	0.193
Religion [Catholic, Protestants, Muslims]	2	0.084	0.775	0.035	0.555
Birth Weight [Low, Normal]	1	0.196	0.428	0.650	0.589
Mother's Survival [Dead, Alive]	1	0.076	0.292	0.379	0.585
Father's Survival [Dead, Alive]	1	0.154	0.282	0.101	0.885
Child School Status [Yes, No]	1	0.692	0.397	0.242	0.250

The study examined whether there is a difference in survival curves of groups of independent variables based on a log-rank test. That is, stratification of survival functions by groups (indicated in brackets) on

independent variables (background characteristics) of children under study. The survival curves of girls and boys were not different for HIV infection progression in all stages of HIV infection. On the other hand, a significant difference in ages of children on HIV infection progression in stage I, the differences disappear with progress to a higher HIV infection stage.

Caregiver are important persons to children on treatment, they give them comfort and support they need to comply with lifelong treatment of HIV/AIDS treatment. They help them deal with adherence and stigma associated with the infection and routine medication. Table 5 indicates that there is significant difference between caregiver in HIV infection stage I and stage III. Likewise, differences in survival curves based on religion show a similar pattern to that of caregivers. Religion offers a similar psychological support to patients as caregivers does, it instils a sense of belongingness and self-esteem. Furthermore, results show no significant differences in survival probabilities between children born of low birth weight and those born of normal weight. Table 5 indicates that the survival probabilities of children living with HIV infection are not difference for those who lost their mothers or fathers for all the four stages of HIV infection. In addition, there is no difference in survival curves for children living with HIV infection whether they were going to school or not.

Risk Factors for HIV Infection Progression

This section examines the effect of each independent variable on HIV infection progression. To achieve this through both bivariate and multivariate Cox regression model specification. Relative risk (RR), the ratio of the exponent to the reference category in a specified factor was the basis for estimation of the effect of the risk factors on HIV infection progression. Relative risk is thus the measure of the likely effect of risk factors on HIV infection progression among children who received HIV/AIDS care and treatment.

Bivariate Analysis of Risk Factors

A first step in the analysis of risk factors is to estimate the estimation of the relative risk for each factor individually. Table 6 below presents bivariate results of risk factors and Asymptomatic HIV infection progression from a Cox proportional hazard model.

Table 6 Relative Risk of HIV Infection Progression from Stage I (Bivariate Results)

Risk Factors		B	SE	Sig.	Exp(B)	95% CI for Exp(B)		-2 LL
						Lower	Upper	
Sex	Male	0.003	0.265	0.991	1.003	0.507	1.984	370.3
				0.052				361.8*
Caregiver	Grand parents	-0.727	0.447	0.104	0.483	0.201	1.161	
	Mother/father	0.203	0.335	0.545	1.225	0.635	2.363	
	Other persons	0.601	0.353	0.089	1.824	0.912	3.645	
				0.058				364.5*
Religion	Pentecostals	-0.589	0.293	0.044	0.555	0.312	0.985	
	Moslems	0.394	0.488	0.420	1.482	0.570	3.858	
BW	Low	-0.365	0.287	0.203	0.694	0.331	1.454	368.6
Mother	Living	0.454	0.345	0.189	1.574	0.647	3.832	368.4
Father	Living	0.491	0.298	0.099	1.634	0.758	3.521	367.4
				0.034				364.2*
Age at registration	0-4	-0.700	0.381	0.067	0.497	0.186	1.326	
	5-8	-0.965	0.373	0.010	0.381	0.146	0.994	

*p-value<0.05

Table 6 indicates that being a boy is not strong risk factor to HIV infection progression from stage I compared to girls. The relative risk for boys living with HIV to progression from Asymptomatic to a higher HIV infection stage is unitary (RR=1.00, CI: 0.51-1.98) to that of girls. Care giving depicts a significant predictor of HIV infection progression from Stage I. Note that, children receiving care from their grandparents have a low hazard rate to progress from Asymptomatic that is 48% of that of children receiving care from their Aunts (RR=0.48, CI: 0.20-1.16). However, children under care of their parents (mother/father) and those having care form other persons have higher hazards of progression from Asymptomatic HIV infections (RR=1.23, CI: 0.64-2.36) and (RR=1.82, CI: 0.91- 3.65) respectively. A significant effect of Religion on HIV infection progression is also evident. The relative risk for children affiliated to Pentecostal to progression from Asymptomatic is significantly low (RR=0.56, CI: 0.31-

0.99) and not significantly high for Muslims (RR=1.48, CI: 0.57-3.86) of that of Catholics at $p<0.05$. Birth weight, survival of mother or father reveals no significant effect on child's HIV infection progression from Asymptomatic to a higher Infection stage.

Results further shows that age at which children starts care and treatment of HIV/AIDS is a significant predictor of HIV infection progression among children. The hazard of children aged 5-8 years progressing from Asymptomatic is 38% (CI: 0.15-0.99) of that of children aged 9 and more years. The study notes that, age at registration remained the only significant predictor of HIV infection progression at all stages of HIV infection. It was observed that with Mildly asymptomatic children age 0-4 and 5-8 have lower risk of HIV infection progression 21% (CI: 0.09-0.47) and 23% (CI: 0.10-0.52) respectively of that of children aged 9 years and over. For stage III ages 0-4 had (RR=0.30, CI: 0.11-0.81) and ages 5-8 (RR=0.28, CI: 0.10-0.76) compared that of ages 9 years and over. Likewise, with severely asymptomatic, children aged 0-4 and 5-8 have a 20% (CI: 0.05-0.80) and 26% (CI: 0.06-1.04) respectively HIV infection progression risk rate of those aged 9 years and over.

The -2 log likelihood (-2LL) ratio in Table 6 represents the improvement in the model fitting of the data when a covariate is added to an empty model. That is, the null hypothesis that regression coefficients for predictor variables are zero or equal to that of an empty model. The -2LL for caregivers, religion and age at registration indicates that the regression coefficients are significantly different from zero. We accept the null hypothesis for the variables sex, birth weight and parental survival, for -2 partial log-likelihood does not change significantly when they are added to a model.

Multivariate Analysis of Risk Factors

We examined the relative risk of HIV infection progression in the presence of multiple risk factors by specifying a multivariate model estimates with all covariates as listed in Table 1. Due to a small sample size, interaction of factors is not examined in this analysis. Therefore, in order to predict well the HIV infection progression, we specified a simpler model by eliminating extraneous covariates in the model; this reduces standard errors of the coefficients and improves prediction (Table 7) by introducing in Stepwise variable selection method to improved model fitting. As a result, basing variable entry selection on the significance of score statistic (0.05), and removal based on the probability of likelihood-ratio statistic (0.10). A similar procedure for HIV infection stages II up to stage IV is applied. This procedure improves the model fitting (-2 log likelihood) and proper interpretation of the model estimates, thus the models are estimated with only covariates that significantly predict HIV infection progression at each Stage.

For the first stage, backward stepwise selection method, only two covariates qualifies through the selection criterion father's survival and caregiver. Children with surviving fathers have a significantly higher hazard rate of HIV infection progression than those who lost their fathers (RR=2.90, CI: 1.29-6.51). In addition, Caregiving to children living with HIV/AIDS remains a significant predictor of HIV infection progression at stage I. Children receiving care from their grandparents have a significantly lower hazard rate of HIV infection progression (RR=0.28, CI: 0.10-0.76) compared to children receiving care from their Aunts. Receiving care from biological parents is indifferent relative to receiving care from Aunts, while receiving care from other relatives/ persons is only significant relative to receiving from Aunt at $p<0.10$ significance level.

Table 7 Relative Risk of HIV Infection Progression at all Stages (Refined for Multiple Factors)

		B	SE	Wald	df	Sig.	Exp(B)	95% CI for Exp(B)		-2 LL
								Lower	Upper	
Stage I	Caregiver [Aunt]†			12.340	3	0.006				360.1*
	Grandparents	-1.282	0.514	6.224	1	0.013	0.277	0.101	0.760	
	Mother/father	0.117	0.336	0.122	1	0.727	1.124	0.582	2.170	
	Others persons	0.679	0.354	3.683	1	0.055	1.972	0.986	3.945	
	Father [surviving]†	1.065	0.412	6.676	1	0.010	2.902	1.293	6.510	
Stage II	Age at reg. [9- 12]†			15.515	2	0.000				549.7*
	0- 4	-1.585	0.426	13.833	1	0.000	0.205	0.089	0.472	
	5- 8	-1.486	0.419	12.543	1	0.000	0.226	0.099	0.515	
Stage III	Caregiver [Aunt]†			3.813	3	0.282				428.2*
	Grandparents	-1.826	1.033	3.125	1	0.077	0.161	0.021	1.219	
	Mother/Father	0.049	0.387	0.016	1	0.899	1.050	0.492	2.245	

	Others persons	-0.356	0.475	0.561	1	0.454	0.701	0.276	1.778	
	Age at reg. [9- 12]†			6.988	2	0.030				
	0- 4	-1.272	0.535	5.652	1	0.017	0.280	0.098	0.800	
	5- 8	-1.398	0.545	6.588	1	0.010	0.247	0.085	0.719	
Stage IV	Age at reg. [9- 12]†			5.395	2	0.067				110.6*
	0- 4	-1.662	0.719	5.34	1	0.021	0.190	0.046	0.777	
	5- 8	-1.196	0.712	2.82	1	0.093	0.302	0.075	1.221	

†Reference category, Age at reg. - age registration into care and treatment, *P <0.05

For Mildly asymptomatic (stage II), the model result indicates that age of children at enrolment into HIV/AIDS care and treatment is the only significant predictor of HIV infection progression at Stage II. That is, the risk of HIV infection progression is heavily dependent on time of initiation of treatment. Children who started care and treatment at ages 0-4 and 5-8 years had 21% (CI: 0.09- 0.27) and 23% (CI: 0.10-0.52) respectively lower risk of HIV infection progression relative to those who started care and treatment at ages 9-12 years.

At moderately asymptomatic (Stage III), the model retains two variables caregiver and age at initiation of HIV/AIDS care and treatment. The model indicates that caregiver significantly improves model fitting though it is not a strong predictor of HIV infection progression at this stage. It is again observed that children who receive care from grandparents have a lower relative risk of progression than those receiving care from their Aunts ($p<0.10$). Furthermore, age at initiation of HIV/AIDS care and treatment remained an important predictor of HIV infection progression. The model indicate that children who were initiated in care at ages of 0-4 and 5-8 years had a significantly lower risk of HIV infection progression (RR=0.28, CI: 0.10-0.80) and (RR=0.25, CI: 0.09-0.72) respectively than those initiated at nine and more years. For Stage IV, only age at initiation into HIV/AIDS care and treatment passed the criterion. Likewise, the model indicates that the older the age at initiation into HIV/AIDS care and treatment the higher the relative risk of HIV infection severity. This ranged from 19% (CI: 0.05-0.78) for children aged 0-4 and 30% (CI: 0.08-1.22) for children aged 5-8 years at the time when initiated in HIV/AIDS care and treatment relative to children initiated to care age 9 years and older.

Discussion

The results of the study reveals that children spend on average over seven years on the lifecourse of HIV infection, and the duration of exposure contributed in each stage decreases with progressive intensification of HIV infection. This is due to the progressive impairment of the immune system and virulent opportunistic infections (Lawn, 2004). Much of the lifetime exposure to HIV infection is lived with Asymptomatic stage (Stage I) indicates that children live a healthier life within this stage, this is evident by the low or undetectable viral load, high number of CD4 count and there are fewer chances of opportunistic infections (WHO, 2007; NIH, 2010; CDC, 1994). Therefore, increased access to HIV cares services for children is likely to improve child mortality and fertility behaviour as parents adopt positive living and devote care for their children. In turn, limited stress in in terms of time caring for sick children is likely to spur economic productivity in the end. We be sure of a great prospect of life for children occupying infection stage I., so long as they have access to timely care services.

On the other hand, however, failure to avail HIV care services to those who need them most comes with increased burden of increased child morbidity and mortality. This is because luck of timely care children have shorter survival time once they progresses from asymptomatic stage, Feachem, (2001) and Braitstein et al. (2006) due to severely impairing immune system, which gives way for numerous opportunistic infections (WHO, 2007). Furthermore, the observed fluctuations in the transition probabilities among stages II up to stage IV are suggestive of drug interruptions or treatment failures. Treatment failure is fatal to the health of a PLWH as it facilitates rapid viral replication and in many cases; it is a result of non-adherence to therapy (Klimas et al., 2008; MoH, 2009). Indeed, grandparents as caregiver and religious affiliation effect on the risk of HIV infection progression; children need social support, comfort and reminders to adhere to the treatment and to deal with stigma in daily life (Biadgilign, et. al., 2009). Religious bodies do offer counselling for psychological challenges and stigma that befall many PLWH (Nguyen, 2005). This linkage is evident in the Uganda National HIV & AIDS Strategic Plan 2007/8 – 2011/12 (UAC, 2007) that advocates for a multifaceted approach to HIV/AIDS care and treatment.

The absence significant effect of birth weight to HIV infection progression, yet low birth weight is associated with significant absence of certain micronutrients in the body, which is a potent factor

for HIV infection progression (Deschamps et al., 2000; Dennis, 1998). The absence of the effect therefore, might be a masked by the nutrition supplement offered to children with HIV/AIDS as part of care to boost their nutritional status and immune system (Namulema et al., 2007). On the other hand, the survival of the father negatively affects the health of a child living with HIV/AIDS. This is a critical observation since common observation cites the health and survival of a mother to be more important than that of a father (Little et al., 2007). The effect of paternal survival on a child's HIV infection is a new shift on this arena though it is unclear from this study how father's survival amplifies a child's HIV infection progression. Perhaps the tendency for men in African societies to have stigma for public sero-disclosure, which may impinge on the child's ability to access and adherence to treatment.

Though some studies have found an elevated risk of HIV infection progression among females (Rodriguez et al., 2010), this is attributed to the lower viral set point for females (Dennis, 1998; Liu et al., 2004; Liu et al., 2004) than in males. On the other hand, the effect of age on HIV infection progression is evident at each stage of HIV infection. Young ages at initiation of HIV/AIDS care and treatment is associated with lower risk of HIV infection progression than older ages. Indeed, younger ages are associated with longer survival time on HIV infection lifecourse (Zwahlen & Egger, 2006). In fact, WHO (2008) and Abraham et al. (2003) have recorded that initiation of HIV/AIDS care and treatment at infant ages boosts the immune system that suppressed viral replication abilities.

Conclusion

The study attempted to describe the HIV/AIDS lifecourse and the factors associated with HIV/AIDS progression among children on HIV/AIDS care and Treatment by estimating the expected duration, prospect of life, and transition probabilities on different HIV infection stages. The study indicates that the duration of stay and the prospects of life in s given HIV infection stage is a function of the immune system or CD4 count. Children living with HIV infection will stay longer time in Stage I of the infection, and the risk of making a transition differs at all-time point during the lifecourse. Hence the gradual decline in the immune system with time, makes the transition probabilities increases directly with increasing duration of survival with HIV infection Stage I. While drug interruptions or treatment failures is critical for fluctuations in the transition probabilities in advanced stages which, call for strict treatment adherence among patients to avoid drug resistance and viral replication.

Age or time of initiation to treatment and social support appear to be critical factors effecting survival rates on the HIV infection lifecourse. Therefore, to optimize survival time on HIV infection lifecourse, HIV/AIDS care and treatment (ART) should target to control and maintain HIV infection within asymptomatic levels yet initiating care on the earliest time possible. Adequate monitoring and management of the infection should prioritize early diagnosis through strengthening PMTCT services and routine medical reviews. In light of the HIV infection transition probabilities and the access to HIV/AIDS care and treatment services, scaling-up likely gain morbidity and mortality, Uganda has to invest adequately to match the increasing demand for ARVs/T that HIV infection progression rates attenuate.

Acknowledgment

Sincere appreciation to Eric Bleumink Fund -Ubbo Emmius Fonds, Population Research Centre (PRC), Faculty of Spatial Sciences University of Groningen for the teaching support, and Mildmay Uganda for the dataset.

References

Abrams, E. J., Wiener, J., Carter, R., Kuhn, L., Palumbo, P., Nesheim, Lee, F., Vink, P. & Bulterys, M., (2003). 'Maternal health factors and early paediatric antiretroviral therapy influence the rate of perinatal HIV-1 disease progression in children'. *AIDS, 17*(6), 867-77.

AHRQ (2001). *Diabetes Disparities among Racial and Ethnic Minorities, Fact Sheet.* Agency for Healthcare Research and Quality, 2101 East Jefferson Street, Rockville, MD 20852

Antai, D. (2009). 'Faith and child survival: The role of religion in childhood immunization in Nigeria'. *Journal of Biosocial Science, 41*(1), 57-76.

AVERT (2011). http://www.avert.org/worldstats.htm. last visited February 4, 2011.

Ben- Shlomo, Y. & Kuh, D. (2002). 'A lifecourse approach to chronic disease epidemiology: Conceptual models, empirical challenges and interdisciplinary perspectives'. *Inter. Journal of epidemiology*, 31(2), 285-93.

Biadgilign, S., Deribew, A., Amberbir, A. & Deribe, K. (2009). 'Barriers and facilitators to antiretroviral medication adherence among HIV-infected paediatric patients in Ethiopia: A qualitative study'. *SAHARA J.* 6(4), 148-54

Blanche, S. (1997). 'Morbidity and mortality in European children vertically infected by HIV-1 the French paediatric HIV infection study group and European collaborative study'. *Journal of Acquired Immune Deficiency Syndromes, 14*(5), 442-450.

Blossfeld, H. & Rohwer, G. (2002), *Techniques of Event History Modeling: New Approach to Causal Analysis.* Lawrence Erlbaum Associates, Inc. Mahwah, New Jersey.

Bos, V., Kunst, A. E., Keij-Deerenberg, I. M., Garssen, J., & Mackenbach, J. P. (2004). 'Ethnic inequalities in age- and cause-specific mortality in the Netherlands'. *International Journal of Epidemiology, 33*(5), 1112-19.

Carter-Pokras, O., and Baquet, C. (2002). 'What is a "health disparity"?'. Association of Schools of Public Health, *Public Health Reports*, 117(5), 426-434.

Centres for Disease Control and Prevention (1994), 'Revised classification system for HIV infected children (<13 years old)'. *MMWR*, 43(RR-12),1-10.

Elder, G. H. (1998). 'The Life course as developmental theory'. *Child Development*, 69 (1), 1-12.

Elder, G. H., Shanahan, M. J. & Clipp, E. C. (1994). 'When war comes to men's lives: Life-course patterns in family, work, and health'. *Psychology and Aging, 9*(1), 5-16.

Halfon, N., Russ, S. & Regalado, M. (2005). The Lifecourse Health Development Model: A guide to children's health care policy and practice. http://www.zerotothree.org. retrieved on Feb 28. 2011.

Hall, S., Holman, C. D., Sheiner, H. & Hendrie, D. (2004). 'The influence of socio-economic and locational disadvantage on survival after a diagnosis of lung or breast cancer in western Australia'. *Journal of Health Services Research and Policy 9*(2), 10-16.

Hutchison, E. D. (2007). *A Life Course Perspective*. CLC-45347.qxd 7/31/2007. http://www.corwin.com/upm-data/16295_Chapter_1.pdf accessed March, 2011.

Joint United Nations Programme on HIV/AIDS (2006). Overview of the global AIDS epidemic. UNAIDS-2006 Report on the global AIDS epidemic. ISBN 9291734799. http://data.unaids.org/pub/GlobalReport/2006/2006_GR_CH02_en.pdf. retrieved on Feb 22, 2011.

Klimas, N., Koneru, A. O., & Fletcher, M. A. (2008). 'Overview of HIV'. *Psychosomatic Medicine,* 70(5), 523-530.

Little, K., Thorne, C., Luo, C., Bunders, M., Ngongo, N., McDermott, P. & Newell, M. L. (2007). 'Disease progression in children with vertically-acquired HIV infection in sub-Saharan Africa: Reviewing the need for HIV treatment'. *Current HIV Research, 5*(2), 139-153.

Mamun, A. (2003). *Life history of cardiovascular disease and its risk factors*: multistate life table approach and application to the Framingham Heart Study. Population studies, Rozenberg Publishers, Amsterdam, the Netherlands.

Merete, O. (2006). 'The life course perspective: a challenge for public health research and prevention'. *European Journal of Public Health*, 16(3), 230.

Mildmay (2010), Work in Uganda. http://www.mildmay.org/uganda/. Last visited on Feb 22, 2010.

MoH (2009), *National Antiretroviral Treatment Guidelines for Adults, Adolescents, and Children*. 3rd Edition. STD/AIDS Control Programme, Ministry of Health (MoH) Kampala- Uganda.

Morgan, D., Maude, G. H., Malamba, S. S., Okongo, M. J., Wagner, H., Mulder, D. W. & Whitworth, J. A. (1997). 'HIV-1 disease progression and AIDS-defining disorders in rural Uganda'. *Lancet 350*(9073), 245-50.

Mosley, W. H. & Chen, L. C. (1984), An analytic framework for the study of child survival in developing countries. *Population and Development Review* 10:25-45.

Newell, M., Coovadia, H., Cortina-Borja, M., Rollins, N., Gaillard, P., & Dabis, F. (2004). 'Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: A pooled analysis'. *Lancet, 364*(9441), 1236-43.

Niessen, L. (2002). *Roads to Health: Multi-State Modeling of Population Health and Resource Use*. Rozenberg Publishers/Dutch University Press, Amsterdam

NIH (2010), HIV/AIDS. http://www.niaid.nih.gov/topics/HIVAIDS/Understanding/Biology/Pages/factors.aspx. accessed on May 14, 2011.

NIH (2010). Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Available at http://aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf. Accessed (10 Feb, 2010)

Omran, A. R. (1998). 'The epidemiologic transition theory revisited thirty years later'. *World Health Statistics Quarterly, 51*(2-4), 99-119.

Ronsmans, C., Chowdhury, M. E., Dasgupta, S.K., Ahmed, A. & Koblinsky, M. (2010). 'Effect of parent's death on child survival in rural Bangladesh: a cohort study'. *Lancet* 375: 2024–31

Schneider, M. F., Gange, S. J., Williams, C. M., Anastos, K., Greenblatt, R. M., Kingsley, L., Detels, R. & Munoz, A. (2005). 'Patterns of the hazard of death after AIDS through the evolution of antiretroviral therapy: 1984-2004'. *AIDS, 19*(17), 2009-18.

StatSoft, Inc. (2011), Electronic Statistics Textbook.

Tulsa, OK: StatSoft. WEB: http://www.statsoft.com/textbook/, visited on June 6, 2011.

Uganda Bureau of Statistics (UBOS) & Macro International Inc. (2007). *Uganda Demographic and Health Survey 2006.* Calverton, Maryland, USA: UBOS and Macro International Inc.

UNAIDS (2010), Report on the Global AIDS Epidemic: http://www.unaids.org/GlobalReport/Global_report.htm. last visited February 4, 2011.

Weeks, J. R. (2005). *Population. An introduction to concepts and issues.* Ninth edition, Wadsworth Publishing, Belmont.

WHO (2007), *WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.* WHO Press, World Health Organization, Geneva, Switzerland.

WHO (2008). Report of the WHO Technical Reference Group, Paediatric HIV/ART Care Guideline Group Meeting. WHO Antiretroviral Therapy for Infants and Children 2008. WHO Headquarters, Geneva, Switzerland. Retrieved on Feb 28. 2011.

Zwahlen M, Egger M (2006) (PDF). *Progression and mortality of untreated HIV-positive individuals living in resource-limited settings: update of literature review and evidence synthesis*. UNAIDS Obligation HQ/05/422204. http://data.unaids.org/pub/Periodical/2006/zwahlen_unaids_hq_05_422204_2007_en.pdf. Retrieved April 24, 2011