Life Expectancy Simulation Model among HIV (Human Immunodeficiency Virus)-Infected Individuals: A Monte Carlo Approach

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Abstract

The study of life expectancies of HIV infected individuals requires a long term experiment design which may not be feasible due to the immediate need for such information. Alternatively, it is possible to gain insights in the phenomena using a quasi-experimental design through simulation and Monte Carlo methods. This study used the latter design based on the empirical regression function produced by Lancet (2008) which predicts life expectancy of HIV infected individuals as a function of treatment, CD counts and age of the individual. The latter determinants of life expectancy were generated as phenomena by computer simulations. Results revealed that there is an increased lifespan of about six (6) folds of HIV infected individuals who seek treatment than those otherwise. The estimated average lifespan of individuals being treated ranges 38-66 years that is greater than those without treatment of 5-11 years from individuals who do not seek treatment. Computer simulations tended to confirm the efficacy of early diagnosis coupled with antiretroviral therapy (ART) as a means to prolong life expectancy by as much as five (5) to ten (10) more years.

Keywords: life expectancy simulation model, life expectancy, CD4 levels, level of development, age at diagnosis, HIV-infected individuals

1.0 Introduction

Today, the combination of antiretroviral drugs has led to a significant increase in survival and quality of life among HIV infected individuals (The Lancet, 2008). Patient's compliance, early treatment, time of diagnosis, and countries' economic health development are good indicators of disease progression. Typically, HIV management and treatment differ according to thier classifications based on the CD4 level counts. The efficacy of antiretroviral drugs (ARVs) prevented infection related-complications and may prolong life (Granich, Gilks, Dye,De Cock, & Williams, 2009). This paper attempts to predict the life expectancy (LE) in those HIV infected population across the health-illness continuum through Monte Carlo approach.

Human Immunodeficiency Virus (HIV) is a multifaceted disorder that affects community health across the world. The most noteworthy change has greater emphasis on the role of HIV treatment as prevention. Thousands of researchers, doctors, policymakers are working collaboratively to fight this deadly virus. It has been known over the past years that LE and mortality are universally

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viewed as key health indicators. Ironically, though high prevalence is noted there is negative relation between life expectancy at a population level. With the advent of highly active antiretroviral therapy (HAART) it decreases death related to AIDS-defining illnesses. It is expected that a person starting medications may live about 43 years at 20 years of age, about two-thirds as long as the general population. In highly developed countries, HIV infected individuals with antiretroviral therapy (ART) may have increased their longevity (Samji, et al, 2013). However, there is a presence of large discrepancy between the life expectancy of the general population as well as HIV-infected individual. LE can be attributed to active HIV or individual's lifestyle, socioeconomic status, and client's conditions (McGuire, 2005). Furthermore, literature reveals that greater awareness of viral loads and behaviour modification will improve conditions.

Various studies have shown correlation between LE and death rates and have linked economic development in regulating the virus through combination therapy; however researchers failed to provide variations in LE among its CD4 categories. Moreover, there is no contextual model that shows a predictive measure of survival. Noncompliance to treatment is often perceived to be one of major reasons in developing full blown AIDS; without proper management there is a progressive deterioration of illness. Furthermore, a simulation model was formulated to project the LE of HIV infected individuals in terms of CD4 category, age groups, and countries level of socio-economic growth.

2.0 Conceptual Framework

The following factors were included in this study:

One factor that may increase mortality is late diagnosis of HIV (Chadborn, Delpech, Sabin, Sinka, Evans, 2006), yet there are still many people who present for care at an advanced stage of infection. Calculating life expectancy of people with HIV allows us to quantify the improvement in prognosis and to also develop an understanding of the benefits of preventing and testing for HIV and the possible impact of delays in diagnosis. Incorporating current estimates of rates of virologic response to ART and subsequent long-term increases in CD4 cell count relies on building a model that captures the processes underlying HIV progression and the effect of ART and then using this to predict the range of courses of infection and treatment over a long period. This has been done for the USA for example, based on a model that predicted an average 24-year survival after entry into healthcare (Schackman, Gebo, Walensky, Losina, Muccio, Sax, 2006). However, this estimate is now known to be too low, as since then, extensive data from routine clinic cohorts have provided increasingly robust estimates of long-term viral suppression rates (Bansi, Sabin, Delpech, Hill, Fisher, Walsh, 2010; Lampe, Smith, Madge, Loes, Tyrer, Sabin, 2004; Lampe, Gatell, Staszewski, Johnson, Pradier, Gill, 2006) Lampe FC, Gatell JM, Staszewski S, Johnson MA, Pradier C, Gill MJ, 2006; . Gill, Lima, Zhang, Wynhoven, Yip, & Hogg, 2010).

Since the introduction of potent antiretroviral therapy (ART), the outcome of people living with HIV has improved significantly (Patella, 1998). HIV is no longer considered a fatal disease, but one that can be controlled, provided with good adherence to ART can be maintained over the long term (Lima et. al. 2009; Volberding, & Deeks, 2010). This leads us to ask how long people currently infected with HIV can be expected to live. Most studies to date have estimated life expectancy and projected current death rates in people with HIV (Lima, Harrigan, Bangsberg, Hogg, Gross, Yip, 2009; Lohse, Hansen, Pedersen, Kronborg, Gerstoft, Sorensen, 2007).

In this study, the lifespan of persons living with HIV was linked to factors such as CD4 level count, level of countries development, and age at time of diagnosis.

Life expectancy has been linked to CD4 level; CD4 counts ≥200 cells/μl were between 70% and 86% while HIV-negative adults of the same age and sex, for patients who start ART with CD4 count of <50 cells/μl life expectancies that were between 48% and 61% of those of HIV-negative adults. Furthermore, LE were also 15%–20% higher in patients who survived their first 24 months after starting ART than in patients of same age who had just started ART. World Health Organizatons have established criteria for starting ART for stage 3 or 4 diagnosis or a CD4 cell count status of less than 0.250 × 109 cells/L (Katabira, 2009).

Mills, Ford, & Mugyenyi, (2009) found that high income countries commonly reach normal LE of HIV positive individuals receiving ART treatment. In some underdeveloped and developed countries, free medications were provided which lessen their viral loads. Resource constraints settings wherein there are existing chronic comorbid conditions such as TB, Hepatitis and other conditions would affect the infected ones. Developing countries must prioritize in extending access to antiretroviral therapy since it helps in improving viral loads through combination of CD4 counts and plasma viral load (pVL) which is very expensive. WHO classified CD4 counts as a 'desirable' test and pVL as an 'optional' test in the context of introducing HAART regimens into resource-poor settings, but offered no practical direction on monitoring efficacy. Though, it is a good marker but it is not widely used in many countries and more extensive field evaluation of these tests is also required (Florence, Dreezen, Schrooten, Van Esbroek, Kestens, Fransen, De Roo, & Colebunders, 2004). The decision of when to start treatment in an HIV-infected individual has always been problematic.

On the one hand, treatment should be initiated at an early point in the individual's course of disease, prior to a time when CD4 cell loss is such that there is substantial risk of clinical progression. On the other hand, the original antiretroviral drugs were often inconvenient to take, of limited efficacy, and were associated with substantial toxicities. Thus, clinicians balanced the risks of delaying treatment (potentially placing the patient at risk of serious illness and death from AIDS) with the inconvenience and possible long-term effects of taking treatment. On the basis of evidence that clinical progression rates were low while the CD4 cell count remained above 200 cells/μl but increased rapidly at lower levels, most early treatment guidelines recommended that treatment be delayed until the CD4 cell count had fallen below 200 cells/μl. Over time, however, as treatments have improved and the number of treatment options available to patients has increased, this threshold has increased; most treatment guidelines now recommend that all individuals with a CD4 cell count less than 350 cells/μ should be treated (Hammer, Eron, Reiss, 2008; Panel on Antiretroviral Guidelines for Adults and Adolescents, 2008; European AIDS Clinical Society, 2008; Gazzard, 2008). The CD4 cell response to ART is an important predictor of short- and long-term morbidity and mortality. In most, but not all studies, treatment initiation at an older age has been associated with a less robust CD4 count response; starting therapy at a younger age may result in better immunologic and perhaps clinical outcomes (Quinn, Wawer, Sewankambo, 2000).

Collectively, we identified the possible gauge in the disease process which has a probable interaction to other variables in the survival rate of HIV infected population. This study aims to establish this stance.

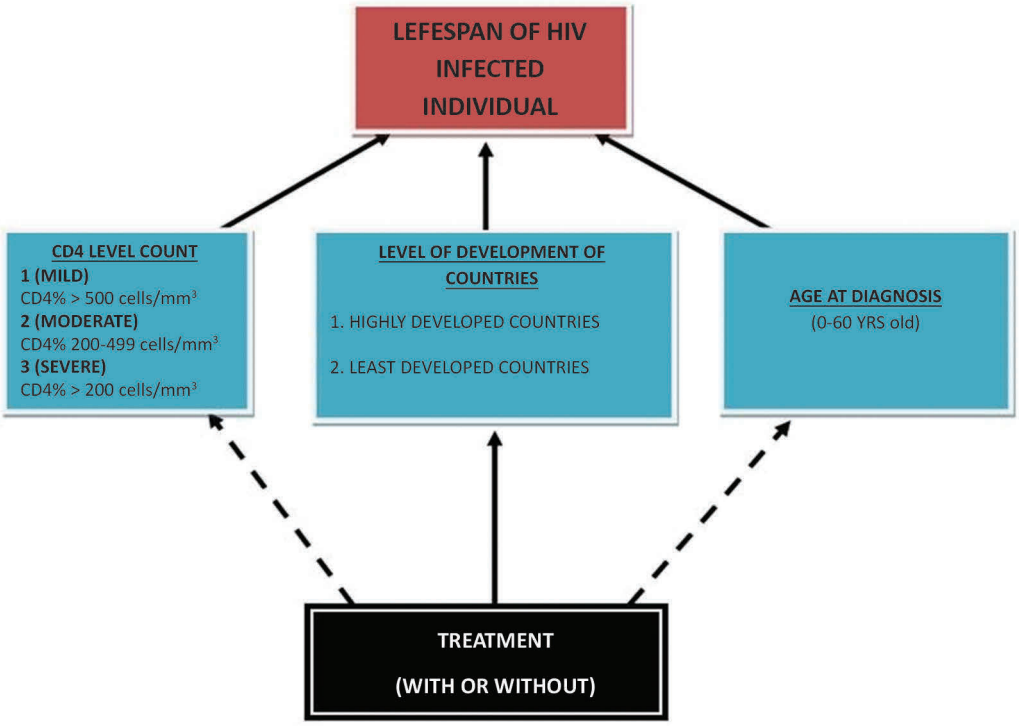

Figure 1: Conceptual Framework of Life Expectancy Model among HIV Infected Population

3.0 Design and Methods

The prevalence rate of Human Immunodeficiency Virus (HIV) infected individual remarkably increased over the period. As the immune system of an individual becomes suppressed due to its pathophysiological changes caused by the virus itself and poor health care services, the existing condition will eventually result to a more fatal condition. Thus, it would develop to Acquired Immunodeficiency Syndrome (AIDS) with numerous observable clinical manifestations leading to complications. The HIV is categorized into three as mild, moderate and severe in terms of the value of CD4 cells. The compliance to treatment is needed in all categories of HIV infection. Those individuals with laboratory results of CD4 cells above 500 cells/mm^3 who seek treatment more likely develop lesser complications than those non-compliant to treatments.

This study utilized an experimental design using simulation modelling. The experimental criterion measure is the life span of HIV infected individual while the simulated experiment treatments are (a) CD4 level, either Category 1 (C_{HIV1}), Category 2 (C_{HIV2}), and Category 3(C_{HIV3}), (b) level of development, either least or highly developed, (c) treatment compliance, either with or without treatment, and (d) age at diagnosis from 0-60 years.

These elements are related this way: The **CD4 level** is the basis in categorizing their conditions as mild, moderate or severe.

Table 1: CD4 Values in HIV Categories

CD4 Category	CD4 Levels
1 (Mild)	>500 cells/mm^3
2 (Moderate)	200-499 cells/mm^3
3 (Severe)	<200 cells/mm^3

The **level of development** among countries is classified as least (1) or highly (2) developed with 0.85 and 0.15 probability values.

Table 2: Level of Development of Countries and its Probability Value

Level of Development of Countries	Probability
1 (Least Developed)	0.85
2 (Highly Developed)	0.15

The treatment compliance is also considered to determine longevity of life of an HIV infected individual either **with or without treatment** compliance.

Table 3: Treatment Compliance either With or Without Treatment

Treatment Compliance	Labelling Assignment
With Treatment	2
Without Treatment	1

The **age from the start of diagnosis** usually starts at birth until 60 years old depending on the availability of resources and awareness to information of its health risk and modalities of care.

Based on available data from the literature (Lancet, 2010), the estimated regression function for the **estimation of lifespan** is:

$$LOG(LIFE) = -2.70 + 2.55\ LOG\ (Treat) - 0.515\ LOG\ (CD) + 1.47\ LOG\ (Age)$$

$$Life\ span = \frac{.0672 \times (Treat)^{2.55} \times (Age)^{1.47}}{(CD)^{.515}}$$

Assumptions:

The simulation model is based on the following assumptions:

1. There are three (3) categories of HIV infection either Category 1, 2 and 3. Each category shows abnormal laboratory findings of CD4 cells with more than 500 cells/mm^3, 200-499 cells/mm^3 and less than 200 cells/mm^3 respectively. We assume that Category 1 has 0.35 probability value while Category 2 and 3 has 0.50 and 0.15 in that order (Center for Disease Control and Prevention, 2008)
2. The level of development among countries worldwide is assumed to be between 1 as least developed and 2 as highly developed. The probability value of least developed countries usually has the highest probability value of 0.85 while highly developed countries have 0.15 probability value (Mills et. al, 2009)
3. HIV infected individual may either seek treatment or not. The treatment derived from the advancement of technology is usually linked to the level of development among counties. We assumed that those HIV infected individuals who do not seek treatment are scored 1 and 2 otherwise, with the probability value of 60% who do not seek treatment and 40% who seek treatment respectively (Fehr, Nicca, Goffard, et. al, 2013)
4. The HIV infection can be developed across the life span starting at birth to 60 years old. We assumed that the distribution is normal with a mean of 30 and standard deviation of 5 (Cairns, 2004).
5. To successfully determine the lifespan of HIV-infected individual in all categories of CD4

cells, the estimated regression function is determined following the derived formula as mentioned (The Lancet, 2008).

4.0 Results and Discussion

Table 4 shows the predicted lifespan (in years) among HIV categories either with or without treatment.

Table 5: Lifespan of HIV Categories With or Without Treatment

HIV Category	Treatment	
	With (in years)	Without (in years)
1	66.25	10.602
2	40.82	7.505
3	38.67	5.440

In the analysis of HIV Life Expectancy Simulation Model, we found imperative insights in improving the quality of life among HIV-infected individuals. It also geared towards more premeditated actions in providing appraisable effort in broadening the life expectancy across all CD4 levels. The following were the findings of the data:

1. There is increase longevity of life in those HIV-infected individuals who seek treatment than those without treatment at all CD4 levels.
2. As the CD4 level declines progressively, the lifespan becomes shorter to those without treatment with an interval difference of approximately 3 years in between each category.
3. There is a significant disparity of lifespan in all CD4 levels who seek treatment. The interval of years between category 1 & 2 is 26 years which is higher than category 2 and 3 with only 2 years interval.
4. The average lifespan of with treatment is 38-66 years while those without treatment ranges from 5-11 years.

In the utilization of simulation methods, the first finding is congruent to the study done by Bor, Herbst, Newell, and Barnighausen (2013) stated that the use of antiretroviral therapy (ART) increases the lifespan of HIV-infected individuals who seek treatment in all CD4 levels. These positive increments in adult life expectancy elucidate the relevance of the primal worth of ART treatment and healthcare cost decision making among infected persons and government support. With the increasing number of epidemic threshold of HIV, momentous numbers of individuals are getting advanced stages of HIV infection. Thus, a global health approach is done to monitor the antiretroviral therapeutic efforts links to its affordability and availability among low and middle resource-constraints countries (WHO, 2011).

The second finding states that the longevity of life becomes shorter as the CD4 level progresses to decline to those without treatment with an interval difference of approximately three years in between and among three categories. The simulated data projected on HIV-infected patient is six (6) folds to those who seek treatment conservatively in all categories. Lima, et.al. (2007) had found out in 12-year study period that there is a significant and progressive decrease in mortality and increase in life expectancy associated with the strict compliance of treatments among HIV individuals. Therefore, those HIV-infected individual without treatment compliance has the highest tendency to live shorter lifespan across all categories in HIV.

Compared to the previous studies, we have noted that there is an increase LE among HIV-infected individuals with treatment due to the persistent actions, advancements to treatment such as ART to HAART. However disparity still exists in mortality and morbidity. The premature death occurs due to disparities due to patients'

demographics, co-morbidities, lifestyle, and psychological support groups.

Lastly, according to the Antiretroviral Therapy Cohort Collaboration (2008) and Loisana, et. al. (2009) there has been an improvement of outcomes among HIV–infected patients with adherence to advanced treatments. This was characterized by a remarkable decrease in mortality rates and likely years of life lost. In effect, there is a significant increase of life expectancy ranges from age 20 to 44 years. The lifestyle, socioeconomic, and health issues attribute to the discrepancy in life expectancy of an HIV infected individual. Another studies by May (2011); Walensky (2006); Holtgrave, & Pinkerton, (1997) & Harrison, Song & Zhang (2010) explained that the life expectancy of females is higher than males. The increase in longevity of life could be the result of earlier diagnosis and appropriate, timely treatment. The results of the average life expectancy after HIV diagnosis of having treatment ranges from ages 10 to 23 years (May, 2011, & Loisana, et. al., 2009) while late treatment initiation in advanced HIV category resulted only to three additional years of life lost. The late compliance or early discontinuation to treatment can all lead to a considerable decline in the longevity of life. Surprisingly, the life expectancy simulated model predicts higher life expectancy compared than those previous studies. It ranges from 38-66 years of life expectancy under treatments while non-compliance, ranges from 5 to 11 years. This change in HIV trends is brought about by the technological advancement in medical treatment and modalities of care. Fang, et. al. (2007) suggested that there must be an aggressive and intensive support on the expansion of HIV screening programs to curtail the delay on the progression of the existing health conditions and strict adherence to HAART that will prolong the lifespan.

5.0 Conclusion

The relationship between demographics, treatment management and countries development contribute to individual's life expectancy. The importance of massive campaign on HIV awareness is necessary for early detection and prompt treatment is to alter the CD4 level counts thereby extending the LE among persons living with HIV. This model, estimated the LE as categorized with their CD4 levels to both compliance and non-compliance to treatment. Despite operant and transformative efforts provided by the government and the health sectors, it is still necessary to further appraise their strategies. Thus, the simulation model is applicable to all existing HIV conditions.

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