



**SURVIVAL PROBABILITIES OF HIV/AIDS
INFECTED WOMEN WITH CERVICAL CANCER IN
KENYA**

I56/75736/2014

MUGENDA NAOMI NJERI

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DECLARATION

I hereby declare that this work has not been presented in any University or any other forum for an award in any degree.

NAME **ADM.NO** **SIGNATURE**

MUGENDA NAOMI NJERI I56/75736/2014

THE SUPERVISOR FOR THIS PROJECT WAS:

NAME **SIGNATURE**

MRS IDAH OROWE

DEDICATION

I am dedicating this study to my parents and brothers for their great support during the reign of this study.

ACKNOWLEDGEMENT

Foremost; I thank God for the wisdom, knowledge and ability to write this project. I am also grateful to my supervisor MRS Idah Orowe for her professional guidance, time and patience in reading through my drafts and suggesting workable alternatives. I also would like to acknowledge the support of the staff of NACC for providing necessary materials and data for this study.

Contents

DECLARATION	1
DEDICATION	3
ACKNOWLEDGEMENT	4
LIST OF FIGURES	7
Abstract	8
CHAPTER ONE	9
1.1 Introduction.....	9
1.1.1 Human immunodeficiency virus infection.....	9
1.1.2 Human Papillomavirus (HPV).....	10
1.1.3 Cervical cancer.....	10
1.1.4 Co-infection of HIV AND HPV	11
1.1.5 HPV and Cervical cancer.....	11
1.1.6 HIV and Cervical cancer.....	11
1.1 Statement of problem.....	12
1.2 Objective of the study	12
1.3.1 Main objective	12
1.3.2 Specific objectives.....	12
1.4 Significance of this study.....	12
Chapter two.....	14
2.0 Literature review	14
2.1 Literature review summary.....	17
CHAPTER 3	18
3.0 Methodology.....	18
3.1 Markov model.....	18
3.2 Transition diagram	20
3.2.2 Transition matrix.....	20
3.3.1 Assumption of this study	20
3.3.2 HIV – Cervical cancer markov process	21
3.3.3 Transition diagram.....	22
3.3.4 Classification of an absorbing Markov chain.....	23

3.4 Life expectancy	25
3.5 Number of years lost	25
3.6 Survival probabilities	26
CHAPTER FOUR.....	27
4.0 Data analysis.	27
4.1 Data source.....	27
4.2.1 HIV-Cervical cancer Markov model	28
4.2.2 Transition diagram	29
4.2.3 Transition matrix.....	29
4.2.4 Classification of an absorbing Markov chain P.	30
4.3 Life expectancy	30
4.3.1 Residual time in each transient state.....	31
4.3.2 Time to absorption for each transient state	31
4.4 Average number of years lost	32
4.5.1 Survival probabilities	32
4.5.2 Discussion	40
CHAPTER FIVE	42
5.0 Recommendation and conclusion.	42
5.1 Conclusion	42
5.2 Recommendation	42
6. References.....	43

LIST OF FIGURES

Figure 1 HIV- CERVICAL cancer markov process	22
Figure 2 Transition diagram of HIV- Cervical process	27
Figure 3 Age specific death rate due to HIV	36
Figure 4 Age specific death rate due to cervical cancer in HIV infected adult female	37
Figure 5 Survival probabilities of HIV infected adult female with cervical cancer	38
Figure 6 Survival probabilities of HIV infected adult female with cervical cancer	39
Figure 7 Comparison of survival probabilities of HIV infected women with and without cervical cancer	40

Abstract

Cervical cancer has become a major issue among HIV infected women. This study evaluates the survival probabilities, life expectancy and the number of years lost among HIV/AIDS infected adult female with cervical cancer in Kenya. This study considers HIV infected women aged between 15 and 54 years .The data used in this study is derived from different epidemiological and demographic research. This study analysis is supplemented by applying a combination of multistate Markov model and survival probabilities with additional force of mortality. The study finds that there is a decrease in probability of surviving for HIV infected women with cervical cancer compared with probability of surviving of HIV infected women without cervical cancer.

CHAPTER ONE

1.1 Introduction

1.1.1 Human immunodeficiency virus infection

Human immunodeficiency virus infection / Acquired immunodeficiency syndrome (HIV/AIDS) is an immune system disease caused by human immunodeficiency virus (HIV). HIV/AIDS was first discovered by the CDC (United States Centre of disease control and prevention) in 1981. HIV started to spread in Kenya between in the end of 1970s and beginning of 1980s.

In the 1980s there was low HIV prevalence in Kenya, the prevalence increased in gradually between 1990 and 2000. The National AIDS and STDs control programme (NASCO) estimated that by mid-2000, prevalence among adults had increased to 13.5% with urban area prevalence been estimated been 17% to 18%. About 470000 adults were infected with the HIV virus, in rural areas HIV prevalence was increasing rapidly. In 2000 it was estimated that the prevalence had been about 12.5% this suggested that there were about 1.5 million HIV infected adults in Kenya.

The Kenya demographic and health survey KDHS (2010) it was estimated that 7.4% of adults between the age of 15years to 49years had been infected with HIV, with those been over the age of 50 accounting to 60000 and approximately 100,000 children. The rate of infection among women been 8.8% was higher compared to that of men which was 5.5%. Urban population had a higher adult prevalence (10%) than rural population (6%). The AIDS death toll in 2010 represents a nearly two-third drop from 2000-2004 death tolls where nearly 130000 people died each year. Peak mortality followed peak high prevalence due to life expectancy of 10years during the pre-ART era.

It has also being proven that with necessary health care of an already HIV/AIDS infected person one can be able to live with the HIV/AIDS virus for more than 10years.

1.1.2 Human Papillomavirus (HPV)

The Human papillomavirus was first discovered in 1954 by a group of scientist. HPV belongs to the papova family and papovida genera. HPV is the most viral sexually transmitted disease worldwide causing warts which are generally non-cancerous. With over 100 types of HPV about 60 types causes warts on non-genital skin. With those associated with genital warts been Types 6 and 11 .Types 16 and 18 are believed to most oftenly lead to cervical cancer.

Two new HPV vaccines have become available to the public since 2006 and licensed for use in a number of countries, some countries have introduced HPV vaccination programmes such as United Kingdom and the United States although the vaccine is available it is too expensive for developing countries. Cervarix is a vaccine that immunize against HPV types 16 and 18, while as Gardasil immunize against types 16, 18, and genital warts causing HPV type. WHO advocate vaccination of adolescent girls aged between 9 and 13 years, aiming to target them before their first sexual experience and hence before any exposure to HPV.

According to a study conducted by primary health Centre Kenya the HPV prevalence was 44.7%, with 58.6% women with cervical abnormalities and 43.2% among female without cervical abnormalities. In total, 23.1% of adult female had single type and 20% had multiple type infections. The HPV type 16 & 18 were more frequent by 34.6% while low risk type were frequent by 21.4%.

1.1.3 Cervical cancer

Cervical cancer is a cancer arising from the cervix. It occurs due to abnormal growth of cells that have the ability to invade or spread to other parts of the body. Cervical cancer is mostly linked to HPV. The high risk HPV types also known as oncogenic type are the ones believed to generally lead to cancer. HPV types 16 and 18 are believed to be the cause of over 70% of the worldwide cervical cancer cases.

Due to lack medical treatment for advanced cervical cancer, expansion of screening and prevention programmes are highly recommended so as to discover pre-cancerous changes in cervical tissue. Some countries have introduced screaning programmes so as to detect cervical abnormalities, preventing over 70% of possible cervical cancer cases.

In a study conducted in 2012 approximately 4,802 new cervical cancer cases are diagnosed annually and 2,500 deaths due to cervical cancer in Kenya. Cervical cancer is the first cause of female cancer in Kenya and most common type of cancer amongst female aged 15 to 49. The crude incidence rate in Kenya is 40.1 per 1000 women; this incidence rate is higher compared world crude incidence rate which is 14 per 1000 women.

1.1.4 Co-infection of HIV AND HPV

HIV infection favors HPV at the molecular and cellular levels during the different phases of the HPV cycle. HIV-positive women who have high-grade cervical lesions are more likely to have high-risk types of HPV. Furthermore, HIV-positive women are also more likely to have non-oncogenic HPV types and precancerous cervical lesions than the HIV negative women.

1.1.5 HPV and Cervical cancer

Persistent infections with carcinogenic HPV cause cervical cancers. Persistent oncogenic HPV infection can lead to pre-cancerous cervical lesions and invasive cervical carcinoma. Oncogenic types HPV lead to cervical cancer .

1.1.6 HIV and Cervical cancer

Cervical cancer is an opportunistic infection and is a symptom of AIDS due to lowered immune system of HIV infected women. Although invasive cervical cancer was classified as ADC in 1993 some studies such as the Swiss cohort study for the years 1990–2001 demonstrated that there is no connection acquiring cervical cancer with either CD4 cell count or progression to AIDS. Due to these results, cervical cancer incidences have not declined in the era of HAART. Currently there are no publications comparing survival probabilities of invasive cervical cancer patients during the pre- and post-HAART eras.

1.1 Statement of problem

With the introduction of HAART there has been a decrease in AIDS mortality and an increase in life expectancy in HIV infected people. Although this has greatly reduced the burden of HIV, it has also caused HIV infected people to be more vulnerable to HPV leading to increase in opportunistic illness such as cervical cancer. Cervical cancer is a leading cause of death among HIV infected women aged between 15 years and 54 years. It affects the current and future productive generation in Kenya. HIV and related cervical cancer death affect both the economic and social welfare in Kenya. This study determines the survival probabilities of HIV infected women with and without co-infection of HPV and cervical cancer.

1.2 Objective of the study

1.3.1 Main objective

The main objective of this study is to come up with survival probabilities for HIV infected adult female with cervical cancer in Kenya.

1.3.2 Specific objectives

- 1) To determine survival probabilities of HIV infected adult female with cervical cancer in Kenya.
- 2) To determine life expectancy of HIV infected adult female with cervical cancer in Kenya.
- 3) To determine the number of years lost due to cervical cancer mortality among HIV infected adult.
- 4) Comparison of survival probabilities of HIV infected adult female with and without cervical cancer.

1.4 Significance of this study

HIV /AIDS is a global epidemic with no vaccine or cure. It affects the immune system of the body making infected individual at high risk of contracting other disease. HIV infected women

are at a high risk of contracting cervical cancer due to been infected with HPV virus which has been proven to be a catalyst of causing cervical cancer.

By coming up with survival analysis of an adult female infected with HIV/AIDS with and without related cervical cancer, it would show reduction of probability of dying if HPV vaccine is administered to HIV infected women thus showing the medical benefit of the HPV vaccine on longevity of HIV infected life.

Chapter two

2.0 Literature review

In this chapter we review the available literature on survival functions for HIV/AIDS infected women with and without cervical cancer.

Anna et al (2015) studied the elevated cancer-specific mortality among HIV-infected Patients in the United States.

They projected an elevated cancer specific mortality among the HIV infected compared to HIV-uninfected counterparts, with colorectum cancer having an adjusted hazard ratio (HR) of 1.49 with a range been between 1.21 to 1.84, pancreas cancer had a HR of 1.71 with the range been between 1.35 to 2.18, larynx cancer had a HR of 1.62 with a range of 1.06 to 2.47, lung cancer had a HR of 1.28 with a range of 1.17 to 1.39 melanoma cancer had a HR of 1.72 with a range of 1.09 to 2.70, breast cancer had a HR of 2.61 with a range of 2.06 to 3.3, prostate cancer had a HR of 1.57 with a range of 1.02 to 2.41 and cervical cancer had a HR of 2.50 with a range of 2.08 to 2.99.

The increase in cancer-specific mortality among HIV-infected patients is caused by decline in Immune system and lesion progression in patient.

The above study did not incorporate the role of HPV on cervical cancer which causes more than 90% of cervical cancer. The study also did not do a comparison of cervical cancer mortality of HIV infected with non-cervical cancer mortality of HIV infected .

Robert et al (2005) conducted a study on survival after cancer diagnosis in person with AIDS; they used life table analysis to compute the unadjusted survival rates. they found about cancer patient 8829 women had invasive cervical cancer with 172 of them also suffering from AIDS , 36 % of this women died within 24 months and AIDS patients had almost double mortality compared to uninfected women .

The study used mortality rate of only patient registered by NY state cancer registry, when mortality was recorded in HIV/AIDS registry the patient was assumed to be still alive. The data was no accurate since majority of cancer patients failed to disclose their HIV status or other

forms of ailment. The study also concentrated on AIDS which is the final stage of HIV ignoring others stages of HIV.

Julius et al (2011) used a Markov state transition model, they found HIV positive women aged 25 had a cumulative cervical cancer mortality of 0.0254. For those women who did not previously undergo cervical cancer screening nor did they receive any HAART treatment. Their Cumulative cervical cancer mortality increased to 0.046. HIV positive women aged 35 who received cervical cancer screening would reduce their mortality from 0.0428 to 0.0417. The study showed that with introduction of HAART cervical cancer did not change much . The analysis was conducted in the absence of any consideration of HPV infections. The study also did not account the average number of years lost among HIV infected females with cervical cancer.

Sabin et al (2015) the study analyzed the life expectancy for patients with HIV enrolled in health care in Rwanda between 1997 and 2011. Life expectancy was estimated using the life table method. The life expectancy of a HIV infected patient aged 20 years was 25.6 years and a person aged 35 years had an additional 23.3 years. Life expectancy was shown to greatly decrease with HIV progression. A patient aged 20 enrolled in care with WHO HIV stage I would have a life an additional life of 42.5 years compared with a patient also aged 20 years enrolled at HIV stage IV who would have an additional life of 8.3 years.

The study also found the mortality rate to be 33.4 per 1000 infected person and the number of years of lost to be 851.2 years per 1000 people. Similarly, the number of years of life lost was less among women 2325.4 per 1000 people than among men 2884.9 years per 1000 people. The mortality rate and potential years of life lost depended on the HIV stage a patient was when admitted into the study.

The Sabin et al study evaluated the overall HIV mortality and life expectancy, the study did not show the burden of cervical cancer on women who are infected with HIV.

May et al (2011) estimated the life expectancy at age of 20 between 1996 and 1999 to be 30 years while between 2006 and 2008 be 45.8 years they also noted that the life expectancy of a HIV infected person was 15 years less than a healthy person. Men had life expectancy 39.5 years while as women 50.2 years. Patients admitted a with low CD4 count had lower life expectancy.

The study had a limitation as it only considered HIV patient with very low CD4 count ignoring those with average and high CD4 count.

Van Sighem et al (2010) compared life span of HIV positive and HIV negative patient using data from Netherlands AIDS registry. The life expectancy HIV infected men at age 25 was 52.7 this life expectancy was less 1 year compared to general population while the life expectancy HIV infected women aged 25 was 57.8 years less 1 year. The study focused on newly infected patient who had an equal cd4 count as a healthy person. The patient was not yet eligible to HAART treatment.

The above study did not account the effect of cancer on HIV infected individuals they also did not show the number of years lost due to HIV mortality.

Harrison et al (2010) used U.S. HIV data to analyze the life expectancy of newly diagnosed patient. They found the life expectancy in 1996 was 10.5 years while in 2005 to be 22.5 years. However, the patient still had a shorter life expectancy by 21 years compared to healthy people in 2005 this difference was less. Men had a lower life expectancy than women.

This study only showed the role of race among the HIV infected which was as biased as HIV infected people with the same medical services have the same life expectancy regardless of their racial background. The study did not show the role of cervical cancer in women infected with HIV.

Sloan et al. [2012] analyzed the life expectancy for a patient aged 38 years old to be 26.5 years, they assumed patients had a CD4 counts below 350 cells/ml and were introduced to HAART. If the patients had just below 500 cells/ml life span increased 27.4 years.

The study computed the life expectancy of HIV infected they did not show the role of opportunistic diseases on life expectancy and the number of years lost due to HIV and the effect of cancer on life expectancy.

Nakagawa et al (2012) used the stochastic simulation model of HIV progression that they had previously developed to estimate the lifespan of men who engaged in gay sex in the UK. The

lifespan of HIV infected gay men aged 30 was 45 years in 2010. They assumed there was no co-infection hepatitis and HIV, the life span lowered with there higher the WHO HIV stage a patient was when admitted.

This study only showed the role of sexual orientation among the HIV infected which was as biased as HIV infected people with the same medical services have the same life expectancy regardless of their sexual orientation background. The study did not show the role of cancer in patient infected with HIV.

Anna E. et al (2013) used the Kaplan Meier product survival estimate method to analyze the mortality among cancer patient with HIV infection in Uganda. The study The study showed that HIV-infected cancer patients had more than double mortality rate compared with HIV negative cancer patients with hazard ratio 2.28. survival was extremely low for HIV patient also diagnosed with cancer survival within one year was lower than that of HIV negative patient .

Although this study was comprehensive in HIV stages they failed to consider the role of HPV in cervical cancer infection, the study also did not compute the life expectancy of HIV infected. The analysis was conducted in the absence of any consideration of HPV infections. The study also did not account the average number of years lost among HIV infected females with cervical cancer.

2.1 Literature review summary

From the literature reviewed we have noticed a few gaps created by the studies and come up with some objectives to cover the gaps. These objectives are

- Determining the survival probabilities of HIV infected adult female with cervical cancer.
- Determining the number of years lost due cervical cancer in adult female infected with cervical cancer.
- Determining the life expectancy of HIV infected adult female with and without cervical cancer.

CHAPTER 3

3.0 Methodology.

There are different methods of obtaining survival probabilities of a certain cohort group such methods include cox proportional hazard model, Kaplan-Meier estimator, Markov chain Monte Carlo simulation, Markov model. In this study we are going to use multistate Markov model to incorporate all the stages from HIV uninfected to death.

3.1 Markov model.

The Markov model is named after Andrey Markov, the markov process possesses a property of memoryness

A stochastic process probability of each event depends only on the state attained in previous events i.e.

$$\begin{aligned} & \mathbf{P}[X_t \in A \mid X_{S_1} = X_1, X_{S_2} = X_2, \dots, X_{S_n} = X_n, X_S = X] \\ &= \mathbf{P}[X_t \in A \mid X_S = X] \end{aligned}$$

For all times $s_1 < s_2 < \dots < s_n < s < t$ all states that $X_1, X_2 \dots X_n$ and X in S and all subsets A of S . This is the **MARKOV PROPERTY**.

Transition probability is a probability of moving one state to another state i.e.

$$\begin{aligned} p_{jk} &= \text{probability of moving from state } E_j \text{ to state } E_k \\ &= \text{prob} (E_j \rightarrow E_k) \\ &= \text{prob} (E_j \setminus E_k) \end{aligned}$$

A sequence $\{ E_1, E_2, E_3, \dots, E_{n-1}, E_n \}$ is called a **Markov chain** if it satisfies the condition;

$$\text{Prob}(E_1, E_2, E_3 \dots E_{n-1}, E_n) = a_1 * p_{12} * p_{23} * \dots * p_{n-1n}$$

Where $a_1 = \text{prob}(E_1)$ is the initial / absolute probability.

A matrix P is a **transition matrix** if

- $0 \leq p_{jk} \leq 1$
- The sum of each row is 1 i.e.

$$\sum_{k=1}^{\infty} p_{jk} = 1$$

p_{jj} = the probability of returning to state E_j in n steps but not necessarily for the first time.

A state E_j is said to be persistent if $f_j = \sum_{n=1}^{\infty} f_{jj}^n = 1$

Transiency

A state E_j is transient, if $\sum_{n=1}^{\infty} f_{jj}^n < 1$ and $\sum_{n=1}^{\infty} p_{jj}^n < \infty$.

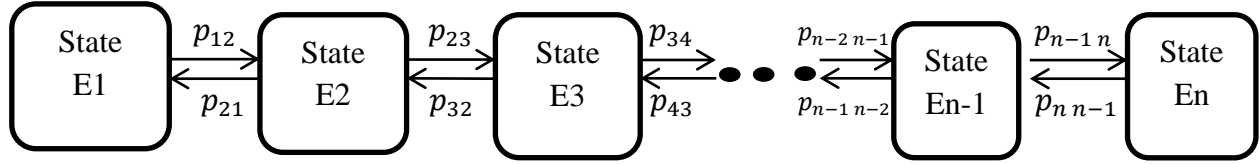
Absorbing state

A state E_j is said to be an absorbing state if $p_{jj}=1$ i.e. once one enters the state they cannot leave the state. An example of an absorbing state is death in a health-illness-death model.

A markov chain is said to be an **Absorbing markov chain** if and only if

- There exist an absorbing state i.e. state j of a markov chain is such that $p_{jj} = 1$
- It is possible to go from any nonabsorbent state to the absorbing state.

3.2 Transition diagram



3.2.2 Transition matrix.

	State E1	State E2	State E3	...	State En-1	StateE n	
P=	State E1	p_{11}	p_{12}	p_{13}	\dots	$p_{1\ n-1}$	$p_{1\ n}$
	State E2	p_{21}	p_{22}	p_{23}	\dots	$p_{2\ n-1}$	$p_{2\ n}$
	State E3	p_{31}	p_{32}	p_{33}	\dots	$p_{3\ n-1}$	$p_{3\ n}$
	:	:	:	:	:	:	:
	State En-1	$p_{n-1\ 1}$	$p_{n-1\ 2}$	$p_{n-1\ 3}$:	$p_{n-1\ n-1}$	$p_{n-1\ n}$
	State En	p_{n1}	p_{n2}	p_{n3}	:	$p_{n\ n-1}$	p_{nn}

3.3.1 Assumption of this study

1. All HIV infected women with cervical cancer are infected with the HPV virus
2. Due to the aggressive nature of cervical cancer among HIV infected women there is no remission of the cervical cancer
3. A healthy woman is subjected to a force of mortality ELT No. 12 males

3.3.2 HIV – Cervical cancer markov process

A Markov model can either be a two state model or a multi-state model. This study covers different stages of co-infection of HIV in women aged between 15 to 54 years. The stages are

- Healthy
- HIV+
- HPV
- Cervical cancer
- Death

Death is an absorbing state of this model once entered one cannot leave. This study will use a five state model

State 1 = healthy state

State 2 = HIV infected

State 3 = HIV infected with HPV infection

State 4 = in this state the woman is infected by both HIV and HPV and also develop cervical cancer.

State 5= Death

3.3.3 Transition diagram.

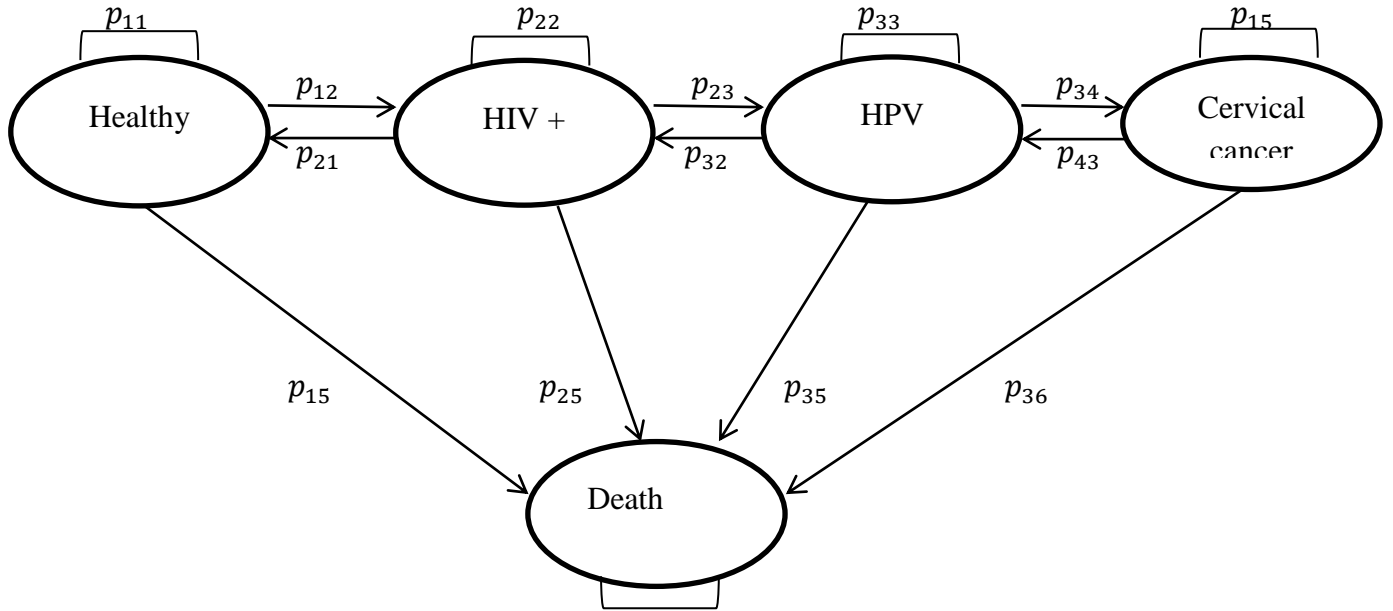


Figure 1

p_{55}

The transition probability matrix of this model;

	Healthy	HIV+	HPV	C.C	Death
Healthy	p_{11}	p_{12}	p_{13}	p_{14}	p_{15}
HIV+	p_{21}	p_{22}	p_{23}	p_{24}	p_{25}
HPV	p_{31}	p_{32}	p_{33}	p_{34}	p_{35}
C.C	p_{41}	p_{42}	p_{43}	p_{44}	p_{45}
Death	p_{51}	p_{52}	p_{53}	p_{54}	p_{55}

3.3.4 Classification of an absorbing Markov chain.

Death state is considered to be an absorbing state i.e. once a patient is in this state they can never leave. The transient states are Healthy, HIV+, HPV and Cervical cancer. The whole process can be summarized into 4 parts: the part labeled **Q** reflects the probability of not dying, conditional on the starting state; the section **R** reflects the probability of dying; the section **O** is a zero matrix, and section **I** is an identity matrix.

	Absorbing state	Transient state
Absorbing state	I	0
Transient state	R	Q

= **P**

$$P = \begin{bmatrix} I & 0 \\ R & Q \end{bmatrix}$$

Multiplication of matrix

$$P^2 = P * P = \begin{bmatrix} I & 0 \\ R & Q \end{bmatrix} * \begin{bmatrix} I & 0 \\ R & Q \end{bmatrix} = \begin{bmatrix} I & 0 \\ R + QR & Q^2 \end{bmatrix}$$

$$P^3 = P * P^2 = \begin{bmatrix} I & 0 \\ R_2 & Q^2 \end{bmatrix} * \begin{bmatrix} I & 0 \\ R & Q \end{bmatrix} = \begin{bmatrix} I & 0 \\ R_3 & Q^3 \end{bmatrix}$$

Where $R_3 = (R + QR) + Q^2R$

$$= R_2 + Q^2R$$

$$P^4 = P * P^3 = \begin{bmatrix} I & 0 \\ R & Q \end{bmatrix} * \begin{bmatrix} I & 0 \\ R_3 & Q^3 \end{bmatrix} = \begin{bmatrix} I & 0 \\ R_4 & Q^4 \end{bmatrix}$$

Where $R_4 = R_3 + Q^3R$

$$R_4 = R + RQ + Q^2R + Q^3R$$

$$R_4 = \sum_{i=0}^3 Q^i R$$

In general,

$$P^n = \begin{bmatrix} I & 0 \\ R_n & Q^n \end{bmatrix}$$

$$\text{Where } R_n = \sum_{i=0}^{n-1} Q^i R$$

$$= R \sum_{i=0}^{n-1} Q^i$$

$$= R (Q^0 + Q^1 + Q^2 + \dots + Q^{n-1}), Q^0 = I$$

But

$$(I - Q)^* (I + Q^1 + Q^2 + \dots + Q^{n-1}) \\ = I + Q + Q^2 + \dots + Q^{n-1} - Q - Q^2 - Q^3 - \dots - Q^n = I - Q^n$$

$$(I - Q)^{-1} * (I - Q) * (I + Q^1 + Q^2 + \dots + Q^{n-1}) = (I - Q)^{-1} (I - Q^n)$$

$$(I + Q^1 + Q^2 + \dots + Q^{n-1}) = (I - Q)^{-1} (I - Q^n)$$

Therefore

$$P^n = \begin{bmatrix} I & 0 \\ (I - Q)^{-1} (I - Q^n) R & Q^n \end{bmatrix}$$

$$\lim_{n \rightarrow \infty} P^n = \lim_{n \rightarrow \infty} \begin{bmatrix} I & 0 \\ (I - Q)^{-1} (I - Q^n) R & Q^n \end{bmatrix}$$

$$= \begin{bmatrix} I & 0 \\ (I - Q)^{-1} (I - \lim_{n \rightarrow \infty} Q^n) R & \lim_{n \rightarrow \infty} Q^n \end{bmatrix}$$

Previously

$$(I - Q)^* (I + Q^1 + Q^2 + \dots + Q^{n-1}) = I - Q^n$$

$$\lim_{n \rightarrow \infty} (I - Q) * (I + Q^1 + Q^2 + \dots + Q^{n-1}) = \lim_{n \rightarrow \infty} I - Q^n$$

$$(I - Q) * (I + Q^1 + Q^2 + \dots + \lim_{n \rightarrow \infty} Q^{n-1}) = I - \lim_{n \rightarrow \infty} Q^n$$

$$(I - Q) * (I + Q^1 + Q^2 + \dots) = I - \lim_{n \rightarrow \infty} Q^n$$

$$I + Q + Q^2 + \dots - Q - Q^2 - Q^3 - \dots = I - \lim_{n \rightarrow \infty} Q^n$$

$$I = I - \lim_{n \rightarrow \infty} Q^n$$

$$\text{But } \lim_{n \rightarrow \infty} Q^n = 0$$

Hence;

$$\lim_{n \rightarrow \infty} P^n = \begin{bmatrix} I & 0 \\ (I - Q)^{-1}R & 0 \end{bmatrix}$$

Where $(I - Q)^{-1} = F$ is called the fundamental matrix.

3.4 Life expectancy

In the HIV- Cervical cancer Markov process death is the absorbing state is death, the time to absorption t is the total time spent in transient state before been absorbed into the absorbing state. The time to absorption is also known as Life expectancy.

.Then,

$$t = Fc, \text{ F is the fundamental matrix and c be a column vector with all entries been}$$

1.

3.5 Number of years lost.

It is a measure of premature mortality

Number of years lost = (life expectancy of population – life expectancy of the infected population) * number of deaths among the infected

3.6 Survival probabilities

$${}_t p_x = \exp - \left| \int_0^t \mu_s ds \right|$$

Where μ_s is the force of mortality.

A person infected with HIV endures an additional force of mortality compared to healthy person
 k is the additional force of mortality

$$\mu^* = \mu + k$$

Where μ is the normal force of mortality

$$\begin{aligned} p_x^* &= \exp - \left| \int_0^1 \mu^* ds \right| \\ &= \exp - \int_0^1 \mu + k ds \\ &= \exp - [\mu + k] \end{aligned}$$

CHAPTER FOUR

4.0 Data analysis.

In this chapter the study uses the acquired data to analyze the survival of adult female infected with HIV with cervical cancer.

4.1 Data source.

Currently in Kenya there is no data on prevalence and mortality rate of cervical cancer amongst the HIV infected women. This is due to lack of screening of HIV amongst women with cervical cancer. It can also be due to lack of cervical cancer screening in rural areas. This study uses secondary and retrospective data.

The number of transition between HPV state for HIV status as recorded by Sandra et al (2013) on HIV positive

Transition between states	No HPV	Acquisition	Clearance	Persistence
No. of women	419	75	79	295

Table 1

According to a study by Mabeya et al, the study found that amongst 150 infected women 4 had cervical cancer and cervical cancer mortality according Anna et al (2015) found that HIV infected women had a mortality hazard ratio of 2.50 compared to their uninfected counterpart. The current cervical cancer mortality is 41 per 1000 women.

The median age of women in this study is 34.5 years old

Below is the data of HIV infection amongst women aged between 15 and 54 years according to *MINISTRY OF HEALTH KENYA: Kenya HIV estimate 2014 and Kenya demographics 2014*

Total number of women aged 15 to 54 years in Kenya	Total number of HIV infected women aged 15 to 54 years	Total number of women uninfected aged 15 to 54 years	New HIV infection amongst women aged 15 to 54 years	No. of deaths of women aged 15 to 54 years due to AIDS	Kenya's crude death rate	Force of transition to death due to AIDS	Force of transition from healthy to HIV infected
12041116	820000	10693272	72450	29848	0.0091	0.0364	0.0681

Table 2 HIV infection amongst women in Kenya.

4.2.1 HIV-Cervical cancer Markov model

The five state of this study will be “Healthy”, “HIV infected”, “HPV”, “Cervical cancer” and “Dead”

Healthy to Healthy	Healthy to HIV	Healthy to Dead	HIV to HIV	HIV to HPV	HIV to Dead
0.9288	0.0621	0.0091	0.7846	0.1790	0.0364

HPV to HIV	HPV to HPV	HPV to C.C	HPV to Dead	C.C to C.C	C.C to Dead	Dead to Dead
0.2112	0.7257	0.0267	0.0364	0.8975	0.1025	1

Table 3

The above table illustrates the transition probability between the states from the mentioned case studies.

4.2.2 Transition diagram

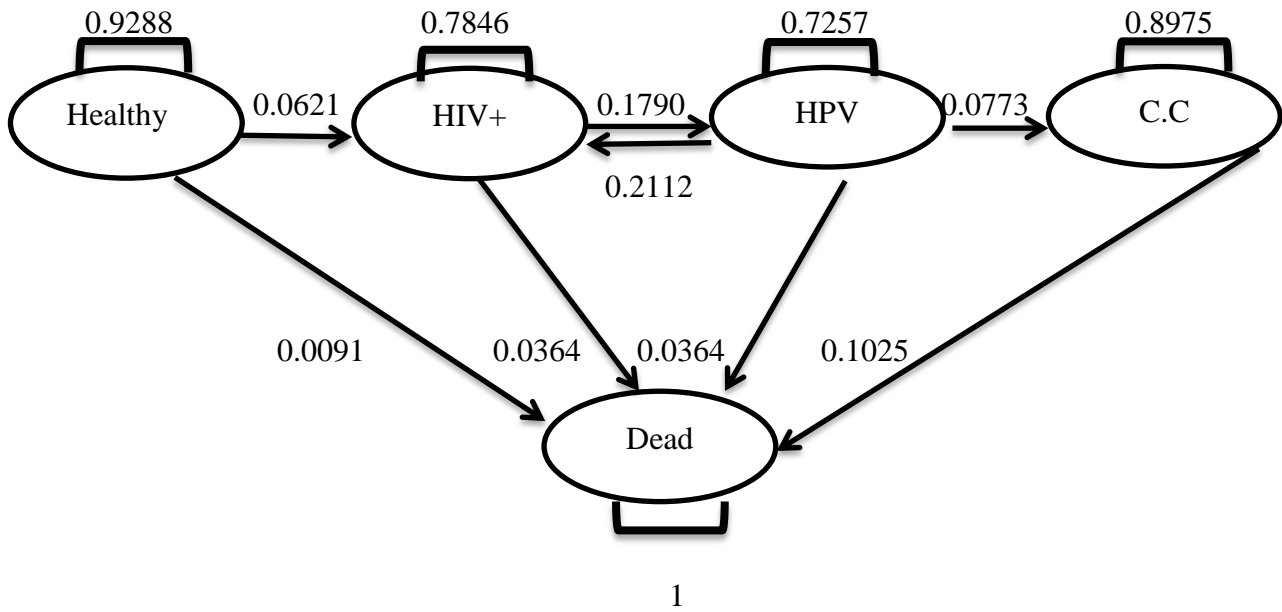


Figure 2

4.2.3 Transition matrix

	Healthy	HIV+	HPV	C.C	Dead
Healthy	0.9228	0.0621	0	0	0.0091
HIV+	0	0.7846	0.1790	0	0.0364
HPV	0	0.2112	0.7257	0.0267	0.0364
C.C	0	0	0	0.8975	0.1025
Dead	0	0	0	0	1

P=

4.2.4 Classification of an absorbing Markov chain P.

$$\mathbf{P} = \begin{array}{c|ccccc} & \text{Dead} & \text{Healthy} & \text{HIV+} & \text{HPV} & \text{C.C} \\ \hline \text{Dead} & 1 & 0 & 0 & 0 & 0 \\ \hline \text{Healthy} & 0.0091 & 0.9228 & 0.0621 & 0 & 0 \\ \hline \text{HIV+} & 0.0364 & 0 & 0.7846 & 0.1790 & 0 \\ \hline \text{HPV} & 0.0364 & 0 & 0.2112 & 0.7257 & 0.0267 \\ \hline \text{C.C} & 0.1025 & 0 & 0 & 0 & 0.8975 \end{array}$$

But

	Absorbing state	Transient state	
Absorbing state	I	O	= P
Transient state	R	Q	

Where Q shows the probability of not dying, conditional on the starting state; the section **R** shows the probability of dying; the section **O** is a zero matrix, and section **I** shows the probability of staying in the death state matrix which is an identity matrix.

4.3 Life expectancy

The matrix

$$\mathbf{Q} = \begin{array}{|cccc} \hline 0.9228 & 0.0621 & 0 & 0 \\ 0 & 0.7846 & 0.1790 & 0 \\ 0 & 0.2112 & 0.7257 & 0.0267 \\ 0 & 0 & 0 & 0.8975 \\ \hline \end{array}$$

The fundamental matrix F is obtained from $(I - Q)^{-1}$

Life expectancy in a markov chain is the number of step a transient state takes before been finally absorbed.

4.3.1 Residual time in each transient state.

		Healthy	HIV	HPV	C.C
F =	Healthy	12.95337	10.369082	6.766554	1.716394
	HIV	0.00000	12.890389	8.411883	2.133746
	HPV	0.00000	9.925083	10.122456	2.567647
	C.C	0.00000	0.000000	0.000000	9.756098

4.3.2 Time to absorption for each transient state

$$t = Fc$$

State	time
Healthy	31.805398
HIV	23.436018
HPV	22.615186
C.C	9.756098

A healthy woman aged 34.5 year old would have a life expectancy of 31.8 years while as a HIV infected woman also aged 34.5 years old would have an additional 23.4 years and a woman aged 34.5 years infected with HIV and also suffering from cervical cancer would have an additional 9.75 years. Women younger than 34.5years would have an increase in additional years while as women older than 34.5 would have a decrease in additional years.

4.4 Average number of years lost

The average number of years lost
= $(\text{life expectancy of a healthy woman} - \text{life expectancy of afflicted woman}) * \text{No of yearly deaths}$.

The average number of years lost due to HIV

$$\begin{aligned} &= (31.805398 - 23.436018) \times 29848 \\ &= 249809.105 \end{aligned}$$

The average number of years lost due to HIV is 8369.38 per 1000 person per year.

The average number of years lost due to cervical cancer in HIV infected women.

$$\begin{aligned} &= 23.436018 - 9.756098 \\ &= 13.67992 \end{aligned}$$

The average number of years lost due to cervical cancer among HIV infected women is 13679.92 years per 1000 women per year.

The average number of years lost due to co-infection of HIV and Cervical cancer.

$$\begin{aligned} &= 31.805398 - 9.756098 \\ &= 22.0493 \end{aligned}$$

The average number of years lost due to co-infection of HIV and cervical cancer among healthy women is 22049.3 years per 1000 women per year.

4.5.1 Survival probabilities

A HIV infected person has an additional force of mortality compared to a healthy woman, a HIV infected woman suffering from cervical cancer also has two additional force of mortality.

p_x^* is the probability an infected woman surviving one more year where k is additional force of mortality

$$\begin{aligned}
p_x^* &= \exp - \left| \int_0^1 \mu^* ds \right| \\
&= \exp - \int_0^1 \mu + k ds \\
&= \exp - [\mu + k]
\end{aligned}$$

p_x^c is the probability of a HIV infected woman suffering from cervical cancer surviving for one year where m is additional force of mortality.

$$\begin{aligned}
p_x^c &= \exp - \left| \int_0^1 \mu^* ds \right| \\
&= \exp - \int_0^1 \mu + m ds \\
&= \exp - [\mu + m]
\end{aligned}$$

Age -specific survival probabilities.

Age	μ_x^h	μ_x^{HIV}	p_x^{HIV}	q_x^{HIV}	$\mu_x^{c.c}$	$p_x^{c.c}$	$q_x^{c.c}$
15	.00052	.03692	0.963753	0.036247	0.10302	0.902109	0.097891
16	.00067	.03707	0.963609	0.036391	0.10317	0.901974	0.098026
17	.00089	.03729	0.963397	0.036603	0.10339	0.901775	0.098225
18	.00107	.03747	0.963223	0.036777	0.10357	0.901613	0.098387
19	.00115	.03755	0.963146	0.036854	0.10365	0.901541	0.098459
20	.00119	.03759	0.963108	0.036892	0.10369	0.901505	0.098495
21	.00119	.03759	0.963108	0.036892	0.10369	0.901505	0.098495
22	.00116	.03756	0.963137	0.036863	0.10366	0.901532	0.098468

23	.00112	.03752	0.963175	0.036825	0.10362	0.901568	0.098432
24	.00105	.03745	0.963243	0.036757	0.10355	0.901631	0.098369
25	.00100	.03740	0.963291	0.036709	0.1035	0.901676	0.098324
26	.00098	.03738	0.963310	0.03669	0.10348	0.901694	0.098306
27	.00099	.03739	0.963300	0.0367	0.10349	0.901685	0.098315
28	.00102	.03742	0.963271	0.036729	0.10352	0.901658	0.098342
29	.00106	.03746	0.963233	0.036767	0.10356	0.901622	0.098378
30	.00112	.03752	0.963175	0.036825	0.10362	0.901568	0.098432
31	.00118	.03758	0.963117	0.036883	0.10368	0.901514	0.098486
32	.00125	.03765	0.963050	0.03695	0.10375	0.901451	0.098549
33	.00132	.03772	0.962983	0.037017	0.10382	0.901388	0.098612
34	.00140	.03780	0.962906	0.037094	0.1039	0.901315	0.098685
35	.00150	.03790	0.962809	0.037191	0.104	0.901225	0.098775
36	.00161	.03801	0.962703	0.037297	0.10411	0.901126	0.098874
37	.00174	.03814	0.962578	0.037422	0.10424	0.901009	0.098991
38	.00189	.03829	0.962434	0.037566	0.10439	0.900874	0.099126
39	.00205	.03845	0.962280	0.037720	0.10455	0.90073	0.09927
40	.00224	.03864	0.962097	0.0378953	0.10474	0.900559	0.099441
41	.00246	.03886	0.961885	0.038115	0.10496	0.900361	0.099639
42	.00273	.03913	0.961626	0.038374	0.10523	0.900117	0.099883
43	.00303	.03943	0.961337	0.038663	0.10553	0.899847	0.100153

44	.00337	.03977	0.961010	0.03899	0.10587	0.899542	0.100458
45	.00377	.04017	0.960626	0.039374	0.10627	0.899182	0.100818
46	.00423	.04063	0.960184	0.039816	0.10673	0.898768	0.101232
47	.00476	.04116	0.959676	0.040324	0.10726	0.898292	0.101708
48	.00538	.04178	0.959081	0.040919	0.10788	0.897735	0.102265
49	.00607	.04247	0.958419	0.041581	0.10857	0.897116	0.102884
50	.00687	.04327	0.957653	0.042347	0.10937	0.896399	0.103601
51	.00777	.04417	0.956791	0.043209	0.11027	0.895592	0.104408
52	.00878	.04518	0.955825	0.044175	0.11128	0.894688	0.105312
53	.00933	.04573	0.955300	0.0447	0.11183	0.894196	0.105804
54	.01121	.04761	0.953506	0.046494	0.11371	0.892517	0.107483

Table 4

Age specific death rate due to HIV

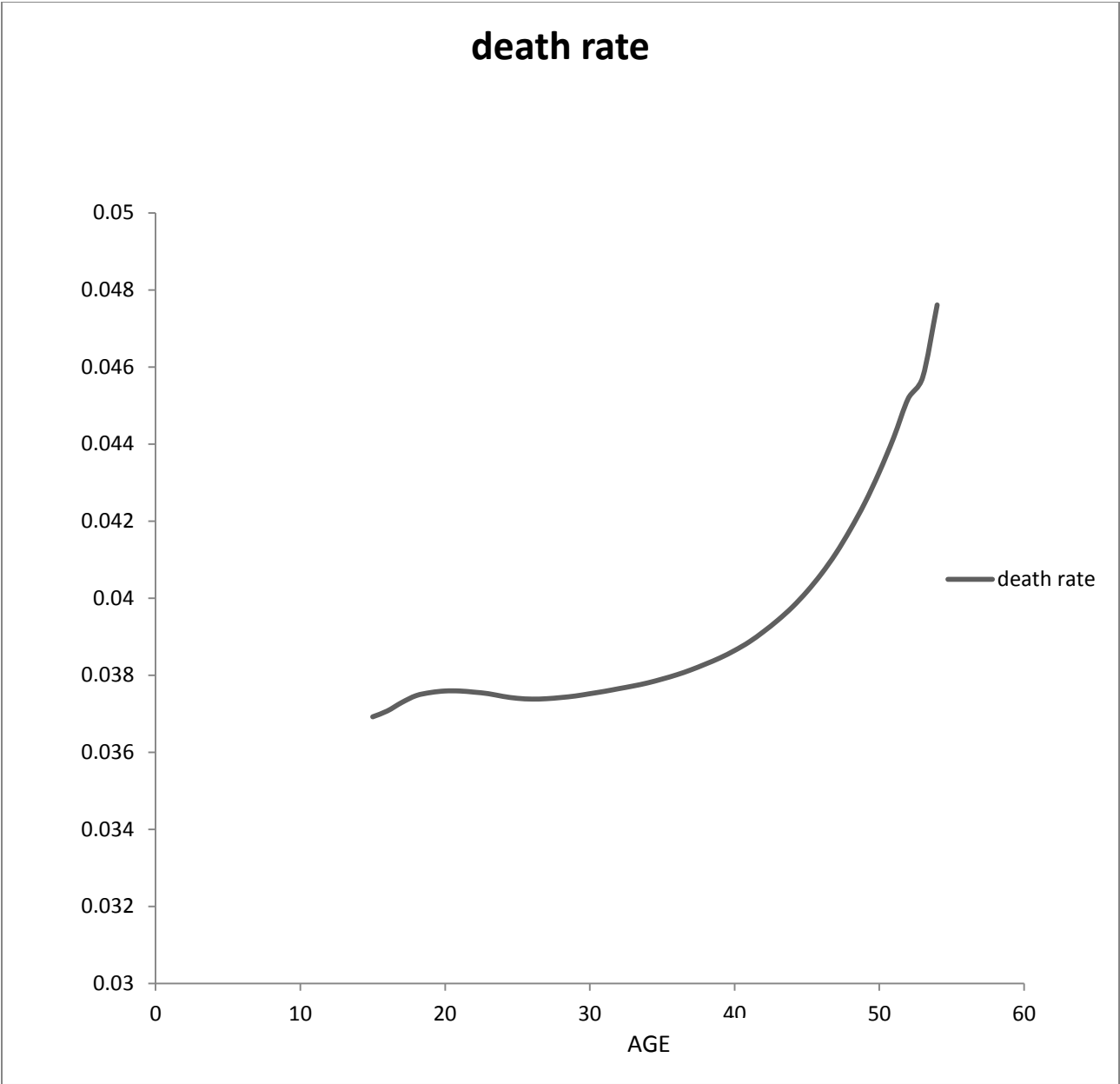


Figure 3

Age specific death rate due to cervical cancer in HIV infected adult female

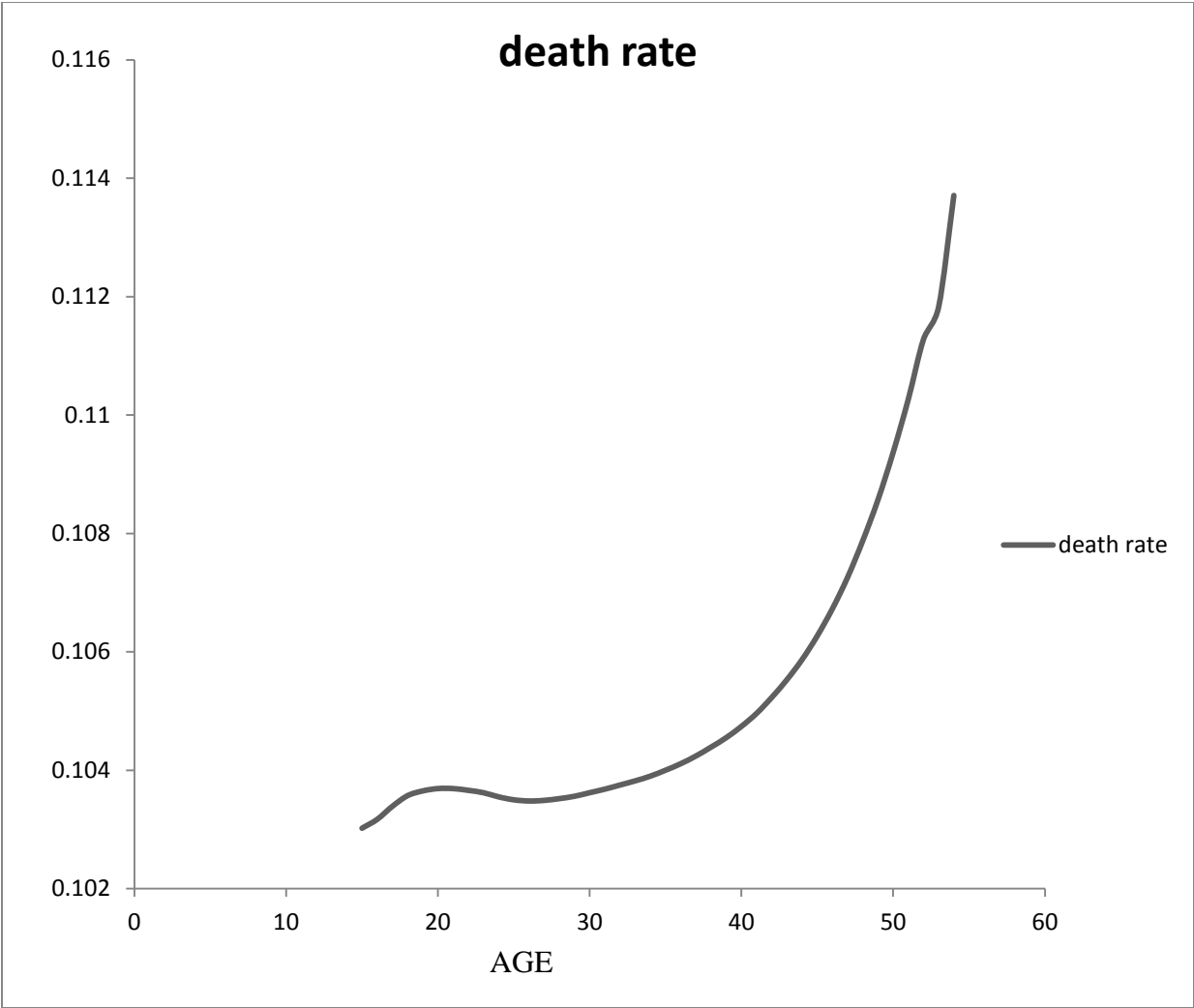


Figure 4

Survival probabilities of a HIV infected adult female

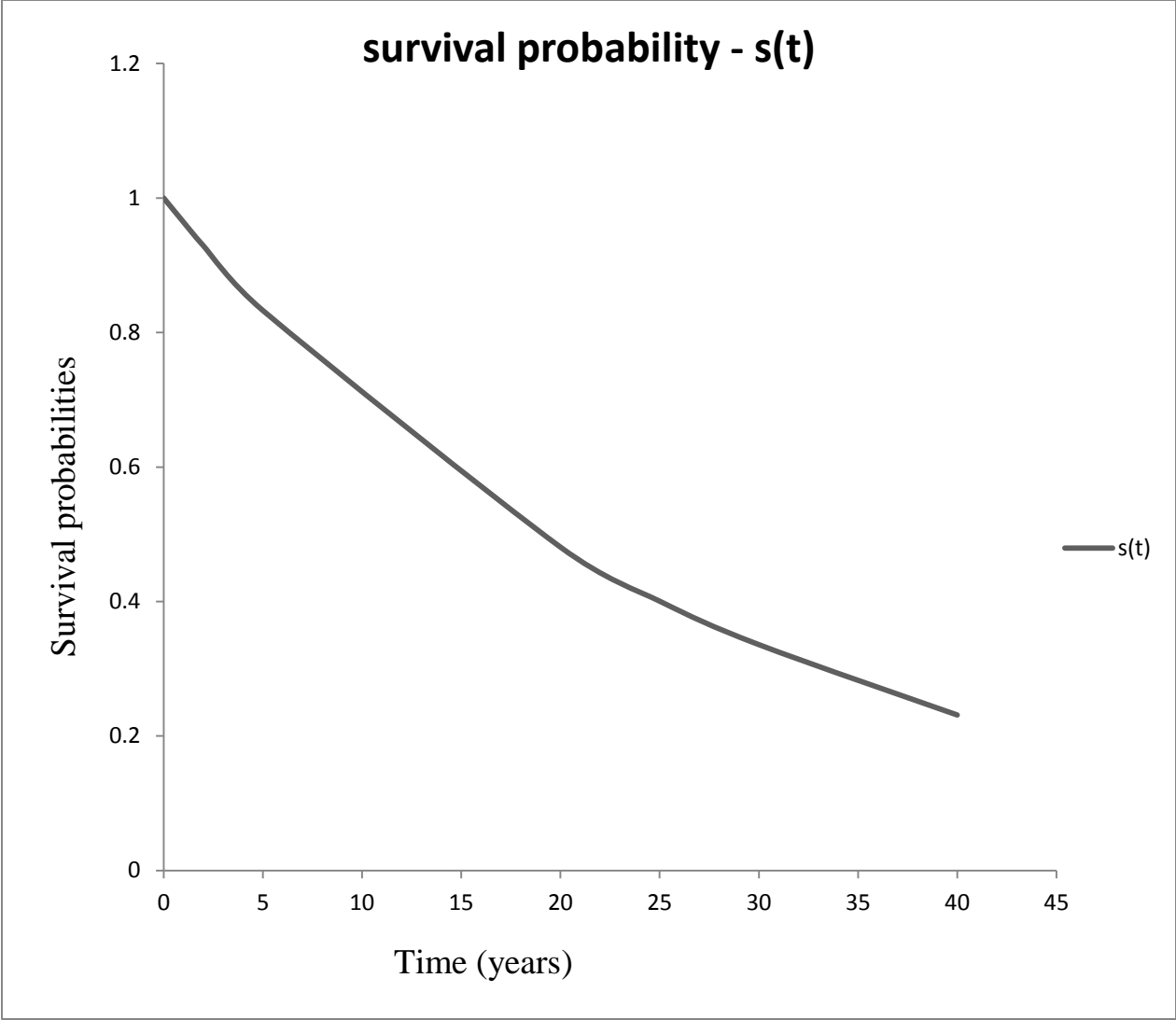


Figure 5

Survival probabilities of HIV infected adult female with cervical cancer.

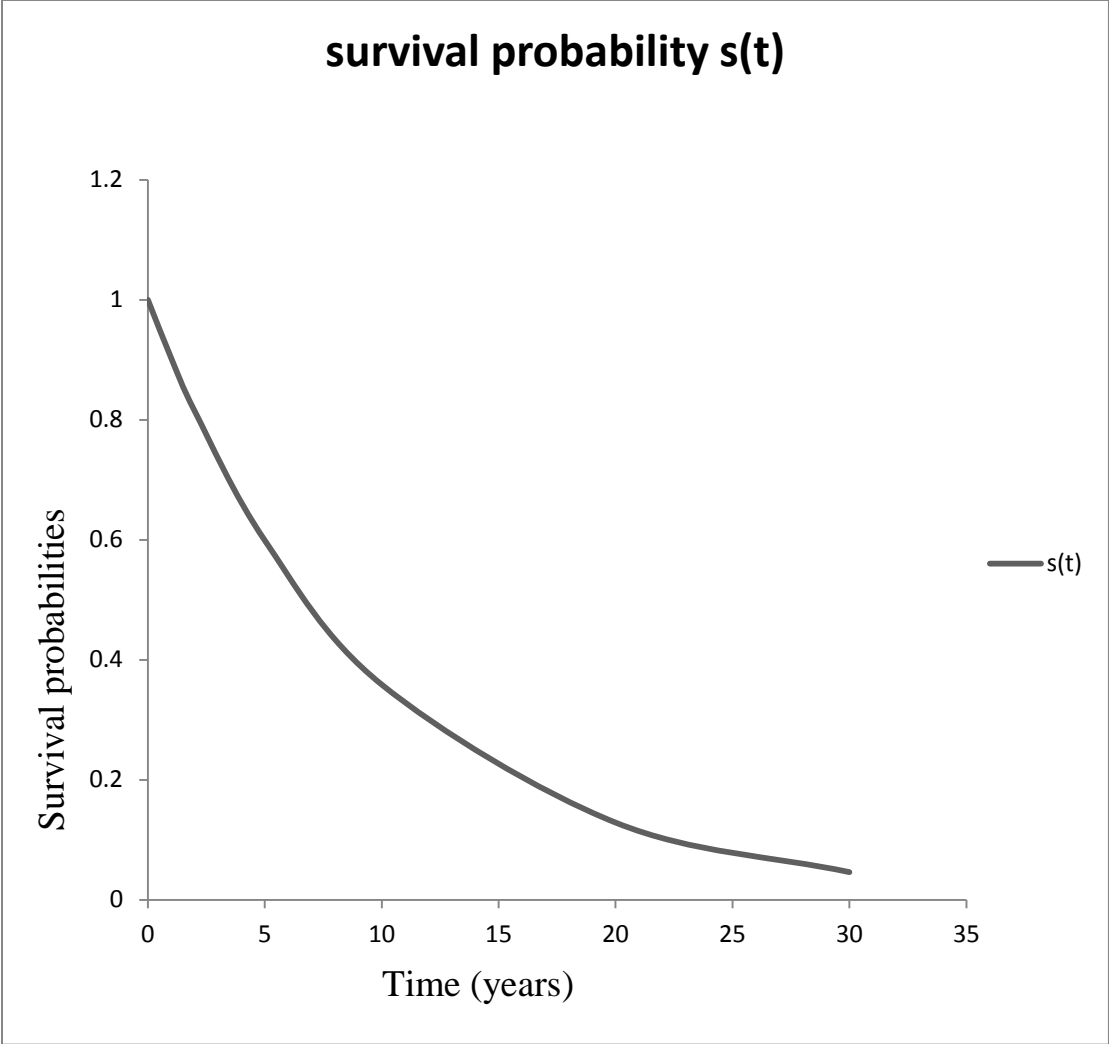


Figure 6

Comparison of survival probabilities of HIV infected women with and without cervical cancer.

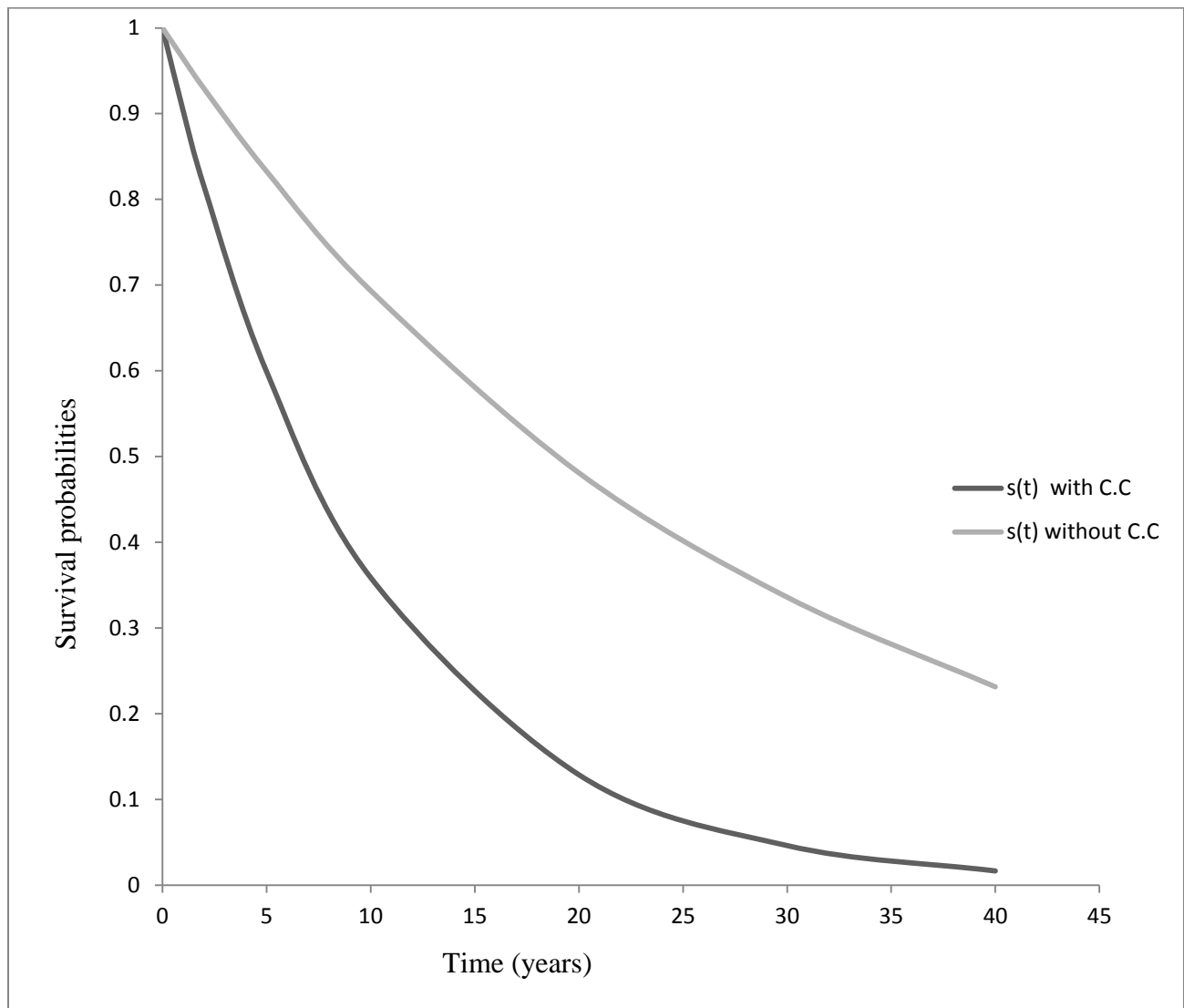


Figure 7

4.5.2 Discussion

Cervical cancer has an adverse effect on survival probability of a HIV infected adult female . HIV infected women with cervical cancer have a have a hazard ratio of 2.81 compared to their counterpart without cervical cancer this HR is almost similar to one found in other studies , Anna et al (2015) found the HR of cervical cancer among HIV infected to be 2.50 with a range of 2.08 to 2.99. Anna E et al (2013) also found the HR to be 2.68 with a range of 1.20–5.99.

We also found that the life expectancy of HIV infected woman of a median age of 34.5 was 23.4 years. The life expectancy differed slightly with the one found in other studies. Sabin et al who found the life expectancy of a 35 year old to be 25.6 years, Harrison et al on average life expectancy on diagnosis also found the life expectancy to be 22.5 years, Sloan et al found the life expectancy of a mean age 38 years to be 26.5 years. Some studies greatly differed with our findings such as Nakagawa et al (2012) who found the life expectancy of a 30 year old to be 45 this difference was caused by the fact Nakagawa concentrated on HIV infected gay men.

This study also found the number of years lost due to HIV to be 8369.38 years per 1000 women per year. These results greatly differed with Sabin et al (2015) who found the potential years lost to be 2325.4 years per 1000 women.

We also found the life expectancy of HIV infected with cervical cancer to be 9.76 years and the number of years lost due to cervical cancer among HIV infected adult female to be 13679.92 years per 1000 women per year.

CHAPTER FIVE

5.0 Recommendation and conclusion.

5.1 Conclusion

Cervical cancer has an adverse effect on survival of HIV infected women, administering of HPV vaccine would lessen the risk of cervical cancer in women especially those infected with HIV this would increase the life expectancy and reduce the number of years lost due to cervical cancer. By comparing the survival probability of a HIV infected woman with and without cervical cancer would show the importance of HPV vaccine.

5.2 Recommendation

- All HIV infected women should be screened for HPV and cervical cancer more often so as prevent the pre-cancerous lesion turning into cervical cancer.
- The government should provide more cervical screening services within the country especially in the rural areas where the is high prevalence of HIV
- The government should also raise awareness of cervical cancer especially in rural areas where women are at a higher risk of developing cancer.
- Women above the age of 15 should be vaccinated against HPV lessening the probability of developing cervical cancer.
- The overall population should be educated on ways of preventing contraction of HIV virus.

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