DYNAMIC SIMULATION MODEL FOR SOCIO-ECONOMIC IMPACT OF e-HEALTH TOOLS IN CERVICAL CANCER MANAGEMENT IN KENYA

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DECLARATION

This thesis is my original work and has not been presented in part or whole for a degree in this or any other University.

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DEDICATION

Samuel Kivuti Ngari, my late Dad and Friend. Thank you for your support and encouragement. I made it dad! I know from heaven, your cute smile is on me.

My dear Sis Sophy, this year, July 2014, I lost you to cervical cancer. God helping me I will do all that I can to ensure that no lives are lost unnecessary to Cervical Cancer. I miss you dearly my friend.

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ABSTRACT

Apart from cost effectiveness, e-health tools optimize cervical cancer management. An understanding of the impact of e-health interventions will inform policy.

The aim of this study was to assess the clinical and social economic impact of e-health in Cancer management in addition to traditional vaccination and screening interventions. System Dynamics(SD) modelling was applied. Ethical clearance was sought from relevant research bodies and study institutions. The study comprised of four phases.

In Phase onequalitative evaluation to establish experiences, opportunities and challenges- Cervical Cancer managers in Kenya was done. 33 Cervical cancer managers drawn from 4 provincial hospitals and 2 main National public referral hospitals were interviewed .Their responses were audio recorded, transcribed verbatim ,content analyzed in emerging themes.Four themes related to; Patients, health care providers, Health facility and Information Technology were identified. Mobile phones were highly accessibility. Negative attitudes towards screening procedure and Cervical Cancer patients need urgent attention.

In phase 2, a cross sectional survey to establish; the extent of use of e-health tools by Cervical Cancers clients, the characteristics of patients and identify barriers faced in internet use was done. Stratified random sampling of 199 Cervical Cancer clients from two main National referral hospitals. A structured questionnaire was administered. Low level (7.5%) use of the internet was reported. The main barriers to internet use were; lack of IT knowledge, no access to computer and high cost at cyber.

In phase 3SD Simulation model to evaluate possible effects of vaccination, screening and e-health tools wad developed using iThink™ version 10.0.6. Virtual experiments to assess socio-economic impact of various interventions were done. Secondary vaccination was found to have the highest impact followed by , primary vaccination and screening . e-health would be a complementary measure.

In Phase 4, Differential equations for population in each stage of diagnosed and undiagnosed cervical cancer were generated. Base Year (2010).Co efficients of model were estimated using published data. Equations were run through Matlab ™ Output graphs showing the rate of change of population in each stage of disease were generated. The SD model may act as an informed policy guide in management of Cervical Cancer in Kenya

LIST OF ACRONYMS

AAR	African Air Rescue
ABCSim	Activity Based Construction Simulation
E-health	Electronic Health
HPV	Human Papilloma Virus
IOM	Institute of Medicine
KNH	Kenyatta National Hospital
MATLAB	MATrix LABoratory.
MCH/FP	Maternal Child Health and Family Planning
MRI	Magnetic Resonance Imaging
MTRH	Moi Teaching and Referral Hospital
NCVHS	National Committee on Vital and Health Statistics
PETs	Position Emission Tomographies
RAND	Research and Development Corporation
RE-AIM	Reach, Effectiveness, Adoption, Implementation and Maintenance
SD	System Dynamics
LEEP	Loop Electosurgical Excision Procedure
VIA	Visual Inspection with Acetic Acid
VILLI	Visual Inspection with Lugol's Iodine

OPERATIONAL DEFINITIONS

Clinical Impact	Any effect of e-health on management of conditions of patients positive or negative.
Discrete Events Simulation	Concerns the modelling of a system as it evolves over time. The system's individual elements or events vary over time and at a countable number of times. It includes a set of equations describing the interaction of these variables.
Economic Impact	Any financial implication, costs or savings realized due to implementation and use of e-health tools.
e-health Tools	Any telecommunication equipment used in delivery of health information or care e.g. phones, fax, internet, etc.
e-health	Delivery of health (promotive, preventive, curative and/or rehabilitative) through telecommunication technologies.
Health Experts	Nurse managers or doctors who work with Cervical Cancer patients or patient at the operational/Functional level of health Institutions.
iThink™	A computer software used to develop and simulate models.
MATLAB	A high-performance modern programming language environment for technical computing which integrates *computation*, *visualization*, and *programming* environment.
Model	A mathematical or computational representation of a process (e.g. Cervical Cancer management) or concept by means of a number of variables which are defined to represent the inputs, outputs, and internal states of the process or concept.
PAP smear	Its full name is Papanicolaou, a medical procedure in which a sample of cells from a woman's cervix is collected and spread (smeared) on a microscope slide. The cells are examined under a microscope in order to look for pre-malignant (before-Cancer) or malignant (Cancer) changes.
PAPNETIs an	automated interactive computer-assisted screening procedure developed in the late 1980s to identify and display abnormal or Cancerous cells in 97% of abnormal cases. It utilizes an automated microscope, a full-color camera, and a high-speed image-

	processing computer. It is used for analysis of PAP smears and has been shown to detect abnormalities that were repeatedly missed on manual screening.
Simulation	The technique of imitating the behaviour of some situation or system (Economic, Clinical or Social) or a real world process or system over time. It generates artificial history of a system. It is done by means of a computer and analyzing the execution output which allow decisions to be made regarding the characteristics of the systems.
STELLA	Computational software utilized in developing simulation models.
Systems Dynamic	An approach to understanding the behavior of complex systems over time.The tests are done to ensure that the model addresses the right problem, provides accurate information about the system being modeled, and enable the model to be actually used. Validation will be done through use of the experts in the various institutions using animation or through expert systems.
Validation	The tests done to check whether the model represent and correctly reproduce the behaviors of the real world system.
Verification	Any test procedure done to ensure that the model is programmed correctly, that the algorithms have been implemented properly and that the model does not contain errors, oversights, or bugs. Verification ensures that no mistakes have been done in implementing the model. It is performed as more tests are performed on the model, errors are identified, and corrections are made to the model developed.

CHAPTER ONE: INTRODUCTION

This chapter consists of basic concepts on Cervical Cancer, e-health tools solutions, problem description and justification of the study.

1.1 Basic Concepts

The cervix is part of a woman's reproductive system. It is the lower, narrow part of the uterus (womb), a hollow, pear-shaped organ in the lower abdomen. The cervix connects the uterus to the vagina which leads to the outside of the body. Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems (Hajdu 2012; Lewin et al. 2010). All Cancers begin in cells, the body's basic unit of life. To understand Cancer, it's helpful to know what happens when normal cells become Cancerous.

The body is made up of many types of cells. These cells grow and divide in a controlled way to produce more cells as they are needed to keep the body healthy. When cells become old or damaged, they die and are replaced with new cells in a programmed process called apoptosis. Sometimes this orderly process, however, goes wrong. The genetic material Deoxyribonucleic Acid (DNA) of a cell can become damaged or changed, producing mutations that affect normal cell growth and division. When this happens, cells do not die when they should and new cells form when the body does not need them. The extra cells may form a mass of tissue called a tumor. Not all tumors are Cancerous; tumors can be benign or malignant.

Benign Tumors aren't Cancerous. They can often be removed, and, in most cases, they do not come back. Cells in benign tumors do not spread to other parts of the body (Hajdu 2012)

Malignant Tumors are Cancerous. Cells in these tumors can invade nearby tissues and spread to other parts of the body. The spread of Cancer from one part of the body to another is called metastasis. Some Cancers do not form tumors. For example, leukemia, a Cancer of the bone marrow and blood.There are more than 100 different types of Cancer. Most Cancers are named for the organ or type of cell in which they originate; for example; colon Cancer, lung Cancer, and skin Cancer for Cancer that

begins in basal cells of the skin. Therefore Cervical Cancer basically denotes that the Cancer begins from the cervix (Hajdu 2012) .

1.2 Causes of and Factors Associated with Cervical Cancer

The specific cause of Cervical Cancer is not known; however, there are risks and predisposing factors associated with Cervical Cancer. We discuss some of these risk factors below:

Human Papilloma Viruses (HPVs): Cervical Cancer is gradually being recognized as a sexually transmitted disease. The sexually transmitted etiological agent has been identified as the HPV, a group of viruses with over 100 sub-types that can infect the cervix. These viruses can be passed from person to person through sexual contact (Schlecht et al. 2003).

Some types of HPV can cause changes to cells in the cervix. These changes can lead to genital warts and genital Cancers.

Weakened Immune system: Women with Human Immune Deficiency Virus (HIV) infection are more likely to have a concurrent HPV infection (Baseman & Koutsky, 2005;WHO/ICO, 2010). Some studies suggest that HIV infection is associated with the rapid progression of HPV-related Cervical pre-malignant lesions to invasive Cervical Cancer or to advanced invasive Cervical Cancer (Omack et al., 2000).Women + who take drugs that suppress the immune system have a higher-than-average risk of developing Cervical Cancer (Baseman & Koutsky, 2005). In Kenya, the HIV rate in adult women with Invasive Cervical Cancer is estimated at 15% hence the need to tackle both HIV and Cervical Cancer concurrently (Ministry of Public Health and Sanitation and Ministry of Medical Services, 2012).

Age: Cancer of the cervix occurs predominantly in women over the age of 40 (WHO/ICO, 2010). Average number of new cases of Cervical Cancer reported in Kenya by age are: 1002 (15−44 yrs), 650 (45−54 yrs), 555 (55−64 yrs) and 428 (65+ yrs) (WHO/ICO, 2007). Even though the incidence rates of Cervical Cancer are lower in women below 15 years of age, it is important to vaccinate these women against HPV, if the war against Cervical Cancer is to be won (Biddlecom et al. 2006).

Sexual History: Because HPV can be transmitted by sexual contact, women who had early sexual contact, who have had many sexual partners or who have men with many sexual partners, have a higher-than-average risk of HPV infection (WHO/ICO 2010; Biddlecom et al. 2006)

Smoking Cigarettes: The chemicals in cigarette smoke interact with the cells of the cervix, causing pre-Cancerous changes that may progress to Cancer over time. Among women with an HPV infection, those who smoke cigarettes have a higher risk of Cervical Cancer than women with HPV infection who do not smoke (WHO/ICO 2010, Kjellberg et al. 2000). However other studies have yielded no association between smoking and HPV infection with some reporting even lower risks of HPV infection among smokers(Wang et al. 2003) . In Kenya the Smoking prevalence in women is 1 percent.

Use of Birth Control Pills: Use of hormonal birth control pills for five or more years has been associated with increased risk of Cervical Cancer especially in women with HPV(Baseman & Koutsky, 2005;WHO/ICO, 2010). In Kenya, 7.5% of women of reproductive age use Oral Contraceptives (WHO/ICO 2010).

Multiparity: Studies suggest that giving birth to many children may increase the risk of Cervical Cancer among women with HPV infection (Baseman & Koutsky, 2005;WHO/ICO, 2010). The current Fertility rate (live births per woman) in Kenya is estimated at 5.0 (WHO/ICO, 2010;Kjellberg *et al*. 2000).

Lack of Regular Pap Tests: Cervical Cancer is more common among women who do not have regular Pap tests. The Pap test helps doctors find pre-Cancerous cells. Treating pre-Cancerous cervical changes often prevents Cancer. It is estimated that only 3.2% of all Kenyan women between the age of 18 to 69 years are screened every three years (WHO/ICO, 2010)

Low Educational Attainment: It was associated with the risk of invasive Cervical Cancer (Ombech & Muigai, 2012); however, another study found that educational attainment and social class were not related to risk(Cuzick *et al*., 2000).

Genetic Factors: Different studies have demonstrated the hereditary link to Cervical Cancer. It is possible that genetic factors influence ceviral persistence and specific more virulent strains of HPV especially in early onset cases (Wang *et al,*. 2010).It has been reported in one analysis that at least 15% to 20% of women diagnosed with Cervical Cancer had a close relative with the Cervical Cancer (Patel *et al*., 2012).

Occupational Health and Pollution: The daughters of women exposed to Diethylstilbestrol (DES) used as an estrogen compound were at a higher risk of developing Cervical Cancer and women working in environments which expose them to environmental chemicals are more likely to die from Cervical Cancer (Hatch *et al*., 2001). Other causes are unknown or unreported.

1.3 Pathophysiology of Cervical Cancer

Cervical Cancer is caused by the invasion of the cervix by different types of Human Papilloma virus (HPV). However, a period of time lapses before the HPV infection can be visible, which is called the incubation period (Schlecht et al. 2003). The range of incubation period depends on the structure of the healthy tissue, the type of HPV infection, the Zero status (HIV) co-infection, age and sexual activity of the women, *inter alia* (Duraisamy *et al*., 2011). The HPV mostly attacks the EndoCervical region of the cervix, where the squamous and the columnar epithelium meet. This section is also characterized by maximum metapastic changes at puberty and at first pregnancy which on average occurs between 18 to 30 years (Duraisamy *et al*., 2011). Below the age of 9 years, the girls are not susceptible to HPV. This is because the conversion of dormant columnar epithelium of endocervical canal into squamous epithelium has not yet occurred (Hwang *et al*., 2012). It is assumed that at this age the girls are not yet sexually active.

After 10 years, HPV infection and spread is associated with the following parameters; The age of the girl, sub-Type of HPV present, Sexual activity including number of sexual partners and age of first intercourse, Co-Infection with HIV, the health status of the Cervical tissue and health risky behaviours e.g. smoking, poor dietary habits (Kjellberg *et al*., 2000).

It takes a period of up to 15 years for the HPV virus to spread from the End Cervical region to other regions of the cervix (Woodman *et al*., 2007). This period is called the Latent period. During this period, HPV infections clear naturally in over 80% of women. This clearance has been attributed to the natural cell mediated immune response where by 'HPV infected epithelium undergoes differentiation and maturation, and exhibits only minor cellular abnormalities.' In the remaining 20%of women, 'HPV infection of replicating immature cells prevents epithelial maturation and differentiation leading to continued replication of immature cells and accumulation of genetic abnormalities that could ultimately lead to a clone of Cancer cells (Ibeanu, 2011).

The clone of Cancer cells may remain in situ (Dysplasia, stage 0) wherebythe Cancer is found only in the top layer of cells in the tissue that lines the cervix), or progress to stage 1, where Cancerous cells are confined to Cervical region, extend to the upper third of the vagina, or the tissue around the uterus, but not the pelvic wall (stage 2). At stage 3, the cells metastatise to the lower third of the vagina and/or the pelvic side-wall and possibly the kidneys. At stage 4, the Cancer cells spread beyond the reproductive tract to involve the bladder or rectum, and invade distant organs (most often the lungs or liver), the bones, or other body systems (Baseman & Koutsky 2005; Kim et al. 2007) For a uniform description and staging of Cervical Cancer, the International Federation of Gynaecologists and Obstetricians (FIGO), in the year 2009, came up with a common platform described below (Adapted from Lewin & Wright, 2011).

FIGO staging of Cervical Cancer, 2009.

Stage I: The carcinoma is strictly confined to the cervix.

1A: Invasive carcinoma identified only microscopically.
Invasion is limited to measured stromal invasion with a maximum depth of 5mm and no wider than 7mm.

1A1: Measured invasion of stroma no greater than 3mm in depth and no wider than 7mm.

1A2: Measured invasion of stroma greater than 3mm and no greater than 5mm in depth and no wider than 7mm

Stage 1B: Clinical lesions confined to the cervix or pre-clinical lesions greater than stage 1A.

IB1: Clinical lesions no greater than 4cm in size.

IB2: Clinical lesions greater than 4cm in size.

Stage II: The carcinoma extends beyond the cervix, but no extension to pelvic side wall. The carcinoma involves the vagina, but not as far as the lower third.

IIA: Involvement of up to the upper two thirds of the vagina. No obvious parametrial involvement.

IIA1: Involvement of the upper two thirds of vagina, less than 4cm in greatest dimension.

IIA2: Involvement of the upper two thirds of vagina, greater than 4cm in greatest dimension.

IIB: Obvious parametrial involvement but not onto the pelvic side wall

Stage III: The carcinoma extends to pelvic sidewall. The tumour involves the lower third of the vagina. All cases of hydronephrosis or non-functioning kidney should be included unless they are known to be due to other causes.

IIIA: Involvement of the lower vagina but no extension onto pelvic sidewall.

IIIB: Extension onto the pelvic sidewall, or hydronephrosis /non- functioning kidney.

Stage IV

IVA: The carcinoma extends beyond the true pelvis or clinically involves the mucosa of the bladder and/or rectum.

IVB: Spread to adjacent pelvic organs and extends beyond the true pelvis. Spread to distant organs outside the true pelvis.

This classifications guide the managers in course of management and possible prognosis of Cervical Cancer.

1.3.1 Signs and Symptoms of Cervical Cancer

Pre-Cancerous changes and early Cancers of the cervix generally do not cause pain or other symptoms. When the disease gets worse, women may notice one or more of the following symptoms: Abnormal vaginal bleeding which includes bleeding that occurs between regular menstrual periods, bleeding after sexual intercourse, douching, or a

pelvic examination and menstrual periods that last longer and are heavier than before. Bleeding after menopause, pelvic pain during intercourse and increased vaginal discharge (Pitts & Clarke, 2002;Hanisch & Gustat, 2008; Kjellberg, *et al.*, 2000).

It is important to note that these symptoms alone may not be an indicator of Cervical Cancer since infections or other health problems may also cause these symptoms. It is therefore necessary to perform further diagnostic tests to confirm these clinical signs and symptoms.

1.3.2 Diagnosis of Cervical Cancer

Cervical Cancer can be diagnosed through a number of tests and procedures which include Pap smear, colposcopy, biopsy, endoCervical Curettage, and conization, among others (Schiffman *et al.* 2000,WHO/ICO 2010, Duraisamy *et al*. 2011). Early diagnosis of Cervical Cancer is the key to any successful management of the condition.

A positive diagnosis of Cervical Cancer is a life changing experience, since Cervical Cancer may be a terminal illness. The woman may be faced with a difficult decision of whether or not to disclose the illness to others (Molefe & Duma, 2009). The woman may have her life dreams and aspirations shattered and may face a bleak future. Hence, the woman experiences physical pain, social, emotional and economic impact upon diagnosis. Emotionally, fear of anticipated outcome including death lingers, socially she is concerned with what could happen to her children (if any), while economically she fears loss of employment and cost of health care among others (Gatune & Nyamongo, 2005).

1.3.3 Treatment of Cervical Cancer

Treatment of Cervical Cancer depends on the stage of the disease and recurrence. Recurrent Canceris Cancer that was previously treated, but has returned after a period of time (Duyn et al. 2002). The Cancer may be diagnosed in the cervix or in other parts of the body. At any stage of disease, women with Cervical Cancer may have treatment to control pain and other symptoms, to relieve the side effects of therapy, and to ease emotional and practical problems. Cervical Cancer may be treated with

surgery, chemotherapy, radiation therapy and/or a combination of all the three intervention methods (Anderson et al. 2010).

1.4 The Burden of Cervical Cancer

Cervical Cancer continues to be a global burden to women's health, which does not only affect older women. It is the second most common Cancer in women under 45 years of age after breast Cancer and commonly strikes women early, often in their mid-thirties, at an age when they are in the prime of their lives (Fernández de Larrea-Baz et al. 2009; Forouzanfar et al. 2011; Linkov et al. 2011). Many affected women will be caring for young children and extended families, so one death from Cervical Cancer can devastate the lives of many people (Gatune & Nyamongo, 2005).

1.4.1 The Burden of Cervical Cancer in Developed Countries

Cervical Cancer is the third commonest Cancer worldwide, after breast Cancer and lung Cancer. Every two minutes a woman dies of Cervical Cancer (Anderson et al. 2010). In the United Kingdom there are around 2,800 new cases and 1,100 Cervical Cancer deaths a year, while in the US there are 10,000 new cases and 3,700 deaths per year (Shin et al. 2010; Baseman & Koutsky 2005).

1.4.2 The Burden of Cervical Cancer in Developing Countries

Over 80%-85% of Cervical Cancer cases occur in the developing world (Anderson et al. 2010). It is the leading cause of death from Cancer among women in developing countries, where it causes about 190,000 deaths each year (Chirenje *et al*. 2001, Duraisamy *et al*. 2011, Biddlecom *et al*. 2006). Sub-Saharan Africa is the worst-affected region. In Zambia, for example, Cervical Cancer affects 63 women in 100,000 per year, which is nine times Australia's rate of 7 per 100,000 women (Singh et al. 2012).

1.4.3 Burden of Cervical Cancer in Kenya

Cervical Cancer is the most frequent Cancer among women in Kenya, and the 2nd most frequent Cancer among women between 15 and 44 years of age after breast Cancer (WHO/ICO, 2010). A Crude incidence rate of 16.5 per 100,000 people per year has been reported in Kenya. With a population of 10.32 million women aged 15 years and older who are at risk of developing Cervical Cancer, it is estimated that 38.8% of women in the general population harbor Cervical HPV infection at a given

time. Estimates indicate that every year 2635 women are diagnosed with Cervical Cancer and 2111 die from the disease (WHO/ICO 2010).

It is also projected that in 2025, there will be 4261 new cases of Cervical Cancer in Kenya and that 3293 deaths will be likely as a result of Cervical Cancer. In Nairobi alone, 520 to 780 new cases are reported every year. At Kenyatta National Hospital, Cervical Cancer accounts for over 70% of Cancers of reproductive health (Ministry of Public Health and Sanitation and Ministry of Medical Services 2012; WHO/ICO 2010).

1.5 Addressing the Challenge of Cervical Cancer

Many solutions have been suggested and /or have been implemented in management of Cervical Cancer in both developed and developing countries. These have included screening, vaccination, health education, surgical and chemotherapy interventions among others (Claeys *et al*. 2003; Schiffman et al. 2000; Rositch *et al*. 2012)

1.5.1 Vaccination

A vaccine has been developed against HPV; however, these vaccines are not designed to treat the infections once it occurs and should therefore be given before infections, in order to achieve maximal effect (Biddlecom et al. 2006; Hwang et al. 2012). The evaluation of vaccines has been done while others is still underway, however, Modeling studies indicate that HPV vaccines could be effective in preventing Cervical Cancer provided vaccination is done at adolescence and before a woman becomes sexually active (Kim & Goldie 2008; Jit et al. 2008; Biddlecom et al. 2006). There is need to sensitize these young women on the importance of the HPV vaccine and research needs to be done in areas of coverage and modalities of delivery to these adolescents.

Primary vaccination against HPV infections has demonstrated high efficacy, immunogenicity and safety (Maine et al. 2011). Since HPV is sexually transmitted, Pre-exposure Vaccination may be administered to both young boys and girls. However, vaccination of boys has been found to be less cost-effective in low resource setting (Kim et al. 2007). For the vaccine to be effective there must be high coverage of vaccination among pre-adolescent girls and lowering of vaccine costs. Catch up

vaccination usually performed among older women is effective as a preventive strategy; however not all women qualify for vaccination since catch up vaccination is recommended for women between 10 to 45 years (Rama et al. 2010).

Women who are already infected with HPV would also not benefit from vaccination (Rama et al. 2010). HPV has been known to have over 100 sub-types. There is no single vaccine which can provide immunity against all these strains of HPV. Even among the few women receiving vaccine against HPV, around 15% do not complete the vaccination doses , while acceptability of the vaccine vary among different groups of women (Kumar & Whynes 2011; Rama et al. 2010)

1.5.2 Screening

Cervical Cancer screening is a procedure which involves opening the vagina using a speculum with the woman lying on lithotomic position and taking a sample of cells from the cervix (Ibrahim et al. 2011). Even though there are a number of screening methods available; Cytology, Visual Inspection with Acetic Acid (VIA), Visual Inspection with Lugol's Iodine (VILI) and HPV DNA testing, Colposcopy, Liquid based Cytology, Sure path, Cytoscreen, Speculoscopy, cervicoscopy, laser induced, and computer imaging (Duraisamy et al. 2011), not all methods can be deployed in developing countries due to limited resources (Anderson et al. 2010). The type of screening chosen by the specific country depends on a number of factors, including availability of resources, infrastructure, health seeking behaviors, frequency of screening and nature of screening test (Anderson et al. 2010; Kim & Goldie 2008).

For developing countries to have effective Cervical Cancer screening, systematic screening coupled with treatment options must be available. These screening interventions must be integrated into the existing health systems and should be economically, socially and culturally acceptable. Goldie (2005) estimated the total discounted cost of screening utilizing VIA at $15; use of HPV DNA testing which required two visits was estimated at $18, while cytological examination was estimated at $25. It is to be noted that the low specificity of some screening methods results in false positive results which may result in unnecessary treatment and increased anxiety among women (Mayrand et al. 2007; Duraisamy et al. 2011).

1.5.3 Treatment Strategies

Many solutions have been suggested and /or implemented in order to deal with the challenge of Cervical Cancer in both developed and developing countries. These include use of vaccination, Cervical Cancer screening, health education, radiation, chemotherapy treatment and a chemotherapy/radiation combined therapy among others (Yin et al. 2012; McAdam et al. 2010; Bergmark et al. 2002; Claeys et al. 2003).

Treatment of Cervical Cancer is dependent on the stage of infection. Treatment methods include cryotherapy, Lloop Electrosurgical Excision Procedure (LEEP), cone biopsy and Laser ablation (Maine et al. 2011). These methods are effective as long as the Cervical Cancer has not spread beyond the local level. Once metastasis has commenced then other interventions must be considered including surgery, chemotherapy, radiation or a combination of any of the interventions.

Treatment intervention of Cervical Cancer has been estimated to reduce mortality rate by 76 % (Goldie 2005). Different stages of HPV infections have different treatment costs. Goldie et al (2005) estimated the cost of treatment of invasive Cancer stage one at 1552.45 at 2000 International Dollars, stage two at 1925.20 while distant stage which included stage 3 and 4 at 1,995.20 while use of VIA ranged from 4.93 US$ to 14.75 US$ while cryotherapy ranged from 47.26 US$ and 84.48 US$ in Ghana. Few studies, if any, have been done to estimate the cost of treatment in Kenya.

1.5.4 Strategies Employed in Management of Cervical Cancer in Kenya

Given the rising incidence and mortality rates from Cervical Cancer in Kenya, it has become necessary to take measures to curb this preventable yet devastating disease. Different stakeholders have taken different measures to curb Cervical Cancer in Kenya. These interventions range from inclusion of Cervical Cancer in training curricula, prevention and promotion services such as screening, vaccination as well as health education. Treatment interventions have also been undertaken (Biddlecom et al. 2006). For those with positive tests, provision of curative services which include Cryotherapy, Loop Electrosurgical Excision Procedure (LEEP), cone biopsy and laser ablation at different levels of health institutions may be provided (Maine et al. 2011). In general Cancer control in Kenya is an integrated evidence-based activity consisting

of primary prevention, early detection, treatment and rehabilitation. All these measures require good health infrastructure in order to be successful (Were et al. 2010)

1.6 Challenges Faced in Management of Cervical Cancer in Developed Countries

Both developed and developing countries face a myriad of challenges in management of Cervical Cancer. In developed countries, poor attitude to HPV vaccination and fear of increase in risky sexual behaviour after HPV vaccination has been reported (Clifford et al. 2003; Shrestha 2011). There is still high prevalence of Cervical Cancer among the poor, the elderly and a few minorities even in developed countries which has been linked to low information and lack of screening (Anderson et al. 2010).

1.7 Challenges of Cervical Cancer Management in Developing Countries

These include low levels of screening due to poor access to organized Cervical Cancer screening, lack of or low information on Cervical Cancer screening, women's perception of low threat of disease, to over burdened health care facilities which lack equipment and are understaffed (Gakidou et al. 2008; Rositch et al. 2012; Chirenje et al. 2001). Poor road infrastructure as well as long distance between facilities' and clients' homes increases transportation costs. The long distance between the facilities and laboratories not only increases cost but also leads to delay in reporting results (Chirenje et al. 2001). Screening is associated with high costs which may not be affordable to most women (Goldhaber-Fiebert et al. 2006; Quentin et al. 2011)

Staffing has been identified as a challenge in screening and management of Cervical Cancer. (Chirenje et al. 2001) reported that if there were adequate number of staff for Cervical Cancer screening services, these personnel may not have the required screening skills or equipment.

Human Papilloma Virus (HPV) Vaccination is, on the other hand, expensive and may not be affordable to most women in developing countries. There is limited knowledge and information on HPV vaccination (Fernandes 2013;DiAngi et al. 2011).

Health Information management is a challenge. There is evident lack of timely Cancer registries with incomplete risk factors. This poor quality data curtail reliable population-based estimates for incidence rates, mortality rates and effectiveness of interventions(Hanna *et al*. 2010).Other challenges faced as a result of health system

deficiencies include; limited training among health care providers, lack of resources and poor data management systems (Louie et al. 2009).

Chirenje et al (2001) however, argue that health care institutions in East and Central Africa have the necessary infrastructure for Cervical Cancer screening, but these facilities experience frequent shortages of materials needed for taking Pap smears.

1.7.1 Challenges Faced in Management of Cervical Cancer in Kenya

Kenya, like other developing countries, is a low in resource setting facing a number of similar challenges. Many women cannot afford the cost of screening. In the Kenyatta National Referral Hospital, Pap smear costs KShs 550 (Approx $7). However, the client must pay for a file or identification card of KShs 500 (Approx$ 6.5). The client then needs to wait for the Pap results from the pathologist which takes a minimum of two weeks. At the leading private hospitals, Pap smear costs on average KShs 1200 ($15) with a waiting time of 2 days for the pathology results. At the public Hospitals, however, the Pap smear procedure is subsidized by the government and the client only pays KShs 20 (Approx $0.25) for registration. The waiting period is two weeks.

Public Hospitals use of Visual Inspection with Acetic Acid (VIA) and Visual Inspection with Lugol's Iodine (VILLI) as screening methods in low resource settings and results are available immediately. Of the few women who undergo screening a large portion of them do not return for their test results (Denny 2008).

Despite the infrastructure challenges of existing health care systems in Kenya, including the shortages of doctors and nurses(Biddlecom et al. 2006).there is a wide gap between the quality of care the health system should be capable of delivering today. Although there are fairly advanced technological and medical science headways in Cervical Cancer management, due to financial constraints, the benefits do not reach the lower income strata. Poorly designed health care process could be responsible for a large proportion of low quality of care Cervical Cancer patients receive. The 21st century health care system at whatever level should be capable of delivering safe, effective, timely, patient centered, efficient and equitable health care (Nishtar 2010).

1.8 Possible/ Proposed Innovative Ways of Dealing with the Challenges

One possible way of improving access, quality, efficiency, effectiveness and equity of Cervical Cancer care is through the appropriate use of e-health tools; such as mobile phones, internet and decision support tools. However, the health care system should be provided with effective models in order to identify, develop and apply methods, tools and indicators for evaluating and measuring the impact of telemedicine and e-health services provision and outcome (Sorensen 2008).

At the same time, health systems engineering and mathematical modelling would be utilized in guiding health system managers on the possible options or alternative actions and their consequences. Health systems engineering is an academic discipline, where researchers and practitioners treat health care industry as a big complex system and further identify and apply engineering principles in health care systems. Industrial Engineering tools such as optimization, stochastic processes, and simulation can be used to model, measure and manage the technological change in Cervical Cancer management. These engineering tools are used for systems design, analysis and control (Reid et al. 2005).

Modelling implies some degree of abstraction, using a wide array of methods, approaches and frameworks of analysis, such as human factors, kaizen, and operations research and Simulation Modeling (Brailsford 2004). Measurements focus on performance evaluation, outcomes analysis, and benchmarking as the key elements in designing and improving health systems. Management of change focuses on needs analysis and design of innovative solutions, to timely execution, sustaining, and spreading the gains/ recommendations from study results.

An understanding of the basic structure, process, and outcomes related to use of internet resources in management of Cervical Cancer will essentially form the basis for the systems perspective, where the dynamic environment influences e-health seeking behaviour, which in turn leads to specific events (Reid et al. 2005; Sorensen 2008). The systems engineering process is based on an iterative, top down, hierarchical decomposition of system requirements. The systems-level considerations are recognized as being paramount in design of new products or delivery systems (Reid et al. 2005; Brailsford 2004).

1.8.1 e-health Solutions

e-health is an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the internet and related technologies (Neuhauser & Kreps 2003; Bright & Fleisher 2005; Maeder 2008). e-health is part of the broad cultural shift toward Internet and technology use, such as portable music devices, cell phones, instant messaging, and interactive voice-response systems, as a normal part of everyday life (Neuhauser & Kreps 2003).

The main e-health domains of activity consist of Health Information Systems (data and software tools) and Health Services Delivery (work practices and processes).
e-health has contributed to changingbehavioursof health professionals, care personnel, citizens and improving patient safety in general. Due to its impact on medico-cultural, legal/regulatory and socio-economic factors, e-health is a new way of thinking and a commitment to networking globally with the aim of improving health care globally (Maeder 2008).

e-health services are established with the intention to improve access to health care services, quality of services and cost-effectiveness especially in low resource setting (Gustafson et al. 2005). e-health systems tap the growing momentum of the consumer e-health phenomenon, in which consumer engagement, decision making, and tools come together to support and enhance health (Bright & Fleisher 2005). The internet facilitates health information exchange. Investment in e-health as well as benefits and risks need to be evaluated. In-order to realize maximum benefits of e-health, using e-health as an enabler of re-engineering and redesigning health care need to be considered if positive economic and clinical benefits are to be realized (Eysenbach 2001; Neuhauser & Kreps 2003)

These benefits range from better coverage of the underserved populations with chronic illness, improvement in quality and safety of care and saving time spent in searching for information. This time is refocused to patient care thereby reducing health care system costs , increasing opportunities for clinicians as well as allowing patients to seek care closer to home, so they need not to travel long distances to receive consultations (Gagnon & Scott 2005; Sorensen 2008; Bright & Fleisher 2005).

In Kenya, a number of studies on Cervical Cancer have focused on the effects of Cervical Cancer screening, prevalence of Cervical Cancer and HPV in relation to HIV (Ombech &Muigai 2012; Were et al. 2010; A. Rositch et al. 2012). However, few if any, studies have focused on the impact of e-health in Cervical Cancer management or application of engineering tools in Re-designing of health care systems. The management of Cervical Cancer, a major cause of mortality among women in Kenya, would therefore act as a useful example for assessing the potential impact and the drivers and barriers to e-health in Kenya. The application of e-health tools does not occur in a vacuum. It needs to be incorporated in the existing infrastructure. System Dynamics (SD) becomes an appropriate tool in evaluating the impact of e-health tools in Kenya. SD is a methodology of mapping and then modeling the forces of change in any dynamically complex system, so that their influences on one another can be better understood and overall direction of the system can be better governed.

1.9 Problem Description

This section is divided into two parts. The first part describing the background of Cervical Cancer in Kenya and the second outlining the problem statement.

1.9.1 Background of Cervical Cancer in Kenya

In Kenya, Cervical Cancer is common among women aged between 15 to 44 years. This is a peak productive age of most women. At this age a woman may be at the peak of career, starting a family or in a relationship among other life developments. Therefore, diagnosis of Cervical Cancer may shatter any dreams and aspirations that a woman may have. Kenya reports a Crude mortality rate of 13.2/100,000, an age-standardized mortality rate of 23.4/100000 and annual number of deaths is 2111(WHO/ICO 2010).

Cervical Cancer screening in Kenya, like in other developing countries, is low at less than 5 % (Ministry of Public Health and Sanitation and Ministry of Medical Services 2012). This has been attributed to less efforts in increasing awareness of Cervical Cancer among women, especially those in rural areas, which would otherwise lead to women submitting early to regular checks hence increase chances for mitigation (Gatune & Nyamongo 2005).

By the year 2005, women in Kenya generally obtained information on Cervical Cancer from friends, radio, books and magazines and educational talks in Hospital respectively, in order from the most accessed source. A few women got the information from Television, seminars and conferences, and knowledge of someone who had suffered from the disease. Women in Rural Kenya preferred different available sources of information on Cervical Cancer; from church seminars, health education talks in hospitals, seminars for women groups, outreach by community leaders and radio in that order (Gatune & Nyamongo 2005).

Radios, TV and films were ranked low as most families did not own them. With about 30% of homesteads in Kenya owning a mobile phone, it would be important to assess the impact of use of mobile phones as one of the e-health tools in raising awareness of Cervical Cancer. There is an expected trend of changes in source of health information. It is important to establish changes in lieu of this wave in Information Communication and Technology.

The formulation and evaluation of health policy in the current political, economic, sociological, technical, legal and environmental climate is hampered by growing health system complexity and the inability to reliably predict the outcomes of policy decisions. Health service changes represent prolonged complex interventions in complex systems. Controlled health services trials are difficult to design, conduct, evaluate, interpret and extrapolate for many reasons.

In health policy many real-life experiments are too costly, too risky, time-consuming or impossible to design and implement and face resistance (Sterman 2002;Sterman 2006). Due to the nature of e-health technologies being dynamic and evolving too rapidly, pre- and post- implementation studies tend to be irrelevant and obsolete. Comprehensive economic analysis that determines outcomes such as cost-benefits and cost offsets require considerable time and expertise and are beyond the scope of many e-health projects (Catwell & Sheikh 2009; Glasgow 2007). Even though application of system dynamics including use of static linear methods to complex dynamic non-linear systems could be a possible solution to evaluating the impact of health policy, this has not been exhaustively explored.

Few studies, if any, have been done in Kenya to establish and/or evaluate e-health interventions. This may be attributed to the slow pace of implementation of e-government and e-health policy, hence there is limited data available on clinical, economic, social and psychological variables on e-health interventions (Kalua & Union 2009). While a number of studies have focused on challenges faced by the patients in Cervical Cancer management, few have focused on the challenges faced by the health care workers. It is important to establish the challenges faced by Cervical Cancer managers and identify ways of alleviating these challenges to improve health care system performance.

1.9.2 Problem Statement

This study aimed at assessing the clinical and social economic impact of e-health intervention in Cancer management, in addition to traditional vaccination and screening interventions. Without the cost of controlled health service trials, system dynamics modelling was applied.

1.10 Broad Objective

To model clinical and socio-economic impacts of Vaccination against HPV, screening and use of current and emerging e-health infrastructures on Cancer management under various scenarios and policy interventions.

1.10.1 The specific objectives were to;

i. Establish prevalence and trends of Cervical Cancer and graph its behaviour over time.
ii. Establish the opportunities and challenges faced by Cervical Cancer managers in Kenya.
iii. Establish the trends of e-health tools use among Cervical Cancer clients in Kenya.
iv. Design, implement, test and validate a system dynamics model of Cervical Cancer in Kenya.
v. Design possible health Policies using the SD model.
vi. Develop a mathematical model for Cervical Cancer system in Kenya.

1.11 Justification of Study

Until more is known about the cost and cost effectiveness of e-health interventions, it is unrealistic to expect decision or policy makers to adopt e-health programs without such information. The management of Cervical Cancer, a major chronic illness in Kenya, would act as a reliable basis for assessing the potential impact and the drivers and barriers to e-health in Kenya.

Even though the best conceptual model can only be tested and improved by relying on learning feedback through the real world, this feedback is slow and often rendered ineffective by dynamic complexity, time delays, inadequate and ambiguous feedback, poor reasoning skills, defensive reactions and the cost of experimentation (Sterman 2002). In order to overcome the above mentioned challenges of real world experiments and future uncertainties, we need to perform in silico experiments to design and test policies that cover a range of future possibilities. Simulation becomes a reliable way to test a hypothesis to evaluate the likely effect on policies. Health Systems Simulation is the application of computer simulation to explore, understand and improve the interaction between structure and action in health care and policy (Heffernan & McDonnell 2012).

Computer simulation has been viewed as a mature and powerful tool for modelling the health system to test how different factors may improve efficiency, effectiveness and equity in situations, where it is not possible to conduct real-world experiments (Heffernan & McDonnell, 2012). A range of powerful modelling and simulation tools from systems engineering available to conduct in silico experiments in health services research have for the first time, made it clearly technically feasible to develop simulations which are capable of modelling the complexities of modern health services (Reid et al. 2005).

The use of dynamic systems simulation would then provide a possible answer to most myopic real life experiments. It is important to note that simulation may not be regarded as a tool for deriving solutions to certain problems. In fact simulation is better suited for understanding the problem and enhancing systematic debate between the problem owners (Kotiadis 2007).

Simulation modelling is not forecasting the future, but rather on learning how actions in the present can trigger plausible reactions both far away and over time. Computer simulation methods provide a means to mimic the behaviours of complex real systems both quickly and economically. Simulation models can expeditiously compare the outcomes of alternatives before selecting a course of action. Such "what if?" applications are the staple of many policy and program design evaluations (Barlas 1996).

Simulation models can also provide a dynamic virtual environment for training. All simulation models require the mathematical representation of a real system that exists, or could exist, in time and space. A computational representation of that system then links inputs to outputs through the system architecture. Simulation modelling offers significant advantages in that making the model and analyzing the problem with the aim of better understanding it, does not necessarily rely on the initial collection of data. Dynamic systems simulation incorporates a broad range of variables including important social and psychological variables for which statistical data are not available. Simulation modelling relies on a combination of expert opinion/judgment, previous history and or facts, literature information (Homer & Hirsch 2006).

This study therefore, employs Systems dynamics modelling in assessing the impact of use of e-health tools in concurrence with other Cervical Cancer management interventions.

CHAPTER TWO: LITERATURE REVIEW

This chapter consists of literature review on use of e-health tools, evaluation of e-health tools, systems dynamics and modelling in Cervical Cancer management.

2.1 Electronic –Health (E-health)

The World Health Organization defines e-health as 'the cost-effective and secure use of information and communications technologies (ICT) in support of health and health- related fields, including health-care services, health surveillance, health literature, and health education, knowledge and research' (Hhojaja et al. 2008).Eysenbach (2001), define e-health as '*an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies. In a broader sense, the term characterizes not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve health care locally, regionally, and worldwide by using information and communication technology'.* Eysenbach, (2001) further suggested a broader meaning of the 'e' in e-health which included; efficiency, evidence-based, empowerment, encouragement, education, enabling, extending, ethics and equity and enhancement of quality. e-health then is broader than the mere use of technology. Other definitions appreciate the use of e-health as a support and platform for service delivery and not directly linked to health of the individual (Oh et al. 2005).

The wide aspect of e-health means that it is even more complex to quantify. The boundaries of e-health are therefore porous. With exponential growth of consumers of e-health, the expected benefits as well as risks associated with use of e-health grow broader. Evaluation of the impact of use of e-health tools becomes more complex. Oncologists view the use of e-health tools as having both positive and negative effects. Benefits and risks associated with use of e-health have been documented elsewhere (Blaya et al. 2010; Stroetmann & Jones 2006; López-Gómez et al. 2012; Helft et al. 2003; Healy 2008).

In other areas, e-health can help improve access to healthcare in settings, where traditional delivery of health care is affected by geographical barriers, poor

infrastructure, socio-economic disparity, high cost of transportation as well insufficient number of local healthcare specialists to deliver services particularly for management of chronic conditions (PATIL 2011). Benefits of internet use to patients include; more informed patients, ability of patients to seek second opinions, patients joining online communities for support, patients being able to communicate online with health care providers, supplementing information provided by health care providers and improving conceptualization of information gained, patients enjoy more privacy than face to face consultations. It can enable clinical consultation, strengthen and better the client's/physician relationship, improve continuing professional education, health promotion, and healthcare management and administration (Helft et al. 2003; PATIL 2011).

However, use of e-health tools can also be challenging for consumers and can create financial, technological, and informational demands that for many, could be overwhelming. Use of e-health technologies may also create a negative attitude towards physicians, create negative relationship between patients and their physicians as well as create anxiety and unrealistic expectations (Helft et al. 2003).

2.1.1 Use of e-health Tools in Cancer Management

e-health tools in Cancer management have been developed to perform different functions for the end user. These range from health education, online communities, Physician order entry and electronic health records. e-health tools have also been used in preventive, promotion and curative aspects of Cervical Cancer management.

Consumers have become comfortable with the Internet as a health resource thus providing access to much needed health information on Cancer management and other disease conditions (Diaz et al. 2002). A large number of Americans use the internet to search information on health issues. According to Helft et al. (2005), forty to eighty (80) percent of adults use the internet for medical information.

Many health educators and healthcare practitioners, rather than producing their own educational materials, refer patients to Web-based resources or download and provide the information. According to López-Gómez et al. (2012) oncologist should prescribe authentic websites for their clients as the information obtained helps the clients cope

better and foster the physician-client relationship, as long as the web content are of good quality.

a) **Access to Health Information**

Cancer clients and their relations have not been overlooked in e-health. Goldsmith (2002) interviewed parents of children with Cancer and found that 38 per cent of them used internet weekly to find information on Cancer. Parents of children with Cancer also cited getting information and sharing experiences on the internet (Schwartz et al. n.d.). Bright & Fleisher (2005) established that 40% of Cancer clients and 60% of their companions used internet to find information on Cancer. In the Netherlands, one study reported as high as 84% of direct and indirect internet use by Cancer patients, while in the USA over 50% internet usage by Cancer patients has been reported (Poll-Franse 2008).

b) **Interaction of Care Providers and Clients**

For Public Health Records to impact positively on disease management, the consumers must have access to the electronic resources which include both physical connection and appropriate content. e-health tools facilitate interaction between patients, clinical professionals and healthcare organizations. Hassol & Walker (2004) evaluated 'my chart', an electronic health record which allows patients to view selected portions of their Electronic Health Records (EHR) and exchange electronic messages with their doctors. Sixty five % of them rated the information complete while 75% rated their medical history as accurate.

c) **Self Management Tools and Online Communities**

The internet has led to development of online communities. Internet-based communities facilitate interaction around common health concerns among consumers; provide support systems and virtual self health care networks(Seçk 2009).

d) **Decision Support Tools**

Decision support has been enabled via e-health tools. The tools in this category provide structured support to consumers. Some tools support treatment decisions, such as weighing the trade-offs between different Cancer treatments while others have acted as links to clinical trials (Eysenbach 2003). Other ways in which e-health tools

have been used in health care provision include: Transmission of medical images for diagnosis (often referred to as store and forward tele-health), groups or individuals exchanging health services or education live via videoconference (real-time tele-health), transmission of medical data for diagnosis or disease management (sometimes referred to as remote monitoring), Health advice by telephone in emergent cases (referred to as teletriage) (Albrecht & Ku 2005).

In non clinical aspects, e-health tools have been utilized in Distance education including continuing medical education, grand rounds, and patient education.
e-health administrative uses including meetings among tele-health networks, supervision, research, asset identification and listing, patient to asset matching, overall healthcare system management as well as monitoring of patient movement and remote admission (Al-Shorbaji 2008; Gagnon & Scott 2005).

Most e-health tools support several of the above functions, generally structured around a primary purpose such as disease management. Most prevention-related tools are developed through research with defined target audiences under controlled conditions.

2.1.2 Effects of e-health of Cervical Cancer Management

While access to information on cervical cancer management has contributed to reduction in cervical cancer in developed countries, information access has no significant difference in developing countries (Hanisch & Gustat 2008). Lack of access to quality information on cervical cancer screening and management has been attributed to the low health status in developing countries(Chingore-Munazvo 2012).It has been argued that investment in Information and Communications Technologies (ICT) in the health care sector has greatly improved health status in developed countries. According to Odutola (2003), developing countries are lagging behind in utilization of ICT in health care and hence may not realize the potential benefits of e-health. Development and investment of e-health in developing countries need to be contextual in nature in order to meet the peculiar characteristics of developing countries whereby; use of the mobile phone is the sole ICT communication gadget catching up rapidly and the use of mobile phone in e-health will be proportionally greater in low resource setting (PATIL 2011).

Different stakeholders will benefit from ICT investment in Health care. The health care providers would benefit from decision making tools, time efficiency and cost containment (Kasiri et al. 2011). It is hoped that the same kind of investment in ICT could benefit developing countries.

It is important to note that investment in e-health may result in overwhelming technological, financial and informational demands on the clients. Use of internet for health management has been known to have possible detrimental effects on the patients. Even though many websites containing Cancer information are available, much of the information contained in these websites may be incorrect, hence of poor quality (Selman et al. 2006). Lack of information on the other hand may increase anxiety among patients as well as hinder their health seeking behaviours(Kasiri et al. 2011). There are other factors that affect the use of e-health tools in Cancer management. It is important to study the characteristics of patients who use internet as a source of health information. Previous reports have established that factors such as level of education, age, sex, stage of progression of disease, computer access and economic status influence internet use among patients (McAdam et al. 2010; Odutola 2003). Identification of barriers to internet use by these patients is important in planning how to overcome the barriers in order to encourage use of ICT in Cervical Cancer management. Studies elsewhere have identified barriers related to users; including lack of computer skills, computer illiteracy, and inability to interpret the available information, slow internet connection and high subscription costs (Christensen & Remler 2007; Gatero 2011).

Few studies, if any, have been done in sub-Saharan Africa to determine levels of internet use among Cancer patients.

2.2 Impact of e-health Tools

The potential impact of e-health tools is enormous. Studies have been done to model and /or measure the clinical and economic impact of e-health solution (Stroetmann & Jones 2006). Other studies have focused on health belief model, on patient empowerment through e-health tools and services (Huang & Lin 2009; Bensley & Mercer 2004; Wijethilake et al. 2010). Several factors have been identified as relevant for assessing e-health for diverse populations; access, availability, appropriateness, acceptability, and applicability of content. Patients not only enjoy private, full time

access to resources but also have expanded choice and autonomy. The patient has access to new forms of social support through e-communities as well as a possibility of better health. Health institutions could enjoy more efficient record management while utilizing e-health tools and avoid duplication of recording hence lowering the cost of health care services. The clinicians on the other hand benefit from greater efficiency in the provision of services and health promotion enhanced through better communication. This results to a population of more adherent and satisfied patients. Health care organizations enjoy the benefit of more patient self-care and health management resulting to not only improved quality and patient outcomes but also lower administrative costs. The benefits of e-health tools are enjoyed by e-health tools developers, policy makers and funding agencies as well as other stakeholders. These benefits are not only economic in nature but also extends to clinical quality and social equity (Eysenbach 2003; Hhojaja et al. 2008). Appendix 2 details the possible steps of e-health journey of a Cervical Cancer client.

The Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) model (www.re-aim.org), has been used extensively to evaluate programs including context and external validity, issues relevant to program adoption, implementation and sustainability as well as evaluate e-health and dissemination research (Glasgow 2007). Estimating public health impact, comparing different health policies, planning policies designed for increased likelihood of success, and identifying areas for integration of policies with otherhealth promotion strategies has also been done using RE-AIM model (Jilcott 2007). The RE-AIM model, however, does not consider the individual attitudes towards e-health. It is important to note that, most of these models have been developed to meet the needs of developed countries, which already have established Information technology infrastructure. At the same time, most of the models are developed for general application and not developed to address specific disease conditions.

Drury (2008) developed an e-health model for developing countries. Although this model was geared for utilization in developing countries and considered important aspects of context, content, connectivity, capacity and community, the model did not consider the attitudes of stake holders towards e-health.

2.3 Application of Modelling and Simulation in Cancer Management

Health care is operating in an unpredictable and volatile environment where survival requires the key players being at the cutting edge. The need to choose among alternatives instead of allowing the market to make choices has led health care professionals to rely on scientific information as an aid in decision making (Bloom & Bloom 1999). Simulation models can expeditiously compare the outcomes of alternatives before selecting a course of action.

The outcomes of options and the decisions of choice are the backbone of applications of many policy and program design and evaluations. Simulated experimentation accelerates and replaces effectively the "wait and see" anxieties in discovering new insight and explanations of future behaviour of the real system (Bloom & Bloom 1999).

Simulation is an excellent and flexible tool to model different types of environments. It is best applied in Systems that change with time, such as an outpatient Cancer clinic, where patients come and go or one cannot be able to predict the exact time the patient will arrive or exact time the doctor will consume on a patient (Sepúlveda & Thompson 1999).

Computer simulation has been utilized in health care policy making, health services planning, biomedical applications from the systems to the cellular and genetic level, and education (Anderson et al. 2010). Cancer managers have been compliant in utilizing computer simulation at different levels and structures of Cancer management.

2.3.1 Understanding of Cancer Pathology and Development

Modelling has been utilized in understanding Cancer pathology, in diagnosis, in screening as well as in decision making. Cancer as a system has been treated as a mathematical model to study the organizational principle of Cancer and to show its growth using 3D simulations. A logarithmic three dimensional Simulation has been used to model the use and benefits of mammographic screening of breast Cancer as well as calcification, and has proven to be more effective in diagnosis than the radiographic images of real breast calcification (Näppi et al. 2001). Fett (2001) used

dynamic simulation to model the use and benefit of mammo-graphic screening for breast Cancer.

Opell et al. (2002)investigated the distribution of prostate Cancer using three-dimensional (3-D) computer simulation. The results illustrate that prostate Cancer is least commonly located in the anterior half and base regions of the prostate. Through an analysis of the spatial distribution of prostate Cancer, new optimal biopsy strategies and techniques have been developed.

Abbott et al. (2006) used agent based simulation model to demonstrate how cell acquire Cancer. Myers & McCrory (2000) developed a Mathematical model for the natural history of human papillomavirus infection and Cervical carcinogenesis; while Ebe & Matsunaga (1997), performed Magnetic Resonance (MR) simulation system for intracavitary brachytherapy for Cervical Cancer and subsequent treatment results. They found that the system promised to be useful in customizing the dose distribution.

Michelow et al. (1997), while simulating primary Cervical Cancer screening by the PAPNET system in an unscreened, high-risk community compared their results with those of original manual screening and concluded that there was a significant superiority of the PAPNET over conventional screening in low grade lesions including a typical squamous and a typical glandular cells of uncertain significance.

Sawaya (2003) used a Markov model to estimates the rate at which dysplasia will progress to Cancer, in relation to the number of Papanicolaou tests and colposcopic examinations in a specified period of time that would be required to avert one case of Cancer given a particular interval between screenings. This study revealed that extending the intervals between screenings to three years, after three or more consecutive negative Papanicolaou tests is a safe option.

2.3.2 Decision and Planning

a) Managerial Decision Making

Simulation allows analysis and exploration of different decisions which enable decision-makers to quickly determine optimal system configurations and the impact of these decisions on future action. Simulation modelling, offers significant

advantages in that making the model, and analyzing the problem does not rely on the initial collection of data. Coupled with expert opinion it offers considerable benefits for those involved in the decision-making process. However, simulation modelling is done with the aim of better understanding problems, but not necessarily solving the problems. The key variables of the problem are identified early in the process (Jilcott 2007).

Sherlaw-Johnson et al. (1999), developed a mathematical model which systematically analysed the consequences of screening options, chart the clinical course of pre-cancerous lesions and the accuracy of the testing procedure.
Baldwin et al. (1999) utilized discrete events simulation in supporting decision making in Randomized clinical trial (RCT) using Activity Based Construction Simulation (ABCSim), which offered insight in to which data to collect.

Different models have been used to evaluate Cervical Cancer management. Sanders & Taira (2003) used decision maker software to develop a Markov model in evaluation of effectiveness and cost effectiveness of prophylactic HPV vaccine, while Goldhaber-Fiebert et al. (2007) modelled HPV for analysis of screening and vaccination in United States and found that while screening reduced the life time risk of Cervical Cancer by 76%, vaccination reduced the same by 75%, while a combination of both reduced the same by 89%. Other mathematical models that demonstrated reduction of Cervical Cancer through both vaccination and screening include (Goldie 2005; Ginsberg et al. 2012; Ribassin-Majed et al. 2012). Therefore, mathematical models are useful to assess the expected trends of Cervical Cancer

b) Public Health /Consumer Decisions

Simulation modelling (SM) is a powerful tool that has been applied to a wide range of topics and research questions in population health and health care. SM has been utilized in making decision on vaccination against HPV, map breast Cancer incidence and mortality in the United States Population, as well as map the impact of several smoking cessation-based scenarios on the future of Cancer of the pancreas(Mulder et al. 1999)System Dynamics modelling has been used to evaluate immunization policy in Uganda(Semwanga & Williams 2006).

c) Service Planning

Simulation has been applied in process improvement in Cancer treatment centre as well as emergency departments, on reduction of waiting time in the emergency room of a Hospital, to support strategic resource planning in healthcare and simulate patient flow, physical and human resources in a Cancer treatment center (García & Centeno 1995; Pitt 1997; Baesler et al. 1998).

Baesler et al. (2003), simulated the maximum capacity of an emergency department of a private hospital. This included the maximum number of patients the department could serve, the number of doctors required as well as the time the patients could spend at the department on average. Sepúlveda & Thompson (1999) used SM to analyze patient flow through a Cancer treatment centre, evaluate the impact of alternative lay floor layouts and analyze resources and patients flow requirements of a new building. The study demonstrated that improvement inpatient flow time could be achieved. The number of patients seen in a day could be increased up to 20%, without materially affecting the closing time of the facility. Other decisions included identification of bottle necks, analysis of patient flow and operating efficiency.

Goldie (2005) used computer-based models to assess the cost-effectiveness of a variety of Cervical Cancer screening strategies in selected developing countries.

Computer models are frequently employed to analyze and assess the value of new health care technologies in order to help demonstrate their health benefits and associated costs even before implementation (Gantner-Bär et al. 2012).

2.3.3 Clinical Interventions

Computer based Cancer management decision making model have been used to produce individualized, rational, clinically appropriate disease management decisions without physicians' bias. It has been used to model Cancer behaviour, predicting tumour growth and guiding treatment options (Gatenby et al. 2006). Even though these mathematical models may not be able to predict the invasiveness of Cancer cell, they can predict the size of the tumour in a given period of time.

Despite all the above advances in use of simulation in cervical cancer management no benchmark exists against which a model can be evaluated in determining neither the best fit of parameters nor representation of disease process (Kim et al. 2007). At the same time few if any, model focused on Kenya as a developing country or

modelled the impact of e-health tools on trends of Cervical Cancer. The following section therefore looks at the impact of use of e-health tools in cervical cancer management leading to hypothesised increase in utilization of e-health tools in cervical cancer management in Kenya.

This study seeks to assess the socio-economic and clinical impact of using e-health tools in Cervical Cancer management in Kenya, alongside the traditional screening and vaccination intervention. This study will also incorporate the attitudes of the users in the existing mathematical models.

The implementation of e-health tools as well as vaccination and screening interventions stratifies the population into those who have benefited from these interventions and those who have not benefited.

There is expected to be a difference between the population at the status quo interventions and the population who benefit from e-health interventions. These interventions then divide the population into vaccinated, unvaccinated, screened and unscreened. The overall health status of the population of the women is affected by this status. The number of women in these groups is altered by their exposure to e-health tools. Implementation of e-health tools occurs in a dynamic environment hence there are confounding variables during implementation. Figure 2.1, the Conceptual Framework further illustrates this interaction.

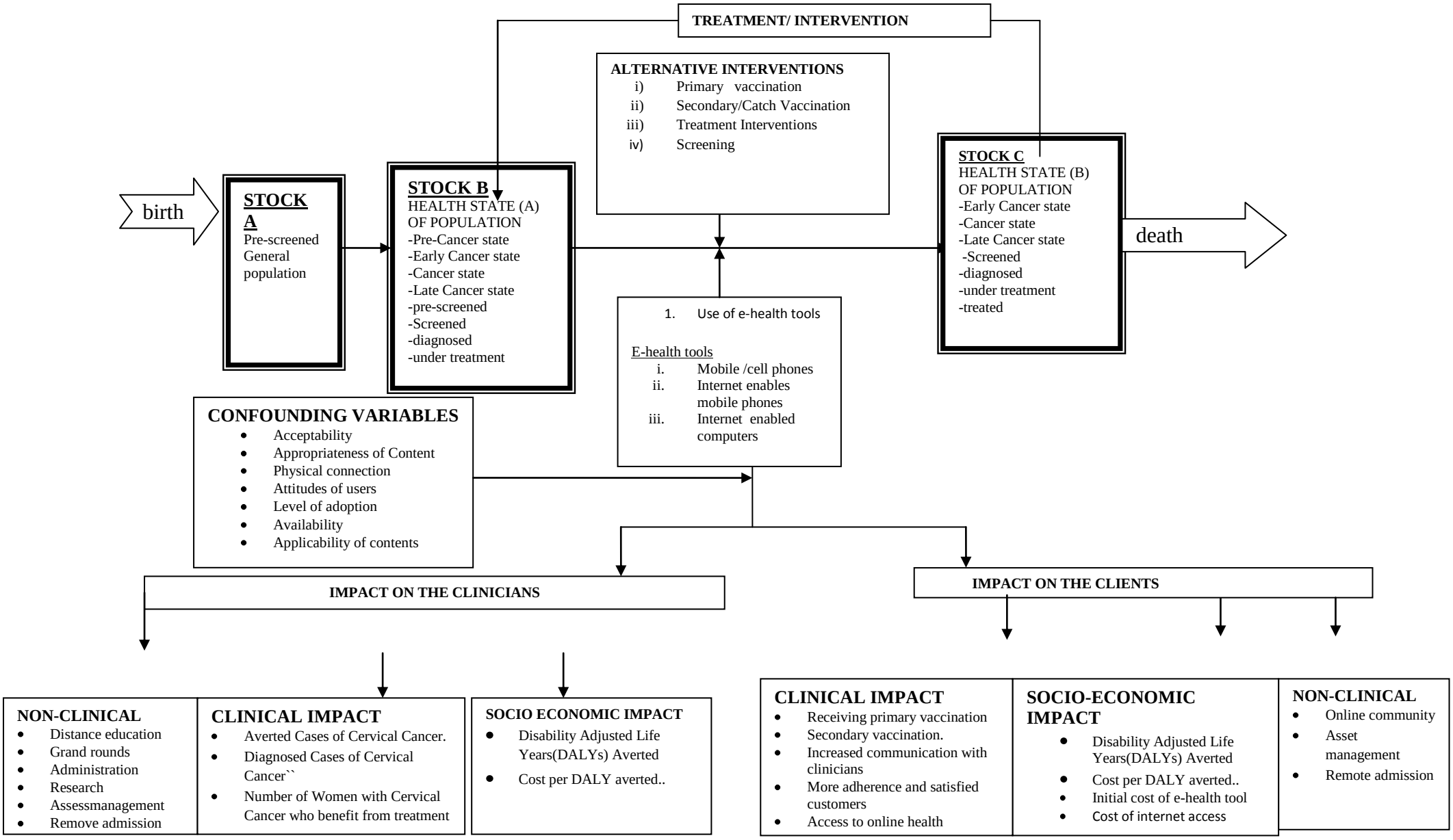


Figure 2.1. Conceptual Framework

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Introduction

This chapter provides an overview of the study methodology that was utilized, aims and objectives of the study, a description of study area, study population, subjects and tools.

3.2 Aims of Study

The main aim of this study was to analyze possible clinical and socio-economic impact of

Screening and vaccination campaign against Human Papillomavirus (HPV) in Kenya as well as use of consumer e-health tools in Cancer management through System Dynamics simulation modelling.

3.3 Study Design

The overall approach to this research was System Dynamics (SD) simulation modelling. SD is a methodology of mapping and then modelling the forces of change in any dynamically complex system so that their influences on one another can be better understood and overall direction of the system can be better governed. According to Milsten and Homer (2006), SD should answer five key questions;

i. What aspects of a system's behavior are of concern?
ii. Why are those features changing in those ways at those times?
iii. Where is the system headed, if no new action is taken?
iv. How else can the system behave, if different decisions are made?
v. Who has the power to move the system in a more desirable direction?

Different researchers have proposed a number of SD approaches. Structured approach to System Dynamics approach by Wolstenholme (Wolstenholme 1990) , SD analysis by(Coyle 1996) the Dynamic Synthesis Methodology(DSM) by(Williams 2002) and Managing from Clarity Methodology(MCM), which combines SD and systems thinking by (Ritchie-Dunham & Rabbino 2001) , the health Systems Dynamics Framework by Marchal et al. (2012)among others. Though with a few variations, these methodologies describe a four to five stage approach emphasising on Problem description, casual loop/ qualitative analysis, construction of

SD model and Policy testing except (Williams 2002) who came up with six stages which included case study stage.

The advantages of SD methodology have been documented elsewhere. These include enabling a deeper understanding of the system, comprehension of complex systems, variation of policies via simulation, inclusion of linear and non linear relationships, incorporation of time delays and soft behavioural relationships as well as understanding management strategies from systems approach to organizations (Cavana & Maani 2000)(Williams 2002)(Ritchie-Dunham & Rabbino 2001). An analysis of the enumerated SD methods are as stipulated in Table 3.1

Table 3.1 Analysis and Comparison of SD Methodologies

Researcher's Approaches	**Wolstenholme (1990)**	**Coyle (1996)**	**Williams (2002)**	**Ritchie-Dunham and Rabbino (2001)**	
Problem Definition	✓	✓	✓	✓	
Qualitative Analysis	✓	✓	✓	✓	
Model Building	✓	✓	✓	✓	
Case Studies	×	×	✓	×	
Simulation Experiments	✓	✓	✓	✓	
Test and Design Policies	✓	✓	✓	✓	
Previously Applied in Health Sector	×	×	✓	?	

This study focused on management of cervical cancer in Kenya. Hence it was viewed as a case study and finding of various branches of science was fused into a holistic and coherent view. For this reason, a powerful Dynamic Synthesis Methodology (DSM) developed by D. W. Williams (2002) which combines System Dynamics (SD) simulation modelling and case study method was adapted. Williams describes DSM as comprising of six stages .

The research design Framework adapted from (Williams 2002)is illustrated in Figure 3.1

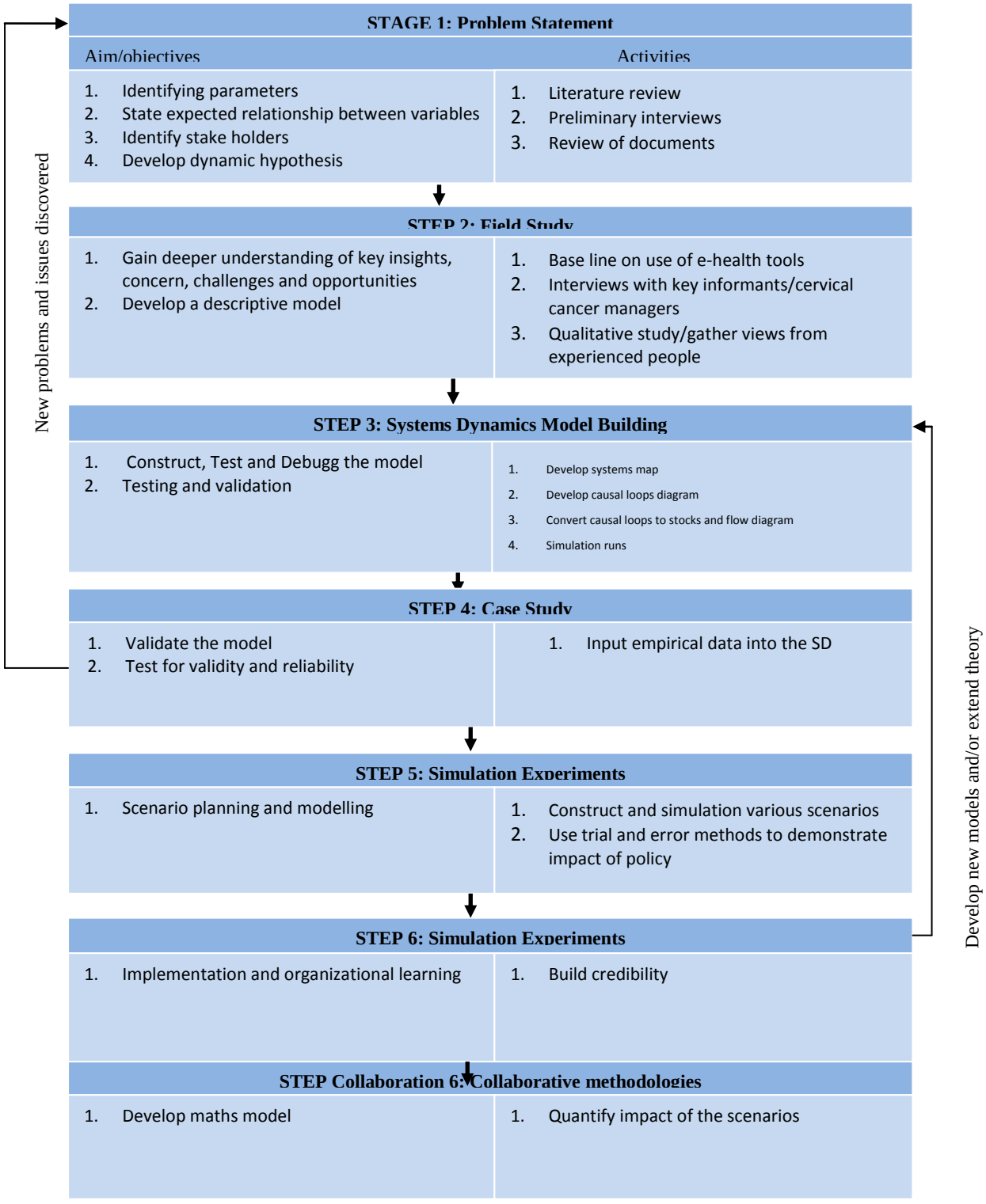


Figure 3.1 Research design Framework adapted from (Williams 2002)

Stage one. Problem Statement

This refers to a statement of the problem to be solved rather than the research question(Williams 2002). According to Sterman (2000), problem statement should include a theme selection of what the problem is and why it occurs. The key variables and the concepts to be considered are identified, systems behaviour (in relation to key concepts and variables) as a function of time (historical) are represented in reference mode. The reference mode should look into both the past and the future. The problem is identified and its behaviour graphed over time. At this stage, the researcher formulates his own mental understanding of the problem, variables interactions, identifies endogenous factors and formulates a dynamic Hypothesis. Hence, the problem statement phase is an important stage in SD modelling.

Stage Two. Field Studies

At this stage, the researcher applies strangulation of research methods in order to study and understand the research problem/ phenomenon in its natural occurring environment. According to (Williams 2002), the field studies collect on site information on the system of study at present, identifies the key stakeholders, their roles in the whole system, their requirements for systems performance and their constraints. The output of this stage is a descriptive model of the system under study. Even though case studies have been argued to be of weak standing as research method, their strength in data collection and description of the study phenomenon in its natural setting is a strength that SD builds on.

Stage Three. System Dynamics Model Building.

According to Williams (2002) the result of field studies should provide a descriptive model, on which SD conceptual feedback structure can be developed. Stage three involves formally presenting the Dynamic hypothesis and the descriptive model into structural model using casual loops diagram or other appropriate methods. Structural model is then converted into stocks, flows and feedback loops using appropriate computer software. According to (Sterman 2000), this stage should include , specification of structure, decision rules, Estimation of parameters, behavioural relationships, and initial conditions and Tests for consistency with the purpose and boundary.

The model is quantified using available scientific evidence. Mathematical relationships between the variables are established. Simulation is run on important variables. Confidence on the model is built through ownership by stakeholders. The model is then deemed ready for hypothesis and policy testing. Williams(2002) notes that models may be validated as a post-mortem or using case studies. Other best practice approach to model validation include Animation, Face Validity, predictive validation and extreme condition tests(Wakeland and Hoarfrost, 2013). The DSM then proceeds to case study stage.

Stage Four. Case Study.

At this stage empirical study of the phenomenon and system is performed. Both exploratory and explanatory approaches are used. Multiple sources of data are recommended providing collaborative evidence. The data gathered which should be of good quality must cover all the inputs, through puts and output processes and requirements in the requirements engineering (RE) process which captures the stakeholder's understanding of how requirements changes over time(Williams 2002). Involvement of stakeholders in this process enhances ownership of the model.

Stage Five. Simulation experiments

At this stage simulation experiments are run. Health systems simulation is the application of computer simulation to explore understand and improve the interaction between structure and action in health care and policy as well as model the complexities of modern health services. Computer simulation has been viewed as a mature and powerful tool for modelling the health system to test how different factors may improve efficiency, effectiveness and equity in situations where it is not possible to conduct real-world experiments(Heffernan & McDonnell 2012). The simulation should mimic behaviour of the real system under study. Ideally the model should assist users make better decisions.

Stage Six. Model Building and Theory Extension.

At this point the model is expected to take a philosophical approach that can explain changes is model behaviour. Various stakeholders , though with varying understanding of the model structure should find the model useful and may make different choices depending on their preferences. The model's 'usefulness' is tested and ascertained. The dynamic hypothesis is tested using the model. Therefore ' the simulation model needs to be evaluated by assessing whether it is fit for its intended purpose'(Heffernan & McDonnell 2012).

3.4 Suitability of Systems Dynamics in Management of Cervical Cancer.

SD is better applied to complex macro level view of systems. 'System dynamics methodology is best suited to problems associated with continuous processes where feedback significantly affects the behavior of a system, producing dynamic changes in system behavior'(Sweetser 1999). Management of cervical cancer is a dynamic and complex systems characterised by;

i. Many stakeholders who hold divergent and often conflicting views.
ii. Dynamic with unpredictable changes in relation to time and magnitude.
iii. Feedback where by a change in one subsystem will result into a change in the next subsystem e.g. an increase in number of primary vaccination will result to a decrease in screening demands.
iv. Tightly coupled as actors in the management system strongly interact with each other. For example, Vaccine Manufacturers must interact with funding agencies and government which in turn must interact with health service providers.
v. Cervical cancer management is non –linear. Effects are rarely proportional to cause. For example, an increase in health education and coverage does not necessary result to proportional demand for cervical cancer vaccination and screening.
vi. Policy resistance also exit, whereby obvious interventions do not necessarily result to solutions. For example, an increase in availability of vaccine does not result to an increase in the number of vaccinated women. In fact vaccination coverage could increase in the short term and decrease thereafter due to un-intended effects.

vii. Management of cervical cancer is characterised by time delays and tradeoffs. A decrease in the primary vaccination coverage may have an increase in HPV incidences and prevalence in the future.

Because Cervical Cancer system is complex and experimentation of the systems is impossible, computer simulation becomes a realistic study method (Fone et al. 2003). Cancer management in this study is viewed as deterministic and focuses on the strategic level (Brailsford & Hilton 2004). The researcher aimed at understanding the feedback dynamics and long-term system behaviour in different intervention strategy options.

The Dynamic Synthesis Methodology on the other hand illuminates the dynamics of cervical cancer management characteristics within the Kenyan case study. Thus;

i. Exogenous shocks such as HIV epidemic such that an increase in HPV infections would result to an increase in HPV infections due to weakened immune status of HIV infected women.
ii. Feedback loops whereby an increase in screening coverage will result to an increase in treatment demands, which will result to a possible decrease in performance of the health Systems.
iii. Interventions whether primary vaccination, secondary vaccination or screening will result to unintended consequences for example an increase in risky sexual behaviours. These intended and unintended consequences will be investigated.
iv. The cervical cancer management system has systemic delays. For example a girl who missed primary vaccination may not benefit from HPV vaccine until an opportune time for secondary vaccination.

3.5Hypothetical and Dynamic Patterns

3.5.1 Dynamic Problem Definition (reference modes).

Cervical cancer is described by variables that change significantly over time. These variables range from primary vaccination demands, secondary vaccination demands, screening demands, and treatment demands. These demands are influenced by factors related to the clients, the health care facilities, health care personnel and technology. These variables, which translate to the dynamic pattern of cervical cancer in the population, can be manipulated over time to show how the problem of cervical cancer

can change in the future. This phenomenon of change over time is referred to as the dynamic pattern (Sterman, 2000). The behaviour over time (BOT) /reference mode of cervical cancer screening and vaccination is shown in Figure 3.2. It is noted that due to the low quality data on cervical cancer in Kenya , a number of these variables were estimated.

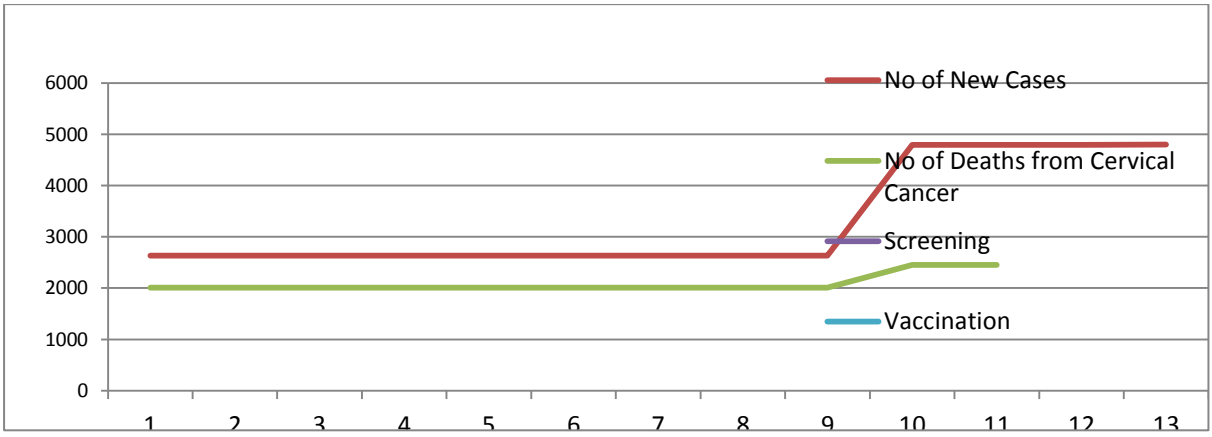


Figure 3.2 Behaviour over Time Mode of Cervical Cancer in Kenya

Figure 3.2 shows that the exponential growth of the number of New cases of cervical cancer as well deaths from cervical cancer.

This study utilized both primary and secondary data.Literature review was done to collect Secondary data on facts on clinical and economic impact reported elsewhere. A checklist (Appendix 1) was developed and used to guide the literature review

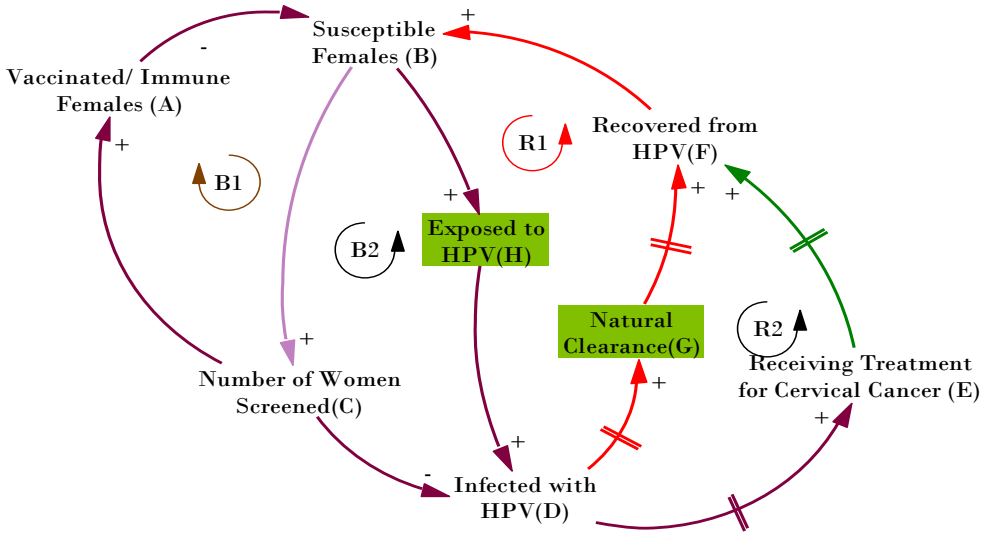
3.5.2 Dynamic Hypothesis

In order to develop the cervical cancer management process, the model boundaries, the key processes and sub-systems were identified. The key players and their roles were also enumerated. These were then synthesized and presented in a high level Dynamic Hypothesis map as shown in Figure 3.3.The dynamic hypothesis is a synthesis of the insight that a modeller has towards to problem of study. It is dynamical in the sense that the systems behaviour changes over time and the hypothesis itself will change continuously during the simulation. Hence it is also called transient hypothesis (Raimo Keroharju n.d.). According to the (Sterman 2000), the generation of Dynamic hypothesis comprises of three major steps which are;

i. Initial hypothesis generation, which addresses the current theories of the problematic behaviour.

ii. Endogenous focus: Formulate a dynamic hypothesis that explains the dynamics as endogenous consequences of the feedback structure.

iii. Developing maps of causal structure based on initial hypotheses, key variables, reference modes, and other available data.



Balancing Loop 1(B1)
Balancing Loop 2(B2)

Reinforcing loop 1(R1)
Reinforcing Loop 2 (R2)

Figure 3.3 Dynamic Hypothesis

The dynamic hypothesis has two balancing loops (HPV vaccination and Screening) and two reinforcing loops (Exposure to HPV loop and HPV recovery loop).

Balancing Loop B1 (Vaccination Loop).

The aim of the vaccination loop is to reduce the number of females susceptible to HPV infection. The model assumes that once vaccinated, life time immunity is accrued HPV can be given prior to susceptibility (Primary Vaccination) or to susceptible groups (Secondary/Catch up Vaccination). This model assumes that once Primary Vaccination is given, then there is no need of Secondary/catch up vaccination. Therefore the higher the coverage rate of primary vaccination, the lower the required number of secondary vaccination. Both primary and secondary vaccinations lower the number of females susceptible to HPV infection. The dynamics involved in the uptake of HPV vaccine are discussed later.

Balancing Loop B2 (Screening Loop)

Screening aims at early detection, diagnosis and treatment of HPV infection and cervical cancer at the earliest opportunity. Women who are susceptible to HPV infection are eligible for screening. The higher the number of susceptible women, the more the demand on screening services. However only exposed women are infected with HPV vaccine. Exposure to HPV depends on a number of factors which are discussed later in this chapter. The more the number of women are screened, the higher the probability of HPV infection detection. This model assumes that once a female is screened for HPV and is found NOT to be infected then, she is offered secondary /catch up vaccination. If she is found to have HPV infection, then treatment options are availed. Screening therefore further increases the demand for both secondary vaccination and treatment for cervical cancer.

As the number of susceptible women increase, there is an increase in the demand and number of screened women. This leads to early detection of HPV infection and an opportunity for health education on HPV infection. With time, these interventions reduce the number of women infected with HPV.

Reinforcing Loop 1 (Exposure to HPV Loop)

It is noted that the higher the number of women exposed to HPV infection, the higher the number of Women infected with HPV, this translated to a higher number of women undergoing natural clearance of HPV as well as an increase in the number of women undergoing treatment for cervical cancer.

Reinforcing Loop 2 (HPV Clearance/Recovery Loop)

It is also noted that HPV infection could clear naturally due to biological mediating factors. The number of women whose HPV infection clears naturally or through treatment are however still susceptible to HPV infection as previous HPV infection does not offer natural immunity. Hence these groups of women, whose bodies undergo natural clearance of HPV, reduce the number of women with HPV infection but also increase the number of women susceptible to HPV infection. At the same time, the females found to have cervical cancer are subjected to appropriate treatment. This is a assuming an effective health care system. The treatment methods availed depends on the stage of the cervical cancer among other health systems factors. The treatment of HPV infections and cervical cancer reduces the number of women with

HPV infection as well as the number of deaths occurring as a result of cervical cancer and its complications. The women 'cured' from HPV/ cervical cancer are still susceptible to HPV infection and hence this group though a small number increases the number of females susceptible to HPV infection.

It is noted that infected females who do not benefit from medical interventions, die from cervical cancer. The death of these females may occur earlier than among those who benefit from treatment interventions.

A certain group of susceptible females, who get infected and do not undergo screening, also contribute to the total death s as a result of cervical cancer.

3.5.3 Scope of the Research

This study covers the activities and strategies employed in management of cervical cancer in Kenya. The relationship and causal effect among key variables are explored. Specific in-depth interviews concerning cervical cancer management were conducted during the field studies.

3.6 Field Studies

For primary data, Twelve (12) medical Doctors and twenty one (21) nurse managers working in oncology centres throughout Kenya were interviewed in order to document their experience in management of Cervical Cancer.

A baseline survey was done among the Cervical Cancer clients in the two national referral hospitals in Kenya to establish their use of e-health tools in management of Cervical Cancer.

Dynamic Model Navigation questions of what, why, where, how and who were utilized as a guide. Seven interactive steps in System Dynamics Modelling were followed (Homer & Milstein 2006).

3.7 Study Setting

Respondents were drawn from the two main National Referral Hospitals in Kenya; Kenyatta National Hospital [KNH] and Moi Teaching and Referral Hospital [MTRH]. KNH is the largest teaching and referral hospital in East and Central Africa. It has a bed capacity of 2500 and is located in the capital city Nairobi. KNH houses the sole radiotherapy facility in public sector and receives patients with different types of Cancer from all over the country. MTRH is the second largest teaching and referral hospital in Kenya and is located in Eldoret city in the Rift Valley province of Kenya

and has a bed capacity of 800. It does not have a radiotherapy machine. The two hospitals serve as the main referral hospitals for the country and receive over 70% of Cervical Cancer patients from all over the country.

Kisumu Provincial General Hospital is located at the Nyanza province, of western region of Kenya. Coast Provincial General hospital represented the experiences from the coast region while Nakuru Provincial General Hospital is located in the rift valley province. Embu General Hospital is located in the eastern Province of Kenya.

3.8 Population

The study considered two population groups which consisted of all Cervical Cancer managers (both Medical doctors and Nurses) and the Cervical Cancer patients under their care.

3.8.1 Sample Size Determination and Sampling Methods

A stratified simple random sampling of 400 patients/clients was calculated using Fisher's formula. The 95% with a confidence interval for population proportion of Cervical Cancer could be estimated using the sampling distribution data. Eight (8) study institutions were selected as part of the main institutions which provide Cervical Cancer patient (Table 3.2). Convenience sampling of the Cervical Cancer managers was prorated based on the size of the health facility. Sequential sampling of the specified number of physicians and nurse managers from each study institution wards or outpatient clinics was done. These physicians and nurse managers have been referred to as experts and their opinion was sought. In-depth qualitative study was done among the Cervical Cancer managers since they are largely responsible for provision of Cervical Cancer care.

Table 3.2. List of Study Institutions

Institution	Region/ Province	% Distribution	No. Of Clients/ Patients	No. Of Physicians	No. of Nurse Managers
Kenyatta National Hospital	Central/Nairobi	30	120	4	6
Kisumu Provincial Hospital	Nyanza	10	40	2	3
Moi Teaching and Referral Hospital	North Rift Valley	15	60	3	5
Mombasa(Coast General Hospital)	Coast	10	40	2	3
Nairobi hospital	Nairobi(private)	10	40	2	3
AAR (Nairobi)	Nairobi(private)	5	20	1	2
Nakuru provincial General Hospital	South Rift Valley	10	40	2	3
Embu Provincial General Hospital	Eastern Province	10	40	2	3
TOTAL		**100**	**400**	**18**	**27**

3.9 Ethical Considerations

Ethical clearance was sought from the Kenyatta National Hospital/University of Nairobi [KNH/UON] ethics and research committee, the National Council of Science and Technology [NCST] as well as individual hospitals where the study was conducted. The participants had full disclosure of information. Written consent was obtained from all participants and confidentiality was upheld.

3.10 Data Collection and Management

3.10.1 Study Tools

Checklist

A checklist was developed to guide literature review and extract of secondary data. The results are as detailed in Table 3.2 (Appendix 4).

Interview Scheduler

An interview guide was used to ensure all coverage of key issues identified which also included use of internet and mobile phones as well as document the experiences of Cervical Cancer managers (Appendix 3).

Self administered questionnaire for clients/patients

A semi-structured self administered questionnaire was used to collect both qualitative and quantitative data from the clients/patients on use of e-health tools in obtaining information on Cervical Cancer (Appendix 4).

3.10.2 Pretest

The interview scheduler and self administered questionnaires were pre-tested at the Nairobi Hospice located at Kenyatta National Hospital (KNH) in April 2011.This site was chosen as it deals with terminal care of Cervical Cancer patients among others types of Cancer cases. The pre-test ensured validity and reliability of the study tool.

Two physicians and two nurse managers were interviewed. Analysis of the interview scheduler had a Cronbach's alpha of 0.71. The interview scheduler was found to be too wide and the interview was narrowed down to issues of e-health, screening and individual health care provider related challenges. Self administered questionnaire was pretested among five clients. The tool was found to be reliable and valid. These participants were not included as part of study subjects during final data analysis.

3.10.3 Data collection

A judgemental sample of all the Cervical Cancer clients attending oncology clinics and all the Cervical Cancer patients admitted in the wards was done. The term clients and patients have been used interchangeably in this document. The staff nurses identified the Cervical Cancer clients and introduced them to the research assistants. A structured questionnaire was then administered to clients and patients between July 2011 and December 2011. Three trained research assistants performed the data collection exercise. Study protocol was follow as detailed in appendix 5.

Cervical Cancer managers were purposefully selected for this study. Qualitative data was collected from the Cervical Cancer managers using the standardised interview. All operational level nurse manager who included in charges of gynaecological and Oncology wards admitting Cervical Cancer clients and radiotherapy departments were interviewed. The Medical doctors who were managing patients in these wards and at radiotherapy departments were also interviewed. Interviews were conducted by the principal investigator and one research assistants who was a holder of MSc in Nursing and were already trained in qualitative research methods and specifically in conducting interviews with health care workers.

The order of the discussion was guided by the interview guide. The respondents were to raise other issues they deemed important in management of Cervical Cancer. Individual Interviews lasted 30 to 60 minutes and took place at the doctors' or/and nurses' office within the work areas. Interviews were audio recorded. The audio recording of the interviews allowed eye contact between the interviewers and the respondents as well as obtaining accuracy from the recordings rather than relying on memory or field notes.

To increase the validity of the interviews, the audio records were played back to the respondents and they were allowed to make alterations of their statements where need arose. However, none of the respondents felt the need of changing their recorded statements.

The researchers listened to the audio recordings and compared them with the transcripts in order to confirm and ensure that the two were identical.

3.10.4 Data Analysis

Data was transcribed verbatim and analysed using emerging themes. Analysis of qualitative data from the scripts generated from the recorded interviews was entered, coded and synthesised using Atlas ti. A mind map was utilised in presenting the summary of qualitative findings. Quantitative data from self administered questionnaires was analyzed using Statistical Package for Social Scientist (SPSS) Version 17.0.

3.11 SD Model Using ithink ^{Tm} Software

A macro-Level population based SD model was developed used iThink™ software to enable Simulation of Cancer of Cervix topography and impact of different management interventions in Kenya. Primary data generated was used to calibrate the parameters thus identify information and knowledge gaps in the dynamic model. This data was used to further redefine the SD model.

3.11.1 Some of the 'What If' Addressed

Use of e-health tools versus no use of e- health tools in Cervical Cancer management.

Primary Vaccination only, secondary vaccination only or a combination of both.

Screening only or a combination of any of the four interventions.

3.11.2 Verification and Validation of the Model

In all these phases, verification and validation was continually performed. Validation of the model means establishment of adequacy with respect to purpose and confidence building. This was done through use of the experts in the study institution.

The following aspects of systems dynamics were validated;

3.11.3 Model qualitative structure

Validity of the model was performed in an informal qualitative nature through; experts review, inspection, walkthroughs and consistency checks. The quality of the map of the model was checked against available clinical knowledge. The map was revised and updated with the research participants until consensus was reached. The feedback from the experts was used to change any aspects of the model as was required. Any discrepancies were addressed based on the experts' experience.

3.11.5 Model behaviour validation/behaviour accuracy

This was checked against the real world cumulative cervical parameters between 2005 to 2010. The entire time frame for simulation was 50 years. The simulation answered the question if the model could replicate historical data with high accuracy and if it can compare with the real world today even under extreme conditions, and possibly predict the future values.

3.11.6 Presenting Cervical Cancer Mathematically

At this stage the Linear and exponential mathematical Models were presented. Differential equations were used to present Cervical Cancer topography in Kenya. Matlab was used to solve differential equations and generate graphical outputs. The results of each equation compared positively with available knowledge on real systems.

3.11.7 Study Limitations

Simulation does NOT rely on learning feedback through real world. There are no established formal tests e.g. statistical hypothesis tests to establish if structure of model is close enough to the real structure. System Dynamics models demand deeper casual theory hence has a greater degree of uncertainty and does not lay concern on a

single individual behaviour hence has a macroscopic point of view. For these reasons No model can claim to be absolutely objective as every model carries its modeller's worldview and assumptions.

The stake holders were Not familiar with most e-health tools or the iThink™ software hence they had limitation in their opinion on possible benefits and limitations of the Model. This model does not allow for volatility of factors which are neither controlled nor deterministically modelled. It is important to note that models are not true or false but lie in a continuum of usefulness**.**

There were very few Cervical Cancer clients in peripheral hospitals as most were referred to the National referral hospitals for management, hence data utilized for internet use by Cervical Cancer clients was based on those clients attended at the referral hospitals only. Even though the researcher would have wished to enrich the study with data from private hospitals, the three main private hospitals earlier sampled declined to participate in the study. One reported to have too many research projects going on at the time while the other reported having too few clients hence declined to participate in the study. The third private hospital wrote an apology for not wanting to be included in the study. No reason was given.

3.11.8 Study Assumptions

For the study to take place, the following assumptions were made;

i) That the experts were aware of some e-health tools.
ii) The study subjects were willing to participate.
iii) That all study institutions proposed for this study and whose authority was sought would grant authority.
iv) That the study subjects would give their honest opinion.

CHAPTER FOUR: RESULTS AND DISCUSSION OF PHASE ONE FIELD STUDY

4.1 Introduction

This chapter provides an overview of the study results and findings of the first phase of the study. The study results are organized into two sections; Qualitative study section and qualitative study phase.

4.2 Results of Experiences of Cervical Cancer Managers in Kenya; Challenges and Opportunities.

4.2.1 Response Rates and Biographical Characteristics

A total of thirty three (33) respondents were interviewed comprising of 12(36%) medical doctors and 21(64%) nurse managers. This was response rate of 73%. This response rate did not affect the results of the study as saturation level was reached and further interviews yielded no new findings. This sample size was deemed sufficient based on recommended sample size of 12 interviews in qualitative studies by Guest et al(2006). The respondents were basically homogenous, were professionals and generally possessed a degree of expertise in their field.

Reasons given for non participation were; being away on other assignments, large workload while one nurse manager was uncomfortable with being audio recorded. Thirty three % (n=11) were from the National referral hospitals and 67% (n=33) from peripheral hospitals. The average age of the respondents was 41.1 years with a standard deviation (sd) of 5.6. The average length of experience of working with Cervical Cancer was 7.29 year with sd 5.4. The respondents' distribution and biographical characteristics are indicated in Table 4.1.

Table 4.1. Biographical Characteristics of Cervical Care Managers

Workstation	**Sex**			**Profession**			
	Females	**Males**	**Total**	**Medical Doctors**	**Nurse Managers**	**Total**	**%age**
Coast Provincial General Hospital	2	2	4	1	3	4	12.1
Embu Provincial General Hospital	4	1	5	2	3	5	15.2
Kenyatta National Hospital	4	4	8	3	5	8	24.2
Kisumu Provincial General Hospital	3	2	5	1	4	5	15.2
Moi Teaching and Referral Hospital	4	3	7	2	5	7	21.2
Nakuru Provincial General Hospital	1	3	4	3	1	4	12.1
Totals	**18**	**15**	**33**	**12**	**21**	**33**	**100**

4.2.2 Emerging Themes

Key themes were described using direct quotes from the respondents against their profession and area of work. Medical Doctors (MD), Nurse Managers (NM).The four themes which emerged were patient related challenges, individual health care provider challenges, health facility related challenges and technology related challenges. Figure 4.1 is a summary of the key challenges identified.

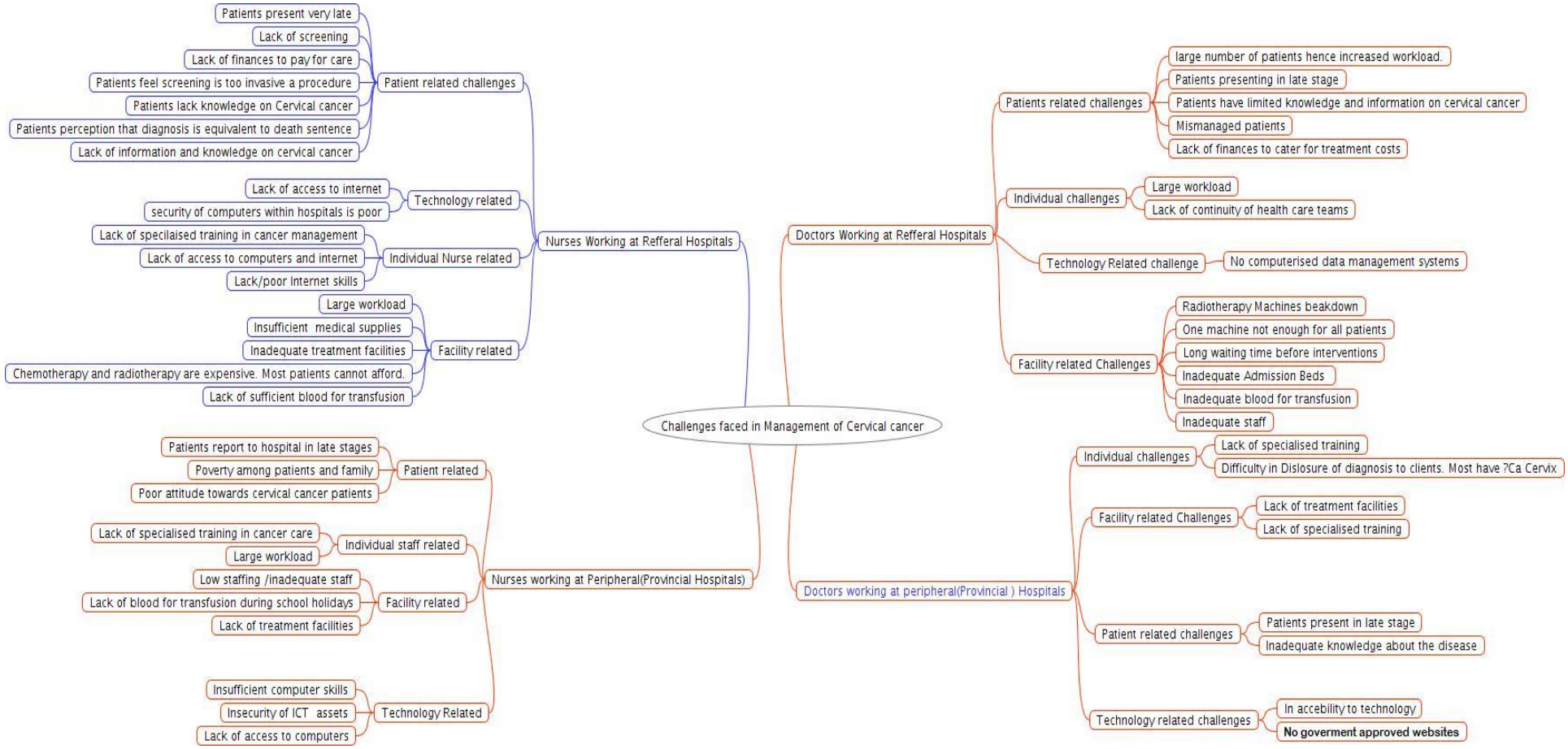


Figure 4.1. Summary of Challenges Faced By Cervical Cancer Managers

* Ca Cx means Cancer of Cervix

4.2.2.1 Patient related challenges

These were identified and included large workload, presenting in late stage, limited knowledge about Cervical Cancer, poor attitudes of some health care providers and relatives towards the patients and poor attitudes towards Cervical Cancer by patients themselves.

a) Large workload.

Cervical Cancer managers in Kenya often find themselves taking care of large number of patients. Large workload hinders quality of care provided to the Cervical Cancer patient. Both nurses and doctors equally reported feeling overwhelmed with the large number of patients. The increase in the number of clients was also attributed to long waiting times before clinical intervention.

> *'The patients are so many, the gynaecologists see the patients but the oncologists do not get to see most of these patients' [NM-**4].***
>
> *'It is over whelming. We get 5-10 patients a day' **[NM- 6]***
>
> *'These patients are chronic patients, once they land in the ward, we are meant to stabilize them for radiotherapy. Bed occupancy goes higher because stabilizing the patients takes longer' **[NM-2].***

b) Inadequate knowledge about the disease

The patients have limited knowledge about Cervical Cancer. Lack of awareness of disease signs and symptoms as well as interventions available is a big challenge.

> *'Many women are not aware of Cervical Cancer; the government needs to step up health education and campaigns about Cancers in general' [NM-8]*
>
> *'Even the nurses themselves have the knowledge and are not using the knowledge. How to integrate knowledge and practice is a problem. Let the survivors speak to the other because they have moral courage' [NM-11].*

Health care managers felt that the responsibility to educate the population about Cervical Cancer is not of the government alone. They felt that use of mobile phones could reach a wider coverage in health education even as an initiative of the health facilities and health care workers.

'Almost every homestead has a mobile phone0 nowadays. Even if the women do not know how to read sms, we could use voice messages in their local language to educate them' [NM 12]

There was a feeling that too much knowledge of Cervical Cancer screening procedures may have a negative effect on the clients seeking screening services. Health care workers also have hidden fears about the screening procedure as reported by one Nurse Manager.

'Too much knowledge may also have a negative effect on screening. The scraping of Cervical cells creates a wound which may act as entry point for other infections including HIV. Once many women realize this, they may decline to have the screening procedure done'[NM-19]

c) Low screening levels and poor attitude towards Cervical Cancer screening procedure

Low screening coverage is a big challenge for the health care workers. Even though screening is integrated in the Family Planning clinics and Maternal Child health care units, many felt that more can be done to mobilize women to seek screening services. Use of mobile phones was identified as a big opportunity in campaigning for screening.

'Whoever is in health facilities has contacts of the phones. If even us we used contacts of 50% of women you have on phone and tell them to come for screening the impact would be great' [NM-16]

Health care workers reported that many clients find the screening procedure too invasive and is viewed as embarrassing and against the African culture. Some women find it culturally unacceptable to have young nurses and doctors see their private parts. Others felt that it was culturally unacceptable to allow a male to see their private parts. Even among health care workers, screening is still seen as an uncomfortable procedure associated with risk of infections.

'Many women feel embarrassed about the screening procedure. Even my fellow health care workers find it too invasive' [MD-4]

'It's difficult because, not many will say that I have a problem in my genital area. They will not encourage a man especially to view their private parts' [NM-19].

'Others have a problem with exposing their bodies to the young doctors and nurses, who they view as their children'[NM- 23]

'Even I with all my medical Knowledge find it hard to expose my body every three years. I am also suspicious of HIV infection from the use of speculum. I am not sure of the sterility methods they use' [NM-18]

'Disposable speculums are expensive and their supply may not be sustainable in Government facilities' [NM-18]

The health managers suggested vaccination as an alternative measure to screening**.**

'Screening in itself has been found to be effective in developed countries. However, our people do not like the procedure and their health seeking behaviour is dictated a lot by their cultural beliefs. Even though vaccination is expensive, it may be more beneficial for us as a country' MD-6

d) Patients Presenting in Late Stage.

Many of the patients present in late stage of Cervical Cancer. This was attributed to lack of proper diagnosis at the peripheral facilities as well as mismanagement of patients before referral to provincial and tertiary facilities.

'I have only seen one patient who came with stage one. All the others come after stage 2'.[NM-4].

'Others come totally for palliative care. So they just bring them here and no active management is being done. They come when they are at the last point of death.'[NM-21]

'Majority of patients come at stage three and four' [M *D- 4]*

'Being referred as too late a case. People come thinking that they coming to get healing or get cured. It's very challenging during counselling to tell patients that even though you have come it is too late and there is nothing much we can do'[MD-6].

'We witness presentation because of symptoms meaning it's a stage where palliative care is needed' [NM-19]

e) Lack of finances to cater for treatment costs

Inability of the patients to pay for Cervical Cancer treatment was attributed to poverty of most patients as well as the high cost of chemotherapy and radiotherapy. Patients lacked health care insurance and only a few were reported to be members of National Hospital Insurance Fund [NHIF]. Since many patients could not afford care, hospital facilities ended up waiving their medical bills hence a loss of revenue to the hospitals.

'Some come from far and are very poor. I advice them to join NHIF. The bills become a problem. They stay until the hospital waves them' [NM-6]

'Poverty is the one killing our people' [NM-8]

'Without money you cannot do all the things required in time. Even if the doctor would want to treat immediately, Staging changes as patients await money. Patients have to cough money' [NM -17]

'Patients can't afford care. Cancer treatment is expensive. Unless there is a donor, poverty is a major challenge. Those unable to afford just stay home and die.'[MD-10]

'Those with NHIF card benefit but some can't even afford the 300 shillings to registers for NHIF'. [MD-13]

'They may miss treatment as chemotherapy is very expensive. Others may die before they receive treatment. Some have no dependants who are capable' [NM-6].

f) Poor attitude towards Cervical Cancer patients by the relatives, public and some healthcare workers.

Some healthcare workers view Cervical Cancer patients as a burden. Some are allocated care of the patients a 'disciplinary' measure. Some health care managers utter negative comments about the Cervical Cancer patients. As one nurse manager reported her experience in accompanying Cervical Cancer patients to one of the National referral hospitals;

'The patients would cry, smell, stink and nobody would move near them. I would be sent to escort the patients to KNH for radiotherapy. I would find myself

travelling to the KNH with public means. The people would move away from us in the Nissan because of the stench!!

'Minute you get to radiotherapy unit and get to consultation room a doctor would ask 'who is that stinking like the X hospital patients'

Other health care managers appreciate the uniqueness of Cervical Cancer care and view it almost as a calling

'Not many health care professionals are interested in management of Cervical Cancer or preventive measures. If interested even those at periphery facilities can do something. However much you try to prevent not many people has shown interest in preventing Cancer. If they were interested we would be receiving earlier stages. Pap smear can be collected in a dispensary or elsewhere. Not many people have come up to fight against Cancer.' NM-17

'Cancer management is not just work. You must have passion for the patient'.MD-12

Some patients and relatives perceive diagnosis with Cervical Cancer as equivalent to a death sentence. Some relatives on the other hand abandon the patients in the hospital to die. As reported by one NM-9

'We witness abandonment of patients by relatives. I had one client who stayed here for five months. Nobody ever visited her. The day she died, the husband was here at 8.30 am.'NM-6

'So they just bring them here and no active management is being done. They came when they are at the last point of death. Some leave patient in the ward to die '[NM-14]

4.2.2.2 Individual Cervical Cancer manager related challenges.

a) Lack of Specialized training

Lack of specialized training in Cancer care and its management was reported as a challenge faced by health care managers themselves. Many feel ill equipped to manage the condition. A number however reported having been trained in palliative care. This lack of specialised training has been attributed to mismanagement of patients at peripheral levels.

'Many health personnel are not aware of what Cancer is. It takes 6 months to 12 months for referral to take place' [MD-4].

Other health care managers have had on job training in Cervical Cancer management. As reported by one doctor

> '*I remember seeing Cervical Cancer patients when I was still at Medical school. Now I am working as an MO and I am expected to manage Cervical Cancer in the ward. I have learnt a lot from the more experienced nurses. I think we need an induction course in managing Cervical Cancer.'MD-9*
>
> *'Poor training and development in area of Cancer management compromises patient care' [NM-17]*
>
> *'Not many health care providers are trained especially in narcotic analgesics' [NM-15]*

However some nurse managers in referral hospitals reported having received adequate training in Cervical Cancer care.

> *'Nurses are aware of screening and procedures. We had training from Americans. Nurses and doctors can now do screening and treatment procedures e.g colonoscopy and leep. Pap smear, a primary screening can be done by everybody' NM -3*

b) **Lack of continuity of health care teams.**

This was attributed to the inadequate numbers of health care workers and frequent change of team members.

'Every week the teams of doctors change and change the management decisions too' NM

c) Difficulty in Disclosure of diagnosis to clients.

It was reported that it takes a long time before a Cervical Cancer diagnosis can be confirmed. Many of the patients in the peripheral facilities are 'suspected' to have Cervical Cancer as the medical team awaits confirmatory test results.

> *'Most patients in the ward are query ca cervix. Many do not know their disease conditions'***[**MD-4]

4.2.2.3 Facility related challenges

a) Inadequate treatment facilities

Facility related challenges were identified as inadequate treatment facilities, long time of wait before interventions, inadequate inpatient facilities, and lack of blood for transfusion and inadequate number of staff. Inadequate treatment facilities in relation to numbers, location and availability were identified as a major challenge. It was noted that radiotherapy facilities were only available at Kenyatta National Hospital. This facility serves the whole country as well as some patients from the neighbouring countries. This one machine is not enough for all the patients. The machine itself is characterized by frequent breakdowns.

> *'….mode of management is radiotherapy which is only available at KNH'[MD-4]*
>
> *'The machine is overbooked or unavailable machines. Patients are booked 3-4 months down the line'[MD-7]*
>
> *'Most come from rural areas where they have no treatment. By the time they come very little can be done'.* NM-3
>
> '*Even though we should not wait and treat immediately we are forced to schedule patients. Scheduling a patient means you are not doing much for them'.* MD-8

They either go to KNH or Uganda for radiotherapy' [NM 18]

Laboratory and theatres facilities were also identified as inadequate.

> *'They come late, staging in theatre takes time, results and treatment can delay. Process of biopsy takes a long time'.MD 9.*

Other facilities have inadequate beds for admission

> 'Cancer *does not have a real ward. Space is limited'NM-6*
>
> *'These patients are chronic patients, once they land in the ward, we are meant to stabilize them for radiotherapy. Bed occupancy goes higher because stabilizing the patients takes longer*.'NM-1

b) Insufficient blood for transfusion

It was noted that blood for transfusion was a big challenge in the referral hospitals.

> *'Patients come with very low Hb of 1 to 2. No blood available. Within the hospital the blood is not available'NM-6*
>
> *'Kenyatta doesn't not have blood. It may take up to 3 months to raise the Hb to 10. Let the peripheral institutions first bring the hb up' NM-2*

'Anemia, getting blood is a challenge and this also causes delay in intervention' NM 3

However lack of blood was a challenge in provincial hospitals only when schools and learning institutions were closed for holidays.

'Blood for transfusion is a problem when school is closed'. NM -23

4.2.2.4 Technology Related challenges

Cervical care managers expressed their inadequacies in Utilization of ICT in management of Cervical Cancer. The challenges identified included lack of computerized data management systems, Lack/poor Internet skills, inadequate access to computers and internet, security of computers and other ICT assets within hospitals is poor, inaccessibility to technology as well as lack of government approved websites.

'Both patients and health care provider need to be computer literate. Only few of us are competent in computer skills' NM-19

'We need to develop a website that will serve the sub-Saharan Africa'.NM-9

The managers reported use of internet in continuing education, updating themselves on management protocols and students education.

'I search on Cases within my wards. I update myself on computers so as to update my students. Just Google' NM-14.

The respondents acknowledged the accessibility of mobile phones by almost all patients who visited the health facilities. They felt that mobile phones could be used to reach a wider population.

'even if the woman does not have a mobile phone, at least one person in the family is likely to have a cell phone' NM- 17.

Potential use of cell phones was identified in health education, reminder alert; follow up of patients as well as database management.

'We can use the mobile phones in helping patients set reminders for pain control. An alarm to remind patients to take medication. If not in pain they forget' NM-9.

'We have not used computers yet. Computer system is not well developed. No access to computers at the hospital. Access is through commercial cyber which are expensive and sometimes are congested' NM-16

'However there is no way of authenticating the information from the internet. You either take it or leave it'NM 11

Even though facilities may not have mobile phones, health care providers extend use of their personal cell phones in management of Cervical Cancer patient

'We give the patients personal numbers. It's a very friendly department. We get attached to our patients. There is now an office number phone. Over the weekend some patients prefer specific persons and may request for specific phone number'
NM -9.

What is already known about the study?
Challenges faced by health care workers include large workload, low knowledge levels on Cervical Cancer management and inadequate facilities

What does this study reveal?
Some Cervical Cancer managers have negative attitude towards Cervical Cancer screening procedure, care of Cervical Cancer clients and feel inadequate in computer and internet skills.

Lack of Blood for transfusion is a big hindrance to Cervical Cancer treatment.

Vaccination is seen as a more culturally accepted form of Cervical Cancer prevention measure.

Acceptability of screening and vaccination are important indicators of potential success of Cervical Cancer management.

Mobile phones have great potential in health education, reminder alert and information management in Cervical Cancer.

4.2.3 Discussion of Qualitative study

A myriad of challenges are faced by cervical cancer managers in Kenya. These challenges influence their view and management of Cervical Cancer. The challenges ranged from individual, to facility, patient as well as technological. The challenges identified in this study concurs with previous studies which found challenges associated with infrastructure, inadequate health care workers, low screening coverage, low knowledge about Cervical Cancer, high cost of screening as well as high cost of vaccines(Arrossi et al. 2010; Denny et al. 2006; Bingham et al. 2003; Fort et al. 2011; Mutyaba et al. 2007; Were et al. 2010).

While screening with concurrent treatment has been associated with high success rate in developed countries(Gakidou et al. 2008) this may not necessarily be the case in Kenya. Cervical Cancer screening is a procedure which involves opening the vagina using a speculum with the woman lying on lithotomic position and taking a sample of cells from the cervix. This study found that screening procedure has been viewed negatively by both clients and health care worker. Cultural, personal and procedural factors were associated with the negative attitudes. Generally Traditional African culture dictated that women expose their private parts only to their spouses and female midwives. Age and Sex differences between the Cervical Cancer managers and women who may require Cervical Cancer screening may be a hindrance to the screening practice.

The results support studies done elsewhere which revealed that women found the whole practice of Cervical Cancer screening embarrassing, uncomfortable and too intimate especially in exposing such personal parts of their body. For these reasons some women dislike the procedure yet acceptability of the screening procedure by the women is a big factor in success or failure of cervical cancer screening programs(Armstrong et al. 2012; Julinawati & Cawley 2013).The results of this study however contradicted Claeys et al. (2003), who found that women had positive attitude towards screening. A study done among HIV positive women in Kenya also revealed positive attitudes towards screening (Huchko et al. 2011). At the same time (Lyimo & Beran 2012) found that embarrassment and fear of pain as a result of the procedure did not significantly affect the uptake of cervical cancer screening in Rural Tanzania.

Vaccination in this study was mentioned as an alternative to screening. However, there has been a reported low level of knowledge on vaccination among women in developing countries(Becker-Dreps et al. 2010; DiAngi et al. 2011). Even with increased level of knowledge on vaccination, there is no guarantee that the community will have a perpetual positive attitude towards vaccination. There is potential challenge of resistance to vaccination due to low acceptability among possible recipients. This has been implied in a study done in France in uptake of Hepatitis Vaccine(Kumar & Whynes 2011) whereby resistance to vaccination was reported.

It is important to note that women in Kenya and Botswana have been reported to have a high level of acceptability of HPV vaccines (Becker-Dreps et al. 2010; DiAngi et al. 2011). The positive attitude towards vaccination may be related to its being less invasive to privacy and less embarrassing. The positive attitude towards HPV vaccine is a strength which the stakeholders would base HPV vaccine on in these countries.

Cervical Cancer managers reported feeling of inadequate training in management of Cervical Cancer. This concurs with findings of Chirenje et al. (2001), who found that health care workers lacked the necessary skills in Cervical Cancer management. This may mean that such a Cervical Cancer manager, who feels ill equipped and has a negative attitude towards screening procedure, is less likely to encourage women to undergo screening.

Technology related challenges included digital divide characterised by inaccessibility to hardware as well as internet. Cervical Cancer managers also reported feeling of inadequate computer skills. This has the implications that the Cervical Cancer managers may not have access to research results or evidence based practice. Their knowledge levels on Cervical Cancer may also not be up-to-date. Few public hospitals are computerised in Kenya hence the medical staff generally do not have access to a computer at the work place. Investment in ICT in most government facilities in Kenya is still rudimentary. At the same time, it was not compulsory to have ICT training as a component of both nursing and Medical curriculum in the yester years hence with a mean age of 7.9 years of experience in Cervical Cancer management, these health care

providers may not have trained in computer skills. Those who have computer skills trained on their own volition.

The results of this study support those done elsewhere that reported low computer skills and inadequate access to ICT in developing countries. The ICT investment in health care in developing countries is also uncoordinated (Bukachi & Pakenham-Walsh 2007). However, the potential impact of use of mobile phone in Cervical Cancer management supports the finding of a study done by Gormley et al. (2010) in Botswana which indicated that mobile phones could be useful in remote access to specialist for diagnosis and direction on management of diagnosed Cervical Cancer.

4.2.4 Limitations of the Qualitative Study

Judgemental sampling has inherent selection bias hence generalization of the results is limited. Three (3) of the researchers have a Medical background hence may have influenced the formulation of the research questions. To eliminate bias, an independent person who was not part of the research team reviewed the questionnaire.

Even though Cervical Cancer care is also offered at the public Health Institutions of lower levels; from Dispensary (Level 2) to District (Level 4) hospitals, this study focused on the National referral Hospitals and provincial Hospitals. It would have been enriching to involve the lower level health facilities as well as private hospitals. This was however not possible due to limited resources.

4.2.5 Strengths of the Qualitative Study

This verbatim transcription avoided complex statistical analysis. The thirty three (33) interviews was sufficient given the aim was to understand and document challenges and experiences of Cervical Cancer managers in Kenya and the group was generally homogeneous.

4.2.6 Conclusion of the Qualitative Study

The results of this study have limited generalization. However, they provide an insight into challenges faced in Cervical Cancer management from the health care providers' perspective. Of interest were the negative attitudes towards screening procedure and

care of patients with Cervical Cancer. This peculiar attitude of health care providers needs urgent attention. With a large population with access to mobile phones and the positive attitude towards use of mobile phone in management of Cervical Cancer, the stakeholders need to exploit this opportunity. The negative attitude towards Cervical Cancer screening procedure may necessitate the stakeholders' redress of the negative attitudes or provide HPV vaccination, which though expensive may be more culturally acceptable. There is need to address the low level of Knowledge, access to Internet and computers use by Cervical Cancer managers. Further research to establish how these factors interact and affect management of Cervical Cancer in Kenya is recommended.

4.3 Results of the Baseline Survey on Use of E-health Tools by Cervical Cancer Clients

The objective of this part of phase one was to establish the extent of internet use by Cervical Cancer patients in seeking information related to Cervical Cancer; identify barriers faced by the patients while using internet and find out the characteristics of patients associated with internet use. The use of mobile phones by the patients was also explored.

4.3.1 Socio demographic characteristics cervical cancer patients at KNH and MTRH

A total of 199 female clients attending KNH (n = 129, 64.6%) and MTRH (n = 70, 35.4%) were identified and included in the study. The average duration since diagnosis with Cancer of the cervix in the sample was 2.48 years (sd ± 3.0). The duration of illness ranged from one month to 24 years. The median duration of illness was 1.5 years (inter-quartile range 11 months to 5 years).

The socio demographic characteristics of the 199 female patients with Cervical Cancer at both study sites are summarized in Table 4.2.The mean age of participants was 47.8 ± 11.2 years, and the median age was 47 years (inter-quartile range 41 to 53 years). The percentage distribution of patients by ten-year age groups is presented in Table 4.1Most participants were middle-aged, with 42.2% (n = 84) of the patients in the age group 40–49 years.

Mobile phone access was reported by 96.5 % (n=192) of the respondents.

The married patients (n=143) constituted 71.9% of the participants and represented the most common marital status followed by single patients comprising 12.6% (n=25) of patients. Approximately one third of the patients in this study reported that they were housewives (n = 63, 31.7%). A similar number of patients reported that their main occupation was farming (n = 61, 30.7%). The other commonly reported occupations were business and formal employment with 11.1% and 5.5% of all patients indicating they were engaged in these occupations respectively.

4.3.1.1 Formal education

A cumulative proportion of 86.4% of patients reported having had formal education. Conversely, 13.6% of patients in the study did not have any formal education (Table4.2). Most (40.7%) patients had completed upper primary education while 18.1% had post primary (ordinary level education).

Table 4.2. Socio-demographic characteristics of clients with Cancer of the cervix

Demographic characteristics	Frequency (n)	% (%)
Age category		
20-29 years	9	4.5
30-39 years	28	14.1
40-49 years	84	42.2
50-59 years	43	21.6
60-69 years	19	9.5
70 + years	10	5.0
Not stated	6	3.0
Highest level of education		
No formal education	27	13.5
Pre-primary	16	8.0
Lower primary	25	12.5
Upper primary	81	40.5
O-level	36	18
A-level	5	2.5
Diploma	6	3.0
Degree	3	1.5
Masters degree	1	0.5
Marital status		
Single	25	12.6
Married	152	76.4
Separated	9	4.5
Divorced	1	.5
Other	12	6.0
Occupation		

House wife	63	31.7
Farmer	61	30.7
Business	22	11.1
Formal employment	11	5.5
Casual labour	6	3.0
Retired	6	3.0
Others	30	15.1

Table 4.3. Level of Education of Cervical Cancer Clients

Category	No	Percentage
Pre-primary	16	16
Lower primary	25	12.6
Upper primary	81	40.7
O-level	36	18.1
A-Level	5	2.5
Diploma	5	2.5
Degree	3	1.5
Masters	1	0.5
No formal education	27	13.6

When socio-economic status was examined, 65.3% (n=130) of patients were found to be in the lowest income category with monthly income below Kenya Shillings 10000(Approximately $150), and 11.1% (n=22) with income between Kenya Shillings 10000-50000(Approximately $150 to $600) per month.

Table 4.4 shows that majority 93% (n=185) of the respondents sought information on Cervical Cancer form their doctors.

Table 4.4Cited sources of information on Cervical Cancer

Source of Cancer information	Frequency	%
Doctor	185	93.0
Nurse	72	36.2
Friend	36	18.1
Relatives	24	12.1
Radio	63	31.7
Television	47	23.6
Mobile phone	5	2.5
Billboard	7	3.5
Other source	5	2.5

This was followed by Nurses 36.2 % (n-=72), the Radio as reported by 31.7% (n=63) while the T.V. accounted for 23.6% (n=47) as a source of information. Only 2.5 % (n=5) of the patients used their mobile phones to source for information on Cervical Cancer despite 96.5% (n=192) of them having access to a mobile phone.

4.3.1.2 Use of mobile phone in managing Cervical Cancer

It was noted that 96.5 % (n=192) had access to a mobile phone .The respondents were asked to give their opinion on use of mobile phone in Cancer management. The results were as shown in Table 4.5.

Table 4.5. Use of mobile phones by Cervical Cancer clients

Use of mobile phones	Frequency	%
Number of reported uses		
Participant did not state any use	86	43.2
Single use	72	36.2
At least 2 uses	41	20.6
Specific uses Reported		
Booking appointment	43	21.6
Reminder alerts for medication	59	29.7
Health education messages	63	31.7
Other use	4	2.0

4.3.1.3 Patient self-reported use of internet in Cancer diagnosis and treatment

Table 4.6 shows details of the patients' use of internet with regards to their illness. Only fifteen (7.5%) of the patients in the study reported that they used the internet to get information on Cancer of the cervix. The most common reasons for this low usage of the internet were lack of knowledge on how to use computers (70.9%) and lack of access to a computer (29.2%).

Table 4.6. Use of Internet by Cervical Cancer Clients and Reasons Given for Not Using Internet

	Number (%)
Use internet to get information on Cancer	
Yes	15 (7.5)
No	184 (92.5)
Reasons for not using internet	
Don't know how to use computers	141 (70.9)
Lack access to a computer	58(29.2)
Lack money to use a computer	29(14.6)
Any other reason	22(11.1)

Among the 15 patients who used the internet regularly to search information on Cancer, three patients reported that they were directed by a nurse/ doctor and five reported that they used local search engines. Approximately half of these patients (n = 7) reported that they gained more knowledge about their disease or condition from using the internet.

The patients reported that internet had an important role in the management of Cancer of the cervix. The different uses suggested by patients for IT in Cancer treatments are shown in Table 4.7 below.

Table4.7. Use of Mobile Phone Technology as suggested by Cervical Cancer Clients

Category	No	Percentage
Booking	27	13.6
Referral	17	8.5
Consultation	29	14.6
Data collection	14	7.0
Consumer health education	35	17.6

The respondents were asked to identify functions they wished to be performed on the internet. Majority17.6 % (n=35) of the respondents preferred health education, this was closely followed by online consultation and booking. Less that 10% of the respondents chose referral and data collection functions.

4.3.1.4 Association of Income and Internet Use

There was a statistically significant association between income of the patients in this study and internet use (p = 0.026) as shown in Table 4.8. The highest rate of internet usage was among patients with incomes of between Kenya Shillings 10,000 to 50,000 per month (13.6%). The lowest rates of usage among patients who had some income were in the group of patients earning less than Kshs 10,000 a month (6.9%).

Table 4.8. Level of Income of Cervical Cancer Clients

	Internet use			
Income in KSHS	**Yes**	**No**	**Total**	**Fishers exact P value**
<10,000	9(6.92)	121(93.08)	130(100)	0.026
10,000 to 50,000	3(13.64)	19(86.36)	22(100)	
50,000 to 100000	1(100)	0(0)	1(100)	
missing	2(4.35)	44(95.65)	46(100)	
Total	**15(7.54)**	**184(92.46)**	**199(100)**	

4.4 Discussion

Access to quality information is paramount in the management of Cervical Cancer. The respondents in this study revealed different sources of Cervical Cancer information. These results supported studies done elsewhere, which identified radio and television among the leading electronic sources of Cancer information(J. Gatune & Nyamongo 2005; Omack et al. 2000; Noh et al. 2009).The internet was a less preferred source of information accounting for 38.8% in comparison to television and radio which accounted for 52 % (Noh et al. 2009). This contradicted a study done earlier in Kenya which showed only 4.3% prevalence in the use of television and radio as sources of information on Cervical Cancer (J. Gatune & Nyamongo 2005). This trend may be attributed to the rising number of households with access to a television and radio in developing countries(Pakenham-Walsh & Bukachi 2009).

This study confirmed reports that mobile phone access was higher than internet access in developing countries (Tryhorn 2009) and Patil (2011) who reported that 64% of all

mobile phone users are found in developing countries. The finding that 96.5% of the respondents had access to a mobile phone indicates a high level of cultural and social acceptance of mobile phones and high potential for their use(PATIL 2011; Drury 2008) . Even though a high percentage of the respondents in this study had access to a mobile phone none of them reported access of internet from their mobile phones. It is possible that the cell phones offer very basic services and may not be internet enabled.

This study found a low level of self reported use of internet among Cervical Cancer patients in Kenya with only 7.1% of patients reporting use of internet in Cervical Cancer management. Few comparable studies if any have been done in developing countries. A study done in Malawi among health care professionals revealed that on 5.3% of respondents had access to internet facilities (Muula et al. 2005). Other studies have been done in economic transitional nations. These are nations which have changed from traditional agricultural to industrial based economies and include; Malaysia, Singapore, South Korea Hong Kong, Indonesia and Thailand. Although the setting may not be comparable to developing countries, they may act as a guide in establishing the trends of internet use as a source of Health information. Noh et al. (2009) found that in South Korea, 38.8% of Cervical Cancer patients aged less than 45 years used the internet as source of information. Muhamad et al. (2011)found that 22.5% of breast Cancer patients in Malaysia used the internet for seeking information on health. Huang & Penson (2008) reported internet access of 16-64% among Cancer patients in developed countries while (Edejer 1998) noted technology accessibility is low in developing countries and rarely will a poor woman in a developing country have access to the internet. Even when the poor woman in a developing country had access to internet, quality of the information accessed, poor connectivity, low capacity to interpret and utilize the information and decision making as well as cultural barriers may still be a hindrance to expected health benefits.

This study concurs with studies done elsewhere which identified lack of computer skills, lack of internet access and low income as a barrier to use of ICT in healthcare (Helft et al. 2003; Crow et al. 2012; Odutola 2003). The identification of potential functions of

internet in management of Cervical Cancer is a good indicator of positive attitude towards e-health. This forms a good basis for developing a needs based e-health system and hence avoid the danger of pushing use of ICT down to the users.

4.5 Conclusion of the Baseline Survey

This study found that only a very small percentage of Cervical Cancer patients had access to the internet. The patients have a positive attitude towards use of internet in management of Cervical Cancer, hence acceptability and uptake of internet use is likely to be high. A large percentage of respondents had access to a mobile phone. This is an indicator of great potential for use of mobile phones in the management of Cervical Cancer, through short messaging services (sms), where internet connectivity is low or unavailable. There is even greater potential to internet use through web access via mobile phones thus, a great promise in use of mobile technologies in management of Cervical Cancer.

4.6 Limitations of the Quantitative study

This study was done in public referral hospitals in Kenya and did not include data from Private institutions and Faith Based Organizations. Even though the two main private hospitals were approached to participate in this study, one declined as they indicated that they rarely received Cervical Cancer clients and hence had insufficient numbers, while the other reported that they had too many research projects going on in the institution at the time and hence could not accommodate one more. The results can therefore not be generalized to the private institutions. Judgemental sampling on the other hand has potential researcher bias. Generalization of these findings is therefore limited.

4.7 Conceptual Model of the Cervical Cancer Management System

In order to understand the cervical cancer management system in Kenya, the variables operating in the system were synthesised into relationship sectors as detailed in figure 4.2.

In order to understand the relationship and interrelation between the sectors there is need to understand the cause-effect linkages between the different variables. The variables in each of the sector are compiled and presented in causal loop diagrams.

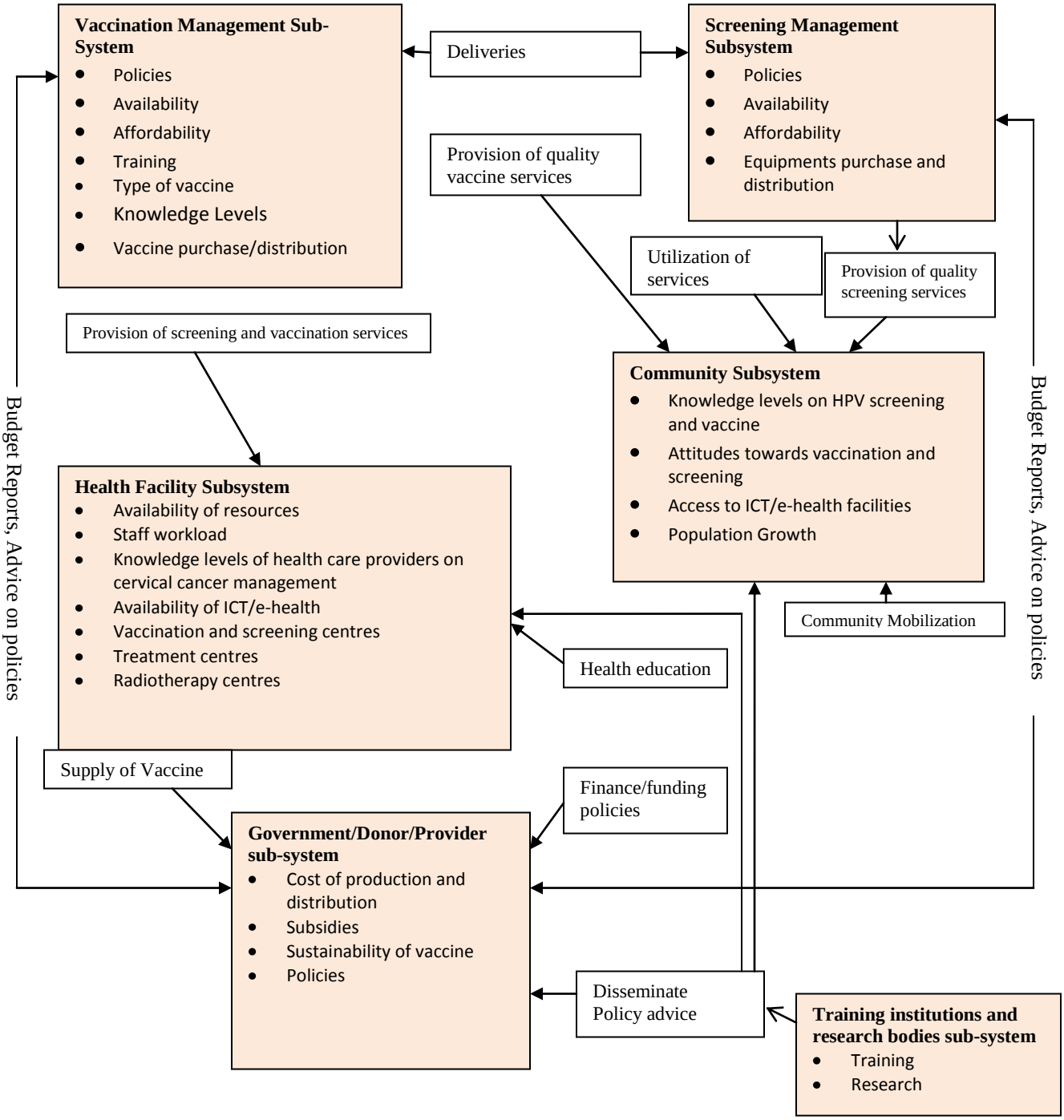


Figure 4.2 Model Boundaries for Cervical Cancer Management in Kenya (Author,2014)

Dynamics Involved in uptake of HPV vaccine,

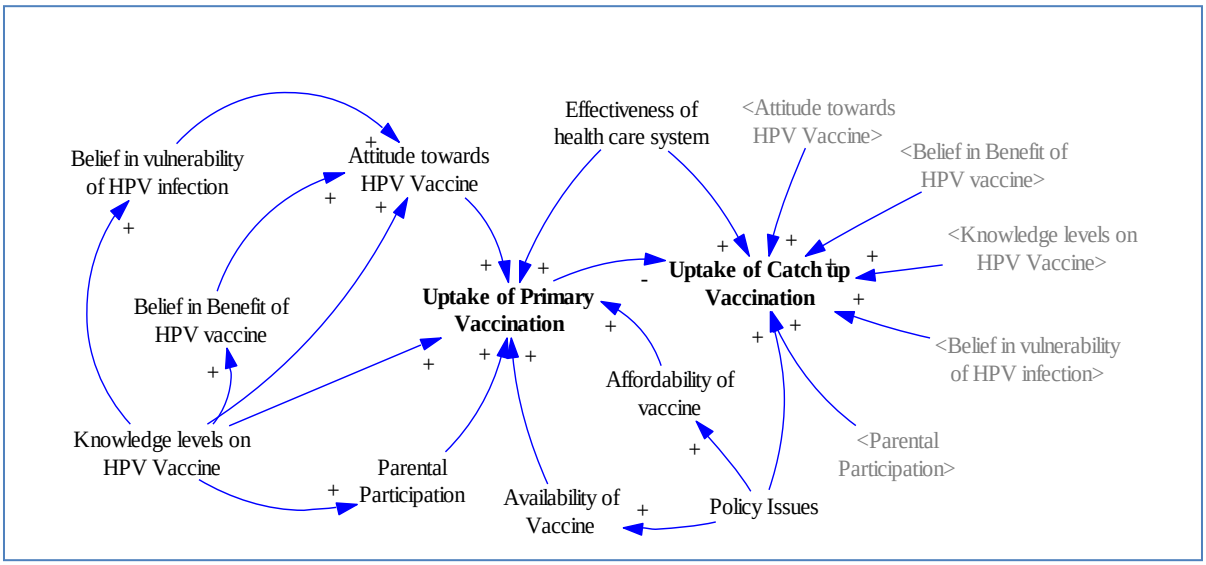


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Figure 4.3 Causal Loop Diagram Showing Demand for HPV vaccine(Author 2014)

Whether given as a primary or catch up vaccination, HPV vaccine uptake is influenced by a number of factors. These include Knowledge level, which increase in belief on Knowledge levels of benefits of HPV vaccine. This belief in benefits, perceive parental approval and belief in vulnerability of HPV infection increase intent of uptake of HPV vaccine both by males and females (D. A. Patel et al. 2012; Galagan et al. 2013; Schmeink et al. 2011). After health education, acceptance of catch up vaccination among general females was 51% while that of 12 years old was highest at 79%(Schmeink et al. 2011). Parental participation is influenced by safety concerns of their daughters with as much as 16% of parents in USA citing this as the reason they would stop their daughters from receiving HPV vaccine(Castillo 2013), while low knowledge levels would reduce the HPV vaccine uptake(Okoronkwo et al. 2012). Other studies however noted no correlation between knowledge levels of HPV and completion of vaccine. In fact, distorted knowledge that HPV could cause HIV/AIDS would drive more recipients to completion of HPV vaccine dose(Stern et al. 2013). A study done in China showed that after health education the number of women willing to vaccinate their daughters increased by 84%(Chang et al. 2013)

Policy issues have been a vibrant debate on HPV vaccination with some of studies advocating for blanket vaccination of eligible women. HPV is primarily transmitted via sexual contact. Hence not all females are at risk; therefore a policy subjecting all the females at whatever age to HPV vaccine may be seen as unethical. It may be more beneficial to only vaccinate those at risk(Zimmerman 2006).

Impact of HPV Vaccine

HPV vaccine may reduce the cases of cervical cancer by as much as 51% (Goldie et al. 2003). Studies done in East Africa found that catch up vaccine would reduce the life time risk cervical cancer risk by 86.5% and reduce the overall number of cervical cancer by 26.5% in Kenya(Kiatpongsan et al. 2012). Other genital cancers have been reported to reduce significantly after HPV vaccination(Ali et al. 2013).Vaccination has been preferred to screening(Koutsky et al. 2003).

SCREENING

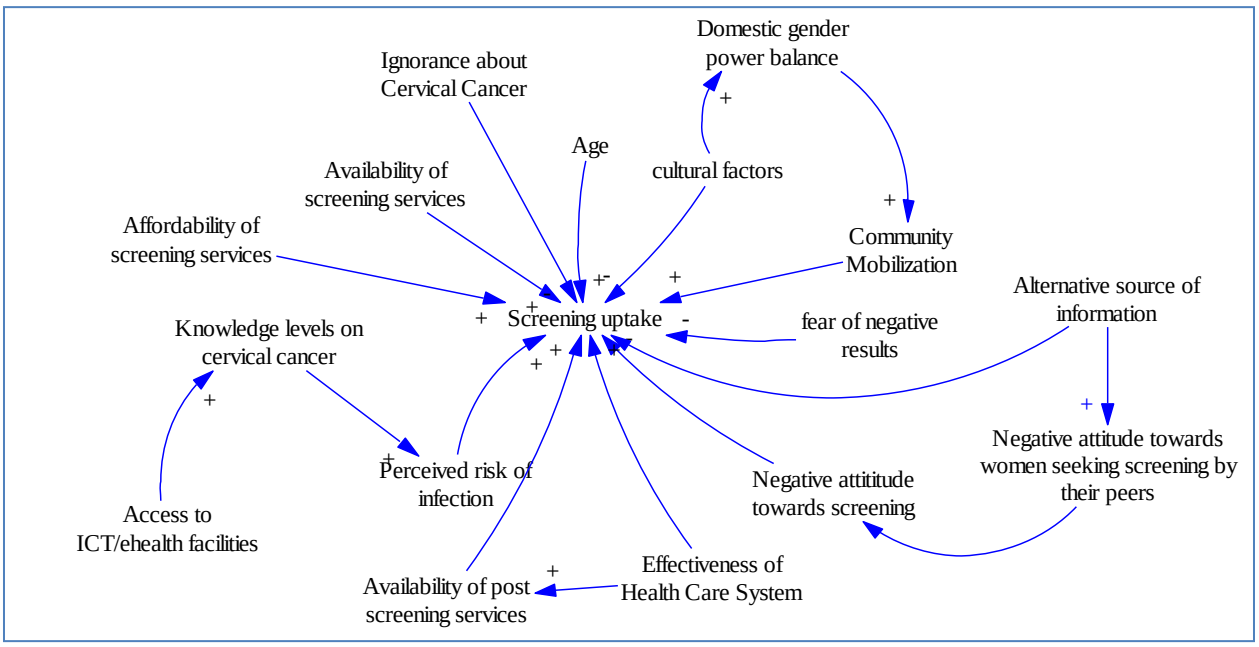

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Figure4.4 Causal Loop Diagram Demand for Screening(Author 2014)

Client related factors

Uptake of screening is influenced by perceived risk of infection, perceived severity of disease, knowledge levels on cervical cancer, fear of screening procedure its self which may go against their cultural practices, age, fear of having negative results and not being able to afford to pay for screening (Sudenga et al. 2013)(Ndikom & Ofi 2012)(Kivuti-Bitok et al. 2013). Other factors associated with uptake of screening services are ignorance about cervical cancer, cultural constructs/beliefs about the illness, domestic gender power relations, alternative authoritative sources of reproductive health knowledge and community participation(Mutyaba et al. 2007). Negative attitude towards women seeking screening services, who may be perceived by their peers as having engaged in unapproved sexual relations is a factors that needs address (Julinawati & Cawley 2013)

Factors related to the Health Care System

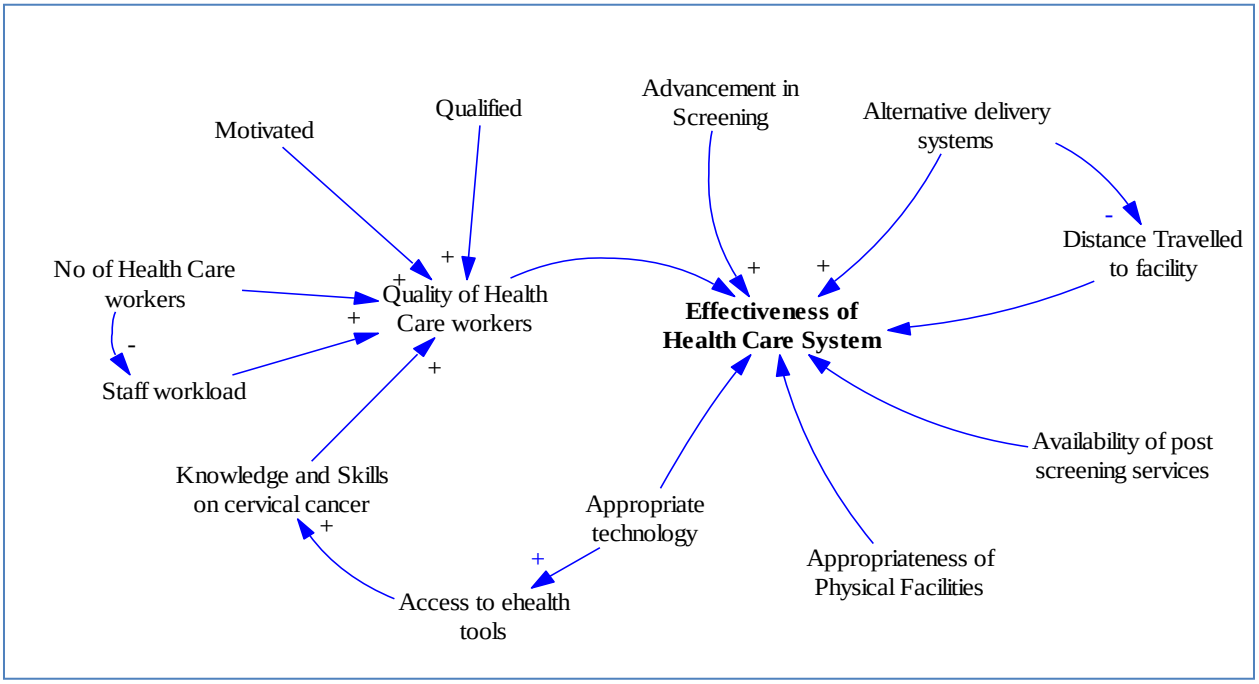

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Figure 4.5 Causal loop Diagram for Factors related to Effectiveness of the Health care Sector (Author 2014)

For screening and vaccination to be effective, health services must be characterized by qualified, motivated and sufficient number of health care workers(Kawonga & Fonn 2008). There is need to strengthen the health care systems not only with adoption of appropriate technological advancement in screening but also in task shifting to enable coverage of screening demands. Structuring of health services delivery and providing alternative delivery methods such as mobile clinics need to be explored (Mutyaba et al. 2007). Other factors such as long distance travelled to access services; post-screening services as well conditions as physical facilities such as cleanliness need to be addressed(Bingham et al. 2003)(Julinawati & Cawley 2013). Unfriendly health care services on the other hand reduce uptake of cervical cancer screening services(Mutyaba et al. 2007), while Appropriate screening policies enhance demand for screening services.

Factors associated with Susceptibility and HPV Infection

Several factors have been associated with HPV infection. Women whose first sexual contact was at less than 20 years have been found to have a 63.5% higher rate of HPV infection(Trang et al. 2012). Circumcised male sexual partners are 37% less likely to have penile HPV infection(Castellsagué et al. 2002). Other risk factors documented include previous abortions, smoking and not using condoms(Trang et al. 2012).

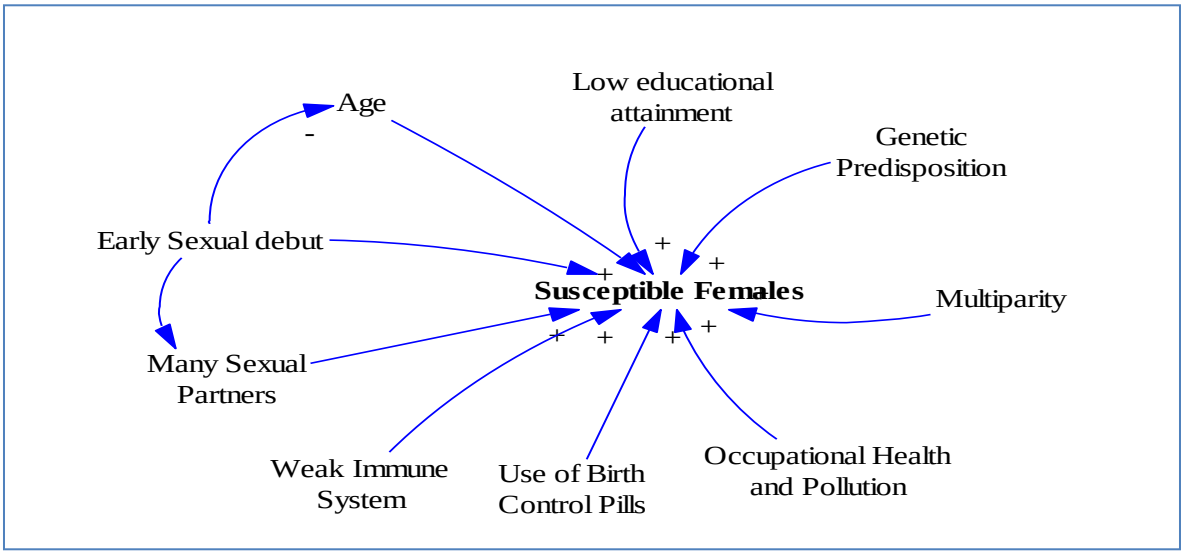

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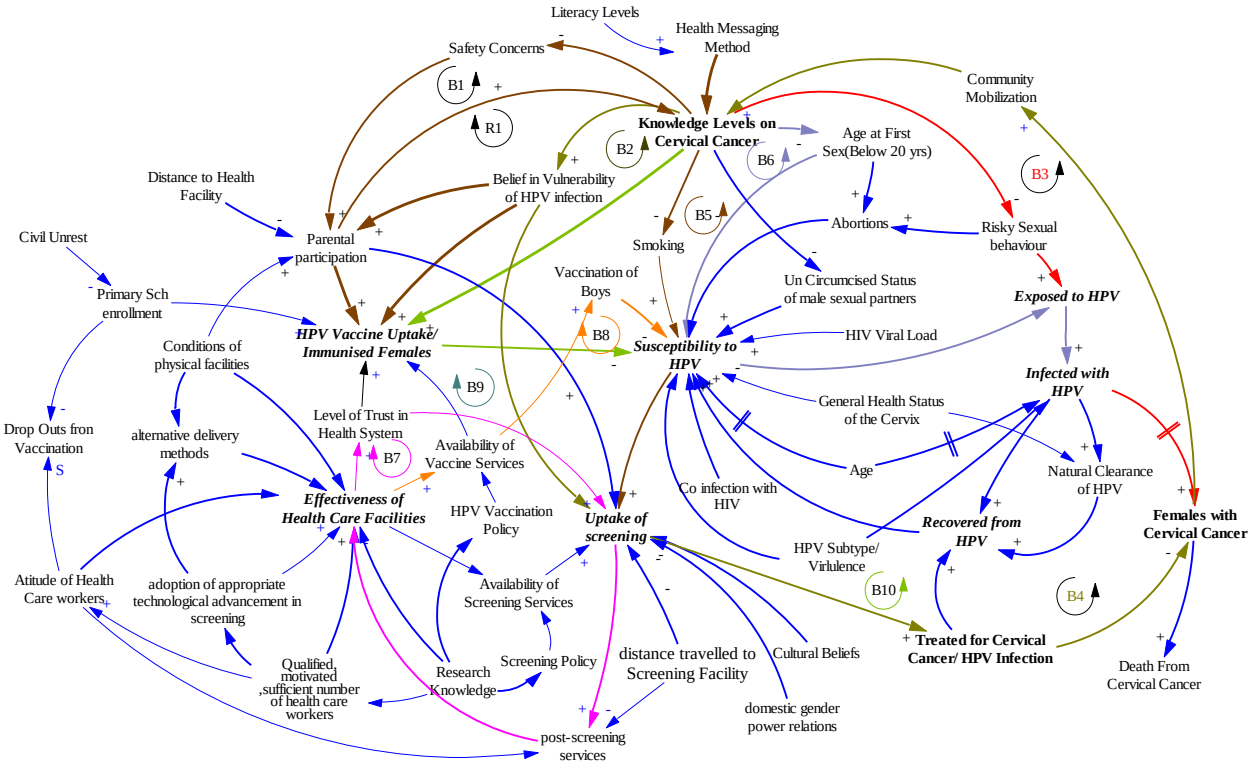
Figure4.6 Factors related to Susceptibility of HPV Infection(Author 2014)

In order to understand the cervical cancer management system, the cause- effect relationships were synthesised into a conceptual model as detailed in Figure 4.7. The system has more than 40 causal- effect loops. However only a few are shown in the diagram.



\+ denotes an increase in the variable in the direction of the arrow

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Figure 4.7 Causal Loop Diagram of Cervical Cancer Management System(Author 2014)

4.8 Inductions drawn from the Causal Loop Diagram

i. Cervical Cancer management system is a complex system with many stakeholders and is inherently composed of numerous feedback loops.

ii. Delays in each of the feedback loops affect the whole cervical cancer management system.

iii. Increase on the knowledge levels of cervical cancer is key in enhancing management of cervical cancer.

iv. Screening and vaccination uptakes are influenced by complex factors, which include effectiveness of the health care system.

v. Motivated and well trained health care worker would increase positive attitudes of the health care worker, hence increasing the overall effectiveness of the care system.

This causal loop diagram presents cause-effect linkages that benefit managerial decision making enabling managers to better understand complex system, identify data that need to be collected and share observations.

The results of field studies and the causal loop diagram are used to develop a simulation model in chapter five.

CHAPTER FIVE: SYSTEM DYNAMICS MODEL OF CERVICAL CANCER IN KENYA

5.0 Introduction

This chapter comprises of a simulation model for cervical cancer management in Kenya. The objective of the model was to show the relationship between different variables, show trends of cervical cancer in Kenya and where possible, show the impact of different proposed interventions.

5.1 Methods

A system dynamics model was developed using iThink™ version 9.1.3 software package. The three basic elements namely stock, flow and converter.

i. **A stock** represented as a rectangular shape is a generic symbol for an anything that accumulates or drains. Stocks can represent a physical entity such as number/ population of women or non physical entity such as quality of care. Stock values depend on the systems past behaviour, hence survival of system depends on the stocks.

Figure 5.1 Stock

ii. **Flow.** The flow represent the rate at which the stock is changing at any given instant, they either flow into a stock (causing it to increase) or flow out of a stock (causing it to decrease). They provide the dynamics of the system

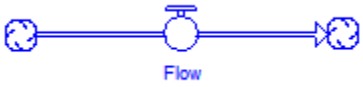


Figure 5.2 Flow

iii. **Converter.** These represent auxiliary valuables. They hold values of constants and defined external inputs. They represent the decision process in the system.

Figure 5.3 Converter

iv. **Connector(s).** The connectors are curved lines that connect model elements. There are two distinct types of connector: the action connector and the information connector. Action connectors are signified by a solid, directed line Information connectors are signified by a dashed line. Connectors show how parts of a system influence each other.

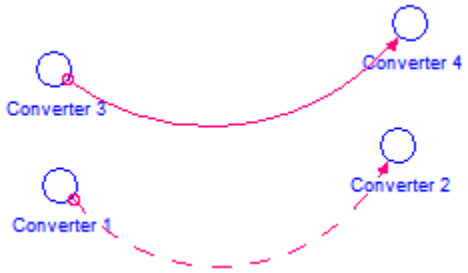


Figure 5.4 Connector(s)

v. Types of equations supported.

The types of equations supported by ithink^{TM} software illustrate the general flow from one stock to the next is represented as;

$$Stock\ (t) = \int_{t_0}^{t} inflow - outflow \ * dt + Stock(t_0) \qquad (5.1)$$

where

Where t represents the stock, $t_0$represents initial value of stock;dt is a time step which represents the rate of change with respect to time.

This is simplified by the ithink^{TM} software to;

$$S(t)=S(t-dt)+ (1-0)dt \qquad (5.2)$$

5.2 Overview of the Dynamic Model Structure and its use.

The model comprised of a population of aging chain of girls/women with or without HPV infection.

Boxes represent population stock; clouds represent births and deaths, Single arrows represent flows from one stock to the next while single circles with linking smaller arrows represent causative/ influencing factors.

The model is an open, dynamic, deterministic, lumped compartmental model consisting of stocks and flows. The female population was stratified according to vaccination and screening status. A set of ordinary differential equations were used as SD is a system of differential equations solved using Integral Calculus approximations.

The choice of model and software took into consideration the availability of data, availability of software, background skills of the researchers, structure of Cervical Cancer, management process as well as objectives of the study.

The general population structure of the model is as shown in Figure 5.6while the Female population structure is shown on Figure 5.7. Data was derived from previous published literature, Cancer registries and where data was not available experts opinion was sought. This methodology is in line with documented methodologies of(Homer & Hirsch 2006)

Appendix 1 provides the details of the values of variables used and their sources.

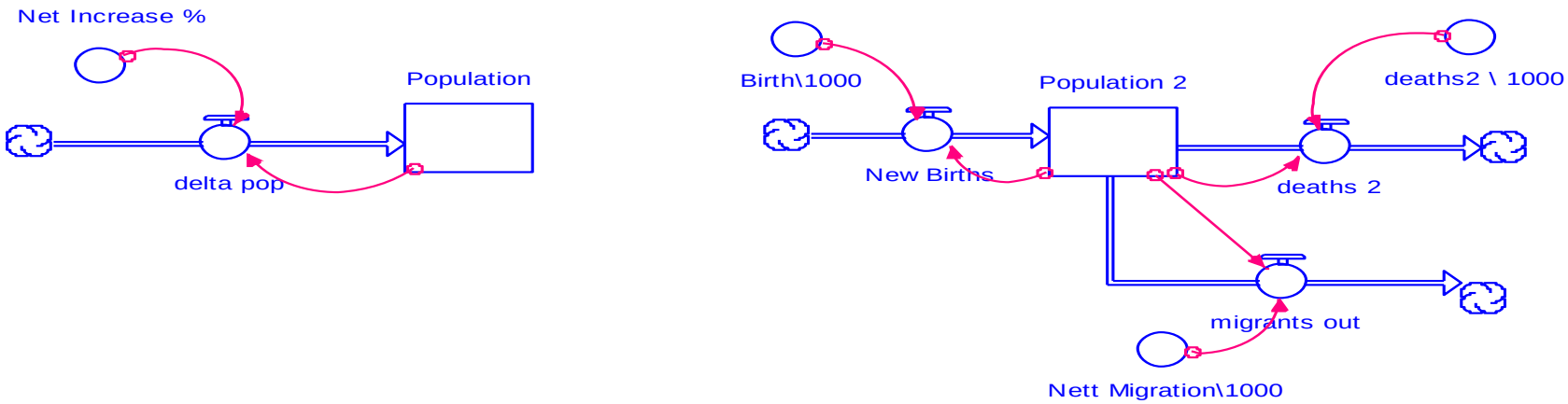


Figure 5.5 Overview of General Population Sector.(Author 2014) * reffer to Section 5.1 for meaning of symbols

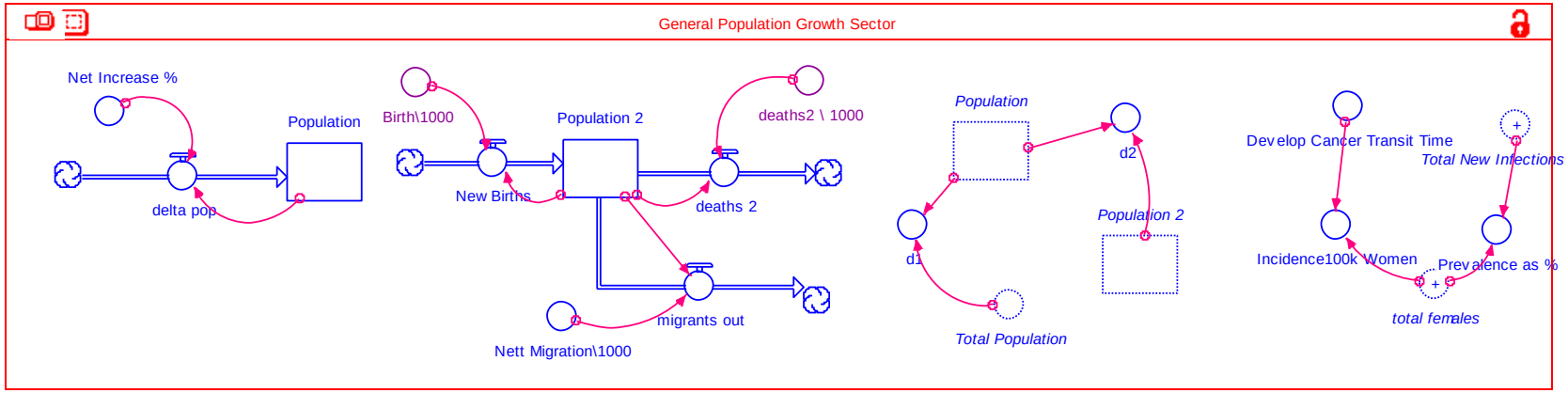


Figure 5.6 General Population Sector(Author 2014)

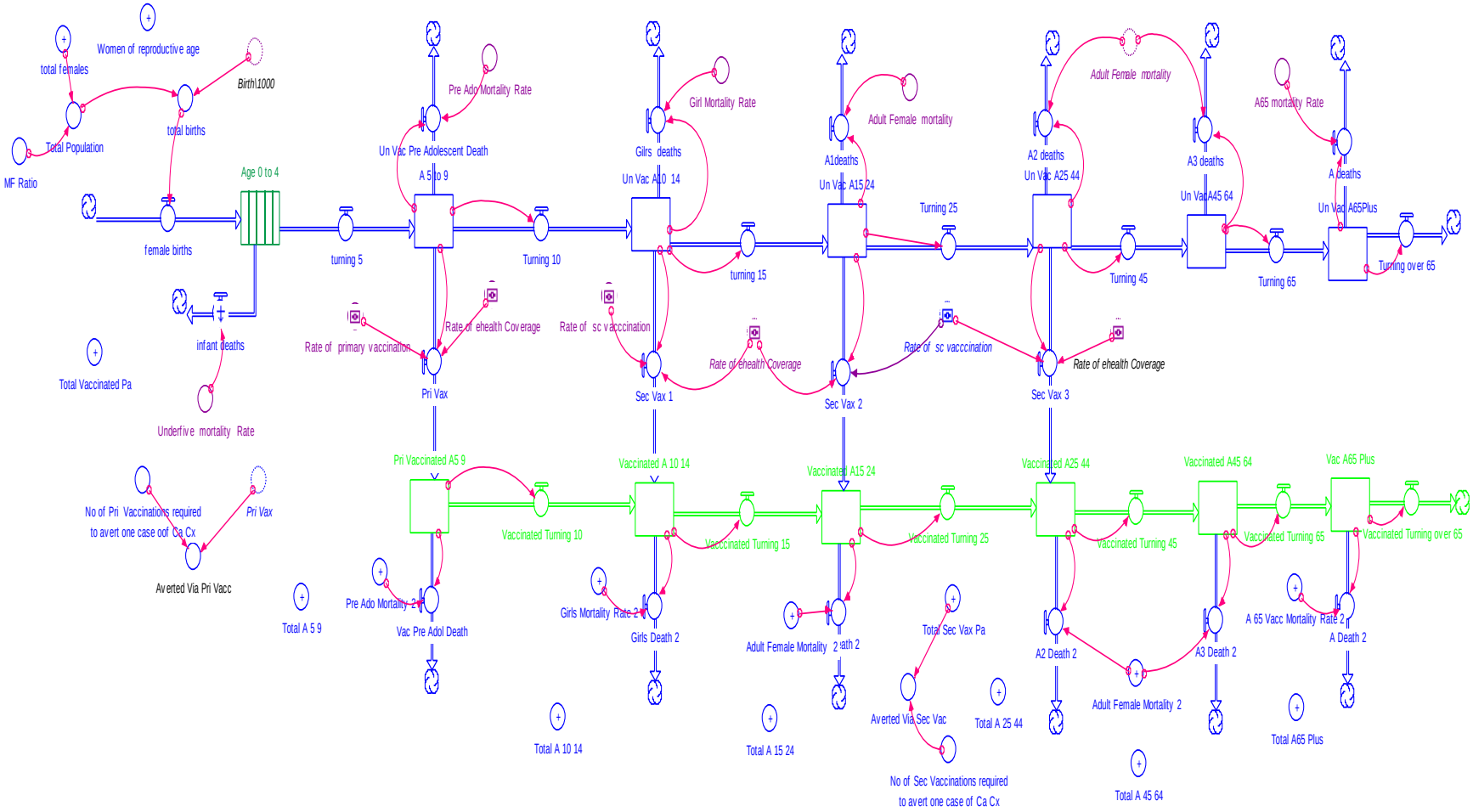


Figure 5.7. Schematic Snapshot of the Female Population Sector and Vaccination Sector (Author 2014)

5.3 Stratification of the Female Population

The population of females is stratified by age group, primary vaccination status, secondary vaccination status, screening status and HPV infection status. The health states are mutually exclusive. The health states characterized by vaccinated or non vaccinated status, HPV infection status, stage of Cancer and screened or non screened, detected or undetected Cancer. Aggregate data was utilized. The population of interest consists of girls born and living in Kenya assuming a birth rate of 3.5%. The females were divided into seven age groups; [0-4], [5-9], [10-14], [15-24],[25-44], [45-64] and over 65 years based on age groups of published data on Cervical Cancer(WHO/ICO 2010). The girls are then vaccinated by age 9 (at beginning of adolescence). This is because the conversion of dormant columnar epithelium of endo-Cervical canal into squamous epithelium has not yet occurred, hence the cells are still not susceptible to HPV infection(Martens et al. 2009; Di Bonito & Bergeron 2012). It is also assumed that at this age the girls are not yet sexually active. The efficacy of the vaccine was assumed to be lifelong. The rate of Primary vaccination is a factor of accessibility and the attitude of care givers towards the primary vaccination. It is assumed that the rate of use of e-health tools will proportionally affect the attitudes. Hence, a high rate of access to e-health tools will translate to a population with more information and knowledge on HPV vaccine and hence a positive attitude towards vaccination. The [5-9] nine years age group is stratified into the Primary vaccinated and non primary vaccinated. The efficacy of the vaccine is assumed to be lifelong hence life time immunity against HPV once vaccinated. The population of girls who received primary vaccination permanently exist the model.

The model then follows up on the girls who did not receive primary vaccination. It is assumed that all the non primary vaccinated girls are exposed to HPV infection. As the girls progress through the aging chain, they are eligible for catch up or secondary vaccination between the ages of [10-44] years. The rate of secondary vaccination is also assumed to be a factor of accessibility, coverage of use of e-health tools and hence knowledge and attitude towards catch-up vaccination. Those receiving secondary vaccination permanently exit the model, assuming lifelong efficacy of the Vaccine. .

The model further assumes;

i. That all the females seeking vaccination will complete the full dose of vaccine.
ii. That 38.8% of all the never vaccinated females will acquire HPV infection based on the prevalence of HPV in Kenya.
iii. That only the females who missed both Primary and secondary vaccination are eligible for screening against HPV.
iv. That only a proportion of the women who missed both primary and secondary vaccination will undergo Cervical Cancer screening later in life while others will miss this vital intervention.
v. That all the HPV infections among the screened women will be detected and subjected to treatment.
vi. That HPV infection among the unscreened women will progress naturally except these women will not benefit from treatment.
vii. That a small proportion of the population of women with unscreened /undiagnosed Cervical Cancer may have 'accidental' opportunity for screening in the course of their seeking health services.
viii. That depending on the stage of this 'accidental' screening and diagnosis, they move to the group of screened and diagnosed population and subsequently benefit from treatment interventions.

The model then follows up on the prognosis of the population women with diagnosed and the non diagnosed Cervical Cancer. This group of women exits the model permanently through death.

The main input variables are Primary vaccination, secondary vaccination, screening and use of e-health tools. Treatment is considered in contextual setting. The potential impact fore mentioned interventions on reduction of Cervical Cancer was studied. The main output variables were; the number of women receiving primary and secondary vaccination, number of women screened against HPV, averted cases of Cervical Cancer and mortality rates from Cervical Cancer. Disability adjusted Life years (DALYS) were used to estimate the burden of disease. DALYS are used as an indicator of burden of a

particular condition. DALYS are calculated by adding the total sum of years lived with disability caused by the condition ,otherwise referred to as Years of Life lived with Disability(YLD) and years lost due to early death as a consequence of the disease condition; Years of Life Lost(YLL). These values are based on the present value of years of future lifetime. DALYs adjustment is based on the severity and duration of illness. One DALY is equivalent to loss of one year, which would otherwise have been lived in full health. DALYs therefore are an indicator of something lost and hence the aim of interventions is to reduce the DALYs. DALYS are a recommended measure of health benefits in developing countries(Fox-Rushby & Hanson 2001).

The prognosis of Cervical Cancer with and without treatment is as indicated in Table 1. It is assumed that once the disease has progressed to stage 3, treatment options are geared towards improving quality of life and palliative care rather than elimination of the infection (Were et al. 2010).

The indicators for this model include incidence rates of Cancer, expected rise in Cancer cases, averted cases of invasive Cancer and DALY's estimates. The effects of different interventions were then studied and compared. Synergy between two or more alternative strategies was evaluated.

5.4 Validation and verification of the SD Model

The model was validated through Animation, Face Validity, predictive validation and extreme condition tests(Wakeland & Hoarfrost n.d.). The demographic sector of the model was first validated through checking if it could produce close estimates of referenced demographic characteristics elsewhere (http://esa.un.org/unpd/wpp/unpp/p2k0data.asp). Error of Estimation of 30% was deemed acceptable level. The error of estimate may be attributed to imperfect calibration and unaccounted for environmental interferences. Calibration is aimed at minimizing the error of Estimate (Corner 1999). Calibration was done by adjusting the parameter values.

5.4.1 Sensitivity Analysis

Sensitivity analysis assessed the effect of parameter variations on model results. The level of screening, primary and secondary vaccinations was varied from 0.001 to 1.0. A slider input device was provided in the interface of the model. For accurate integration of equations, the forth order Runge Kutta and a DT (Step Size) of 0.25 were applied.

5.4.2 Model Simulation

Simulations were then run with different levels of parameters. The population dynamics in relation to Cancer are simulated over a period of 50 years (2010-2060). It is assumed that with a life expectancy of 60.9, the model follows a birth cohort to estimated life expectancy. These experiments attempt to demonstrate the current landscape of Cervical Cancer prevention and control strategies in Kenya as well as simulate possible future landscapes. A number of 'what if' scenarios were simulated.

The prognosis of Cervical Cancer with and without treatment is as indicated in Table 1. It is assumed that once the disease has progressed to stage 3, treatment options are geared towards improving quality of life and palliative care rather than elimination of the infection (Were et al. 2010).

The simulated results of different proposed interventions are presented. The policy experiments include;

i. Business as usual (base-case) scenario.
ii. Varying the levels of primary vaccination.
iii. Varying the levels of catch up/secondary vaccination.
iv. Varying the levels of screening.
v. Varying e-health coverage rates.
vi. Combining and varying screening, vaccination and e-health coverage levels. .

Even though the model can perform different levels of experiment values, for the purposes of this paper, WHO-CHOICE standard geographical coverage of 50%, 80% and 95% of eligible cases receiving intervention are utilized. A 'realistic' scenario of 30% coverage was also simulated. This was based on a study done in France (Ribassin-Majed et al. 2012). The results were compared against base-case scenario.

RESULTS OF THE SD MODEL EXPERIMENTS

Simulations were done using ithink [Tm], however the outputs were exported into excel for ease of reference to the readers who were not familiar with ithink [Tm], software and/or were not willing to explore ithink software outputs. The ithink [Tm] model as well as outputs are also available on the CD attached.

POPULATION TRENDS

Figure 5.8 shows the general population trends . The data generated from simulation of this model was (Simulated Population) was compared with Kenyan population data as projected by the United Nations . This projected data is available on (http://esa.un.org/unpd/wpp/unpp/p2k0data.asp). The results as well as the respective error of estimations are shown in Table 8 and Table 9.

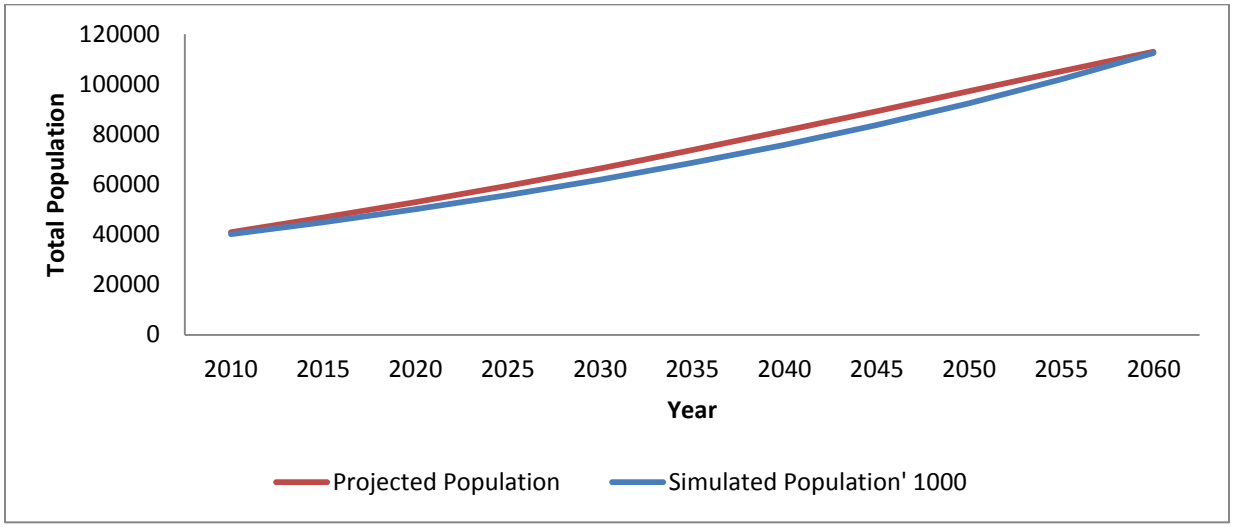


Figure 5.8. General Population Trends in Comparison to Population Projected Using Known Methods(Author 2014).

The error of estimate can be attributed to the changing birth rate over time due to family planning practice, increasing levels of education, urbanization and economic empowerment(Blacker et al. 2005). The model however utilized a constant birth rate (3.2%). While Figure 5.9 shows the trends of Women population in comparison to the general population.

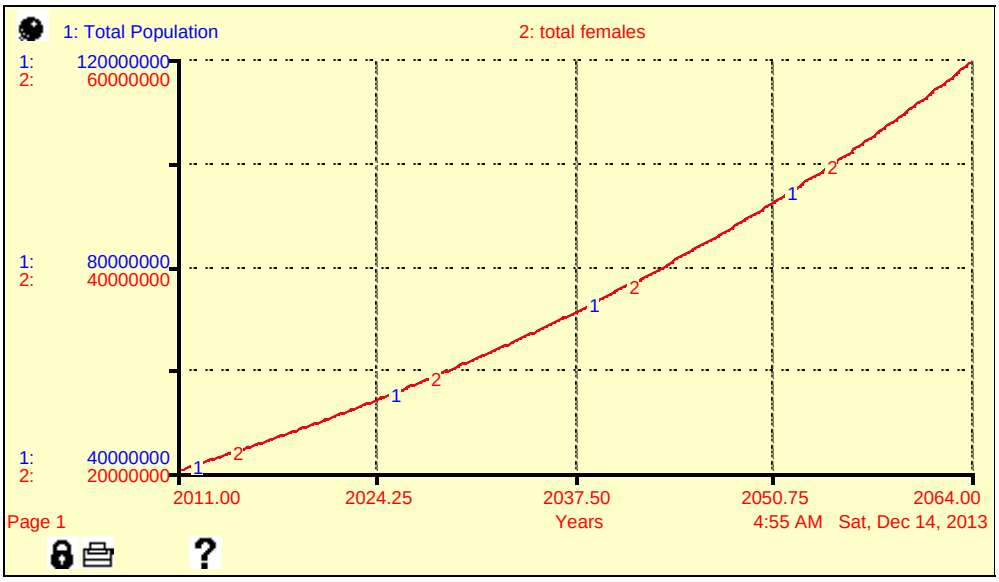


Figure 5.9 trends of Women population in comparison to the general population.

A comparison of the projected population trends and Simulated Population trends is shown in Table 5.1 and Table 5.2.

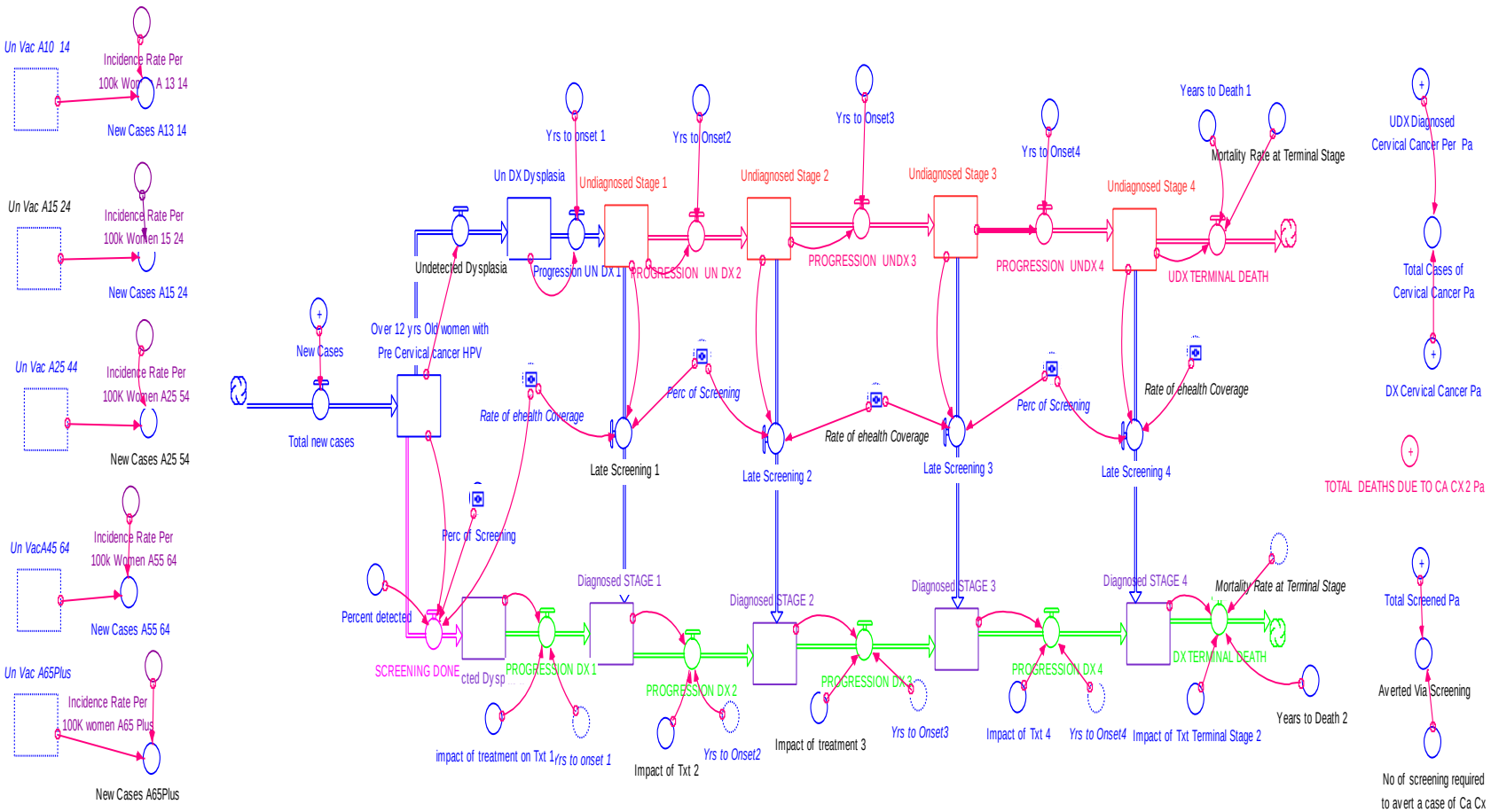
Table 5.1 Comparison of Projected and Simulated Total Population

Kenya	**Projected Population** is derived from Published data.
Population (thousands)	**Simulated Population** is an output from the SD model developed from this study.
Medium variant	
2010-2060	

Year	Projected Population	Simulated Population	Simulated Population' 1000	Error of Estimation%
2010	40909	40,158,000.00	40,158	-1.8
2015	46749	44,889,025.02	44,889	-4.0
2020	52906	50,121,709.73	50,122	-5.3
2025	59386	55,818,815.46	55,819	-6.0
2030	66306	62,004,661.87	62,005	-6.5
2035	73666	68,727,085.45	68,727	-6.7
2040	81354	76,052,305.05	76,052	-6.5
2045	89219	84,060,118.89	84,060	-5.8
2050	97173	92,840,240.50	92,840	-4.5
2055	105071	102,490,087.78	102,490	-2.5
2060	112869	113,113,961.35	113,114	0.2
		Standard Error of Estimate		1947

Table 5.2 Comparison of Projected and Simulated Female Population in Specific Age Groups

Year	Age Group	Projected Population	Simulated Population	Error of Estimation	Year	Age Group	Projected Population	Simulated Population	Error of Estimation
2010	0-4	3345	3045	-9.0%	2035	15-24	7163	6271	-12.4%
2015	0-4	3584	2664	-25.7%	2040	15-24	7628	6831	-10.5%
2020	0-4	3792	2972	-21.6%	2045	15-24	8171	7492	-8.3%
2025	0-4	4024	3314	-17.7%	2050	15-24	8770	8252	-5.9%
2030	0-4	4315	3684	-14.6%	2055	15-24	9316	9107	-2.2%
2035	0-4	4606	4087	-11.3%	2060	15-24	9750	10059	3.2%
2040	0-4	4849	4525	-6.7%	2010	25-44	5041	4929	-2.2%
2045	0-4	5029	5003	-0.5%	2015	25-44	6129	5721	-6.7%
2050	0-4	5183	5527	6.6%	2020	25-44	7057	6527	-7.5%
2055	0-4	5290	6103	15.4%	2025	25-44	7911	7329	-7.4%
2060	0-4	5396	6736	24.8%	2030	25-44	8879	8112	-8.6%
2010	5-9	2887	2887	0.0%	2035	25-44	10018	8902	-11.1%
2015	5-9	3276	3227	-1.5%	2040	25-44	11348	9735	-14.2%
2020	5-9	3525	3217	-8.7%	2045	25-44	12663	10647	-15.9%
2025	5-9	3742	3451	-7.8%	2050	25-44	13802	11664	-15.5%
2030	5-9	3981	3797	-4.6%	2055	25-44	14850	12803	-13.8%
2035	5-9	4277	4206	-1.7%	2060	25-44	15936	14080	-11.6%
2040	5-9	4573	4662	2.0%	2010	45-64	2013	2013	0.0%
2045	5-9	4821	5163	7.1%	2015	45-64	2376	2723	14.6%
2050	5-9	5004	5711	14.1%	2020	45-64	2822	3445	22.1%
2055	5-9	5159	6312	22.3%	2025	45-64	3471	4177	20.3%
2060	5-9	5266	6970	32.4%	2030	45-64	4349	4915	13.0%
2010	10-14	2421	2421	0.0%	2035	45-64	5352	5656	5.7%
2015	10-14	2855	2832	-0.8%	2040	45-64	6228	6404	2.8%
2020	10-14	3250	2993	-7.9%	2045	45-64	7070	7172	1.4%
2025	10-14	3505	3145	-10.3%	2050	45-64	8033	7976	-0.7%
2030	10-14	3724	3390	-9.0%	2055	45-64	9167	8833	-3.6%
2035	10-14	3965	3717	-6.3%	2060	45-64	10479	9760	-6.9%
2040	10-14	4263	4105	-3.7%	2010	65+	580	580	0.0%
2045	10-14	4560	4544	-0.4%	2015	65+	703	687	-2.3%
2050	10-14	4809	5029	4.6%	2020	65+	895	861	-3.8%
2055	10-14	4992	5561	11.4%	2025	65+	1121	1068	-4.7%
2060	10-14	5148	6145	19.4%	2030	65+	1356	1292	-4.7%
2010	15-24	4204	4204	0.0%	2035	65+	1617	1525	-5.7%
2015	15-24	4509	4591	1.8%	2040	65+	1987	1764	-11.2%
2020	15-24	5192	5046	-2.8%	2045	65+	2540	2009	-20.9%
2025	15-24	6026	5425	-10.0%	2050	65+	3283	2261	-31.1%
2030	15-24	6684	5811	-13.1%	2055	65+	4119	3120	-24.3%
					2060	65+	4888	3498	-28.4%



Un Vac Unvaccinated Yrs Year(s)
Un Dx Undiagnosed Dx Diagnosed

Figure 5.10 HPV Infection and Screening Sector (Author 2014)

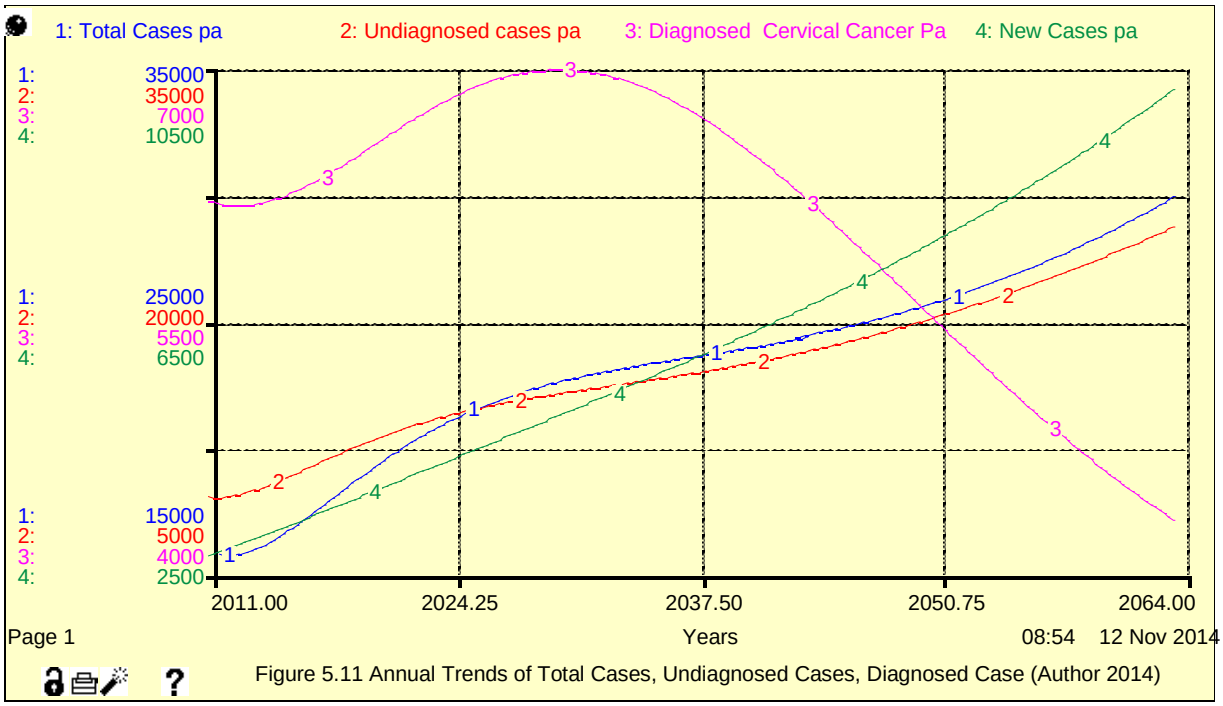


Figure 5.11 Annual Trends of Total Cases, Undiagnosed Cases, Diagnosed Case (Author 2014)

Figure 5.11 shows simulated Annual trends of diagnosed, undiagnosed, new cases, total Cases of Cervical cancer and total deaths due to cancer. This is taken as the base case scenario, using age standardized incidence rates per 100000 Population. The e-health coverage rate of 7.5% established in the first phase of study was used. The rate of primary and secondary vaccinations could not be established and expert opinion (done in Phase one) estimated coverage at 0.1% and 0.3% respectively and the rate of screening was taken at 3.2% (WHO/ICO 2010). A birth rate of 3.2 and an average life expectancy rate of 60.9 years were utilized in simulation. This trends closely Mirrors other projections which estimated the annual death rate among cervical cancer clients at 65%, and estimated 2454 new and 1676 deaths each year (Of et al. 2011).

Figure5.12 shows trends of new cases of cervical cancer at status quo. The women aged 55 to 64 years have the largest number of new cases of cervical cancer. This age group also has the highest level of aged specific incidence rate estimated at 105/100000 women(WHO/ICO 2010).

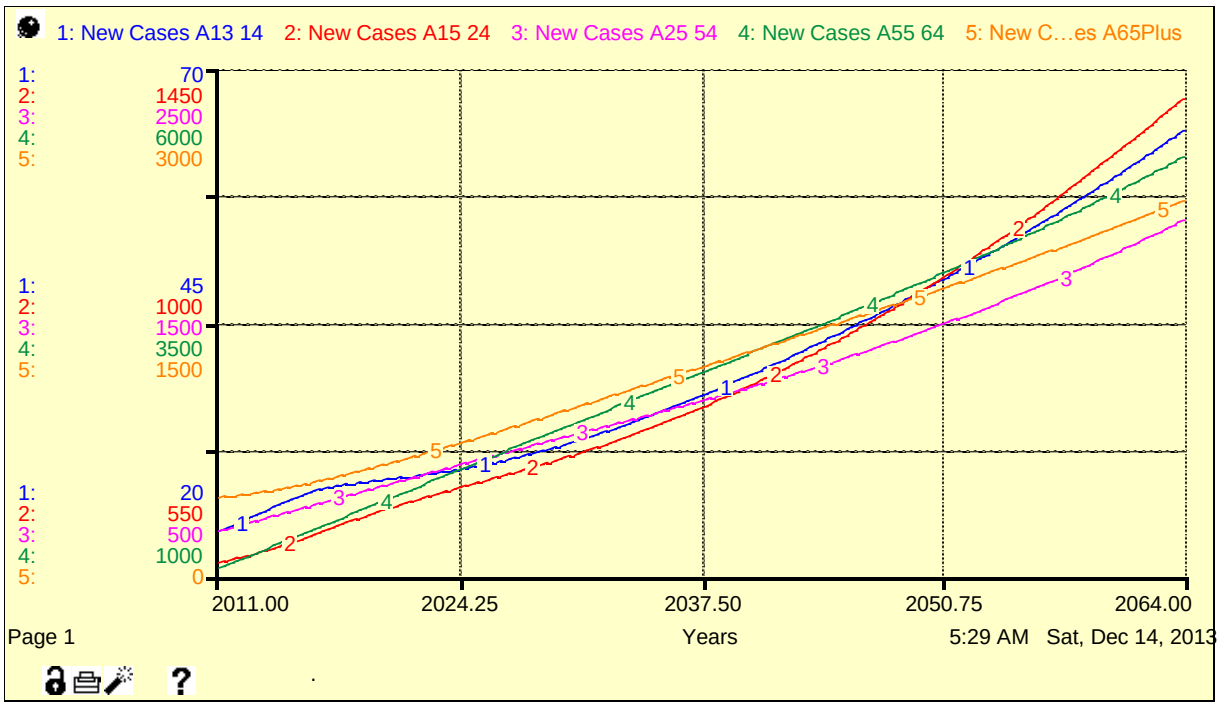


Figure 5.12 Trends of New Cases of Different Age Groups at Base Case Scenario

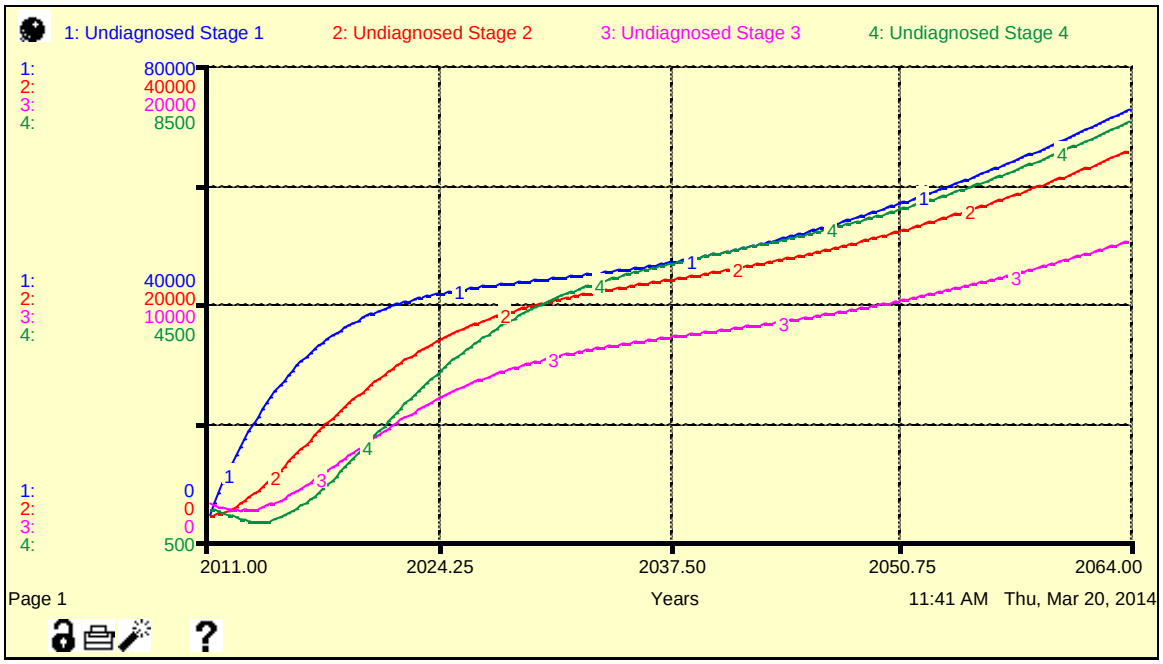


Figure 5.13 Trends of undiagnosed Cases of Cervical Cancer

Figure 5.13 shows the trends of Undiagnosed Cervical Cancer among women who missed primary vaccination, secondary vaccinations and screening. Undiagnosed stage 1has the highest number of undiagnosed patients. This may be attributed to the slower rate of disease progression from stage one to stage two. Undiagnosed Stage 4 has the least number of clients among the undiagnosed group. This may be attributed to the fast rate of progression from stage 3 to stage 4 as well as the high death rate

(Approximately 65%) of clients at this stage as the clients rarely benefit from Medical Intervention.

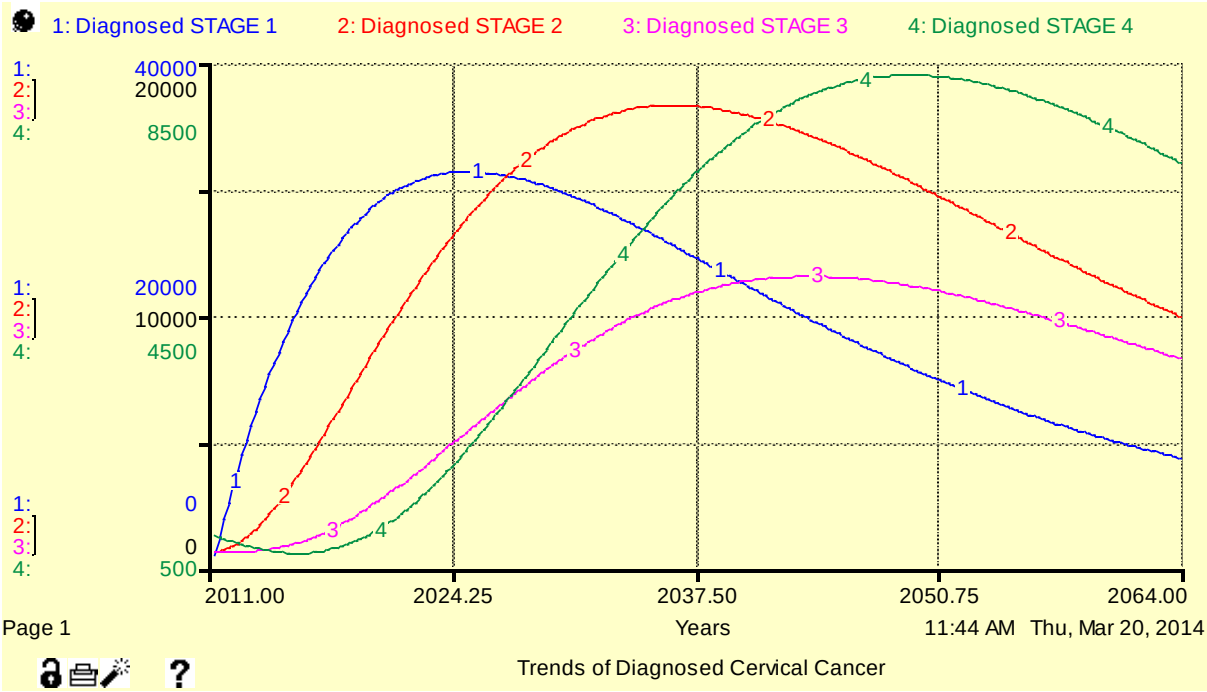


Figure 5:14 Trends of Diagnosed Cervical Cancer

Fig 5.14 Shows trends of Cases of Diagnosed Cervical Cancer. For diagnosed cervical cancer patients, majority are in stage one. This may be attributed to the treatment impact at this stage with probability of regression and Cure. Diagnosed Stage 4 has more clients compared to the undiagnosed stage 4. This may be attributed to early intervention at stage one and two among the diagnosed group as well as delayed death at stage four of diagnosed patients due to treatment interventions. The treatment interventions delay progression from one stage to the next.

5.4.3 Output Indicators

Cost Utility analysis was used as indicated by changes in Disability Adjusted Life Years [DALYs] and Total Cost of averted DALYs. DALYs consisted of Years of Life Lost (YLL) and Years of Life Lived with Disability (YLD).

The cost per averted DALY was based on simplified calculation based on the total cost of intervention divided by the DALYs averted.

DALYs = YLD + YLL. Fox-Rushby and Hanson(Fox-Rushby & Hanson 2001) calculation method was adopted.

	YLD
[K] Age weighting modulation factor	1
[W] is a constant	0.1658
[y] Discount rate expressed as decimals	0.03
[Alpha] Age at Diagnosis of Cervical cancer	45
[Beta] Parameter for age weighting Function	0.04
[l] Average Duration of Disability	15
[D] Disability Index of cervical cancer	0.81
	YLL
[alpha 2] Age of death	60.7
[life2] Standard expectation of life at age of Diagnosis with Cervical cancer	15.7

IMPACT OF DIFFERENT INTERVENTIONS ON DALY TRENDS

The model sort to estimate the impact of combined intervention strategies on the trends of DALYs and averted DALYs

i. At a base case scenario,
ii. 30% (realistic Coverage) of Primary Vaccination, Secondary Vaccination and screening.
iii. 50% Coverage of Primary Vaccination, Secondary Vaccination and screening.
iv. 80% Coverage of Primary Vaccination, Secondary Vaccination and screening.
v. 95% Primary Vaccination, Secondary Vaccination and screening.

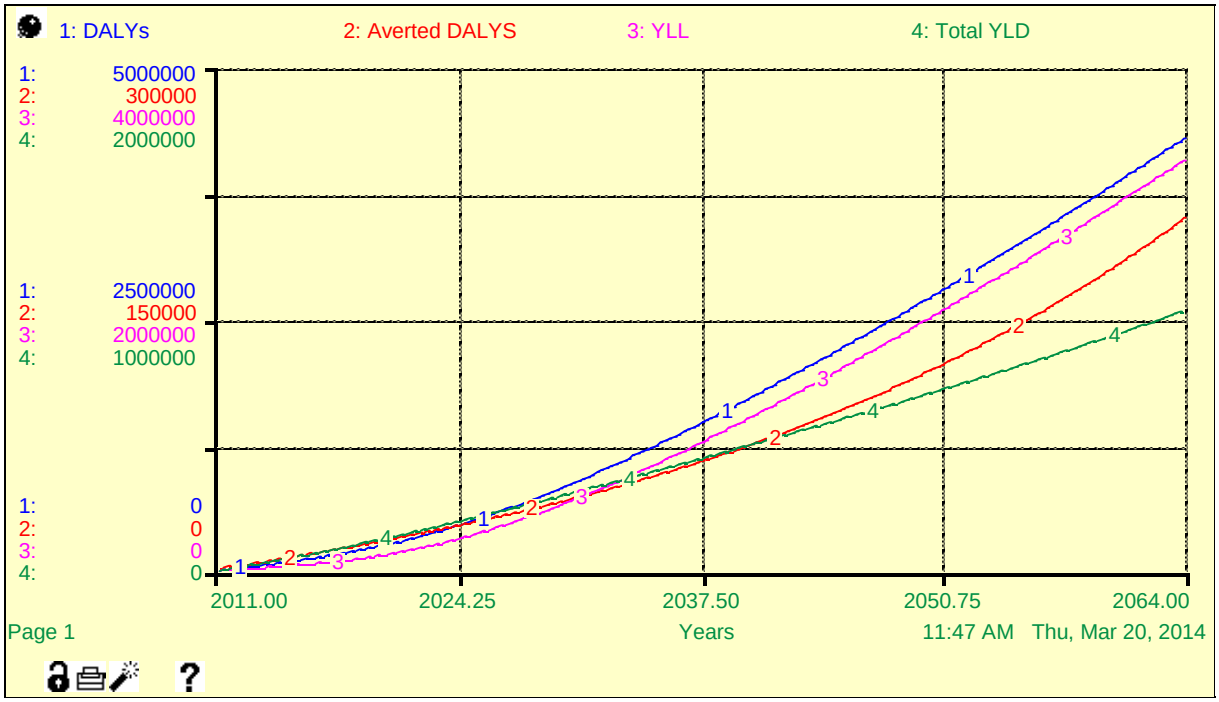


Figure 5.15 Trends on DALYs and DALYs Averted Base Case Scenario

Figure 5.15 demonstrates expected trends of DALYs and DALYs averted at Base Case Scenario. In the year 2060, Only 215,589 DALYs would be averted at the current state of intervention in management of cervical cancer. At a realistic coverage of 30% of the three interventions, 3,222,424 DALYs will be averted, while 2,958,736 would be averted at 50% coverage levels with 80% and 95% coverage levels accounting for 2,674,020 and 2,433,440 respectively. This would then mean that even a realistic coverage of the three interventions would be effective target in management of Cervical Cancer in Kenya.

Figure 5.16shows a general reduction in DALYs with increase in coverage rates a reflection of the impact of the three traditional interventions.

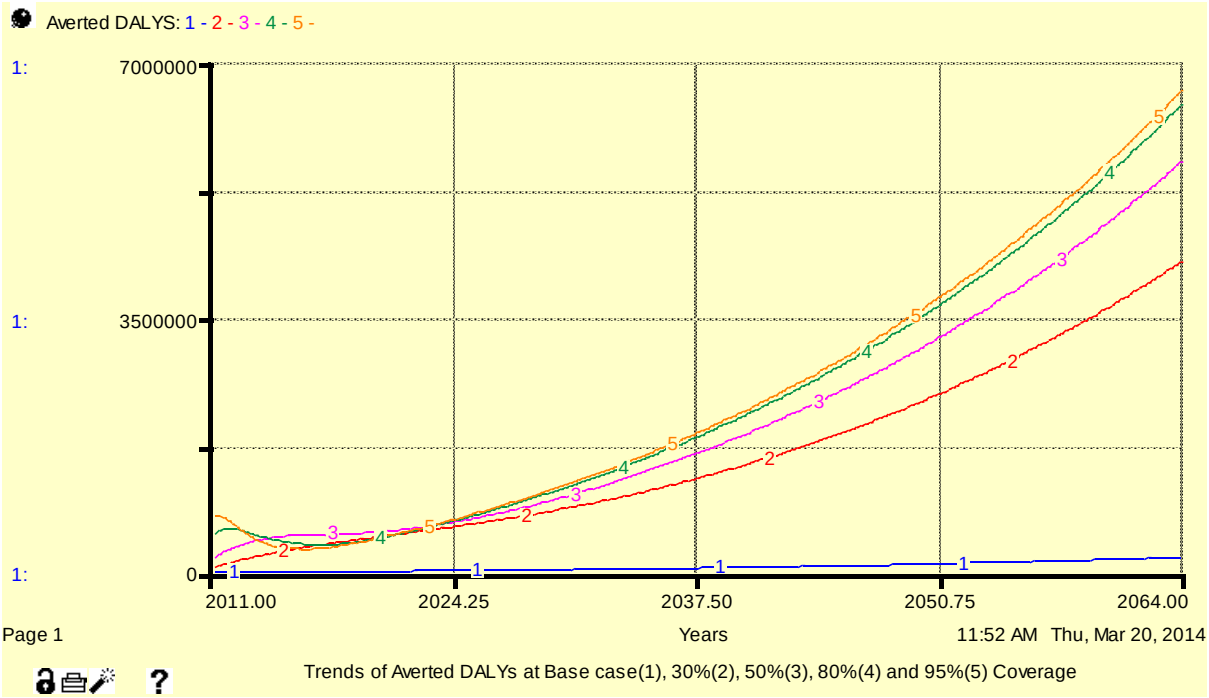


Figure 5.16. Trends of DALYs at Base case Scenario, at 30%, 50%. 80% and 95% Coverage rates of the three Interventions.

Impact of Primary Vaccinations

The model sought to estimate the impact of primary vaccination. In this model, Primary vaccination refers to vaccination at 9 years of age only. Other models have set primary vaccination from age 9 to age 12(De Visser et al. 2011; Situations 2010; Milne et al. 2007). It has been reported that 250 vaccinations among girls less that 12 years are required to avert one case of cervical cancer assuming immunity of a life span and 600 with waning immunity after 10 years (Sanders & Taira 2003).

The impact of different rates of Primary vaccination coverage.

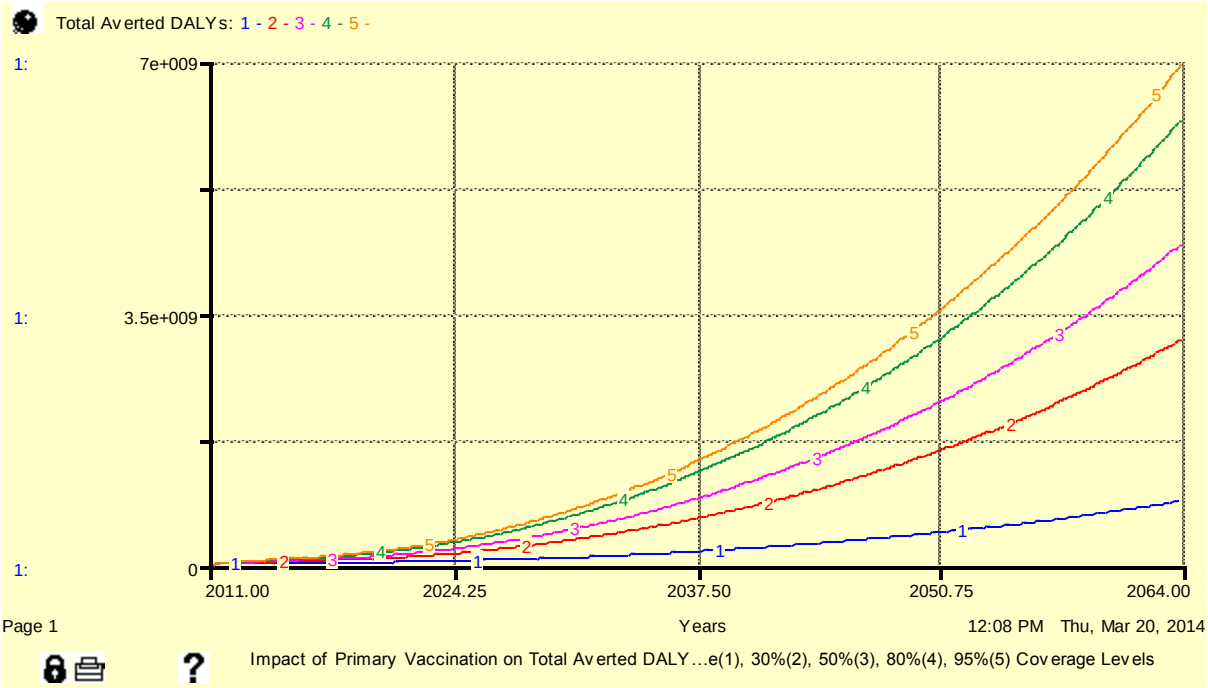


Figure 5.17. Impact of Primary Vaccination

Figure5.17show predicted levels of DALY in different levels of coverage of primary vaccination coverage. The DALYs averted increase with increase in coverage of Primary Vaccination.

Impact of Secondary Vaccination

The impact of Secondary Vaccination on DALYs averted was simulated. It was noted that 324 Secondary vaccinations are required to avert one case of cervical cancer among eligible women(Brisson 2007). This is a 29.6% increase in the number of vaccinations required (in comparison to primary vaccination) and hence an increase in cost of vaccination. For the purposes of this model, Secondary Vaccination has been defined to cover the women aged 10 to 44 years. Other studies have set the age bracket at different figures ranging from 10 to 45 years (De Visser et al. 2011; Situations 2010; Milne et al. 2007).

Figure 5.18, shows simulated trends of DALYs averted at different levels of secondary Vaccination.

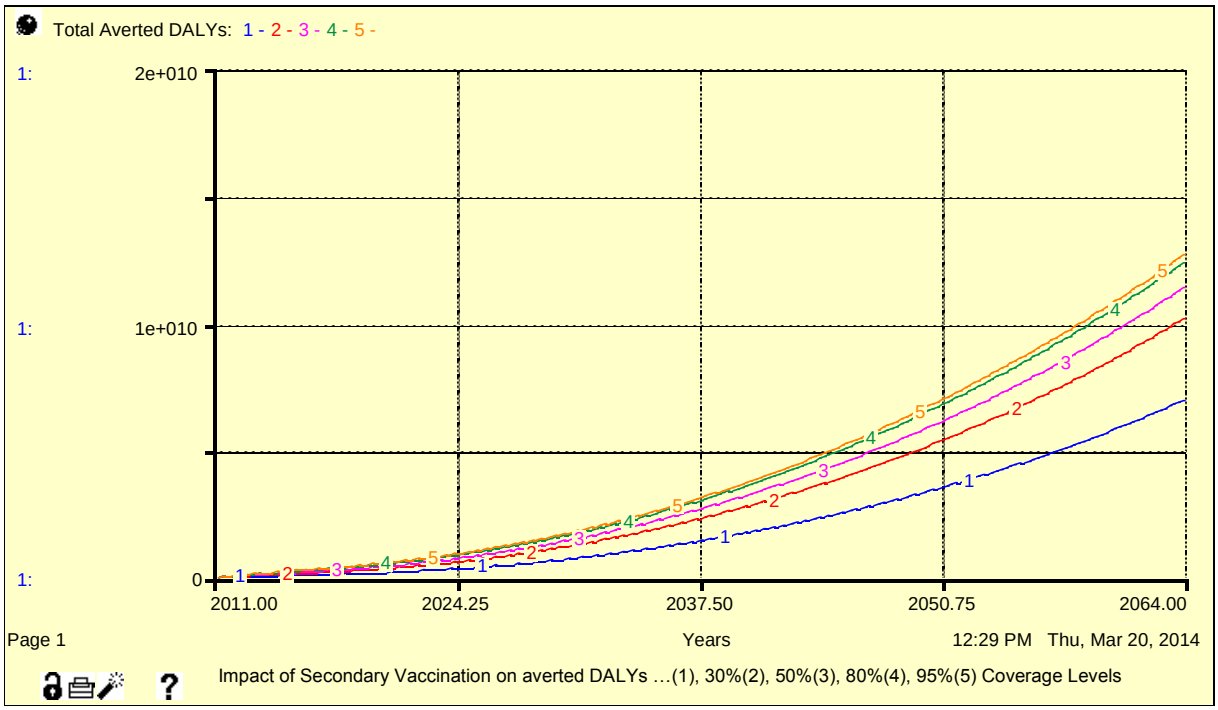


Figure 5.18 Impact of Secondary Vaccination on Averted DALYs

The impact of secondary vaccination will be realized earlier in time in comparison to the impact of primary vaccination. The results in Figure 5.16 and Figure 5.17demonstrated that catch up vaccination would be a more effective approach in the prevention of HPV infections as compared to primary vaccination. Over the simulated 50 year period, secondary vaccination would result to aversion of 52% to 56% more DALYs in comparison to primary Vaccination. These figures however can change depending on the set age limits of both primary and secondary Vaccination.

Impact of Screening

Screening intervention has been identified as an effective preventive measure as long as it is done systematically, covering large proportion and is done concurrently with treatment. Apart from resources needed, effectiveness of screening is also affected by such factors as the number of tests required, the sensitivity and specificity of screening methods available as well as the recommended screening intervals(Bingham et al. 2003). This model assumes effective cervical cancer screening coverage.

It is assumed that the proportion of girls who were not vaccinated are at risk of HPV infection. This is taken as the beta transmissibility. This is the group which is subjected to HPV screening and that all the women who have been confirmed to have HPV are subjected to appropriate treatment options. The base case rate of 0.1% of primary and 0.3% secondary vaccination remains.

Screening was shown to have reduction on DALYs. DALYs reduction was noted with increase in screening coverage.

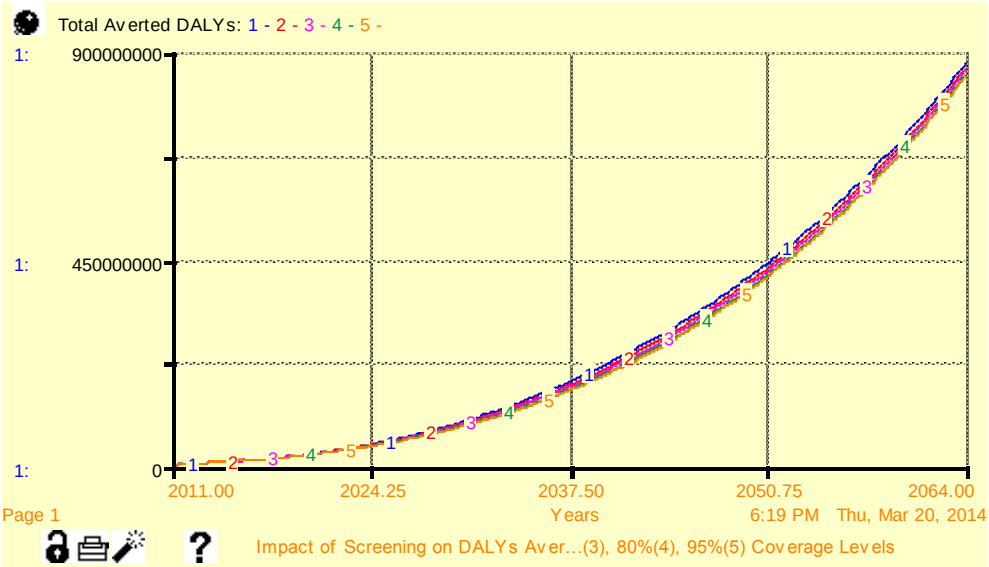


Figure 5. 19. Impact of Screening

The rate of change however reduced after 50% coverage rate as noted from Figure 19. However, at a realistic coverage (30% of all the interventions) screening contributed to less averted DALYs in comparison to Primary and Secondary Vaccination. Screening would contribute 85% to 89% less DALYs than secondary vaccination and 68% to 75% less averted DALYS than primary vaccination (Table 5.3). The impact of Screening is expected to be realized latter in comparison with primary vaccination and catch up vaccination.

Table 5.3 Comparison of averted DALYs Contributed by different 'traditional' interventions

YEAR	30% Secondary Vaccination	30% Primary Vaccination	30% Screening	Screening Versus Sec Vaccination%	Screening Versus Primary Vaccination%	Secondary Vaccination Versus Primary Vaccination%
2010	13695	6074	1,537	89	75	56
2015	86355	39299	10,520	88	73	54
2020	165278	72503	21,330	87	71	56
2025	251780	113154	34,117	86	70	55
2030	350937	162767	49,293	86	70	54
2035	468579	222221	67,405	86	70	53
2040	610620	292595	89,086	85	70	52
2045	783085	375271	115,038	85	69	52
2050	992382	471922	146,034	85	69	52
2055	1245647	584522	182,934	85	69	53
2060	1551093	715357	226,708	85	68	54

Impact of e-health

The e-health scope of this study referred to use of internet in accessing information on cervical cancer among the clients. This was established at 7.5%. It is assumed that the population with access to these e-health tools would benefit from the health education messages relied to through these tools. The impact of this knowledge would be translated to increased positive attitude towards vaccination and screening as well as an increase in demand for these interventions.

The model sought to find the impact of e-health tools on the DALY trends in addition to the traditional (Screening, Vaccination and treatment) approaches to management of cervical cancer. Figure 5.20 shows the possible impact of e-health tools while holding all other interventions at the base case scenario.

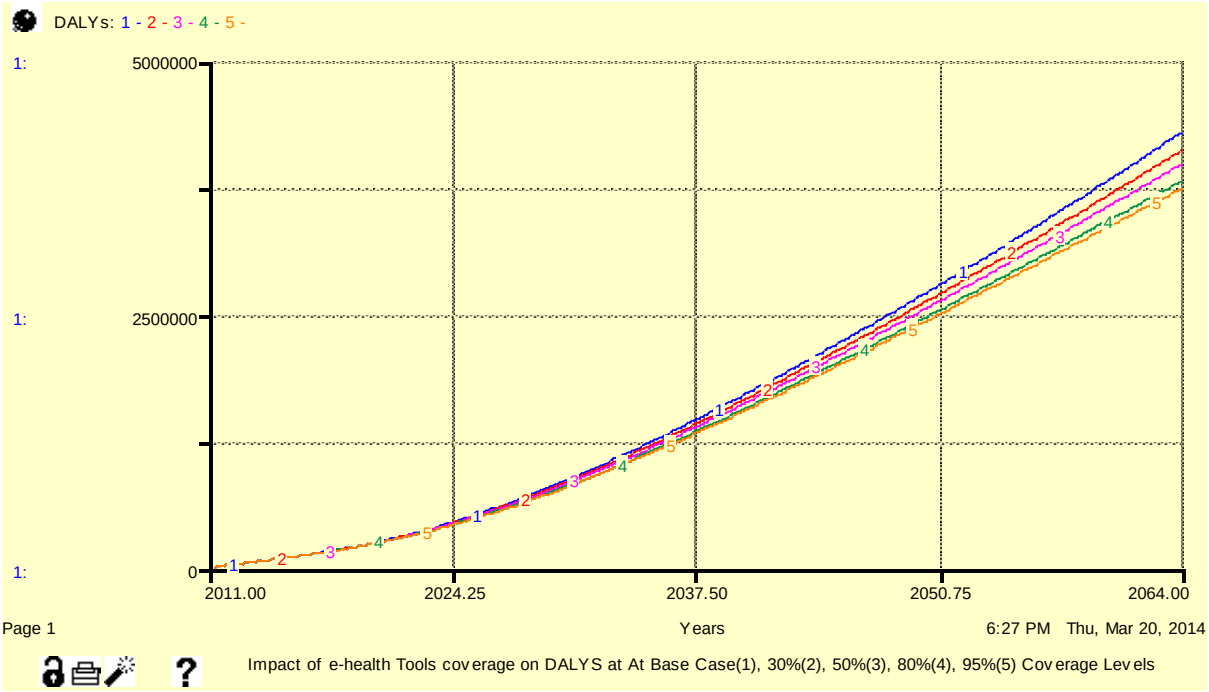


Figure 5. 20: Impact of e-health Tools

Figure 5.21 shows predicted trends of DALYs at Base case scenario and different levels of e-health coverage while holding at realistic coverage of 30% of the three (Primary Vaccination, Secondary Vaccination and Screening) interventions.

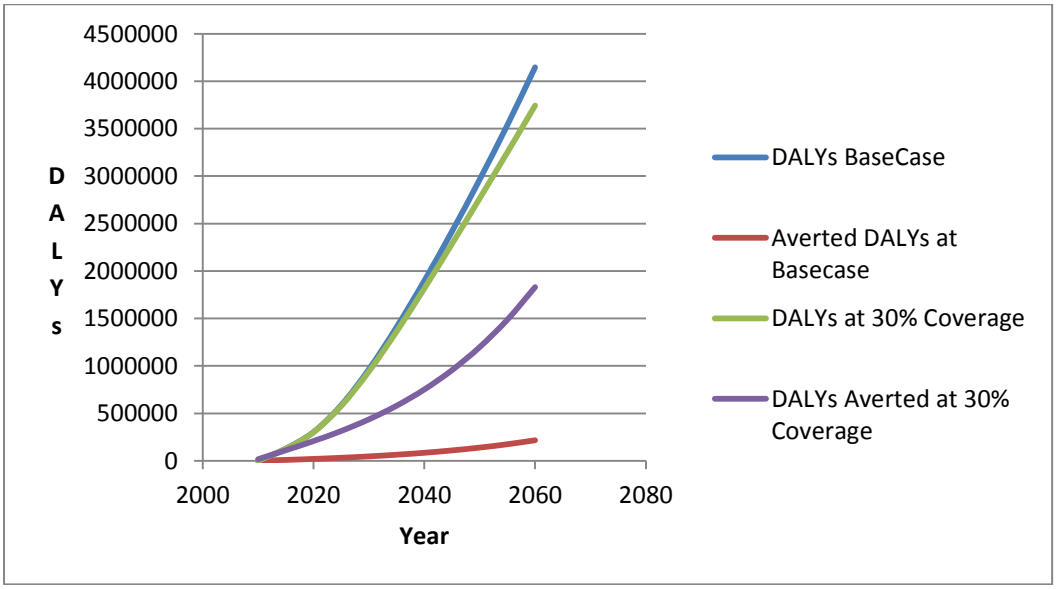


Figure 5. 21. Trends of DALYs and Averted DALYs at Base case and Realistic Coverage

Holding a realistic coverage of 30% of primary vaccination, secondary vaccination and screening, variation of e-health coverage levels would have varying impact as shown in Figure 5. 21.

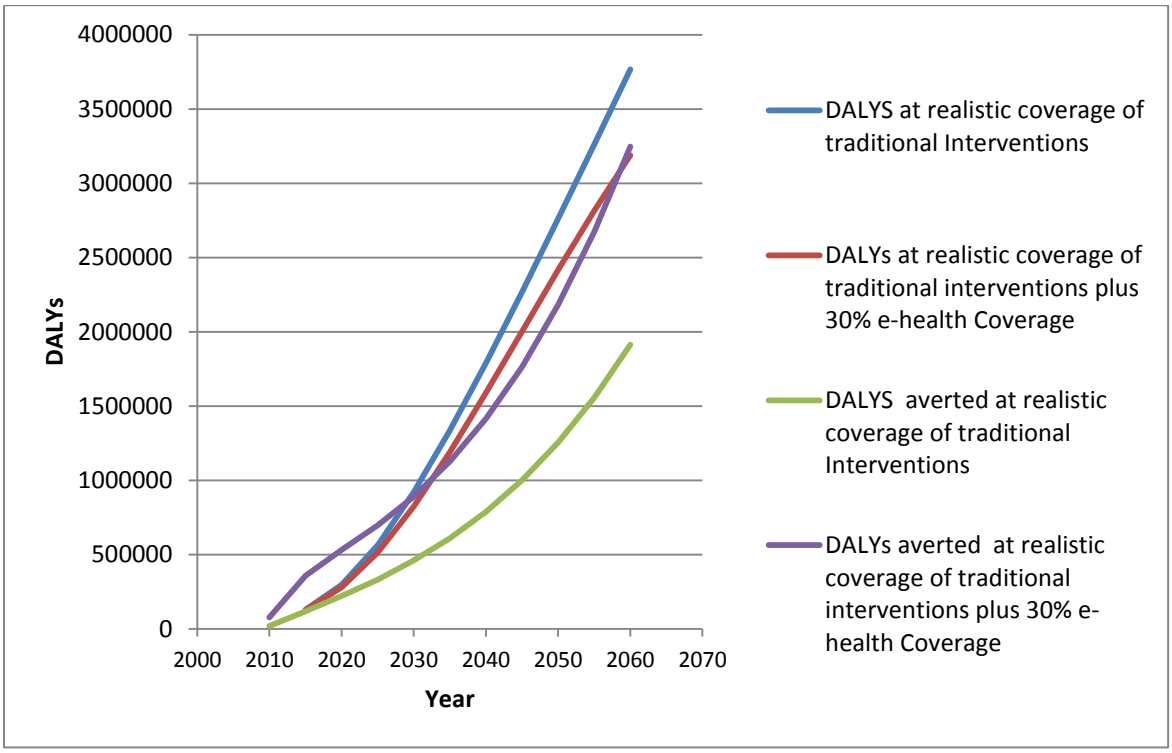


Figure 5. 22. Impact of e-health Tools.

A realistic coverage (30%) of e-health tools resulted to between 2% to 15% reduction in the number of DALYs and between 41% to 75% increase in DALYs averted.

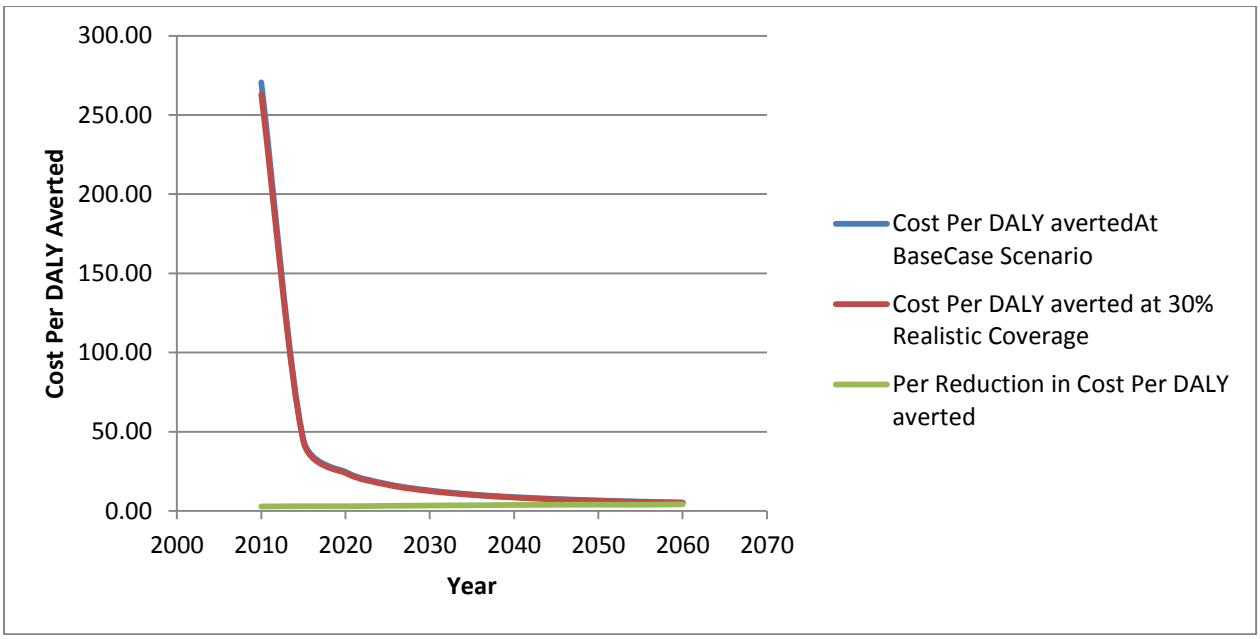


Figure 5.23 Trends in cost per DALY averted

Figure 5.23 compare the cost of averting each DALY at base case and at a realistic coverage of the three interventions. The cost per DALY averted decreases

significantly with increase in intervention coverage. By the year 2016 and at realistic policy at 30% coverage of screening, primary and secondary vaccination would yield a 28.5%reduction in DALYs; [18355212] DALYs at Base case and [17174968] at a realistic coverage.

By the Year 2060, and at a realistic coverage, Secondary Vaccination would account for the largest portion of averted cases(at 98%)followed by Primary Vaccination(1.2%) while screening would contributed the lowest with less than 1%.

Discussion

This model assessed the possible impact of primary vaccination, secondary vaccination, screening and use of e-health campaigns in management of cervical cancer in Kenya. Current levels of coverage were compared with different intervention scenarios including a 'realistic' coverage of 30% of the interventions. The model confirmed effectiveness of the three 'traditional' intervention strategies in management of cervical cancer; however the possible impact of the interventions varied according to the various scenarios simulated. The impact of a more 'recent' e-health intervention was also simulated.

Secondary vaccination against HPV was found to have the highest impact of the three choices of intervention. Different studies have emphasized the potential impact of vaccination as an intervention in reduction of HPV infection and Cervical Cancer mortality(Maine et al. 2011). Secondary Vaccination would account for a reduction of over 50% incidence rates. This is in consistence with Baussano et al. (2013) who simulated a 50% reduction in HPV prevalence after introduction of catch up vaccination. It is noted that even with higher primary vaccination coverage, the impact of vaccination is realized only after 10-15 years. This is consistent with findings of Franco and Cuzick (2008). After rolling out an extensive HPV vaccination a recent study in Australia reported a reduction ranging from 0.1 to 0.38% in both Low grade and High Grade abnormalities in a period of 3 years(Brotherton et al. 2011).Five years later the AustralianNational HPV vaccine programs reported success in reduction of not only HPV Cervical Cancer related lesions but also a reduction of 9.65% in genital warts(Fairley et al. 2009).

Primary Vaccination can only achieve it potential impact if it reaches all vulnerable groups. National wide School based vaccination programs may go along away in meeting this need(Franco & Cuzick 2008) The trade off in vaccination intervention must be considered in relation to age specific incidences, vaccination coverage rate, efficacy of the vaccine and risk of viral re-infection among others (Goldie et al. 2008; Brotherton et al. 2011)A challenge of resistance to vaccination due to low acceptability among respondents is possible. This has been reported in France in uptake of Hepatitis Vaccine (Ribassin-Majed et al. 2012) as well as HPV vaccination uptake in USA where less than 50% of teenage girls completed the three doses of HPV vaccine. The reasons associated with resistance included some parents of teenagers feeling that the vaccine was not needed, safety concerns and fear of increase in sexual activity, convenience of completion of the vaccine and lack of factual information on the vaccine (Bartlett & Peterson 2011). It is important to note that women in Kenya and Botswana have been reported to have high levels of acceptability of HPV vaccines (DiAngi et al. 2011; Becker-Dreps et al. 2010). This is a strength which the country would base HPV vaccine on in these countries. Low income countries have been documented to have more supportive environment and school based HPV vaccination programs model have been documented to result to high coverage rate (Tsu 2012).

Primary vaccination must take into account economic considerations. It has been argued that HPV vaccination exercise may not be economically viable in developing economies due to the high cost of vaccination, the un-sustainability of such an economic endeavour by GAVI as well as other more competing health priorities(Kane et al. 2012; Ouedraogo et al. 2011) However HPV vaccine may be the most effective measure in the future(Hessel 2009; Bosch et al. 2008)

Screening was shown to have the lowest impact of the three choices of intervention in terms of the number of cervical cancer cases averted and impact on reduction of DALYs. However it is important to note that the primary purpose of screening is early diagnosis and treatment and does not prevent HPV infection. Cervical Cancer screening has been considered as an effective method of reduction in Cervical Cancer mortality , accounting for a 70% reduction in mortality rate in developed countries and contradicting results in developing countries (Denny et al. 2006). The Nordic and

some European countries have succeeded in reduction of Cervical Cancer where systematic screening was done. However Cervical Cancer screening has been reported to have a low rate of success attributed to a number of factors which include low test sensitivity of HPV testing, uneven access to screening and coverage, lack of follow up in women with abnormal results, poor treatment and poor quality of care among others(Franco & Cuzick 2008). It has been suggested that in low resource setting, women of over 30 years should have at least one screening done. However depending on the screening method adapted, screening has a 30%-50% probability of false negative results(Gakidou et al. 2008). This would result in missed treatment intervention.

The simulated results of this model concur with the theory that screening may have minimal effect in control of Cervical Cancer with coverage of less than 50%. The results support Goldie et al., who reported that coverage of over 50% of HPV screening resulted in minimal change to Cervical Cancer rate. (Denny et al. 2006)Denny et al. (2006) suggested that for successful Cervical Cancer screening in low resource setting to take place, a number of essential requirements must be met. These include but are not limited to low cost, low screening technology , diagnosis and treatment offered on site, wide coverage of majority of at risk women, appropriate educational programs for both clients and health care workers as well as built in mechanism for evaluating of screening programs. It is important to not only have massive screening but also have surveillance programs with recall and follow up embedded in the existing health services (Gakidou et al. 2008). It has been urged that it is unethical to provide screening services in the absence of a treatment option(Were et al. 2010). Screening has also been found to be less acceptable with some women describing it at ‘invasive’ to their privacy and being against the cultural expectations (Kivuti-Bitok et al. 2013). These factors pause a challenge to screening as an intervention. The long term effect of the negative attitude towards screening interventions should not be ignored.

Use of Information Communication and Technology (ICT) and its dynamism among cervical cancer clients as well as the general community has been shown to be on the increase. This model demonstrated that an increase in use of e-health tools to a realistic coverage of 30% would results to 2-15% reduction in DALYs and 41-75%

increase in averted DALYs. With the rising accessibility of mobile phones among families and in translation among cervical cancer clients in Kenya, there is need to explore use of e-health in health messaging on cervical cancer in Kenya. This would result in possible increase in demand for screening and vaccination services. This would translate to raised awareness and better management of cervical cancer in Kenya.

Limitations of the System Dynamic Model

The model did not distinct between regularly screened and occasionally screened women. Efficacy of vaccine was assumed to be life-long. However vaccine affects lasts for a limited period of time, usually around 10 years and hence a boaster is required later. If efficacy of the vaccine is poor, then there is poor impact on reduction of Cervical Cancer. The need for vaccination booster was not included in the model. The impact of male circumcision and Vaccination of Boys against HPV were also not modelled. HPV has been known to cause other genital cancers. Effects of HPV vaccination on these other cancers were not simulated and hence it may be necessary to develop a model which incorporates the impact of HPV vaccine on all these other cancers

There is limited cervical cancer epidemiological data available in Kenya. Therefore this population based model relied majorly on aggregate point data which did not allow for probability variations. Even though Population based models are easier to construct, they may miss out on uniqueness of individual clients and hence may not allow the history of each individual client to be tracked. The model was not differentiated by socioeconomic status hence socioeconomic status interventions could not be established.

All the interventions occur in a dynamic environment affected by Information Communication and Technology (ICT), politics, economic forces , socio-cultural, legal and possible unknown factors. The model was limited in its ability to include all other possible confounding variables. However the models allows for modification to accommodate for new research findings.

Recommendations Based on the SD Model

As a matter of policy, Kenya should consider secondary vaccination and primary vaccination as a matter of priority. Screening should be complementary to primary and secondary vaccination. This is based on assumption that the country could afford all options. With the proposed financial support of HPV vaccine by GAVI, the expected cost will be between $5 and $15 which is close to the average cost of screening. There is need to develop a model on the implication of Vaccination in developing economies, and Africa in particular.

Conclusion based on SD model

This model generated reasonable estimates in evaluation of effects of different interventions on Cervical Cancer management in Kenya. Interim Cervical Cancer management policy is derived. The model charts informed debate leading to development of new consensus policy on screening and vaccination. Cervical Cancer needs to be managed and monitored continuously with screening being implemented as a complimentary intervention to vaccination. Kenya as a country need to consider implementing catch up and primary vaccination as an urgent measure to curb Cervical Cancer.

CHAPTER SIX: MATHEMATICAL MODEL FOR CERVICAL CANCER

6.1 Introduction

Dynamics of Cervical Cancer in the population can be presented mathematically using differential equations. All deductions in mathematical formulas ensure that even the smallest implication is noticed. In their nature, mathematical formulas are relatively 'short' hence are easier to express an idea and memorize issues concisely. However, mathematical formulas may be based on assumptions and strict definitions hence may prevent further indulgence into the issues expressed.

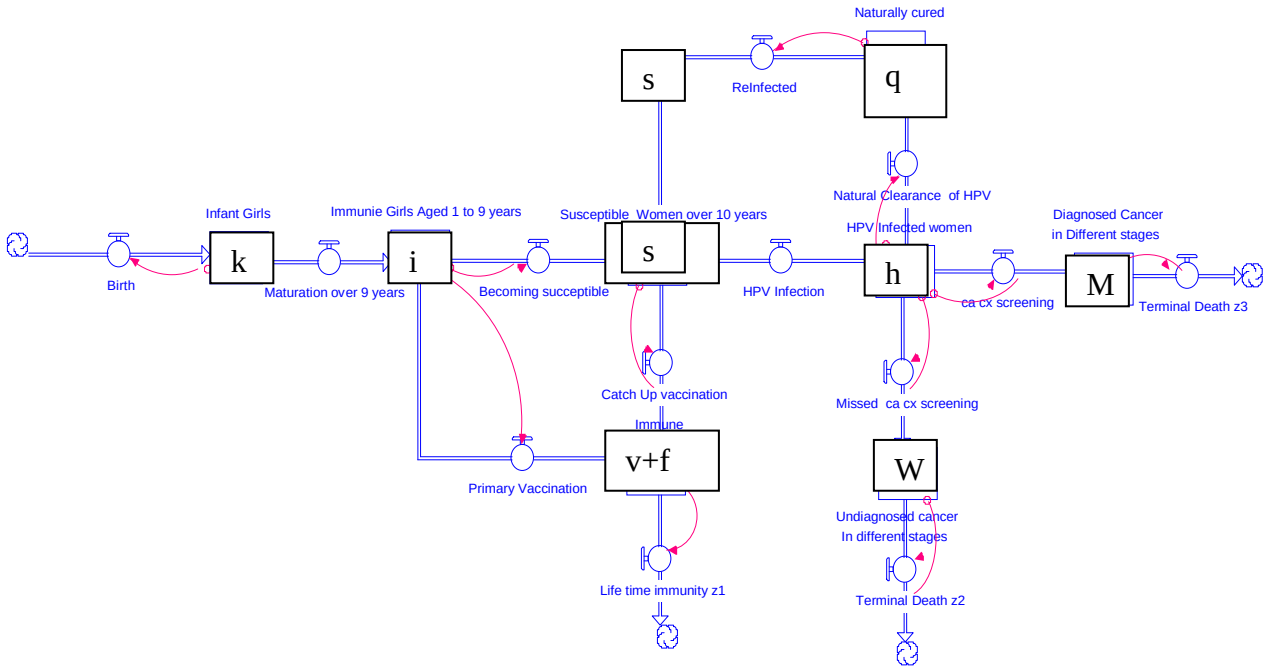
This chapter shows that the topography of Cervical Cancer cases can be modelled and expressed mathematically. Modelling trends of Cervical Cancer requires accurate estimation of control variables. The initial conditions are estimated as 'posteriori' conditions by the model. The model assumes that Cervical Cancer can be described by two main variables, control and state variables which reflect on the structure and intervention topography of Cancer of cervix. It further assumes that Cervical Cancer exists over a span of time with interplaying variables that can be dynamically modelled along with boundary conditions.

Different preventive and interventive approaches have been proposed in management of Cervical Cancer. These include pre-exposure /primary vaccination of pre-puberty girls and secondary /catch up vaccination of women aged between 10 and 45 years. Currently two main vaccines are available. Gardasil is only given to females' aged 9 to 26. A complete cycle of HPV vaccine is given in three equal doses over a period of six months. The second dose is given 1 to 2 months after the first dose while the last dose is given at six months after the first dose. Women who are pregnant should not get the HPV vaccine until after the baby is born. Cervarix is recommended for 10 to 45 year olds(Markowitz et al. 2007; Baussano et al. 2013 and Situations 2010).

Different screening methods have also been employed. The methods have differing sensitivity and specificity levels. These methods include Visual Inspection with Acetic Acid (VIA), Visual Inspection with Lugol's Iodine (VILLI), DNA Testing and Cytology(Duraisamy et al. 2011). Clinical management of the Cervical Cancer which includes; surgical intervention , chemotherapy, radiotherapy or a combination of any two or three methods have been employed(Legge et al. 2010; Mucheusi

2012).These management approaches have different impacts and outcomes on Cervical Cancer.

System Dynamics(SD) can be employed to better understand Cervical Cancer in Kenya and be used as a basis for informed decisions to policy makers. System Dynamics models can be expressed as a set of differential equations using theory of Dynamic systems to determine equilibrium and stability of the system. The summarized schematic structure of the System Dynamics model of Cervical Cancer is presented in Figure 6.1.



k= number of infant girls
i= immunized girls (aged 1-9 years).
v= Girls who receive primary vaccination at age 9
s = Susceptible (girls or women of age>9 years)
f = the Portion females eligible for catch up vaccination.
r = be the women aged 15 years eligible for screening.
z_2= Death from undiagnosed Cancer ,
z_3= Death from diagnosed Cancer
M= Total population of women with diagnosed cervical cancer.
W= total population of women with undiagnosed cervical cancer.
q= total number of women who had natural clearance of HPV infection

Figure 6.1. Schematic Diagram of SD Model of Cervical Cancer(Author 2014)

6.2 Mathematical Models

Various mathematical models to represent the dynamics of HPV are given in this section.

6.2.1 Linear Model

Cervical Cancer is best described as a dynamic system due to the nature of the disease condition as well as the population in which it occurs. Since dynamic systems use continuous time formulation, it is assumed that absolute change with respect to time is equal to a constant and the average change is constant with respect to time and hence the Dynamic System can be expressed as a linear model. The dynamic system at each moment in time is expressed as a function of the state variables, control variable and a given time. A system is completely observable on $(t_0\ t_f)$if for the same arbitrary initial state$[y(t_0)=y(0)]$, there is a finite output uniquely determined such that from the measurement of the output $y_{(0)}, y_{(1)}, y_{(3)}$--------$(m)$, the initial state $y(t_0)=y=0$ can be computed.

The phenomenon of Infection and growth of HPV infection in the population is such that initially there are the numbers of women with; dysplasia (Pre-Cancer stage), stage 1, stage 2, stage 3 and Stage 4(terminal stage) of Cervical Cancer were considered.

These stages may be undiagnosed or diagnosed, depending on whether the affected women underwent screening of Cervical Cancer or not. Since the trends and intervention of Cervical Cancer are dynamic then SD becomes an appropriate model. Linear and exponential function of time was used to describe how the system changes and evolves over time. The model follows a cohort of all the female population in Kenya in the year 2010.

6.2.2 Exponential Model

Cervical Cancer can also be modelled as an exponential Model in a dynamic system represented by; Pop (t) = Pop (0)*Expon (Variable Fraction*t), where *Variable* Fraction is taken as a constant.

The variable in the model are taken to be birth fraction, Primary vaccination fraction, secondary vaccination fraction or screening fraction. One major characteristic of the exponential curve is that it doubles its value in constant time intervals. The formula for the doubling timecan be derived tobe:

Td = ln2/(*Variable Fraction*) ≈ 0.70/ *variable Fraction* (Barlas 1996).

Variable fraction indicates exponential growth of Cervical Cancer or exponential decline of Cervical Cancer cases depending on the management interventions availed. The linear Model and the exponential model were found to be not completely adequate to describe HPV dynamics. Therefore, dynamical models for various stages for diagnosed and undiagnosed patients have been developed and analysed. The equations were simulated on Matlab software to forecast trends of Cervical Cancer, to estimate the standard errors and compare historical data to simulated rates. The results were as illustrated in Fig 25, Fig 26, Fig 27 and Fig 28. The Matlab codes used are detailed in appendix 21.

6.3 Dynamical Representation of Cervical Cancer.

An understanding of the typical course of HPV infection within the population and the quantification of the women within the different stages of infection is essential in determining effectiveness of primary (Vaccination), secondary vaccination, screening and tertiary (Treatment) intervention strategies. For purposes of specification the girls and women are stratified for modelling purposes according to the following categories;

k=number of infant girls (age less than 1 year) in Kenya

i=immunized girls (aged 1-9 years). These are immunized by physiologically derived factors)

v=Girls who receive primary vaccination at age of 9

s =Susceptible (girls or women of age>9 years) who missed primary vaccination.

Susceptible $=(i-v)-f=i-v-f$ (6.1)

The model assumes life time immunity for girls receiving primary vaccination.

Let *f* be the Portion of girls and women who missed the primary vaccination and are given secondary (catch up) vaccination. It is also assumed that with this secondary vaccination, they get life time immunity from HPV infection.

Girls and women who miss secondary vaccination are eligible for screening.

Let *r* be the women aged 15 years and over who are eligible for screening.

Let *M* bethe number of screened girls and women who have been confirmed to have HPV infection. These have been further stratified as:

- Diagnosed dysplasia denoted by (m_0)
- Diagnosed stage 1 denoted by (m_1)
- Diagnosed Stage 2 denoted by (m_2)
- Diagnosed Stage 3 denoted by (m_3)
- Diagnosed stage 4 denoted by (m_4)

Such that $M = m_0+m_1+m_2+m_3+m_4$. (6.2)

The women who miss Primary and secondary vaccination as well as screening are denoted by *W*. It is assumed that this population of women may be infected with HPV and undergoes the similar stages of Cervical Cancer albeit undiagnosed. Thus this population is further stratified as;

- Undiagnosed dysplasia stage denoted by (w_0)
- Undiagnosed Stage 1 denoted by (w_1)
- Undiagnosed Stage 2 denoted by (w_2)
- Undiagnosed Stage 3 denoted by (w_3)
- Undiagnosed Stage 4 denoted by (w_4)

Such that $W = w_0+ w_1+w_2+w3+w_4$. (6.3)

It is assumed that 80% of the clients who may have detected Cancer at the time of screening have natural clearance of HPV infections. Let the number of women who had HPV infection but clear naturally be denoted by *q*. Some of the women among those testing negative for HPV may previously have had HPV infections which cleared naturally.As shown in Figure 23, the women exit from the system model through three main ways;

- Through permanent immunity (z_1) via primary and secondary vaccination.
  Such that $z_1 = v+f$
- Death as a result of undiagnosed Cancer (z_2,),
- Death from diagnosed Cancer (z_3)

The total number of women exiting the model at any given time

$=v+f+z_2+z_3$, (6.4)

Thus total exit from the system = $z_1+z_2+z_3$ (6.5)

Deaths from other causes among the cervical cancer clients (other than Cervical Cancer) were estimated to be minimal and hence considered not Significant to the

undertaken study. They were therefore not included in the model. For the purposes of this model 2010 was considered the base year. According to UNDP the projection of female population in Kenya was as elaborated in Table 9. Calculations from Table 9 indicate that; the total Number of females regardless of age in Kenya as at year 2010 was 20,492,000, while those females aged 10 to 0ver 65years comprised of 14,260,000. The WHO report documented the incidences of HPV in intervals of 10 years from age of less than 14 years, 15 to 44 years, 45 to 54 years, 55 to 64 years and over 65 years(WHO/ICO 2010). To describe the number of girls and women in various stages of HPV infection, corresponding differential equations showing the rates of change in the number of girls and women in respective stages with the help of the relevant parameter were formulated. Mathematical modelling has been done in line with HIV/AIDS infection model, using differential equations by Simwa and Pokhariyal (2003).In practice, the age groups are recorded as 0-4.5, 4.5 to 9.5, 9.5 to 14.5, and so on till 64.5 and above.

6.4 Modelling of Various stages of Cervical Cancer.

Representation of females at various stages and the rate of change in these stages have been done using differential equations. The boundary conditions for respective stages were derived from data of WHO country report for Kenya(WHO/ICO 2010).

a) Infants Born in the Country

Let $k(t)$ be the population of infant girls (Numbers) at any given time t, with k_0 being the number of infants girls born in the base year, 2010. The total number of infant girls was computed by using the birth rate and infant mortality rate.

Thus at any given time t, $k(t)=k_0$(Birth Rate-Infant Death Rate). This is based on assumption that the death rate and Birth rate are proportional to the female population.

.

$$\frac{dk(t)}{dt}= 0, \quad \text{when } 0 \leq t \leq t_s \quad \text{and } k_0 \geq 600000 \qquad (6.7)$$

$$\frac{dk(t)}{dt}= 0, \quad \text{when } t > t_l, \qquad (6.8)$$

wheret_l is the level off time after which no more infants are born.

Thus $k_{(t)}$ is equal to k * birth rate- k*death rate;

Pop $k_{(t)}$=Pop $k_{(0)}$ *Expon (Variable Fraction*t),

Thus $\frac{dk(t)}{dt} \propto (k - g)$. (6.9)

Changing the proportionality into equation, we get

$dk(t)/dt = \alpha_1(k-g)$, (6.10)

where α_1 is the constant governed by the factors responsible for population growth mechanism and $g = infant\ mortality\ rate$ of 5% or 50/1000 life births with birth rate at 3.2%. g is also infant survival rate of 3.04%(which is 5% of 3.2%).

Thus, k_t is the total number of infants surviving at any given time which can also be presented in Integral form as

$$k_{(t)} = k_{(0)} + \int_0^t \alpha_1 (k-g)dt. \quad (6.11)$$

b) The Population of Girls with Natural mediated Immunity.

Up to the age of 9 years, the girls are assumed to have a naturally mediated immunity due to the fact that the conversion of dormant columnar epithelium of endocervical canal into squamous epithelium has not yet occurred, hence the cells are still not susceptible to HPV infection (Makin &Kamanu 2010; Adekunle 2010). It is also assumed that at this age the girls are not yet sexually active and hence are not exposed to HPV infections.

c) Population of Primary Vaccinated Girls

The model assumes that on reaching 9 years the girls are subjected to pre-exposure primary vaccination against HPV. The model considers that a life time immunity against HPV is achieved once the girls are vaccinated and all the non vaccinated girls are susceptible to HPV infection.

Pre-exposure vaccination may be administered to both young boys and girls. Even though vaccination of boys has been documented to have some positive impact on prevention of HPV transmission, it has been found to be not cost effective in low resource setting (Kim, Andres-Beck and Goldie 2007). For this reason the model does not include vaccinating boys as a preventive measure.

The rate of vaccination at this stage is affected by a number of factors including; the attitude of mothers and care givers towards Primary HPV vaccination which directly influences acceptability of the HPV vaccine, level of knowledge about HPV vaccine,

use of e-health tools for health education and raising awareness about cervical cancer. Studies done among women of lower economic status in Kenya and Botswana reported that 0% of the women sampled in Kenya and 9% of women sampled in Botswana had knowledge on HPV vaccine. However, after giving the basic information on HPV vaccine and its advantages, as high as 88% to 95% of the same women shown positive attitude towards primary vaccination of their daughters(Becker-Dreps et al 2010; DiAngi et al. 2011). This positive attitude may be a predictor of the level of acceptability of HPV vaccine among mothers and families of pre-adolescence girls.

Infant girls (*k*) grow within one year to be adolescent girls and enter into the age group between 1-9 years. This population of girls aged between 1-9 years is denoted by *i*. Let *i(t)*be the number of pre-adolescence girls at any given time *t* such that $t>t_s$, then we have the following rate of change and boundary conditions;

$\frac{d(\mathrm{i})}{dt}$=0, when 1≤t≤9, and $i(t_0)$=5632,400 (6.11)

These girls *i(t)*are immunized by physiologically derived factors (Kawana et al, 2012).

The model assumes that the girls receive pre-exposure /primary vaccination just after completing age 9. Primary vaccination at this age ensured that the girls are vaccinated within the Centre for Disease Control(CDC) recommended Minimum age of 9 to 12 years (Situations 2010). It has been documented that this is one of the best age group for inculcating healthy living habits and normalize health care utilization (Evans et al. 2009).

Let the number of primary vaccinated girls be denoted by *v* and these are immunized by vaccine derived factors and the initial population of primary vaccinated girls be $v(t_0)$. This remains constant up to a time say $t_{s..}$ Let *v(t)* be the proportion of primary vaccinated girls at any given time *t* such that $t>t_s$, then we have the boundary conditions using the values of Table 9; then the number of girls eligible for primary vaccination are 5632000(All the girls, 1 to 9 year olds, who would be given primary vaccination immediately on reaching 9 years of age.

Limited data is available on the rate of primary vaccination in Kenya. Therefore, the exact number of girls given primary vaccination in Kenya is cannot be known. For this reason, expert opinion was taken to estimate the primary vaccination coverage. The experts for this study were defined in phase one as the doctors and Nurses involved in operational level management of Cervical Cancer clients in the national referral hospitals as well as provincial hospitals in Kenya. The experts estimate that only 0.1 to 0.3 % of girls aged 9 years receive primary Vaccination. Calculation of the vaccination rate based on 0.3% of this age group give 16,896 girls. However, given the current cost of HPV Vaccine ($150 for Gardasil and $300 for Cervirax) per full dose it seems that the number, 16,896 is an overestimation.

It can be noted that not all girls aged 9years will receive primary vaccination hence they need not be 100%. In this case the level off value is denoted by $L<1$. Let $v(t)$ be the number of girls receiving primary vaccination out of the entire population of girls aged 1- 9years at any given time. The rate of change and the boundary conditions of the girls receiving primary vaccination can be expressed as

$$dv(t)/dt \propto (i\text{-}v,) \qquad (6.12)$$

where $i\text{-}v$ denotes the number of girls at age 9 not yet vaccinated and

$\frac{dv(t)}{dt}=0$, when $1 \leq t \leq 9$ and $v(t_0) = 16896$.

Changing the proportionality into equation we get;

$$dv(t)/dt = \alpha_2 (i\text{-}v), \qquad (6.13)$$

where α_2 is a constant and depend upon;

i. The number of girls aged 9 years available for primary vaccination.
ii. Resources existing to conduct primary vaccination.
iii. The prevailing attitude of the general population towards primary vaccination.
iv. Coverage of e-health tools.

It has been reported that in order to avert one case of Cervical Cancer, 250 girls aged 9 to 12 must be given primary vaccination (Sanders & Taira 2003). The number of averted cases through primary vaccination at any given time is given by; $dv(t)/250$,

where $dv(t)$ is the number of girls receiving Primary Vaccination at any given time and 250 is the number of girls required to be vaccinated in order to avert one new case of Cancer of the cervix.

d) The Susceptible and Infected Groups

The population of girls who miss primary vaccination are assumed susceptible to HPV infection. Of this group 38.8% harbour HPV infection at any given time. Eighty Percent (80%) of HPV infections in these women clear naturally. This has been attributed to the natural cell mediated immune response where by 'HPV infected epithelium undergoes differentiation and maturation, and exhibits only minor cellular abnormalities.' In the remaining 20% 'HPV infection of replicating immature cells prevents epithelial maturation and differentiation leading to continued replication of immature cells and accumulation of genetic abnormalities that could ultimately lead to a clone of Cancer cells(Baseman & Koutsky 2005; Duraisamy et al. 2011).

Even though this natural clearance of HPV infection is derailed by sero conversion(HIV Positive status) and co-infection with different types of HPV, these confounding factors were not included in the model. It is also noted that the clearance does not provide immunity as the women could be re-infected with same strains or different strains of HPV, hence the women move back to susceptible group.

Let s, be the number of susceptible women in the population and h be the number of infected women in the population. The rate of change of number of infected women is proportional to the number of susceptible women.

It is important to note that the susceptible population consists of the women aged 10 to 44 years; who are eligible for catch up vaccination as well as the women aged over 45 years who are not eligible for catch up vaccination.

Thus $s = s_1 + s_2$, (6.14)

Where; s_1= 10 to 44 year old who are eligible for catch up vaccination

s_2=Women over 45 years of age who are not eligible for secondary vaccination

With 14260000 being the population of girls and women aged $\geq$ 10 years denoted by N_1. It is estimated that 38.8% of this population harbours HPV infection. Thus, a total of 5532880 women may be infected with HPV. This group which is assumed to be infected with HPV is denoted by N_2. The number of women not infected with HPV is 8,727,120 and is denoted by N_3.

In this manner $N_1 = N_2 + N_3$, (6.15)

It is estimated that 80 %(4,426,304) of these Infections clear naturally therefore only 20% (1106576) in the population of women harbouring HPV would have progressive

HPV infections. This group is further sub classified depending on whether they underwent Screening against HPV or not.

Let the initial number of infected women be denoted by $h(t_0)$which is assumed to be at constant up to time t_s. Let $h(t)$ be the number of infected women at any time $t > t_s$.

The rate of change and the boundary condition of infection is therefore

$\frac{dh(t)}{dt} = 0$when t<10 years and $10 \leq t \leq$ over 80 and $h(t_0) = 1106576$ and$t > t_l$, (6.16)

where t_l is known as the level off time after which there is no more appreciable incidence of HPV infection in the population (which is taken to be 80 year).

Thus, rate of infection is dependent on the number of women available for infection (susceptible) and is given by

$\frac{dh(t)}{dt} \propto s - h$, where $s(t_0) \leq 14260000 \leq s(t)$

Changing the proportionalities to equation , we get .

$$dh(t)/dt = \alpha_3(s-h), \quad (6.17)$$

where α_3 is the constant governed by the factors responsible for the susceptibility and infections with HPV. These include; incidence rate, the rate of natural clearance, risky sexual behaviours, smoking and some unknown risk factors.

e) Group Vaccinated Through Secondary/Catch Up Intervention.

The girls who reach 10 years of age and missed the primary vaccination are also eligible for catch up or secondary vaccination. This vaccine is given in equal doses and route as per the Primary vaccine.

Secondary /Catch up vaccination is recommended for women aged between 10 to 45 years (Graham & Mishra 2011; Baussano et al. 2013). This model assumes eligibility of Catch up vaccination at 10 to 44 years. From http://esa.un.org/unpd/wpp/unpp/p2k0data.asp report, the women aged 10 to 44 years are estimated at 11,666,000. Assuming that this group includes the girls who previously receive primary vaccination then number of females eligible for secondary/catch up vaccination in the year 2010 is 11649104, derived from 11666000 (Total Number of women aged 10-44 years) minus 16896

(the population of girls who received primary vaccination on turning 9)

Only 0.3% of eligible women receive catch up vaccination. This gives a total of 34,947women.

Let the Initial number of women receiving catch up vaccination be denoted by $f(t_0)$ which is assumed to be at constant up to time t_s. Let f(t) be the number of women who receive catch up vaccination at any time t(where $t>t_s$), then .

$\frac{df(t)}{dt}$=0, when t<10 years and $t>t_l$ with $f(t_0)\leq 0\leq f$(t) *and* $f(t_0)$ =34947. (6.18)

The time $t_l$is known as the level off time after which there is no more women in the population are available for catch up vaccination.

The number of women receiving catch up vaccination varies and is proportional to the number of women eligible for catch up vaccination in the population (s_1). Thus, the rate of change in catch up vaccination,

$df(t)/dt \propto s_1-f$ (6.19)

Changing the proportionality into equation we get

$df(t)/dt=\alpha_4(s_1-f)$, (6.20)

where ;

$s_1(t_0)$= 11649104 when $10\leq t\leq 45$, α_4 is the constant governed by factors that influence catch up vaccination coverage and practices. These include level of knowledge about catch up vaccination, access and coverage of e-health tools and attitude towards catch up vaccination.

It has been argued that it takes secondary vaccination of 324 women in order to avert one case of Cervical Cancer when life time protection is assumed from HPV vaccination and 600 assuming waning off of vaccine protection after 10 years (Sanders & Taira 2003). The number of cervical cancer cases averted at any time through secondary vaccination is $df(t)/324$ or $df(t)/600$ depending on the protection offered by the HPV vaccine.

6.5 Screening for Cervical Cancer

A portion of the populations of unvaccinated women who miss both the primary and catch up vaccination are assumed to be susceptible to HPV infection. This group is subjected to screening for HPV as a measure aimed at early detection and treatment.

Only a fraction of women not vaccinated undergo screening. This is because the rate of screening is affected by level of knowledge on Cervical Cancer screening, access to e-health tools, access to other modes of health education and the attitude towards screening. Literature has shown that female clients as well as some health care providers have negative attitudes towards Cervical Cancer screening. Other factors negatively affecting the screening trends are; the screening procedure itself being viewed as too invasive to privacy by many women, cultural factors where some women are uncomfortable with the procedure being performed by a male health care worker or younger female health care workers. Other women fear that scrapping the cells of the cervix is likely to expose the client to more infections such as HIV while other clients lack faith in the sterilization status of the equipments utilized during screening (Kivuti-Bitok et al. 2013). Routine Screening for HPV has however, been recommended for all the women aged 15 years and above, whether they received primary and catch up vaccination or Not(Bosch &. SAnjosé, 2003).

For the purpose of this model, it is assumed that only women who missed both Primary and catch up vaccination will receive screening intervention. From the population estimates of 2010 and the trends of both primary and secondary vaccination the women who would be eligible considered for screening are 11614157(Women eligible for Secondary Vaccination – women who received catch up vaccination). Assuming that only 3.2% of eligible women would undergo screening(WHO/ICO 2010) theoretically 371, 916 would be screened through national, provincial, district and sub-district hospitals in Kenya. Thus 96.8 % (11242504) of eligible women miss this vital procedure.

Let $q(t)$ be the number of women eligible for screening at any given time, when $t \leq 14 \leq 65$ years, *and* $dq(t)/dt = 0$ when $t<15$, and $t>80$ $q(t_0) = 11614157$. (6.21)

Let $r(t)$ be the number of screened women at any given time and $r(t_0) = 371, 916$ such that the number of screened women keeps on changing within the study interval.

Hence, the boundary condition and the rate of change of screened women are;

$\frac{dr(t)}{dt} \propto q\text{-}r$ and $d\,r(t))/dt = 0$ when $t<15$, and $t>80$. (6. 22)

Changing the proportionality this gives

$dr(t)/dt = \alpha_5(q\text{-}r)$, (6.23)

where: α_5 is aconstant which depends on; the attitude towards screening, resources existing to conduct screening, the prevailing attitude of the general population towards screening and coverage of e-health tools

It is estimated that each year approximately 2454 women are diagnosed with Cervical cancer and approximately 1676 die from it.Using the incidence rate of 16.5 per 100,000 women, it is projected that there will be 4261 new cases in the year 2025 and 2955 will die from Cervical Cancer in the year (WHO/ICO 2010). If only 3.2% of the women with new HPV infection underwent screening in the year 2010, and considering the HPV prevalence of 38.8%, then it would follow that o38.8% of the women undergoing screening would be found to be infected with HPV.

Let $r(t_0)$be the number of women who theoretically underwent screening in the year 2010 and let $M(t_0)$ be the number of women who were found to have HPV.

Thus $r(t_0)$ =371653

M=144201(38.8% of $r(t_0)$) and $(r-M)$ are susceptible to HPV

However only 20% of the women diagnosed with HPV will progress to have cervical cancer. This gives 28840 cases

Let the initial number of screened women found to have HPV and progress to Cervical Cancer be denoted by $M(t_0)M(t)$ denote the number of women found to have HPV infection at any given time t. The rate of change of number of women found to have HPV will be proportional to the number of women who are susceptible to HPV and undergo screening, thus

$$\frac{dM(t)}{dt} \propto r\text{-}M \qquad (6.24)$$

and$\frac{dM(t)}{dt}$=0, when 15≤t≤ t_l(over 65years)$M(t_0)$≤144201. (6.25)

where t_l is known as the level off time after which there is no more women undergoing screening. Changing the proportionalities this gives,

$$d\,M(t)/dt = \alpha_6\,(r\text{-}M), \qquad (6.26)$$

where α_6 is a constant that depends on; HPV prevalence, Sensitivity of screening method and Specificity of screening method.

Since HPV infection progress from dysplasia to terminal stage 4, the women screened for HPV are categorized depending on the stage of disease. Women older than 9 years infected with HPV (Sufferers) are divided into 10 categories within the *M* (diagnosed)and *W*(undiagnosed) as previously stated so that.

$W+M=N_2$ and $N_2(t_0)=901259$. (6.27)

Based on the screening trends, this figure can be proportionally allotted to 3.2% (*M*) and

96.8 %(*W*). Thus$M(t_0)=28841$.and$W(t_0)=872418$.

It has been reported that approximately 80% of women in Kenya seek health intervention at stage 3 and stage 4 of disease (Gichangi et al. 2002). Hence for the purpose of this model the *M* and *W*are divided proportionately among all the five categories as shown in Table 6.1.

Table 6.1 . Distribution of HPV Infected Women

Stage	**Percentage**	**Number of Women**	**Stage**	**percentage**	**Number of Women**
m_0	5	1442	w_0	5	43621
m_1	5	1442	w_1	5	43621
m_2	10	2884	w_2	10	87242
m_3	40	11536	w_3	40	348967
m_4	40	11536	w_4	40	348967
Total	**100**	**M= 28840**		**100**	**W= 872418**

6.5.1 Screened and diagnosed Cervical Cancer cases.

The women screened and diagnosed with HPV infection develop cervical cancer and advance to different stages. The changes from one stage to another are represented with the help of differential equations and the proportionality constants are estimated with the help of observed/published data. The changes in stages are then graphically demonstrated. In this section, the changes in the number of women in different stages of diagnosed Cervical Cancer are discussed.

a) Diagnosed Dysplasia

Dysplasia stage is characterized by HPV presence however there is no conversion of epithelial cells to Cancerous stage. Let the number of women in Dysplasia stage be denoted by $m_0(t_0)$ which is assumed to be at constant up to time t_s then we have .

$dm_0(t)/dt = 0$, when $0 \leq t \leq t_s$ and $m_0(t_0) \leq 1442 \leq m_0(t)$.

The total number of Women with Diagnosed Dysplasia is proportional to the number of women susceptible to HPV and underwent screening and the number of women who with medical intervention regress from stage 1 to Dysplasia minus the Number of women who progress from Dysplasia to Stage 1. Therefore, the rate of change in the population of women with Diagnosed dysplasia can be expressed as;

$$dm_0(t)/dt \propto (r)(m_1). \quad (6.28)$$

Changing the proportionality this give

$$dm_0(t)/dt = \alpha_7 r + \beta_1 m_1 - \alpha_8 m_1, \quad (6.29)$$

where $\alpha_{7=}0.2$ which is the progression factor of HPV from normal cells to m_0. This constant depends on; Virulence of HPV, General health status of the cervix and healthy living behaviour of the client.

$\alpha_{8=}5\%$ depicts the progression factor from m_0 to m_1;

$\beta_{1=0.8}$ represents regression factor (due to treatment intervention/natural clearance)

$r=1$, (Constant of proportionality r is taken as 1 for simplicity)

$$dm_0(t)/dt = 0.2 + 0.8\, m_1 - m_1 \quad (6.30)$$

$$= 0.2 - 0.2 m_1$$

$$m_1 = 1442$$

$$m_0 = (\alpha_7 r + \beta_1 m_1 - \alpha_8 m_1)t + k. \quad (6.31)$$

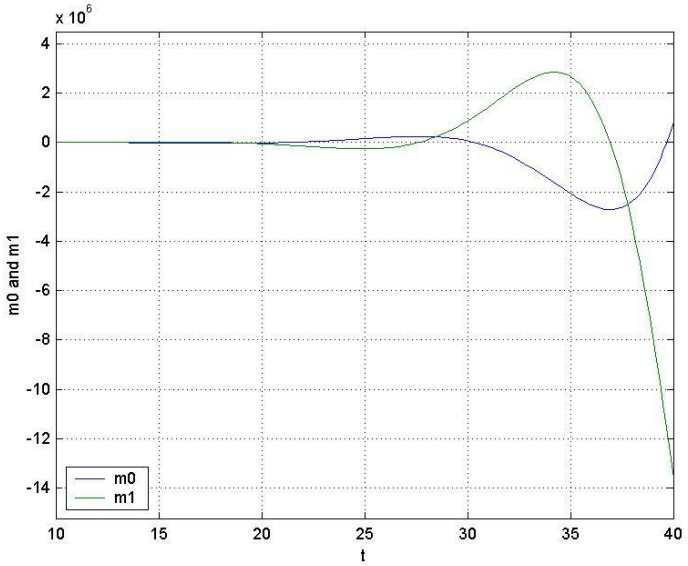


Figure 6.2. Progression from Diagnosed Dysplasia to Diagnosed Stage 1

Figure 6.2 shows a gradual increase in $m_0$until t_{29}after which m_o decreases up to $t_{38.}$ The period t_{38} to $t_{40}$is characterized by an increase in m_0. At the same time m_1 is marked by gradual increase up to t_{34} and thereafter m_1 decreases sharply up to t_{40}. This sharp decline in m_1 may be explained by the regression of the m_1 to m_0. Hence as the m_1 declines, the $m_0$increases slightly.

b) Diagnosed Stage 1

The initial number of women at Diagnosed stage 1 be denoted by $m_1(t_0)$ which is assumed to be at constant up to time $t_{s.}$ Let $m_1(t)$ be the number of women at stage 1 at any time $t>t_s$. The rate of change and the boundary condition are therefore;

$dm_1(t)/dt=0$ when $0\leq t\leq t_s$, $m_1(t_0)_{)}= 1442$ and $t > t_l$

The total number of Women with stage 1 among the diagnosed women is proportional to the number of women with dysplasia and the number of women who regress from stage 2 to stage 1.

Thus, the rate of change in the population of women at diagnosed stage one is expressed as,

$$dm_1(t)/dt= \alpha_9 m_0+\beta_2 m_2-\alpha_{10} m_{2.} \qquad (6.32)$$

where; α_9 =1, is the progression factor from dysplasia to stage1, β_2 =0.5, is the regression factor from stage 2 to stage 1, α_{10} =2,is progression factor from stage 1 to stage 2.

Time of progress from dysplasia to stage 1 is approximately 15 years and the time taken to regress from stage 1 to dysplasia is 1.4 years (Schlecht et al. 2003).

$dm_1(t)/dt=m_0+0.5m_2-2m_2$, (6.33)

$=m_0+1.5m_2$

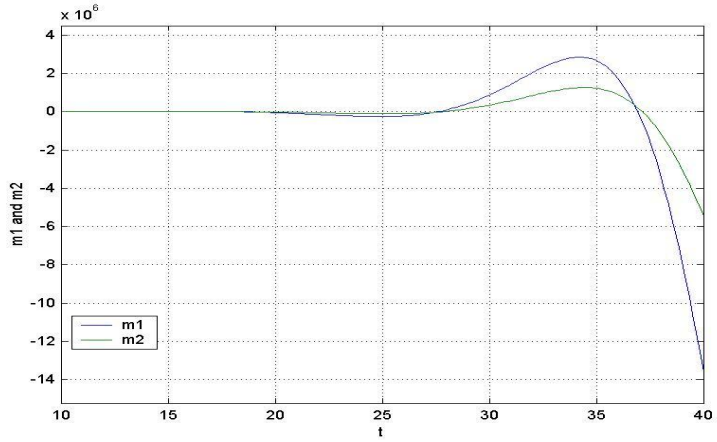


Figure 6.3 . Progression From Diagnosed stage 1 to Diagnosed Stage 2 .

In Figure 6.3, the progression ratefrom m_1 to m_2 is characterized by a relatively slight increase betweent_{10} to t_{20}. However after t_{20} there is slight increase in both m_1 and $m_2$upto t_{30} after which there is a higher increase in m_1 upto t_{35}. This is explained by the regression of a number of cases from m_2 to m_1.

c) Diagnosed Stage 2

Let the initial number of women at Diagnosed stage 2 be denoted by $m_2(t_0)$which is assumed to be at constant up to time t_s. Let $m_2(t)$ be the proportion of women at stage 2 at any time $t > t_s$.

Thus we have $d\, m_2(t)/dt = 0$ when $0 \leq t \leq t_s$ and $m_2(t_0) \leq 2884 \leq m_2(t)$

Thus, the rate of change of the population of women with diagnosed stage 2 is expressed as;

$d\, m_2(t)/dt = \alpha_{11} m_1 - \alpha_{12} m_2 - \beta_3 m_2$. (6.34)

where: α_{11}=2, is a constant dependent on progression factor from stage 1 to stage 2

α_{12} =4, is a constant that depends on the progression factor from stage 2 to stage 3, β_3=0.5, is constant representing regression from stage 2 back to stage 1.

m_1 is obtained from previous equation

$$dm_2(t)/dt=2m_1-4m_2-0.5m_2 \quad =2m_1-4.5m_2 \qquad (6.35)$$

Time of progress from stage 1 to stage 2 is estimated to be 5.6 years and the time taken to regress from stage 2 to stage 1 is 1 year(Schlecht et al. 2003).Even though the modellers appreciate possibility of death among the women Diagnosed with Dysplasia, stage 1 and stage 2 of Cervical Cancer, the death rates were assumed negligible for this study hence were not included in the model.

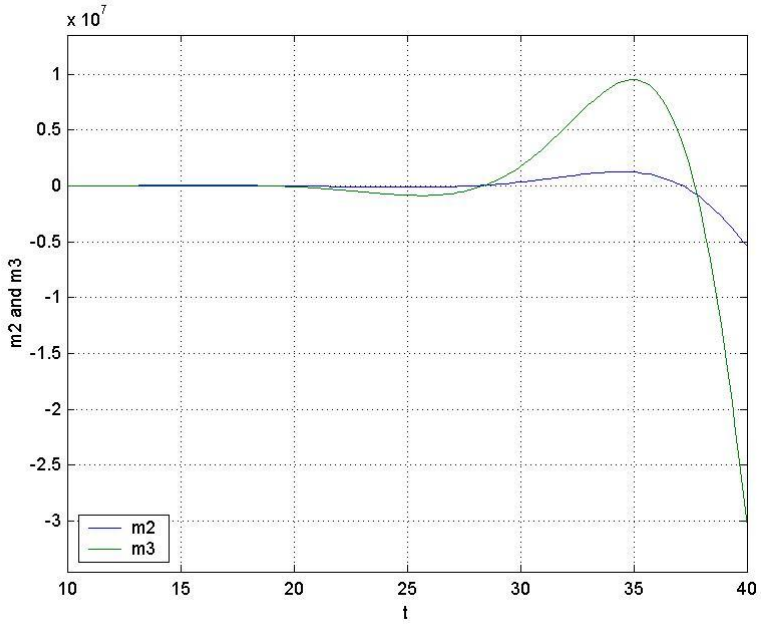


Figure 6.4Diagnosed Stage 2 to Diagnosed Stage 3 .

Figure 6.4 showschanges in m_2 and m_3 are both constant up to t_{22}. The m_3 shows slight decrease between t_{22} to t_{28} where as m_3 still remains constant. . It is noted that the rate of progression of m_3 declines drastically from t_{35}. .After t_{28}, there is a slight increase in m_2, but $m_3$increases sharply up to t_{35}. The progression rate of $m_3$declines sharply as compared to $m_2$after t_{35}. This can be attributed to the deaths at m_3.

d) Diagnosed Stage 3

Let the initial number of women at Diagnosed stage 3, be denoted by $m_3(t_0)$ which is assumed to be at constant up to time t_s. Let $m_3(t)$ be the number of women at stage 3 at any time t is $>t_s$.and$m_3(t_0)=11536$

Therefore, the rate of change among the population of women with diagnosed stage 3 is;

$dm_3(t)/dt = \alpha_{13} m_2 - \alpha_{14} m_4 - \beta_4 m_3,$ (6.36)

$\alpha_{13}=4$, is a constant dependent on progression factor from stage 2 to stage 3

$\alpha_{14}=1$, is a constant that depends on the progression factor from stage 3 to stage 4

$\beta_4=1$, is constant representing deaths at stage 3

$dm_3(t)/dt = 4m_2 - m_4 - m_3$ (6.37)

Time of progress from stage 2 to stage 3 is estimated at 6.1 years (Schlecht et al. 2003). The model also assumes there is no regression from stage 3 to stage 2.

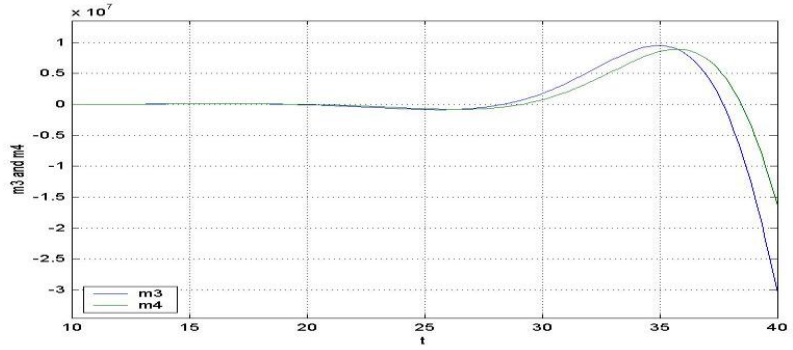


Figure 6.5 Diagnosed Stage 3 to Diagnosed Stage 4.

e) Diagnosed Stage 4

Let the initial number of women at Diagnosed stage 4 be denoted by $m_4(t_0)$ which is assumed to be at constant up to time t_s. Let $m_4(t)$ be the proportion of women at stage 4 at any time *when* $t > t_s$ and $m_4(t_0)= 11536$.

The rate of change in the total number of women with stage 4 among the diagnosed women is

$$d\,m_4(t)/dt = \alpha_{15} m_3 - \beta_5 m_4. \quad (6.36)$$

α_{15}=1, is a constant dependent on progression factor from stage 3 to stage 4

β_5=1, is constant representing deaths at stage 3

$$d\, m_4(t)/dt = m_3 - m_4. \quad (6.37)$$

Time taken for Cancer to progress from stage 3 to stage 4 is 1 year (Schlecht et al. 2003)

Figure 6.5 shows that the progression rates of both m_3 and $m_4$is constant up to time t_{20} and shows a slight decrease upto t_{27}. There after m_3 has relatively higher increase up to t_{35}as compared to m_4. This is followed by a sharp decrease in m_3 as compared to m_4 up to t_{40}. This can be attributed to the fact that deaths at stage three, would leave relatively smaller number to die at stage 4.

The coefficients of the model are estimated as the basis of the HPV infected women data for diagnosed and undiagnosed patients. Based on the proportionalities in Table 11, the trends of the diagnosed and undiagnosed patients are expected to be similar.

6.6 Unscreened and Undiagnosed Cervical Cancer Cases.

In this section the fate of the women who do not undergo screening and the stages they undergo in relation to Cervical Cancer are discussed. The women who missed screening and have undiagnosed HPV infections develop cervical cancer and advance to different stages. The change from one stage to another are represented with the help of differential equations and the proportionality constants are estimated with the help of observed data from documented studies. The changes in stages are illustrated graphically. Those who never go for screening progress through the same stages of cancer invasion but do not benefit from medical interventions. However some of these women may be screened at a later date and benefit from medical interventions. While this model appreciates this phenomenon, the number of women who undergo this late /accidental screening has been assumed negligible and hence are not included in this mathematical model. The total number of women with Undiagnosed HPV is denoted by where $W(t_0)$=872418

a) Undiagnosed Dysplasia

The number of women with undetected/ undiagnosed Dysplasia is denoted by $w_0\ (t_0)$ which is assumed to be at constant up to time t_s. Let $w_0(t)$ be the number of women at Undiagnosed Dysplasia at any time $t > t_s$ and $w_0(t_0)$=43621

The rate of change in undiagnosed dysplasia is therefore;

$d\, w_0(t)/dt = \alpha_7[q-r]$ and $t > t_l$, (6.38)

t_l is the level off time when there are no more women available for progression to Dysplasia stage.

α_7 is the progression factor of HPV from normal cells to w_0. This constant depends on; virulence of HPV subtype, general health status of the cervix and health living behaviour of the client.

q *i*s the proportion of women eligible for screening

r is the proportion of screened women with undiagnosed Stage 1cervical cancer.

The undiagnosed dysplasia stage progresses to be stage 1 of undiagnosed Cervical Cancer.

b) Undiagnosed Stage 1

Let the Initial number of women with Undiagnosed stage 1 be denoted by $w_1(t_0)$ which is assumed to be at constant up to time t_s. Let $w_1(t)$ be the number of women at Undiagnosed stage 1 at any time $t > t_s$ *and* $w_1(t_0) = 43621$.

The change in the proportion of women with undiagnosed stage one Cancer at any given time is

$$d\, w_1(t)/dt = \alpha_{16} w_0 - \beta_6 w_1, \quad (6.39)$$

where; α_{16} is the progression factor from undiagnosed dysplasia to undiagnosed stage1, β_6 is progression factor from undiagnosed stage one to undiagnosed stage 2.

c) Undiagnosed Stage 2

The initial number of women at undiagnosed stage 2, be denoted by $w_2(t_0)$ which is assumed to be at constant up to time t_s. Let $w_2(t)$ be the number of women at Undiagnosed stage 2 at any time $t > t_s$. and $w_2(t_0) = 87242$

and the boundary condition is ;

$dw_2(t)/dt = 0$ when $0 \le t \le t_s$ and $w_2(t_0) \le 87242 \le w_2(t)$, (6.40)

Thus, the rate of change in the proportion of women with undiagnosed stage 2 is therefore,

$$d\, w_2(t)/dt = \alpha_{17} w_1 - \beta_7 w_2, \quad (6.41)$$

where: α_{17} is a constant dependent on progression factor from undiagnosed stage 1 to undiagnosed stage 2, $\beta_7$is a constant that depends on the progression factor from undiagnosed stage 2 to undiagnosed stage 3.

d) Undiagnosed Stage 3

The initial number of women at Undiagnosed stage 3 be denoted by $w_3(t_0)$ which is assumed to be at constant up to time t_s. Let $w_3(t)$ be the number of women at Undiagnosed stage 3 at any time $t > t_s$ and $w_3(t_0) = 348967$.

. The boundary conditions therefore is,

$w_3(t)/dt = 0$ when $0 \leq t \leq t_s$ and $w_3(t_0) \leq 348967 \leq w_3(t)$.

The rate of change of the proportion of women with Undiagnosed stage 3

$$dw_3(t)/dt = \alpha_{18} w_2 - \beta_8 w_3 - \beta_9 w_3 , \quad (6.42)$$

where: α_{18} is a constant dependent on progression factor from undiagnosed stage 2 to undiagnosed stage 3, $\beta_8$is a constant that depends on the progression factor from undiagnosed stage 3 to undiagnosed stage 4, β_9 is a constant of a factor representing death at stage 3.

e) Undiagnosed Stage 4

The initial number of women at Undiagnosed stage 4 be denoted by $w_4(t_0)$ which is assumed to be at constant up to time t_s. Let $w_4(t)$ be the number of women at Undiagnosed stage 4 at any time t is $> t_s$.

$$d w_4(t)/dt = \alpha_{19} w_3 - \beta_{10} w_4, \qquad w_4(t_0) = 348967 \quad (6.43)$$

α_{19} is a constant dependent on progression factor from undiagnosed stage 3 to undiagnosed stage 4 and β_{10} is a constant of a factor representing death at stage 4.

The growth patterns of the various stages for both diagnosed and undiagnosed status in the population were identical with the only difference being the initial values that are taken from the (WHO/ICO 2010) with 2010 as the base year.

6.6 Death from Cervical Cancer

Some of the women are permanently removed from the model through death denoted by (z) .

Let the initial number of women deaths as a result of Cervical Cancer is denoted by $Z(t_0)$ which is assumed to be at constant up to time t_s. Let $Z(t)$ be the number of women who die from both diagnosed and undiagnosed Cervical Cancer at any time t is $> t_s$. The boundary and the rate of change is therefore,

$$\frac{dZ(t)}{dt}=0, \text{ when } 0\leq t\leq t_s \quad \text{and} \quad Z(t_0) \geq 2000 \leq z(t), \tag{6.44}$$

Death as a result of undiagnosed Cervical Cancer

$$z_2=\beta_{12}w_3+\beta_{14}w_4 \tag{6.45}$$

$$z_3=\beta_5 m_4+\beta_4 m_3 \tag{6.46}$$

$$Z \text{ (Total Death from cervical cancer)} = z_2+z_3. \tag{6.47}$$

The proportion of death at any one time is dependent on the women available to die from cervical cancer. The number of women infected with HPV and at different stages of Cervical Cancer at any time in the country though difficult to estimate to exact number can still be estimated.

6.7 Conclusion

In this chapter, the dynamic time varying model for estimating control variables and changes in trends therein has been developed. Baseline data set adapted from WHO and published reports was used to test the model. These initial conditions form the basis for further investigation into the topography of Cervical Cancer in Kenya as well as prediction of the trends that Cervical Cancer is likely to take. The model is dynamic in the sense that it can be adjusted over the time of investigation. The model predicted reasonable estimates of real life expectations of both progression and death from Cervical Cancer.

CHAPTER SEVEN: CONCLUSION, DISCUSSION, AND FUTURE WORK

7.1 Introduction

This chapter summarizes the thesis, discusses its findings and contributions, points out

Limitations of the current work, outlines directions for future research and brings the thesis to a conclusion.

7.2 Summary of the Thesis

This study aimed at evaluating the clinical and socio-economic impact of primary Vaccination, secondary Vaccination, screening and use of e-health tools in Cervical Cancer management in Kenya.

Phase One of the study comprised of a qualitative study aimed at establishing experiences, opportunities and challenges faced by Cervical Cancer managers in Kenya. Four themes of challenges were identified. These were related to; Patients, Individual health care providers.Health facility and Information Technology. Mobile phones were identified as having great potential for improving the management of Cervical Cancer in Kenya. Peculiar negative attitude towards screening procedure and the negative attitude of some managers towards Cervical Cancer patients need urgent attention. Cervical cancer management approaches have consistently advocated for cervical cancer screening oblivious of the socio-cultural barriers to the procedure itself. This was seen as a possible reason as to why rate of cervical cancer screening is low even among health care workers. This model advocates for a systems view of cervical cancer management which must seek to deal with ways of addressing hindrances to the different proposed interventions.

Phase two comprised of a cross sectional survey done to establish; the extent of use of e-health tools by Cervical Cancers clients, the characteristics of patients associated with internet use and identify barriers faced in internet use. The study established low level (7.5%) use of the internet. The main barriers identified to low internet access were; lack of knowledge on how to use computers and lack of access to a computer. High level of access to mobile phones was reported. This is an indicator of great

potential for use of mobile phones in the management of Cervical Cancer through short messaging services (sms), with or without internet connectivity.

In Phase 3, a System Dynamics (SD) model was developed using iThink™ version 9.1.3 software package. Trend of Cervical Cancer was represented using a system of differential equations solved using Integral Calculus approximations.
Validation of the model was done through expert interactive review of simulated experiments and any discrepancies were utilized to modify the model.
Virtual experiments were run to assess the socio-economic impact of different interventions. Current levels of coverage were compared with different intervention scenarios including a 'realistic' coverage of 30% of the three traditional Interventions as well as addition of use of e-health tools intervention. The model confirmed effectiveness of the four strategies in management of Cervical Cancer; however the impact of the interventions varied according to the various scenarios simulated. Disability Adjusted Life Years (DALYs) were utilized as economic indicators. It was implied that as a matter of policy, Kenya should consider secondary vaccination, primary vaccination and use of e-health tools as a matter of priority. These should be complemented by screening.

In phase four, a mathematical model for cervical cancer in Kenya was presented using differential equations. Different stages and status in regards to screening and vaccination were described through Control and State Variables. Coefficients of the model were estimated as the basis of the HPV infected women data for diagnosed and undiagnosed patients.
The study generated an innovative decision support SD model that can guide in designing the health care system in delivery of Cervical Cancer management in Kenya as well as inform Policy formulation based on expected outputs of various interventions.

7.3 Discussion

7.3.1Contribution of the thesis

This thesis presents a simulation model for evaluating the possible effects of screening and vaccination campaign against Human Papillomavirus [HPV], as well as

impact of use of e-health tools in Kenya. In this study, e-health coverage levels among cervical cancer clients was established.

This model builds on the body of Knowledge. It is a unique study done in Kenya and most likely in Africa. Improvement of Health care delivery using existing Health care practices, mathematical modelling, Computer simulation and information technology was achieved. This model provides a policy decision support vehicle that can allow for choice between different interventions based on their expected outcomes. This model can be modified/expanded to include new research findings. Collaborative research between diverse professional and regions (Kenya, Canada and Australia) was achieved

7.3.2Achievements

Two papers were published in International peer reviewed Journals available on http://www.biomedcentral.com/1756-0500/5/559 and http://www.biomedcentral.com/1756-0500/6/136. One other paper submitted to BMC, Cost Effectiveness and Resource Allocation

Journal was in press. The thesis demonstrated that health care workers can partner and collaboration with applied mathematics and engineering disciplines to enhance efficiency of Health Sector. Engineering principles can be successfully applied in redesigning health systems.

7.4 Study Limitations

Each phase of the study had its own unique limitations outlined in specific chapters. This population based model relied on aggregate point data which did not allow for probability variations. There is limited epidemiological data on Cervical cancer in Kenya, hence data availability was a challenge. Even though Population based models are easier to construct, they may miss out on uniqueness of individual clients and hence may not allow the history of each individual client to be tracked. The model was not differentiated by socioeconomic status hence socioeconomic status interventions could not be established. The need for vaccination booster was not included in the model. HPV has been known to cause other genital Cancers. Effects of HPV vaccination on these other Cancers were not simulated and hence it may be necessary to develop a model for these other cancers.

7.5 Recommendations

Women Population

i. Change attitude towards screening
ii. Work to overcome cultural barriers.
iii. Utilize e-health tools for Health education

Policy Formulators

i. Include attitudes and culture in policy development
ii. Incorporate and encourage secondary and primary vaccinations as a matter of priority.
iii. Encourage acceptability of screening preferably provide conducive health facilities which should ensure , cultural sensitivity. , Preferably elderly female health care workers should carry out screening when clients are not comfortable with other age groups and gender.
iv. Incorporate use of e-health tools in the policy on cervical cancer.

The Donors community

i. Address issues of vaccine affordability , availability and Sustainability especially to developing countries
ii. Incorporate Vaccination to existing health systems structures

Health Care Managers

i. Overcome negative attitudes towards screening and cervical cancer clients.
ii. Utilize e-health tools in health education, Dissemination of knowledge and practices, consult and seek advice
iii. Ensure Competence based training on cervical cancer management to relevant health care workers.
iv. Incorporate cultural sensitivity into practice.
v. Increase collaborative multi disciplinary research

Over all, Kenya as a country should consider adoption of secondary catch up vaccination as an immediate measure to curb Cervical Cancer. This should be coupled with pre-adolescent girls' vaccination. Of importance was the consideration of the negative attitude of both Cervical Cancer clients and staff towards Cervical Cancer

screening procedure. Any policy which Kenya adopts must take these attitudes into consideration. Either implements vaccination which though expensive is more culturally acceptable or finds a way of improving the attitude towards screening preferably through use of e-health tools.

7.6 Future Work

Effects of HPV vaccination on these other cancers of reproductive system were not simulated and hence it may be necessary to develop a model in which effects of HPV vaccination to these other Cancers of reproductive system are considered. Incorporate variability effects of HIV, Male circumcision, extended benefits in SD model.

The impact of the private sectors as well as Faith based organizations need to be considered. There is need to develop a model on the implication of Vaccination, screening and use of e-health tools in developing economies, and Africa in particular.

Analyse and design strategies to overcome negative attitudes towards cervical cancer screening procedure and towards the cervical cancer clients.

Strategies to establish and deal with possible negative impact of e-health interventions.

7.7 Conclusion

Systems Dynamics modelling is instrumental in Tests of effectiveness of alternative policies, design strategies and is instrumental in informed decision making. This model generated reasonable estimates in evaluation of effects of different interventions on Cervical Cancer management in Kenya. Interim Cervical Cancer management policy is derived. The model charts informed debate leading to development of new consensus policy on screening , vaccination and use of e-health tools. Cervical Cancer needs to be managed and monitored continuously with screening being implemented as a complimentary intervention to vaccination. Kenya as a country need to consider implementing catch up and primary vaccination as an urgent measure to curb Cervical Cancer.

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APPENDICES

APPENDIX 1: Table 1: PARAMETER(S) Estimates and Sources

Factor[s]	Value	Source of Information	Notes
Cervical Cancer BASE CASE[Year 2010]			
Prevalence rate	38.8	(WHO/ICO 2010)	
Crude Incidence rate/100000	16.5	[(WHO/ICO 2010)	Year 2009
Number of deaths	2100	[(WHO/ICO 2010)	
Number of cases	4178	(WHO/ICO 2010)	
No diagnosed with Cervical cancer Each year	2635	(WHO/ICO 2010)	
2011 life expectancy in Kenya	60.7		
Average age of onset of Cervical Cancer	45 Years	Baseline Survey	
Average Duration of Cervical Cancer	7.5years	Experts Opinion	
DALY assumptions For Cancer			
Age of onset of death or disability in years [a]	40.	Baseline Survey	
Disability weight [D]	0.81		
Percent of surviving cases with sequelae	0%	Expert Opinion	Assumed all eventually will die from Ca Cervix
Mortality to incidence ratio	.55	(WHO/ICO 2010)[36]	
Mortality from other causes not directly connected to Cancer of Cervix	0.008	Experts Opinion	This was considered insignificant hence not modeled.
Crude mortality rate	13.2	(WHO/ICO 2010)	
Age-standardized mortality rate	23.4	[(WHO/ICO 2010)	
Screening coverage rate within 3 years	3.2	(WHO/ICO 2010)	
Rate of Primary Vaccination	0.01	Experts Opinion	Limited data available
Rate of Secondary Vaccination	0.03	Experts Opinion	Limited data available
No of Primary Vaccinations required to avert one case of Ca Cervix	250	(Gillian D Sanders & Taira 2003)	Assuming a life time protection

No of Primary Vaccinations required to avert one case of Ca Cervix	600	(Gillian D Sanders & Taira 2003)	Assuming waning off of vaccine protection after 10 years.
No of Secondary/Catch up Vaccinations required to avert one case of Ca Cervix	324	(Gillian D Sanders & Taira 2003).	
E-health Usage			
Percentage with access to internet	7.5	Baseline Survey	
Percentage with access to Mobile phone	96	Baseline Survey	
Percentage with Positive Attitude towards use of e-health	95	Baseline Survey	
PROGNOSIS OF Undiagnosed Ca. Cervix			
Percentage of death from invasive cancer	33	(Myers & McCrory 2000)	
time span between infection of HPV and development of Carcinoma in Situ	7 to 15 years	(Makin & Kamanu Chuks 2010)[12]	
Years taken by precancerous cells to progress to cancerous cells	5	[12(Makin & Kamanu Chuks 2010)	
Percentage of progress from precancerous stage to undiagnosed stage one	3 – 10%	(Makin & Kamanu Chuks 2010)(Myers & McCrory 2000)	
Percentage of Regression from precancerous stage to 'clean' state through Immune reaction	90-97%	(Makin & Kamanu Chuks 2010)(Myers & McCrory 2000)(Schlecht et al. 2003)	
Progression of undiagnosed cancer from stage 2 to Stage 3	40%	(Schlecht et al. 2003)	
Progression of Undiagnosed cancer from stage 3 to stage 4	80%	(Schlecht et al. 2003)	
PROGNOSIS OF diagnosed Ca. Cervix			
Treatment impact/five year survival rate			
Early intervention Survival rate	92%	(Schlecht et al. 2003)	.277
Stage 1 Survival rate	90%	(Schlecht et al. 2003)	.271
Stage 2 Survival rate	60-80%	(Schlecht et al. 2003)	Average 70% used in this model .211
Stage 3 Survival rate	50%	(Schlecht et al. 2003)	.151
Stage 4 Survival rate	Less than 30%	(Schlecht et al. 2003)	30% used in this model .091

APPENDIX 2: STEPS ON AN E-HEALTH JOURNEY

In order to outline some of the uses of those aspects of *e-health*, which shows possible interaction of patient and care providers' interaction with e-health tools, a simple client's e-health journey will act as an example.

Activity	**E-health Tool**	**Socioeconomic Benefits**	**Clinical Benefits**	**Parameters To Consider**	**INPUTS/ COST**
Client reads information about healthy lifestyles on a government sponsored Website. On the site she finds a questionnaire on possible genetic predisposition to Cervical Cancer. Client completes the questionnaire and realizes she could be at risk of Cervical Cancer. Following the advice on the website, she visits her general practitioner's website to arrange an appointment for further advice.	Internet Electronic booking	Better informed citizens about prevention Confidence in seeking medical help Clients exercise reasonable levels of choice. Access to information Patient is informed about their responsibilities in seeking medical health Client	Clinicians receive clients in less advanced stages of Cervical Cancer hence early diagnosis and treatment.	Availability of internet Connectivity of internet Appropriateness of web content Number of women accessing/reading the website Seeking medical care after reading from the website.	Government develops website Purchase of computer software with Electronic booking system Equip G.P with computers Training of health care providers in Informatics.
Her GP examines her and agrees that something is not quite right. Suspecting that client may be showing early stages of Cervical Cancer, the GP uses the national oncology decision support tool.	Oncology Decision support tools	Clinicians supported by colleagues	Provides informed and patient oriented services	Availability of DSS in oncology GP Use of e-health tools	Cost of computers Cost of Computer software with decision support tools.
Based on result, GP uses the regional health network to book an urgent appointment with a radiologist at the local hospital	Electronic Health Records Electronic booking	Time saved, no traveling to book appointment	Early timely investigations	Availability of HER Willingness of Radiologist to use e-health tools	Cost of established /establishing electronic Cancer registries.

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Activity	E-health Tool	Socioeconomic Benefits	Clinical Benefits	Parameters To Consider	INPUTS/ COST
An entry into her Electronic Health Record using both a natural language description and an internationally recognized code for clinical diagnoses.	EHR	Health information availability to provider	A second opinion can be sought Use of a common international language will guide uniform quality management.	Availability and connectivity to EHR	Established EHR with description of all clinical diagnosis
On returning home, client accesses the internet once more to find a local Women's health support network. Using a specialist health-oriented search engine she finds several national and regional groups whose web pages give helpful outline information about diagnosis and treatment pathways in suspected cases of Cervical Cancer.	1.Internet 2.Online community 3.Cancer management tools	Provide social support Interaction between clients, care givers and clinicians	A well informed client will participate in planning of own care.	Connectivity and availability of internet Availability of online community Willingness of online community to interact Capability of client to make decision Appropriateness of content	Developing and web management cost of a national and international health information providing websites.
The radiologist examines client using a digital imaging system. Immediately after the images are captured, he stores them in her Electronic Health Record and simultaneously forwards the images involving three dimensional pattern recognition and comparison tools with an international quality assured image dataset.	1.Digital imaging systems 2. EMR 3.Internationa quality assured image data bases	Travel costs saved Immediate availability of results to care providers	Accesses to clients information and improves interphase between primary and secondary care	Availability of Digital Imaging systems, HER and interconnectivity of computers systems between radiologist and oncologist.	Cost of Digital Imaging systems
The digital system recognizes that some of the tissue density is indicative of a Cancer. The radiologist interprets the results of the image processing and advises client that she should see a Cancer specialist.	Digital diagnostic system availability	Immediate availability of investigation results	Reduction of diagnostic errors.	Availability of diagnostic systems	Cost of digital diagnostic systems

Activity	E-health Tool	Socioeconomic Benefits	Clinical Benefits	Parameters To Consider	INPUTS/ COST
He makes the necessary appointment using the secure regional health information network. He also advises Sophie to see the Cancer counseling service located in the same hospital	Electronic booking EMR Online counseling services	No traveling to another site to book appointment Saves cost and time.	Psychological care Multidisciplinary care	Availability of online counseling services connectivity	Software supporting online booking /counseling Cost of internet access to client
The specialist is able to access all clients medical notes from both the general practitioner and radiologist using the regional secure network	EMR	Availability of all patients information	The clinician makes a better informed decision with access to all information.	Integration of information systems to all health care providers	Hardware and appropriate software
After examination, the specialist orders a series of blood test and arranges for a biopsy to be taken	Electronic Health records Electronic recall system	Time saved	Investigations ordered right on time	Availability of soft ware with supportive tools. Connectivity within care providers	Hardware and software costs
The tests reveal certain drug sensitivities. These are duly entered into the Electronic Health Record so that they may be linked into the regional electronic prescribing system in order to avoid possible medication errors in subsequent treatments.	Decision support systems Electronic Health records	The patient is protected from erroneous prescription and consequences.	Reduction of medication errors	Availability of accurate information.	Hardware costs Soft ware costs
On receiving the biopsy results, the specialist consults an online database of medical evidence before confirming that client has the early stages of Cervical Cancer. She thinks it would be advisable to start therapy as soon as possible. However, before enrolling her in the therapy, client asks for permission to send the data acquired through radio imaging and biopsy to a colleague in another country for a second opinion.	EMR(Online data bases Decision support tools Second medical opinion Electronic Medical Records	Client involvement Saves travel costs for client in contacting a second care provider	Second medical opinion	Informed clients Willingness to allow information to be shared Appropriate policy for online transmission of medical records.	Cost of online database Hardware costs Soft ware costs
Activity	**E-health Tool**	**Socioeconomic Benefits**	**Clinical Benefits**	**Parameters To Consider**	**INPUTS/ COST**

The specialist uses the hospital's internal booking system to arrange client's first course of treatment to commence in three weeks and makes all the necessary additions to Client's EHR and advises her to seek support from the counseling centre and her general practitioner.	Electronic booking system Decision support tools	Time saving and immediate booking	DST reduce diagnostic error	HER Attitudes of Health care providers to use of e-health tools.	Cost of soft ware Cost of hardwares Training of Health care providers
Client visits the counseling centre where she is able to give a nurse access to her EHR. The nurse considers the medical report in conjunction with the personal information the client gives her. Using a complex database, she is able to retrieve and print several pages of health information targeted at client's current needs. She also gives client some references to trustworthy websites where she can find further information.	EHR WEB sites	Better informed clients	Provision of more informed and patient oriented services Improve interphase between primary and secondary care	Attitudes of clients Attitudes of health care providers Connectivity and information flow between primary and secondary care providers	
Client's radiotherapy treatment is based upon an enhanced planning system which formulates the shape of the beam and dosage to offer minimum dosage and optimum targeting. After three courses a second biopsy and radiogram reveal that all pre-Cancerous tissue has been removed	DSS	Lowered cost of care	Quality effective treatment through DSS planned and formulated dosage and targets.	DSS availability	SOFTWARE costs Hard ware costs
Client is discharged from the care of the oncologist. Her case history is noted and linked to an automatic screening recall system which means that from now on she will be invited to screening mammograms on a regular, 12-monthly basis.	EMR Electronic recall systems	Timely review Reminder alerts	Early detection of relapse	Availability, connectivity and willingness of client to use the e-health tools	Software and hardware costs
Her insurance coverage is automatically initiated and processed at each visit through the use of her health insurance smart card	EMR	Information to manage economic resources	Timely clinical are provide with assumption that economic	Availability of EMR	Software costs Hardware costs

at the point of care.		Application of e-health tools supports business process	constraints do not delay provision of care.		
Client is discharged and find continued support through the online community of people who have had similar experiences. Client continues medical treatment and through her online support system feels empowered to adjust her diet and exercise appropriately. Client begins to make a good recovery.	Online communities Supportive websites	Societal support	Psychological care enhanced	Availability of online communities Willingness of client and online community to interact Internet connectivity	WEB site costs Hard ware costs Internet access costs

APPENDIX 3: INTERVIEW SCHEDULER NURSE MANAGERS & PHYSICIANS

My name is Lucy Wanjuki Kivuti. I am a PhD student at School Of Mathematics University Of Nairobi. As part of my studies I am carrying out a study on;

System Dynamic Simulation Model For Assessing Clinical And Socio-Economic Impact Of The Use Of E-health Tools In Cervical Cancer Management In Kenya.

The study will help policy makers and other key stakeholders understand the impact of use of Internet and other Information technologies in Management of Cervical Cancer in Kenya.

I am requesting for your participation in this study in which you have been purposefully selected. Your anonymity will be ensured as no name will be entered anywhere in the script and you are under no obligation to disclose your name during the interview. Due to the nature of the study, the researcher will be required to tape this conversation with you.

You are free to withdraw from the interview and this study at any point without any repercussions whatsoever.

There will be no compensation or financial benefits awarded to you. Apart from conducting this study as a requirement for my studies and with an aim of improving Cervical Cancer management in Kenya, I have no competing interests in this study whatsoever.

Do you wish to take part in this study? *(Please tick as appropriate.)*

- Yes
- No-

Signature---------- (optional)

Instructions for research assistants. After introduction and signing of consent, Please position the tape recorder in a suitable place. Ensure that the room is as quite as possible and the voices are at a clear level of volume. The interview should not have interruptions however should there be interruption of any nature, pause the recorder until the interruption is sorted out and then continue with your interview.

Inform the respondent that,
THIS INTERVIEW WILL TAKE APPROXIMATELY 45 mins to 1 HOUR.
PLEASE ANSWER THE FOLOWING QUESTIONS AS HONESTLY POSSIBLE. YOU ARE ALLOWED TO VOICE AS MANY CONCERNS/ISSUES AS YOU HAVE DURING THIS INTERVIEW.

1. Age in completed years._____
2. How long have you been involved in care of Cervical Cancer management_____
3. In what capacity have you been involved in care patients with Cervical Cancer? ----------
4. Have you been involved in caring for patients with other types of Cancer? If so which ones? ----------
5. What challenges have you faced in management of Cervical Cancer patients?
6. Please tell me ways in which you have been able to tackle the challenges.
7. What future challenges do you anticipate in management of Cervical Cancer clients?
8. Have you used computer technology in management of Cervical Cancer? If so what ways? If no, give reasons or challenges faced in use of computer in management of Cancer.
9. Do you serve the internet in search of information or in management of Cervical Cancer? If so what sites have you visited in the last three months?
10. In what ways have you used the information obtained from the web?
11. In what ways would the internet and computers be useful in management of Cervical Cancer in Kenya?
12. What would be the role of the following players in ensuring that Cervical Cancer management benefited from use of technology?

a. The government/ ministry of health

b. The hospital

c. The health care provider

d. The patient/client

e. Any other party----------

13. Apart from use of computers and internet in management of Cervical Cancer, what other measures would the key players put in place to ensure successful management of Cervical Cancer in Kenya.
14. Is there is any other comment or issue you would like to add regarding management of Cervical Cancer in Kenya today and in the future?

Thank you for taking part in this study.

APPENDIX 4: INTERVIEW SCHEDULER FOR CLIENTS/PATIENTS

My name is Lucy Wanjuki Kivuti. I am a PhD student at School Of Mathematics University Of Nairobi. As part of my studies I am carrying out a study on

A Model for Assessing Clinical and Socio-Economic Impact of the Use of E-health Tools in Cervical Cancer Management in Kenya.

The study will help policy makers and other key stakeholders understand the impact of use of Internet and other Information technologies in Management of Cervical Cancer in Kenya.

I am requesting for your participation in this study in which you have been purposefully selected. Your anonymity will be ensured as no name will be entered anywhere in the script and you are under no obligation to disclose your name during the interview.

You are free to withdraw from the interview and this study at any point without any repercussions whatsoever.

There will be no compensation or financial benefits awarded to you. Apart from conducting this study as a requirement for my studies and with an aim of improving Cervical Cancer management in Kenya, I have no competing interests in this study whatsoever.

Do you wish to take part in this study? *(Please tick as appropriate.)*

- Yes
- No-

Signature---------- (optional)

Instructions for research assistants. After introduction and signing of consent,

Give the questionnaire to the patient/client to fill if they are literate or read out the questionnaire and fill in if the patient is illiterate or is in a position to write.

THIS INTERVIEW SCHEDULER WILL TAKE APPROXIMATELY 1 HOUR.

PLEASE ANSWER THE FOLLOWING QUESTIONS AS HONESTLY POSSIBLE. YOU ARE ALLOWED TO VOICE AS MANY CONCERNS/ISSUES AS YOU HAVE DURING THIS INTERVIEW.

BIOGRAPHICAL CHARACTERISTICS

Sex
Male

Female

Age at Next Birthday----------

Occupation----------

Highest level of education

- Pre-primary
- Lower primary
- Upper primary
- O level
- A level
- Diploma
- Degree
- Masters
- Phd
- Other----------(please specify)

Background information

1. For how long have you suffered from Cervical Cancer? ----------

   (Please give duration in months or years).

2. How did you find out about your diagnosis?
   - From the doctor
   - By myself
   - As part of routine check up

3. Where do you get information on Cervical Cancer from?(*tick all those applicable*)

- Doctors
- Nurses
- Friends
- Relatives
- Newspapers
- Radio
- Tv.
- Mobile phone
- Bill boards
- Any other(please specify)----------

4. Did you use the internet to search for information about Cervical Cancer?

- Yes(if yes go to question 6)
- No(if no go to question 5)

5. If No? What made you not search for information on the internet?(*tick all the applicable)*

- Don't know how to use computers/internet
- Lack of money to use on the internet
- Don't have access to a computer or internet.
- I do not trust the information from internet.
- Any other(please specify)----------

6. If yes? What made you search the internet for the information?

- Needed to learn more about Cervical Cancer
- Search for a doctor for management
- Connect with other people with the condition.
- Book appointment with the doctor

Any other(specify)----------

7. a) What web sites did you visit?

   Please specify----------.

   What was the content of the web?(please write all that you can remember about the content/issues addresses by the website)----------
   ----
   ----------.

8. Did you find any challenges in using the websites.
   - No
   - Yes(specify challenges faced)
     - Writing too small
     - Language too hard to understand
     - Too much information
     - Any other (specify)----------

       ----

9. How did you go about searching for information?
   - Was directed by the nurse/doctor.
   - Was guided by the cyber attendant
   - Used the local search engine
   - Any other(please specify)----------
     ----

10. In what ways have you used the information obtained from the web?
    - Gained more knowledge about the disease condition.
    - Learnt about online communities
    - Any other (specify) ----------

11. How much does it cost you to have access to internet per minute? _____

12. In what ways would the internet and computers be useful in management of Cervical Cancer in Kenya?
    - Booking patients online
    - Referral of patients online
    - Consulting the doctor/nurse online
    - Data collection
    - Consumer health education
    - Any other(specify)----------

13. How would you like to use a mobile phone in management of Cervical Cancer?
    - Booking appointment
    - Reminder alert of medication
    - Health education messages
    - Any other(specify)----------

14. What would be the role of the following players in ensuring that Cervical Cancer management benefited from use of technology?
    a. The government/ ministry of health.----------
    b. The hospital----------
    c. The health care provider----------
    d. The patient/client----------
    e. Any other party----------

15. Apart from use of computers and internet in management of Cervical Cancer, what other measures would the key players put in place to ensure successful management of Cervical Cancer in Kenya?

    i ----------

    ii ----------

    iii ----------

    iv ----------

    v ----------

    vi

16. Is there is any other comment or issue you would like to add regarding management of Cervical Cancer in Kenya today and in the future?----------
    ----

Thank you for your taking your time to take part in this study.

APPENDIX 5: LETTER TO KNH/UON ETHICS COMMITTEE

LUCY WANJUKI KIVUTI
SCHOOL OF NURSING SCIENCES
UNIVERSITY OF NAIROBI
P.O BOX 19676-KNH-00202
NAIROBI
Tel. 0710-499700
2711250(Office)

15TH JUNE 2009

THE CHAIRMAN
RESEARCH AND ETHICS COMMITTEE
KENYATTA NATIONAL HOSPITAL/UNIVERSITY OF NAIROBI
P.O BOX 20723
NAIROBI

Dear Sir/ Madam,

RE: REQUEST FOR REVIEW AND APPROVAL TO CONDUCT RESEARCH.

I am a lecturer at School of Nursing Sciences, and a PhD candidate with School of Mathematics, University of Nairobi. As part of studies I wish to conduct a study entitled, **A COMPUTATIONAL MODEL FOR ASSESSING CLINICAL AND SOCIO-ECONOMIC IMPACT OF THE USE OF e-health TOOLS IN CERVICAL CANCER MANAGEMENT IN KENYA.**

I hereby submit three copies of the research proposal for review and authorization.

Sincerely

Lucy Wanjuki Kivuti

APPENDIX 6: LETTER TO MINISTRY OF EDUCATION AND TECHNOLOGY

LUCY WANJUKI KIVUTI
SCHOOL OF NURSING SCIENCES
UNIVERSITY OF NAIROBI
P.O BOX 19676-KNH-00202
NAIROBI
Tel. 0710-499700
2711250(Office)

15TH JUNE 2009

THE CHAIRMAN
RESEARCH AND ETHICS COMMITTEE
MINISTRY OF SCIENCE AND TECHNOLOGY
JOGOO HOUSE-B
P.O. Box 30040,
NAIROBI

Dear Sir/ Madam,

RE: REQUEST FOR REVIEW AND APPROVAL TO CONDUCT RESEARCH.

I am a lecturer at School of Nursing Sciences, and a PhD candidate with School of Mathematics, University of Nairobi. As part of studies I wish to conduct a study entitled, **A COMPUTATIONAL MODEL FOR ASSESSING CLINICAL AND SOCIO-ECONOMIC IMPACT OF THE USE OF e-health TOOLS IN CERVICAL CANCER MANAGEMENT IN KENYA.**

I hereby submit three copies of the research proposal for review and authorization.

Sincerely

Lucy Wanjuki Kivuti

APPENDIX 7. LIST OF SD MATHS INTERPHASE

A_5_to_9(t) = A_5_to_9(t - dt) + (Turning_5 - Turning_10 - Pri_Vax - Un_Vac_Pre_Adolescent_Death) * dt
INIT A_5_to_9 = 2887000
INFLOWS:
Turning_5 = CONVEYOR OUTFLOW
OUTFLOWS:
Turning_10 = A_5_to_9/Transit_years
Pri_Vax = A_5_to_9*Uptake_Pri_Vac*Rate_of_ehealth_Coverage
Un_Vac_Pre_Adolescent_Death = A_5_to_9*Pre_Ado_Mortality_Rate
Detected_Dysplasia(t) = Detected_Dysplasia(t - dt) + (SCREENING_DONE - PROGRESSION_DX_1) * dt
INIT Detected_Dysplasia = 80000
INFLOWS:
SCREENING_DONE = Females_with_Pre_Cervical_cancer_HPV*Uptake_of_Screening*Rate_of_detection*Rate_of_ehealth_Coverage

OUTFLOWS:
PROGRESSION_DX_1 = Detected_Dysplasia/Yrs_to_onset_1*impact_of_treatment_on_Txt_1
Diagnosed_STAGE_1(t) = Diagnosed_STAGE_1(t - dt) + (PROGRESSION_DX_1 + Late_Screening_1 - PROGRESSION_DX_2) * dt
INIT Diagnosed_STAGE_1 = 900
INFLOWS:
PROGRESSION_DX_1 = Detected_Dysplasia/Yrs_to_onset_1*impact_of_treatment_on_Txt_1
Late_Screening_1 = Undiagnosed_Stage_1*Rate_of_ehealth_Coverage*Uptake_of_Screening
OUTFLOWS:
PROGRESSION_DX_2 = Diagnosed_STAGE_1/Yrs_to_Onset2*Impact_of_Txt_2
Diagnosed_STAGE_2(t) = Diagnosed_STAGE_2(t - dt) + (PROGRESSION_DX_2 + Late_Screening_2 - PROGRESSION_DX_3) * dt
INIT Diagnosed_STAGE_2 = 600
INFLOWS:
PROGRESSION_DX_2 = Diagnosed_STAGE_1/Yrs_to_Onset2*Impact_of_Txt_2
Late_Screening_2 = Undiagnosed_Stage_2*Uptake_of_Screening*Rate_of_ehealth_Coverage
OUTFLOWS:
PROGRESSION_DX_3 = (Diagnosed_STAGE_2/Yrs_to_Onset3)*Impact_of_treatment_3
Diagnosed_STAGE_3(t) = Diagnosed_STAGE_3(t - dt) + (PROGRESSION_DX_3 + Late_Screening_3 - PROGRESSION_DX_4) * dt
INIT Diagnosed_STAGE_3 = 625
INFLOWS:

PROGRESSION_DX_3 =
(Diagnosed_STAGE_2/Yrs_to_Onset3)*Impact_of_treatment_3
Late_Screening_3 =
Undiagnosed_Stage_3*Rate_of_ehealth_Coverage*Uptake_of_Screening
OUTFLOWS:
PROGRESSION_DX_4 = Diagnosed_STAGE_3/Yrs_to_Onset4*Impact_of_Txt_4
Diagnosed_STAGE_4(t) = Diagnosed_STAGE_4(t - dt) + (PROGRESSION_DX_4 +
Late_Screening_4 - DX_TERMINAL_DEATH) * dt
INIT Diagnosed_STAGE_4 = 1000
INFLOWS:
PROGRESSION_DX_4 = Diagnosed_STAGE_3/Yrs_to_Onset4*Impact_of_Txt_4
Late_Screening_4 =
Undiagnosed_Stage_4*Rate_of_ehealth_Coverage*Uptake_of_Screening
OUTFLOWS:
DX_TERMINAL_DEATH =
Diagnosed_STAGE_4/Years_to_Death_2*Impact_of_Txt_Terminal_Stage_2
Females_with_Pre_Cervical_cancer_HPV(t) =
Females_with_Pre_Cervical_cancer_HPV(t - dt) + (Total_new_cases -
SCREENING_DONE - Undetected_Dysplasia) * dt
INIT Females_with_Pre_Cervical_cancer_HPV = 1000
INFLOWS:
Total_new_cases = New_Cases
OUTFLOWS:
SCREENING_DONE =
Females_with_Pre_Cervical_cancer_HPV*Uptake_of_Screening*Rate_of_detection*Rat
e_of_ehealth_Coverage

Undetected_Dysplasia = Females_with_Pre_Cervical_cancer_HPV*Screening_Gap
Population(t) = Population(t - dt) + (delta_pop) * dt
INIT Population = 43013000
INFLOWS:
delta_pop = Population*Net_Increase_%
Population_2(t) = Population_2(t - dt) + (New_Births - deaths_2 - migrants_out) * dt
INIT Population_2 = Population
INFLOWS:
New_Births = Population_2*Birth\1000
OUTFLOWS:
deaths_2 = Population_2*deaths2__1000
migrants_out = Population_2*Nett_Migration\1000/1000
Pri_Vaccinated_A5_9(t) = Pri_Vaccinated_A5_9(t - dt) + (Pri_Vax -
Vaccinated_Turning_10 - Vac_Pre_Adol_Death) * dt
INIT Pri_Vaccinated_A5_9 = 0
INFLOWS:
Pri_Vax = A_5_to_9*Uptake_Pri_Vac*Rate_of_ehealth_Coverage
OUTFLOWS:
Vaccinated_Turning_10 = Pri_Vaccinated_A5_9/Transit_years

Vac_Pre_Adol_Death = Pri_Vaccinated_A5_9*Pre_Ado_Mortality_2
Total_YLD(t) = Total_YLD(t - dt) + (Yrs_lived_with_Disability) * dt
INIT Total_YLD = 1
INFLOWS:
Yrs_lived_with_Disability = Disabled_person_Year_per_yr
Undiagnosed_Stage_1(t) = Undiagnosed_Stage_1(t - dt) + (Progression_UN_DX_1 - PROGRESSION__UN_DX_2 - Late_Screening_1) * dt
INIT Undiagnosed_Stage_1 = 4000
INFLOWS:
Progression_UN_DX_1 = Un_DX_Dysplasia/Yrs_to_onset_1
OUTFLOWS:
PROGRESSION__UN_DX_2 = Undiagnosed_Stage_1/Yrs_to_Onset2
Late_Screening_1 = Undiagnosed_Stage_1*Rate_of_ehealth_Coverage*Uptake_of_Screening
Undiagnosed_Stage_2(t) = Undiagnosed_Stage_2(t - dt) + (PROGRESSION__UN_DX_2 - PROGRESSION__UNDX_3 - Late_Screening_2) * dt
INIT Undiagnosed_Stage_2 = 2000
INFLOWS:
PROGRESSION__UN_DX_2 = Undiagnosed_Stage_1/Yrs_to_Onset2
OUTFLOWS:
PROGRESSION__UNDX_3 = Undiagnosed_Stage_2/Yrs_to_Onset3
Late_Screening_2 = Undiagnosed_Stage_2*Uptake_of_Screening*Rate_of_ehealth_Coverage
Undiagnosed_Stage_3(t) = Undiagnosed_Stage_3(t - dt) + (PROGRESSION__UNDX_3 - PROGRESSION__UNDX_4 - Late_Screening_3) * dt
INIT Undiagnosed_Stage_3 = 1500
INFLOWS:
PROGRESSION__UNDX_3 = Undiagnosed_Stage_2/Yrs_to_Onset3
OUTFLOWS:
PROGRESSION__UNDX_4 = Undiagnosed_Stage_3/Yrs_to_Onset4
Late_Screening_3 = Undiagnosed_Stage_3*Rate_of_ehealth_Coverage*Uptake_of_Screening
Undiagnosed_Stage_4(t) = Undiagnosed_Stage_4(t - dt) + (PROGRESSION__UNDX_4 - UDX_TERMINAL_DEATH - Late_Screening_4) * dt
INIT Undiagnosed_Stage_4 = 1000
INFLOWS:
PROGRESSION__UNDX_4 = Undiagnosed_Stage_3/Yrs_to_Onset4
OUTFLOWS:
UDX_TERMINAL_DEATH = Undiagnosed_Stage_4*Mortality_Rate_at_Terminal_Stage/Years_to_Death_1
Late_Screening_4 = Undiagnosed_Stage_4*Rate_of_ehealth_Coverage*Uptake_of_Screening
Un_DX_Dysplasia(t) = Un_DX_Dysplasia(t - dt) + (Undetected_Dysplasia - Progression_UN_DX_1) * dt
INIT Un_DX_Dysplasia = 80000
INFLOWS:

Undetected_Dysplasia = Females_with_Pre_Cervical_cancer_HPV*Screening_Gap
OUTFLOWS:
Progression_UN_DX_1 = Un_DX_Dysplasia/Yrs_to_onset_1
Un_VacA45_64(t) = Un_VacA45_64(t - dt) + (Turning_45 - Turning_65 - A3_deaths) * dt
INIT Un_VacA45_64 = 2013000
INFLOWS:
Turning_45 = Un_Vac_A25_44/Transit_to_A45
OUTFLOWS:
Turning_65 = Un_VacA45_64/Transit_to_A65
A3_deaths = Un_VacA45_64*Adult_Female__mortality
Un_Vac_A10__14(t) = Un_Vac_A10__14(t - dt) + (Turning_10 - turning_15 - Gilrs__deaths - Sec_Vax_1) * dt
INIT Un_Vac_A10__14 = 2421000
INFLOWS:
Turning_10 = A_5_to_9/Transit_years
OUTFLOWS:
turning_15 = Un_Vac_A10__14/Transit_to_A15
Gilrs__deaths = Un_Vac_A10__14*Girl_Mortality_Rate
Sec_Vax_1 = Un_Vac_A10__14*Rate_of_ehealth_Coverage*Uptake_of_Sec_Vac
Un_Vac_A15_24(t) = Un_Vac_A15_24(t - dt) + (turning_15 - Turning_25 - A1deaths - Sec_Vax_2) * dt
INIT Un_Vac_A15_24 = 4204000
INFLOWS:
turning_15 = Un_Vac_A10__14/Transit_to_A15
OUTFLOWS:
Turning_25 = Un_Vac_A15_24/Transit_to_A25
A1deaths = Un_Vac_A15_24*Adult_Female__mortality
Sec_Vax_2 = Un_Vac_A15_24*Rate_of_ehealth_Coverage*Uptake_of_Sec_Vac
Un_Vac_A25_44(t) = Un_Vac_A25_44(t - dt) + (Turning_25 - Turning_45 - A2_deaths - Sec_Vax_3) * dt
INIT Un_Vac_A25_44 = 4929000
INFLOWS:
Turning_25 = Un_Vac_A15_24/Transit_to_A25
OUTFLOWS:
Turning_45 = Un_Vac_A25_44/Transit_to_A45
A2_deaths = Un_Vac_A25_44*Adult_Female__mortality
Sec_Vax_3 = Un_Vac_A25_44*Rate_of_ehealth_Coverage*Uptake_of_Sec_Vac
Un_Vac_A65Plus(t) = Un_Vac_A65Plus(t - dt) + (Turning_65 - Turning_over_65 - A_deaths) * dt
INIT Un_Vac_A65Plus = 580000
INFLOWS:
Turning_65 = Un_VacA45_64/Transit_to_A65
OUTFLOWS:
Turning_over_65 = Un_Vac_A65Plus/Transit_to_Over_65
A_deaths = Un_Vac_A65Plus*A65_mortality_Rate

Vaccinated_A15_24(t) = Vaccinated_A15_24(t - dt) + (Sec_Vax_2 +
Vacccinated_Turning_15 - Vaccinated_Turning_25 - A1_Death_2) * dt
INIT Vaccinated_A15_24 = 0
INFLOWS:
Sec_Vax_2 = Un_Vac_A15_24*Rate_of_ehealth_Coverage*Uptake_of_Sec_Vac
Vacccinated_Turning_15 = Vaccinated_A_10_14/Transit_to_A15
OUTFLOWS:
Vaccinated_Turning_25 = Vaccinated_A15_24/Transit_to_A25
A1_Death_2 = Vaccinated_A15_24*Adult_Female_Mortality__2
Vaccinated_A25_44(t) = Vaccinated_A25_44(t - dt) + (Sec_Vax_3 +
Vaccinated_Turning_25 - Vaccinated_Turning_45 - A2_Death_2) * dt
INIT Vaccinated_A25_44 = 0
INFLOWS:
Sec_Vax_3 = Un_Vac_A25_44*Rate_of_ehealth_Coverage*Uptake_of_Sec_Vac
Vaccinated_Turning_25 = Vaccinated_A15_24/Transit_to_A25
OUTFLOWS:
Vaccinated_Turning_45 = Vaccinated_A25_44/Transit_to_A45
A2_Death_2 = Vaccinated_A25_44*Adult_Female_Mortality_2
Vaccinated_A45_64(t) = Vaccinated_A45_64(t - dt) + (Vaccinated_Turning_45 -
Vaccinated_Turning_65 - A3_Death_2) * dt
INIT Vaccinated_A45_64 = 0
INFLOWS:
Vaccinated_Turning_45 = Vaccinated_A25_44/Transit_to_A45
OUTFLOWS:
Vaccinated_Turning_65 = Vaccinated_A45_64/Transit_to_A65
A3_Death_2 = Vaccinated_A45_64*Adult_Female_Mortality_2
Vaccinated_A_10_14(t) = Vaccinated_A_10_14(t - dt) + (Sec_Vax_1 +
Vaccinated_Turning_10 - Vacccinated_Turning_15 - Girls_Death_2) * dt
INIT Vaccinated_A_10_14 = 0
INFLOWS:
Sec_Vax_1 = Un_Vac_A10__14*Rate_of_ehealth_Coverage*Uptake_of_Sec_Vac
Vaccinated_Turning_10 = Pri_Vaccinated_A5_9/Transit_years
OUTFLOWS:
Vacccinated_Turning_15 = Vaccinated_A_10_14/Transit_to_A15
Girls_Death_2 = Vaccinated_A_10_14*Girls_Mortality_Rate_2
Vac_A65_Plus(t) = Vac_A65_Plus(t - dt) + (Vaccinated_Turning_65 -
Vaccinated_Turning_over_65 - A_Death_2) * dt
INIT Vac_A65_Plus = 0
INFLOWS:
Vaccinated_Turning_65 = Vaccinated_A45_64/Transit_to_A65
OUTFLOWS:
Vaccinated_Turning_over_65 = Vac_A65_Plus/Transit_to_Over_65
A_Death_2 = Vac_A65_Plus*A_65_Vacc_Mortality_Rate_2
YLL(t) = YLL(t - dt) + (Years_lost_to_death) * dt
INIT YLL = 1
INFLOWS:

Years_lost_to_death = Total_yrs_lost_due_to_Deaths
Yrs_LD(t) = Yrs_LD(t - dt) + (YLD_2) * dt
INIT Yrs_LD = 1
INFLOWS:
YLD_2 = D*(K*W*EXP(y*alpha)/(y+beta_1)^2)*(EXP(-1*(y+beta_1)*(l+alpha))*(-(y+beta_1)*(l+alpha)-1)-EXP(-1*(y+beta_1)*alpha)*(-(y+beta_1)*alpha-1))+((1-K)/y)*(1-EXP(-1*y*l))
Yrs_LL(t) = Yrs_LL(t - dt) + (YLL_2) * dt
INIT Yrs_LL = 1
INFLOWS:
YLL_2 = (K*W*EXP(y*alpha2)/(y+beta_1)^2)*(EXP(-1*(y+beta_1)*(life2+alpha2))*(-(y+beta_1)*(life2+alpha2)-1)-EXP(-1*(y+beta_1)*alpha2)*(-(y+beta_1)*alpha2-1))+((1-K)/y)*(1-EXP(-1*y*life2))
Age_0_to_4(t) = Age_0_to_4(t - dt) + (female_births - Turning_5 - Female_infant_deaths) * dt
INIT Age_0_to_4 = 3045000
	TRANSIT TIME = 4
	CAPACITY = INF
	INFLOW LIMIT = INF
INFLOWS:
female_births = (total_births)/2
OUTFLOWS:
Turning_5 = CONVEYOR OUTFLOW
Female_infant_deaths = LEAKAGE OUTFLOW
	LEAKAGE FRACTION = Underfive__mortality__Rate
	LEAK ZONE = 0% to 100%
$Cost_of_Screening_Method_Used = 15
$Cost_of__per_Each_Vacination = 15
$Cost_Per__Each_Primary_Vacciantion = 17
$Total_Cost_of_Catch_Up_Vaccination = Total_Sec_Vax_Pa*$Cost_of__per_Each_Vacination
$Total_Cost_of_Primary_Vaccination = Pri_Vax*$Cost_Per__Each_Primary_Vacciantion
$Total_Cost_of_screening = Total_Screened_Pa*$Cost_of_Screening_Method_Used
$_Total_Cost_of_intervention = $Total_Cost_of_Catch_Up_Vaccination+$Total_Cost_of_Primary_Vaccination+$Total_Cost_of_screening
A65_mortality_Rate = 30/1000
Adult_Female__mortality = 2.5/1000
alpha = 43
alpha2 = 60.7
Attitude_to_Primary__Vaccination = 0.9
Attitude_to_Screening = 0.06
Attitude_to_Sec_Vaccination = 0.8
Availability_of_Pri_Vaccination = 0.1
Availability_of_Screening = 0.1

Availability_of_Sec_Vaccination = 0.1
Average_age_of_Dx_death = 45
average_age_of_UDx_death = 49
average_Life_Lost_Due_to_Dx_Death = alpha2-Average_age_of_Dx_death
Average_Life_Lost_due_to_UDx_Death = alpha2-average_age_of_UDx_death
Averted_Via_Pri_Vacc =
Pri_Vax/No_of_Pri__Vaccinations_required_to_avert_one_case_oof_Ca_Cx
Averted_Via_Screening =
Total_Screened_Pa/No_of_screening_required_to_avert_a_case_of_Ca_Cx
Averted_Via_Sec_Vac =
Total_Sec_Vax_Pa/No_of_Sec_Vaccinations_required_to_avert_one_case_of_Ca_Cx
beta_1 = 0.04
Birth\1000 = 32/1000
Converter_1 = 1
Cost_$_Per_DALY_AVERTED =
$_Total_Cost_of_intervention/Total_Averted_DALYs
D = 0.81
d1 = (Total_Population)/Population
d2 = (Population_2-Population)/Population
deaths2__1000 = 7.26/1000
Desired_Level_of_Pri_Vaccination = 1
Desired_Level_of__Screening = 1
Develop_Cancer_Transit_Time = 15
Disabled_person_Year_per_yr =
(Early_Cancer_Diabled_persons_year_Per_yr+LC_Disabled_Persons_year_per_yr)
Early_Cancer_Diabled_persons_year_Per_yr = Total_Early_Cancer_Pa*D
Girl_Mortality_Rate = 7.5/1000
Impact_of_treatment_3 = 0.5
impact_of_treatment_on_Txt_1 = 0.75
Impact_of_Txt_2 = 0.7
Impact_of_Txt_4 = 0.3
Impact_of_Txt_Terminal_Stage_2 = 0.25
Incidence100k_Women = Develop_Cancer_Transit_Time/total_females/100000
Incidence_Rate_Per_100k_Women_15_24 = 13.6/100000
Incidence_Rate_Per_100K_Women_A25_54 = 13.6/100000
Incidence_Rate_Per_100k_Women_A55_64 = 105/100000
Incidence_Rate_Per_100K_women_A65_Plus = 79/100000
Incidence_Rate_Per_100k_Women_A_13_14 = 2/100000
K = 1
l = 15
LC_Disabled_Persons_year_per_yr = D*Total_Late_cancer_Pa
life2 = 15.7
MF_Ratio = 1
Mortality_Rate_at_Terminal_Stage = 650/1000
Nett_Migration\1000 = .23/1000
Net_Increase_% = 2.474/100

New_Cases_A13_14 =
(Incidence_Rate_Per_100k_Women_A_13_14*Un_Vac_A10__14)/2
New_Cases_A15_24 = Un_Vac_A15_24*Incidence_Rate_Per_100k_Women_15_24
New_Cases_A25_54 = Un_Vac_A25_44*Incidence_Rate_Per_100K_Women_A25_54
New_Cases_A55_64 = Un_VacA45_64*Incidence_Rate_Per_100k_Women_A55_64/2
New_Cases_A65Plus =
Un_Vac_A65Plus*Incidence_Rate_Per_100K_women_A65_Plus
No_of_Pri__Vaccinations_required_to_avert_one_case_oof_Ca_Cx = 250
No_of_screening_required_to_avert_a_case_of_Ca_Cx = 600
No_of_Sec_Vaccinations_required_to_avert_one_case_of_Ca_Cx = 352
Prevalence_as_% = Total_new_cases/total_females*100
Pre_Ado_Mortality_Rate = 3/1000
Primary_Vac_Gap = Desired_Level_of_Pri_Vaccination-Uptake_Pri_Vac
Rate_of_detection = 0.7
Rate_of_ehealth_Coverage = 0.3
Screening_Gap = Desired_Level_of__Screening-Uptake_of_Screening
Total_Averted_DALYs = (Yrs_LD+Yrs_LL)*Total__Cases__Averted
total_births = Total_Population*Birth\1000
Total_Cases_of_Cervical_Cancer_Pa =
DX_Cervical_Cancer_Pa+UDX_Diagnosed__Cervical_Cancer_Per__Pa
Total_Population = total_females*(MF_ratio+1)
Total_yrs_lost_due_to_Deaths =
(Years_of_Life_Lost_due_to_UDx_Deaths+Years_of_Life_Lost_due_to_Dx_Deaths)/C
onverter_1
Transit_to_A15 = 5
Transit_to_A25 = 10
Transit_to_A45 = 20
Transit_to_A65 = 20
Transit_to_Over_65 = 8
Transit_years = 5
Underfive__mortality__Rate = 0.0074
Uptake_of_Screening = Attitude_to_Screening*Availability_of_Screening
Uptake_of_Sec_Vac = Attitude_to_Sec_Vaccination*Availability_of_Sec_Vaccination
Uptake_Pri_Vac = Attitude_to_Primary__Vaccination*Availability_of_Pri_Vaccination
W = 0.1658
y = 0.03
Years_of_Life_Lost_due_to_Dx_Deaths =
average_Life_Lost_Due_to_Dx_Death*DX_TERMINAL_DEATH
Years_of_Life_Lost_due_to_UDx_Deaths =
UDX_TERMINAL_DEATH*Average_Life_Lost_due_to_UDx_Death
Years_to_Death_1 = 0.8
Years_to_Death_2 = 0.8
Yrs_to_Onset2 = 10
Yrs_to_Onset3 = 5
Yrs_to_Onset4 = 2
Yrs_to_onset_1 = 10

Adult_Female_Mortality_2 = Adult_Female__mortality/2
Adult_Female_Mortality__2 = Adult_Female__mortality/2
A_65_Vacc_Mortality_Rate_2 = A65_mortality_Rate/2
DALYs = Total_YLD + YLL
DX_Cervical_Cancer_Pa = PROGRESSION_DX_1 + PROGRESSION_DX_2 + PROGRESSION_DX_3 + PROGRESSION_DX_4
Girls_Mortality_Rate_2 = Girl_Mortality_Rate/2
New_Cases = New_Cases_A13_14 + New_Cases_A15_24 + New_Cases_A25_54 + New_Cases_A55_64 + New_Cases_A65Plus
Pre_Ado_Mortality_2 = Pre_Ado_Mortality_Rate
Total_A_10_14 = Un_Vac_A10__14 + Vaccinated_A_10_14
Total_A_15_24 = Un_Vac_A15_24 + Vaccinated_A15_24
Total_A_25_44 = Un_Vac_A25_44 + Vaccinated_A25_44
Total_A_45_64 = Un_VacA45_64 + Vaccinated_A45_64
Total_A_5_9 = A_5_to_9 + Pri_Vaccinated_A5_9
Total_Cases_of_Ca_Cervix_Pa = Total_Early_Cancer_Pa + Total_Late_Cancer_Pa
Total_Early_Cancer_Pa = PROGRESSION_DX_1 + PROGRESSION_DX_2 + Progression_UN_DX_1 + PROGRESSION__UN_DX_2
total_females = Age_0_to_4 + A_5_to_9 + Vaccinated_A_10_14 + Vaccinated_A15_24 + Vaccinated_A25_44 + Vaccinated_A45_64 + Vac_A65_Plus + Pri_Vaccinated_A5_9 + Un_Vac_A10__14 + Un_Vac_A15_24 + Un_Vac_A25_44 + Un_VacA45_64 + Un_Vac_A65Plus
Total_Late_Cancer_Pa = PROGRESSION_DX_3 + PROGRESSION_DX_4 + PROGRESSION__UNDX_3 + PROGRESSION__UNDX_4
Total_Screened_Pa = SCREENING_DONE + Late_Screening_1 + Late_Screening_2 + Late_Screening_3 + Late_Screening_4
Total_Sec_Vax_Pa = Sec_Vax_1+ Sec_Vax_2+ Sec_Vax_3
Total_Vaccinated_Pa = Pri_Vax + Sec_Vax_1 + Sec_Vax_2 + Sec_Vax_3
Total__Cases__Averted = Averted_Via_Pri_Vacc + Averted_Via_Screening + Averted_Via_Sec_Vac
TOTAL__DEATHS_DUE_TO_CA_CX_2_Pa = UDX_TERMINAL_DEATH + DX_TERMINAL_DEATH
UDX_Diagnosed__Cervical_Cancer_Per__Pa = Progression_UN_DX_1 + PROGRESSION__UN_DX_2 + PROGRESSION__UNDX_3 + PROGRESSION__UNDX_4

APPENDIX 8: MATLAB CODES USED

```
function
t=15:0.001:80;
initial_w_4=425462;
a_19=0.5;
beta_10=0.3;
w_3=425462;
[t,w_4]=ode45(@eq10,t,initial_w_4);
plot(t,w_4);xlabel('t');ylabel('w_4');title('Graph of women at
undiagnosed stage 4 against time');
function w_4_dot=eq10(t,w_4)
w_4_dot=a_19*w_3-beta_10*w_4;
end
end
```

```
function
t=10:0.001:80;
initial_m_0=1758;
a_7=0.1;
beta_1=0.1;
a_8=0.1;
r=374800;
m_1=1758;
[t,m_0]=ode45(@eq1,t,initial_m_0);
plot(t,m_0);xlabel('t');ylabel('m_0');title('Graph of women at
dysplasia stage against time');
function m_0_dot=eq1(t,m_0)
m_0_dot=a_7*r+beta_1*m_1-a_8*m_1;
end
end
```

```
function
t=10:0.001:80;
initial_m_1=1758;
a_9=0.2;
beta_2=0.2;
a_10=0.2;
m_0=1758;
m_2=3516;
[t,m_1]=ode45(@eq2,t,initial_m_1);
plot(t,m_1);xlabel('t');ylabel('m_1');title('Graph of women at
diagnosed stage 1 against time');
function m_1_dot=eq2(t,m_1)
m_1_dot=a_9*m_0+beta_2*m_2-a_10*m_2;
end
end
```

```
function
t=10:0.001:80;
initial_m_2=3516;
a_11=0.2;
beta_3=0.2;
```

```
a_12=0.2;
m_1=1758;
[t,m_2]=ode45(@eq3,t,initial_m_2);
plot(t,m_2);xlabel('t');ylabel('m_2');title('Graph of women at
diagnosed stage 2 against time');
function m_2_dot=eq3(t,m_2)
m_2_dot=a_11*m_1-beta_3*m_2-a_12*m_2;
end
end


function
t=10:0.001:80;
initial_m_3=14065;
a_13=0.3;
beta_4=0.3;
a_14=0.3;
m_1=1758;
m_2=3516;
[t,m_3]=ode45(@eq4,t,initial_m_3);
plot(t,m_3);xlabel('t');ylabel('m_3');title('Graph of women at
diagnosed stage 3 against time');
function m_3_dot=eq4(t,m_3)
m_3_dot=a_13*m_1-beta_4*m_3-a_14*m_2;
end
end


function
t=10:0.001:80;
initial_m_4=14065;
a_15=0.8;
beta_5=0.5;
m_3=14065;
[t,m_4]=ode45(@eq5,t,initial_m_4);
plot(t,m_4);xlabel('t');ylabel('m_4');title('Graph of women at
diagnosed stage 4 against time');
function m_4_dot=eq5(t,m_4)
m_4_dot=a_15*m_3-beta_5*m_4;
end
end


function
t=15:0.001:80;
initial_w_0=53183;
a_7=0.1;
q=11712506;
r=374800;
[t,w_0]=ode45(@eq6,t,initial_w_0);
plot(t,w_0);xlabel('t');ylabel('w_0');title('Graph of undiagnosed
dysplasia against time');
function w_0_dot=eq6(t,w_0)
w_0_dot=a_7-(q-r);
end
```

```
end



function
t=15:0.001:80;
initial_w_1=53183;
a_16=0.3;
beta_6=0.1;
w_0=53183;
[t,w_1]=ode45(@eq7,t,initial_w_1);
plot(t,w_1);xlabel('t');ylabel('w_1');title('Graph of women at
undiagnosed stage 1 against time');
function w_1_dot=eq7(t,w_1)
w_1_dot=a_16*w_0-beta_6*w_1;
end
end



function
t=15:0.001:80;
initial_w_2=106356;
a_17=0.3;
beta_7=0.3;
w_1=53183;
[t,w_2]=ode45(@eq8,t,initial_w_2);
plot(t,w_2);xlabel('t');ylabel('w_2');title('Graph of women at
undiagnosed stage 2 against time');
function w_2_dot=eq8(t,w_2)
w_2_dot=a_17*w_1-beta_7*w_2;
end
end




function
t=15:0.001:80;
initial_w_4=425462;
a_19=0.5;
beta_10=0.3;
w_3=425462;
[t,w_4]=ode45(@eq10,t,initial_w_4);
plot(t,w_4);xlabel('t');ylabel('w_4');title('Graph of women at
undiagnosed stage 4 against time');
function w_4_dot=eq10(t,w_4)
w_4_dot=a_19*w_3-beta_10*w_4;
end
end
```

APPENDIX 9: VERIFICATION OF THE CERVICAL CANCER MANAGEMENT MODEL

This conceptual model was designed as part of PHD studies with the aim of capturing the dynamics involved in management of cervical cancer in Kenya.

The target audience is

1. Nurse managers
2. Physicians involved in management of cervical cancer.
3. Public health educators
4. Policy formulators
5. Policy implementers.

QUESTIONS

		Yes	**NO**	**List those missing if any**
1.	Do all sectors stated in the model exist?			
2.	Are all variable within the sector stated?			
3.	Do the relationships stated exist?			
4.	Are the directions of the links right? Do they need to be reversed?			
5.	Are there other effects that could be observed?			

RESULTS

	YES	NO
Sectors exist	9(100%)	0
All variables included	8(89%)	1
Relationships stated exist	9(100%)	0
Directions of links right	8(89%)	1
Other effects that could be observed	9(100%)	0

APPENDIX 10: EVALUATION OF THE CONCEPTUAL MODEL

This too is administered after presentation of the model by the researcher to the individual evaluator or a group of evaluators.

In your opinion rate this cervical cancer management model in the following aspects *(Tick the most appropriate answer)*

		Very reasonable	Reasonable	Fairly reasonable	Not reasonable	MISSING (Please list)
1	Representation of reality					
2	Representation of issues of cervical cancer management in Kenya					
3	A tool to be used for communication on cervical cancer management					
4	Ability to stimulate systems /holistic view of cervical cancer management					
5	A tool useful as an aid to decision making					

RESULTS

	Very reasonable	Reasonable	Fairly reasonable	Not reasonable	MISSING (Please list)
Representation of reality	8(89%)	1(11%)	0	0	0
Representation of issues of cervical cancer management in Kenya	9(100%)	0	0	0	0
A tool to be used for communication on cervical cancer management	8(89%)	1(11%)	0	0	0
Ability to stimulate systems /holistic view of cervical cancer management	8(89%)	0	1		
A tool useful as an aid to decision making	9(100%)	0	0	0	

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THIS IS TO CERTIFY THAT:

Prof./Dr./Mr./Mrs./Miss. LUCY WANJUKI KIVUTI

of (Address) UNIVERSITY OF NAIROBI P.O. BOX 30197 NBI

has been permitted to conduct research in ..... **Location,** RIFT VALLEY , WESTERN, ~~District,~~ NAIROBI , EASTERN, COAST **Province,** s

on the topic Dynamic simulation model for assessing clinical and socio-economic impact of the use of e-Health tools in Cervical Cancer Management in Kenya.

for a period ending 30TH APRIL **,20** 13

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Research Permit No. NCST/RRI/12/1/MAS/56

Date of issue 28/04/2010

Fee received SHS 2,000

Applicant's Signature

Secretary National Council for Science and Technology

CONDITIONS

1. **You must report to the District Commissioner and the District Education Officer of the area before embarking on your research. Failure to do that may lead to the cancellation of your permit**
2. **Government Officers will not be interviewed with-out prior appointment.**
3. **No questionnaire will be used unless it has been approved.**
4. **Excavation, filming and collection of biological specimens are subject to further permission from the relevant Government Ministries.**
5. **You are required to submit at least two(2)/four(4) bound copies of your final report for Kenyans and non-Kenyans respectively.**
6. **The Government of Kenya reserves the right to modify the conditions of this permit including its cancellation without notice**

GPK6055t3mt10/2009

REPUBLIC OF KENYA

RESEARCH CLEARANCE PERMIT

(CONDITIONS— see back page)

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi.
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP", Nairobi.
Email: KNHplan@Ken.Healthnet.org

Ref: KNH-ERC/ A/407

18th February 2010

Lucy Wanjuki Kivuti
School of Nursing Sciences
College of Health Sciences
University of Nairobi

Dear Lucy

RESEARCH PROPOSAL: "DYNAMIC SIMULATION MODEL FOR ASSESSING CLINICAL AND SOCIO-ECONOMIC IMPACT OF THE USE OF E-HEALTH TOOLS IN CERVICAL CANCER MANAGEMENT IN KENYA" (P347/12/2009)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and approved your above revised research proposal for the period 18th February 2010 – 17th February 2011.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

DR. L. W. MUCHIRI
AG. SECRETARY, KNH/UON-ERC

c.c. Prof. K. M. Bhatt, Chairperson, KNH/UON-ERC
The Deputy Director CS, KNH
Supervisors: Prof. G. P. Pokhariyal, School of Mathematics, UON
Dr. Geoff McDonnel, University of New South Wales
Prof. Abdul Roudsari, City University London

Telegrams: "MEDSUP" Nairobi

Tel:2726300-9
2725272

E-Mail: knhadmin@knh.or.ke

KENYATTA NATIONAL HOSPITAL

P.O. Box 20723 – 00202 Fax:
NAIROBI

RE: KNH/OBS/GYN/ETC/16 Date: 15th November, 2010

To

Lucy Wanjiku Kivuti
Lecturer, School of Nursing
UNIVERSITY OF NAIROBI

RE: AUTHORITY TO CONDUCT RESEARCH

I am happy to inform you that authority has been given for you to conduct your study titled: Dynamic Simulation model for assessing clinical and Social-economic impact of use of e-health tools in cervical cancer management in Kenya in the department of Obstetrics and Gynaecology (ward 1B, ward 1D and clinic 18). The study which has been approved by KNH-ERC and National Council for Science and Technology has been further reviewed by the department. The department has noted that the ethics issues have been addressed and the study will not disrupt the services.

I wish you all the best and kindly give the department regular updates on the progress of this study including dessiminition of the final results.

Dr. J. Onge'ch
HEAD OF DEPARTMENT
OBSTETRIC AND GYNEACOLOGY

CC: Deputy Director (Clinical Services)
Assistant Chief Nurse Obs/Gyn
Administrative Officer Obs/Gyn
Chair/KNH Scientific Committee - Dr. Mugo
In-charges wards 1B, 1D and Clinic 18

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2011/09
Approval Number: 000592

17th January, 2011

Lucy Wanjuki Kivuti,
University of Nairobi,
P.O. Box 30196,
NAIROBI, KENYA

Dear Ms. Kivuti,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has received your request for approval of your study titled:

"Dynamic Simulation Model for Assessing Clinical and Socio-Economic Impact of the Use of e-Health Tools in Cervical Cancer Management in Kenya".

On the basis of your study review and approval by the NCST and KNH/UoN-Ethics & Research Committee, IREC is glad to inform you that your study has been granted a Formal Approval Number: **FAN: IREC 000592** on 17th January, 2011. You are therefore permitted to continue with your study.

Note that this approval is for 1 year; it will thus expire on 16th January, 2012. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Yours Sincerely,

APPR
18 JAN 2011

DR. OMAR ALY
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc: Director - MTRH
Dean - SOM
Dean - SPH
Dean - SOD