

**MODELLING SURVIVAL TIME OF CERVICAL CANCER PATIENTS IN  
MOI TEACHING AND REFERRAL HOSPITAL, KENYA**

**BY**

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## DECLARATION

### Declaration by the Candidate

This thesis is my original work and has not been presented for a degree award in any other university. No part of this thesis should be produced without prior written permission of the author and/or Moi University.

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**DEDICATION**

I dedicate this research thesis to my beloved family for their invaluable love and great desire to see me excel to this level of academics.

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I take this opportunity to give thanks to the Almighty God for His guidance, grace, strength and protection throughout the programme.

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## ABSTRACT

Cervical cancer is one of the most prevalent cancers in women. Globally, it is ranked behind breast cancer, lung cancer, and colorectal cancer as the fourth most common cancer killer of females. Cervical cancer has risen 3,211 percent in the last five years, making it the top cancer-related death among women in Kenya. An increase in cervical cancer in Kenya has resulted in an economic burden for patients and families. There is an increase in healthcare spending and productivity losses due to morbidity and mortality at a productive age. The purpose of the study was to model the survival time of cervical cancer patients at the Moi Teaching and Referral Hospital (MTRH) to gain insights into causes and prognostic factors of survival after diagnosis. The specific objectives were to (1) estimate the survival time among cervical cancer patients, (2) determine the predictors of survival after a cervical cancer diagnosis, and (3) evaluate the relationship between a patient's survival and covariates of cervical cancer. The study employed a retrospective cohort design. A population of 175 cervical cancer patients enrolled between 1st January to 31st December 2014 were studied for a follow-up period of five years. Objective one was achieved using the Kaplan-Meier estimator to estimate the median survival time. The Cox proportional hazard regression model was used to achieve objectives two and three. Data analysis was done using R statistical software. The study findings revealed that 144(82.3%) of cervical cancer patients who were considered in the study died within 5 years. Furthermore, 98.6% of patients who had a family history of cervical cancer died within the study period. Only 33.3% (10) of patients diagnosed with stage one of cervical cancer died within the study period. Furthermore, 81.6% and 94.8% of patients diagnosed with stage two and three cervical cancer, respectively, died within the study period. Finally, all patients diagnosed with stage four died within five years. Among the patients whose treatment plan was radiation, 56.4% of them died within the study period across all stages of the disease. The age of the patients [hazard ratio (HR) =0.369; p-value (p) =<0.001], employment status [HR =.328, p=0.042], family history of cervical cancer [HR=0.444, p=0.048], smoking cigarettes [HR=0.807, p=0.002], comorbidities [HR =0.825, p=0.001], cancer grade [HR =.472, p=0.001], staging of cervical cancer [HR =0.265, p=0.015] and treatment plan [HR =-0.124, p=0.043] were significant predictors for survival time of cervical cancer patients. The overall median survival time was two years. The study concluded that age, marital status, employment status, family history, smoking status, comorbidity, cancer grade, staging of the disease and treatment plan were significant predictors of survival after a diagnosis of cervical cancer. However, insurance cover, attaining menopause age, use of contraceptives, types of contraceptives, HIV status and HPV infections were not significant predictors of survival after a diagnosis of cervical cancer. There was an increased chance of survival if cervical cancer patients were diagnosed in stage one. The study recommends that healthcare systems in MTRH and Kenya should consider investing in highly targeted social support services and interventions that may help reduce the significant survival differences due to predictors of survival after a diagnosis.

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**ABBREVIATIONS AND ACRONYMS**

<b>AIDS</b>	Acquired Immuno Deficiency Syndrome
<b>ALP</b>	Alkaline phosphatase
<b>CCCDC</b>	Chandaria Cancer and Chronic Disease Center
<b>CSM</b>	Cancer-Specific Mortality
<b>CTC</b>	Circulating Tumour Cell
<b>DES</b>	Diethylstilbestrol
<b>DSS</b>	Disease-Specific Survival
<b>GLOBOCAN</b>	Global Cancer Observatory
<b>HIV</b>	Human Immunodeficiency Virus
<b>HPV</b>	Human Papillomavirus
<b>HR</b>	Hazard Ratio
<b>IARC</b>	International Agency for Research on Cancer
<b>IREC</b>	Institutional Research and Ethics Committee
<b>LCF</b>	Logic for Computable Functions
<b>LR</b>	Likelihood Ratio
<b>MPMN</b>	Multiple Primary Malignant Neoplasm
<b>MRD</b>	Medical Records Department
<b>MTRH</b>	Moi Teaching and Referral Hospital
<b>NSCLC</b>	Non-small cell lung cancer
<b>OM</b>	Overall Mortality
<b>OS</b>	Overall Survival
<b>PCRD</b>	Pancreatic Cancer Related Diabetes
<b>PH</b>	Proportional Hazards
<b>pN1</b>	Protease Nexin 1

<b>RPA</b>	Recursive Partitioning Analysis
<b>SEER</b>	Surveillance, Epidemiology, and End Results
<b>SSA</b>	Sub-Saharan Africa
<b>STATA</b>	Statistics and Data
<b>STD</b>	Sexually Transmitted Disease
<b>TASH</b>	Tikur Anbessa Specialized Hospital
<b>US</b>	United States
<b>WHO</b>	World Health Organization

## DEFINITION OF TERMS

<b>Cervical cancer</b>	Cancer that starts in the cells of the cervix, which is the lower part of the uterus that connects to the vaginal canal.
<b>Pap Smear</b>	It is a type of cervical screening that looks for precancerous or cancerous changes in the cervix or colon.
<b>Prognosis</b>	It is figuring out how likely it is that someone will get sick, including whether the signs and symptoms will get better, worse, or stay the same over time.
<b>Screening</b>	Is the assumption that an undiagnosed disease is present in a healthy, symptom-free population by using tests, exams, or other procedures that can be quickly and easily used on the target population (WHO, 2018).
<b>Survival time</b>	It is the length of time from a certain point until a certain event occurs, like death.

## CHAPTER ONE: INTRODUCTION

### 1.1 Background of the Study

Cancer is the growth of abnormal cells excessively uncontrollably and can spread to surrounding body parts (Keum & Giovannucci 2019; Frandsen et al., 2016; Salazar-Roa & Malumbres, 2017). There are different types of cancers in the world, for example, skin, lungs, breasts, prostate, pancreas, and cervical cancer. Cervical cancer is a type of cancer that occurs in the cells of the cervix, the lower part of the uterus that connects to the vagina (Ali, Makata & Ezenduka, 2016). Various strains of the human papillomavirus (HPV), a sexually transmitted infection, play a role in causing most cervical cancer (Rasool *et al.*, 2019).

Globally, cervical cancer is ranked as the fourth most common cancer in women, after breast cancer (2.1 million cases), colorectal cancer (0.8 million), and lung cancer (0.7 million) (Bray et al., 2018). In 2018, the Global Cancer Observatory (GLOBOCAN) modelling estimated that there were 569,847 new cases of cervical cancer with an age-standardized rate of 13.1 per 100,000 and there were an estimated 311 365 deaths from cervical cancer worldwide, accounting for 9.5% of all female cancer deaths (Bray *et al.*, 2018). China and India collectively accounted for over one-third of the worldwide cervical burden, with China reporting 106,000 cases and India reporting 97,000 cases. Cervical cancer has resulted in approximately 48,000 fatalities in China and approximately 60,000 fatalities in India. In Nepal, cervical cancer is the most common cancer and the leading cause of death among women (Shrestha *et al.*, 2019). The age-adjusted incidence rate of cervical cancer in Nepal is 21.5 per 100,000 population, with 2,942 new cases and 1,928 deaths (International Agency for Research on Cancer, 2018).

Cervical cancer is a significant cause of morbidity and mortality in sub-Saharan Africa (SSA) (Ferlay *et al.*, 2019). While high-income countries have been able to implement and sustain population-based screening programs with high population coverage, screening has been less effective in SSA due to financial, logistical, and sociocultural barriers (LaMontagne *et al.*, 2017). Additional preventive strategies are needed to address the growing burden of cervical cancer

Malawi, Mozambique, Comoros, Zambia, Zimbabwe, and Tanzania are among the countries with the highest age-standardized incidence rates in the world, at over 50 cases per 100,000 women annually (De Vuyst *et al.*, 2013). Age-standardized incidence and mortality rates are highest in Eastern Africa, which also has the highest HPV prevalence in the general population (20.5%, compared with 18.6% in SSA overall and a global prevalence of 4.1%) (Setiawan *et al.*, 2018).

The leading cause of cancer death in Kenya is cervical, followed by breast, esophageal, colorectal, and prostate cancers Globocan (2020). About 3,286 cervical cancer deaths occur annually in Kenya. Based on age category, cervical cancer is the 1st leading cause of cancer deaths in women aged 15 to 44 years in Kenya (Ferlay *et al.*, 2018). There are 33 per 100,000 women having cervical cancer and 22 per 100,000 who die from the disease (Gatumo *et al.*, 2018). About 5,250 new cervical cancer cases are diagnosed annually in Kenya (Osok *et al.*, 2018).

Risk factors associated with cervical cancer include human papillomavirus (HPV) infection, immune system deficiency, herpes, smoking, age, socio-economic factors, oral contraceptives, and exposure to diethylstilbestrol (DES) (Kessler, 2017). Most people are infected with HPV when they become sexually active, and most people clear the virus without problems (Pandey *et al.*, 2019).

Screening is testing of all women at risk of cervical cancer, most of whom were without symptoms (Walker & Hamilton, 2017). Screening aims to detect precancerous changes, which, if not treated, may lead to cancer. Screening is only effective if there is a well-organized system for follow-up and treatment. Now more than ever, effective cervical cancer control planning requires access to accurate statistics. According to Arbyn *et al.* (2020), one of the fundamental steps in the action plan for non-communicable diseases is to evaluate a high-quality surveillance and monitoring system that provides, as a minimum standard, reliable population-based statistics data on the major non-communicable diseases.

Due to burden of cervical burden in the country, there is a need for statistical modelling, which the government and policymakers can use in the management of the cervical cancer pandemic. Proportional hazard models are a class of survival models in statistics. Survival models relate the time that passes before some event occurs to one or more covariates that may be associated with that quantity of time.

## **1.2 Statement of the Problem**

According to GLOBOCAN (2018) estimates, there were 569,847 new cases of cervical cancer with an age-standardized rate of 13.1 per 100,000, and an estimated 311,365 deaths from cervical cancer worldwide, accounting for 9.5% of all female cancer deaths (Bray *et al.*, 2018). Further, almost nine out of ten (87%) cervical cancer deaths occur in middle-and-low-income countries. According to World Health Organization (2018), 33 per 100,000 women in Kenya have cervical cancer, and 22 per 100,000 dies from the disease. Further, according to Human Papillomavirus and Related Diseases Report (2019), about 5,250 new cervical cancer cases are diagnosed annually in Kenya. In Kenya, cervical cancer is ranked as the leading cause of female cancer. Furthermore, it is the most

common female cancer in women aged 15 to 44 years. Most cancers are often diagnosed at the advanced stages of the disease resulting in structural, physiological, as well as socio-economic challenges (Mwangi, Gachau & Kabiru, 2017).

Cervical cancer has impacted the national economy and society at large through increased health expenditure, labour and productivity losses, and reduced investment in human and physical capital formation (Sawaya *et al.*, 2019). Further, the increasing treatment burden of cervical cancer has depleted family resources, contributing to the cycle of poverty. Cervical cancer has disproportionately affected women in the prime age of life, resulting in significant economic and societal impact in Kenya. A mother's death has complex effects on the children and families she leaves behind.

Despite the availability of effective prevention and treatment strategies, the survival rate for cervical cancer patients in Kenya remains low. There is a lack of comprehensive understanding of the factors that influence survival rates among cervical cancer patients in Kenya. This knowledge gap hinders the development of effective interventions to improve patient outcomes. The available research is from GLOBOCAN estimates and WHO reports, which may not provide the granularity and precision needed for a comprehensive analysis of cervical cancer survival in Kenya. Access to data from Chandaria Cancer and Chronic Disease Center at MTRH or other relevant sources allowed for a more detailed understanding of patient characteristics, treatment regimens, and survival outcomes.

There was need to adopt the Cox regression model and Kaplan-Meier Estimator in order to provide a comprehensive approach to studying survival data on cervical cancer patients at Moi Teaching and Referral Hospital. These methods helped identify prognostic factors, estimate survival probabilities, and assess trends in survival, ultimately contributing to



better understanding of cervical cancer survival patterns and informing interventions to improve patient outcome. Cervical Cancer in Chandaria Cancer and Chronic Disease Center at MTRH serves as a major catchment area for cervical cancer cases.

Despite studies done on statistical modeling there is still need for modeling of survival of the cervical cancer patients since the disease is the leading cause of death in Kenya. Therefore, this study sought to model survival time of cervical cancer patients at Moi Teaching and Referral Hospital. This allowed to know out of the study variables which one can be adjusted in order to prolong the cervical cancer patients. This also allowed for strategies on how to increase the survival rate of cervical cancer patients after knowing the predictors which reduce the life rate.

### **1.3 Objectives of the Study**

This sub-section highlights the general objective and specific objectives.

#### **1.3.1 General Objective**

The general objective of the study was to model survival time of cervical cancer patients at Moi Teaching and Referral Hospital

#### **1.3.2 Specific Objectives**

1. To estimate the survival time among cervical cancer patients
2. To determine the predictors of survival after a diagnosis of cervical cancer
3. To evaluate the relationship between patients' survival and covariate of cervical cancer

#### **1.4 Justification of the Study**

Due to the rise in cervical cancer in Kenya, patients and healthcare systems have had to spend more money on health care and lose money because of illness and early death (Owenga & Nyambedha, 2018). Modelling how long people with cervical cancer survive after diagnosis could help decide how to spend money and where to put resources in programmes to prevent, find, treat, care for, and support people who have survived the disease. So, the goal of this study was to model the survival time of cervical cancer patients at Moi Teaching and Referral Hospital so that decisions can be made about how to use resources and how much to invest in programmes to control cervical cancer. Therefore, the purpose of the study was to model survival time of cervical cancer patients at Moi Teaching and Referral Hospital. The study findings informed policy makers on cervical cancer survival in order to come up with control and intervention measures for cervical cancer burden.

#### **1.5 Significance of the Study**

The study findings would enable the stakeholders and policymakers to realize the benefits of early cervical cancer diagnoses, understand cervical cancer survival trends, and plan prevention measures and resource allocations. The staff would benefit through training to implement cervical cancer prevention and health promotion programs.

The MTRH administration would benefit from the study findings and recommendations on the survival of cervical cancer and the model for prevention and health promotion programs. The results of this study would benefit the communities and government managing cervical cancer patients as they design education materials and strategies to achieve their objectives better. The ministry of health would benefit from the study findings on how to model vaccination against the human papillomavirus (HPV) to reduce

cervical cancer incidence. The study findings would act as a basis for future researchers who focused on the same field of the study.

### **1.6 Scope of the Study**

The study focused on modelling survival time of cervical cancer patients. The research was carried out at Moi Teaching and Referral Hospital, Kenya. Records of women aged 20–70 years presenting with cervical cancer from January 1, 2014, to December 31, 2014 and followed up for a 5 years study period were obtained from MTRH.

## **CHAPTER TWO: LITERATURE REVIEW**

### **2.1 Introductions**

This chapter contains literature review on cervical cancer, underlying cervical cancer incidence, and predictors of survival among cervical cancer patients.

### **2.2 Cervical Cancer**

Cervical cancer is a type of cancer that occurs in the cells of the cervix, the lower part of the uterus that connects to the vagina (Jafri, Shah, Shamim & Bajwa, 2019). Various strains of the human papillomavirus (HPV), a sexually transmitted infection, play a role in causing most cervical cancer. Cervical cancer happens when cells change in a woman's cervix, which connects her uterus with her vagina (Peate, 2019). This cancer can affect the deeper tissues of her cervix and may spread to other parts of her body (metastasize), often the lungs, liver, bladder, vagina, and rectum.

Cervical cancer begins with unusual changes in your tissue. Most cases are linked to infection with human papillomavirus (HPV) (Ali, Makata & Ezenduka, 2016). Different types of HPV can cause skin warts, genital warts, and other skin disorders. Others are linked to cancers involving the vulva, vagina, penis, anus, tongue, and tonsils. Most cases of cervical cancer are caused by infection with human papillomavirus (HPV), which is preventable with a vaccine (Viens et al., 2016). Cervical cancer grows slowly, so there's usually time to find and treat it before it causes serious problems. It kills fewer and fewer women each year, thanks to improved screening through pap tests. Women 35 to 44 years old are most likely to get it. More than 15% of new cases are in women over age 65; however, especially those who haven't been getting regular screenings.

Someone might be at higher risk of cervical cancer if they: Started having sex before age 16 or within a year of starting your period, have multiple sexual partners, take birth

control pills, especially for longer than five years, smoke cigarettes, have a weakened immune system and have a sexually transmitted disease (STD) (Ndejjo *et al.*, 2017).

### **2.3 Underlying Cervical Cancer Incidence**

Cancer is the second leading cause of death worldwide with the types of cancer, incidence and mortality rates, and the burden of disease differing significantly between countries (Ngune *et al.*, 2020). Cervical cancer is the second most common female reproductive cancer after breast cancer, with 84% of the cases being reported in developing economies (World Health Organisation, 2019). With an estimated 570,000 cases and 311,000 deaths in 2018 worldwide, cervical cancer is ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women (GLOBOCAN, 2018).

In Sub-Saharan Africa, cervical cancer is responsible for the highest number of female deaths, with a mortality rate of 23 cases per 100,000 woman-years compared to 2 cases per 100,000 woman-years in the United States of America (USA) (World Health Organisation, 2019). Additionally, it contributes to the largest cause of potential years of life lost due to young age onset in women between 35 and 50 years (Ngune *et al.*, 2020). About 20% of cervical cancers are diagnosed after age 65. These cases usually occur in people who did not receive regular cervical cancer screenings before age 65. It is rare for people younger than 20 to develop cervical cancer. Both the higher incidence and mortality rates result from a lack of or low uptake in screening and preventative measures, late diagnosis, cost and availability of treatments (Ifediora, 2019).

In Kenya, cervical cancer poses a great burden on women's health due to the high incidence and poor prognosis (Globocan 2018). Incidence rates have continued to rise over the years with an estimated tenfold increase between 1998 and 2011 (414 per 100,000 women in 2011 compared to 48 per 100,000 in 1998) (Globocan 2018). Data

from 2018 shows that cervical cancer contributes 5,250 (12.9%) of new cancer cases and 3,286 (11.84%) of cancer deaths. Incidence rates for women aged 15 to 24 years are predicted to exponentially increase by 50% by 2034 (Kivuti-Bitok et al., 2020). Currently, nine women in their twenties die of cervical cancer every day (Ministry of Health Kenya, 2020).

Cervical cancer is mostly caused by a persistent infection with twelve specific carcinogenic types of human papillomavirus (HPV) which is transmitted sexually by males and females shortly after the onset of sexual activity (Chan *et al.*, 2019). The two most common high-risk HPV types that cause cervical cancer in women are 16 and 18, which are responsible for approximately 70% of cervical cancers worldwide (WHO, 2020).

Whilst most HPV infections are transitory, in some women they persist, especially if they are HIV positive (Chan *et al.*, 2019). Human papillomavirus (HPV) is the virtually necessary cause of cervical cancer, with 12 oncogenic types classified as group 1 carcinogens by the IARC Monographs Okunade (2020). Other important cofactors include immunosuppression (particularly human immunodeficiency virus), smoking, parity (a higher number of full-term pregnancies increases risk), and oral contraceptive use (Bruni *et al.*, 2022). Cervical cancer incidence and mortality rates reportedly have been in decline in many populations worldwide. Aside from screening (where available), these declines have been ascribed to factors linked either to increasing average socioeconomic levels or a diminishing risk of persistent infection with high-risk HPV, resulting from improvements in genital hygiene, reduced parity, and a diminishing prevalence of sexually transmitted disease (Barmon *et al.*, 2019). In the absence of effective screening, there is rapid increases in premature cervical cancer mortality.

Strategies to combat incidence and mortality of cervical cancer include HPV vaccines as primary prevention, and cervical screening to identify early changes as secondary prevention (Chan *et al.*, 2019). The HPV testing offered greater protection against invasive cervical cancer than either visual inspection with acetic acid or cytology (Harper & Jimbo, 2021). The effective integration of HPV vaccine programs with HPV-based testing via screening programs has the potential to virtually eliminate the burden of cervical cancer in every country of the world in this century. Despite differing screening and immunisation programs, this has led to a marked decline of cervical cancer and deaths in most developed. Modelling by Hall *et al.* (2019) shows that incidence rates of invasive cervical cancers in Australia will fall by 42 to 51% over the next 15 years. There are some factors, however, that have led to an increase of cervical cancer rates in younger generations of women in some European and African countries, such as changes in sexual behaviours, parity and age at first birth, use of oral contraceptives and tobacco use (Wild, Weilderpass and Stewart, 2020).

Although surveillance programs for cervical cancer for sexually active women and women of reproductive age are in place in Sub-Saharan countries, cervical cancer screening rates have remained relatively low and some of the screening facilities are underutilised (Vermandere *et al.*, 2015). Community awareness of cervical cancer in Kenya may have improved after the introduction of cervical cancer screening programs in 2013 and HPV vaccination in 2019 in Kenya Ministry of Health Kenya (2019), but only 14% of women in the reproductive age participate in screening and nearly 50% of women still present with late disease (Donkor *et al.*, 2020).

High-quality screening programs are important to prevent cervical cancer among unvaccinated older women. The WHO (2020) recommends the screening of women aged

30 to 49 years either through visual inspection with acetic acid in low-resource settings, Papanicolaou tests (cervical cytology) every 3 to 5 years, or HPV testing every 5 years—coupled with timely treatment of precancerous lesions (Aoki *et al.*, 2020).

The 5-year survival rate tells about percent of people live at least 5 years after the cancer is found. Survival rates depend on the stage of cervical cancer that is diagnosed. When detected at an early stage, the 5-year survival rate for people with invasive cervical cancer is 92%. About 44% of people with cervical cancer are diagnosed at an early stage. If cervical cancer has spread to surrounding tissues or organs and/or the regional lymph nodes, the 5-year survival rate is 58%. If the cancer has spread to a distant part of the body, the 5-year survival rate is 18% (Hemminki, Försti & Hansson, 2021).

#### **2.4 Estimate the Survival Time among Cervical Cancer Patients**

The survival time among cervical cancer patients varies depending on the stage of the cancer at diagnosis Sengayi-Muchengeti *et al.* (2020). The 5-year relative survival rate tells what percent of people with the same type and stage of cervical cancer are alive 5 years after their cancer was diagnosed, compared with people in the overall population. For example, the 5-year relative survival rate for cervical cancer diagnosed at an early stage is 91%. This means that people diagnosed with early-stage cervical cancer are 91% as likely as people who do not have cervical cancer to be alive 5 years after diagnosis.

When cervical cancer is diagnosed at an early stage, the 5-year relative survival rate is 91%. When cervical cancer is diagnosed after it has spread to nearby tissues, organs, or regional lymph nodes, the 5-year relative survival rate is 60%. When cervical cancer is diagnosed after it has spread to a distant part of the body, the 5-year relative survival rate is 19%. The 5-year relative survival rate for all people with cervical cancer is 67% (Balasubramaniam *et al.* 2021).



A study conducted in Ethiopia by Mebratie et al. (2022) found that in 2019, the median survival time of cervical cancer patients at 5 years was 37 months. Estimated the median survival time of cervical cancer patients to be 40.21 months. It is important to note that these estimates are based on specific populations and may not be generalizable to all cervical cancer patients.

The median survival time for cervical cancer patients varies depending on several factors, including the stage of cancer, age of the patient, overall health, and access to treatment (Chen, Kung, Wang & Tsai, 2019).

According to the Fontham et al. (2020)., the overall 5-year survival rate for cervical cancer is 66%. This means that 66% of women with cervical cancer will still be alive 5 years after their diagnosis. The 5-year survival rate is much higher for women with early-stage cervical cancer (stage I or II) than for women with advanced-stage cancer (stage III or IV). The 5-year survival rate for women with stage I cervical cancer is 93%, while the 5-year survival rate for women with stage IV cervical cancer is 16%.

The median survival time for cervical cancer patients is also affected by the age of the patient. Women who are younger than 40 years old at diagnosis have a median survival time of 5.7 years, while women who are 70 years old or older at diagnosis have a median survival time of 2.8 years Yang et al. (2019).

Van Krieking, Castellsague, Cibula and Demarteau (2014) focused on estimation of the potential overall impact of human papillomavirus vaccination on cervical cancer cases and deaths. Human papillomavirus (HPV) vaccination offers potential for primary prevention of HPV-related pre-cancers and cancers as demonstrated in clinical trials. Mathematical models have estimated the potential real-life impact of vaccination on the

burden of cervical cancer (CC). However, these are restricted to evaluations in a limited number of countries. Pak *et al.* (2017) by comparing 2 groups in a survival analysis, discussed issues of using the hazard ratio (HR) and present the restricted median survival time (RMST) as a summary measure of patients' survival profile over time. However, the median PFS time of docetaxel was significantly better than that of nivolumab. Therefore, it may be difficult to use median OS and/or PFS to interpret of the HR value clinically.

Landy, Pesola, Castanon and Sasieni (2016) used logistic regression to estimate the odds ratio (OR) of developing stage-specific cancer for women regularly screened or irregularly screened compared with women not screened in the preceding 15 years. Mortality was estimated from excess deaths within 5 years of diagnosis using stage-specific 5-year relative survival from England with adjustment for age within stage based on SEER (Surveillance, Epidemiology and End Results, USA) data. Kim, Uno and Wei (2017) revealed that the restricted mean survival time (RMST) was proposed as an alternative measure of treatment effect that offers some advantages in design, analysis, and interpretation over the conventional measures.

Oza (2015) study powered to detect a difference in overall survival. Analysis was by intention to treat. The study used the difference in restricted mean survival time as the primary estimate of effect. No overall survival benefit of bevacizumab was recorded (restricted mean survival time 44.6 months). A significant difference in overall survival was noted between women who received bevacizumab plus chemotherapy and those who received chemotherapy alone (restricted mean survival time 34.5 months). However, in non-high-risk patients, the restricted mean survival time did not differ significantly between the two treatment groups (49.7 months). An updated analysis of progression-free survival showed no difference between treatment groups.

Latimer (2014) focused on treatment switching commonly occurs in clinical trials of novel interventions in the advanced or metastatic cancer setting. The study demonstrated that methods used to adjust for treatment switching have important limitations and often produce bias in realistic scenarios. Key assumptions include the “no unmeasured confounders” assumption associated with the inverse probability of censoring weights (IPCW) method and the “common treatment effect” assumption associated with the rank preserving structural failure time model (RPSFTM).

## **2.5 Predictors of Survival After a Diagnosis of Cervical Cancer**

Viganó *et al.* (2000) used univariate Kaplan-Meier and multivariate Cox regression analyses to establish relationships between tumor- and treatment-specific, clinical, laboratory, demographic, socioeconomic variables and survival time. The study found out that methodological improvements in the design and implementation of survival studies may reduce prognostic uncertainty and ultimately provide better care for the terminally ill patients and their families.

Ashworth *et al.* (2014) used cox regression to evaluate factors predictive of overall survival (OS) and progression-free survival. Risk groups were defined using recursive partitioning analysis (RPA). The study found out that the long-term survival is common in selected patients with metachronous oligometastases. This risk classification scheme can be used in guiding selection of patients for clinical trials of ablative treatment. Abdollah *et al.* (2014) evaluated 1,107 patients with Protease Nexin 1 (pN1) prostate cancer treated with radical prostatectomy and anatomically extended pelvic lymph node dissection between 1988 and 2010 at two tertiary care centers. Regression tree analysis stratified patients into risk groups on the basis of their tumor predictors and the corresponding cancer-specific mortality (CSM) rate. Cox regression analysis tested the

relationship between adjuvant radiotherapy (aRT) and CSM rate, as well as overall mortality (OM) rate in each risk group separately. These results noted that the beneficial impact of aRT on survival in patients with pN1 prostate cancer is highly influenced by tumor predictors.

An investigation by Wang et al. (2021) found that the overall death rates from cervical cancer rose with women's age. The age effect on cervical cancer death rates was that the rates went up with age. Wang, Xue, Wang, and Bai (2018) said that women over 40 years old are more likely to die from cervical cancer because of their age. According to the results of Luo's (2017) study, the survival rate for cervical cancer patients goes down as they get older.

Several studies and statistics show that the death rate from cervical cancer tends to rise with age. The overall death rates from cervical cancer went up with age and down with birth in three high-income countries (Bedell, Goldstein, Goldstein, & Goldstein, 2020). The high death rate from cervical cancer around the world could be lowered by effective interventions at different stages of life. This shows how important age is when trying to lower cervical cancer mortality.

Lee *et al.* (2015) investigated the epidemiologic predictors and prognostic factors for survival in patients diagnosed with osteosarcoma of the jaws. A retrospective, population-based cohort study of 541 patients in the SEER tumor registry diagnosed with osteosarcoma of the jaws from 1973 through 2011 were reviewed. The study used Kaplan-Meier analysis which demonstrated an overall survival (OS) and disease-specific survival (DSS) of 53% and 62%, respectively, at 5 years and 35% and 54%, respectively, at 5 years. Multivariate Cox regression analysis revealed that independent predictors of

OS and DSS included age at diagnosis, stage at presentation and surgical resection. Tumor size was not significant for OS but significant for DSS.

Bidard *et al.* (2014) aimed to assess the clinical validity of circulating tumour cell (CTC) quantification for prognostication of patients with metastatic breast cancer by undertaking a pooled analysis of individual patient data. The study used Cox regression models, stratified by study, to establish the association between CTC count and progression-free survival and overall survival. The researchers used the landmark method to assess the prognostic value of CTC and serum marker changes during treatment. The researchers also assessed the added value of CTCs or serum markers to prognostic clinicopathological models in a resampling procedure using likelihood ratio (LR) statistics. The study data confirm the independent prognostic effect of CTC count on progression-free survival and overall survival. CTC count also improves the prognostication of metastatic breast cancer when added to full clinicopathological predictive models, whereas serum tumour markers do not.

Cho *et al.* (2019) determined the risk of mortality associated with the use of antidiabetic medications in individuals with pancreatic cancer-related diabetes (PCRD) and post pancreatitis diabetes mellitus (PPDM). Multivariable Cox regression analysis was conducted, and the risk was expressed as hazard ratio (HR) and 95% CIs. A 6-month lag was used to minimize reverse causality. The study found that metformin promotes a survival benefit in individuals with PPDM but not PCRD. Reverse causality may play a role in the association between insulin use and mortality in PCRD.

Stark *et al.* (2012) presented a large single institution patient series evaluated for prognostic factors using uni- and multivariate survival analysis. The association to patient survival was estimated using log-rank test for univariate analysis and cox

regression method for multivariate analysis. The following parameters were significantly associated with survival in multivariate analysis: age, performance, multifocal tumor, total or subtotal resection, radiotherapy, chemotherapy, combined radio-/chemotherapy with temozolomide.

Niegisch *et al.* (2018) described clinical predictors, treatment patterns and subsequent outcomes in the setting. This retrospective observational cohort analysis evaluated 1L and 2L treatment patterns and overall survival (OS) in patients aged  $\geq 18$  years with advanced UC or mUC (T4b, N2-3 and/or M1) at office-based urology and academic as well as non-academic urology clinics throughout Germany between 1 November 2009 and 2 June 2016. Data were obtained through the German Oncology database and additional treatment centers using similar electronic case report forms. The study provides a contemporary multicentre assessment of real-world treatment patterns and outcomes among palliatively treated patients with UC in Germany. The findings were generally consistent with the poor treatment outcomes observed globally, underscoring the need for effective 1L and 2L treatment for advanced UC or mUC.

Cormedi *et al.* (2018) compared the clinicopathological factors and survival rates of younger and older patients with gastric cancer. Patients were placed into the following groups: YA ( $\leq 40$  years; N=71), older adult (OA: 41 to 65 years; N=129) and elderly (E:  $\geq 66$  years; N=94). Differences were assessed through Pearson's  $\chi^2$  test, Kaplan-Meier analysis, Log rank test and Cox regression. The study found out that overall survival was similar among age groups. Metastatic disease at diagnosis was the only factor associated with a poorer prognosis in YA. These results suggest that younger patients deserve special attention regarding the detection of early-stage disease.

Zhang and Gong (2017) investigated the prognostic factors of bone metastases from lung cancer. The Kaplan-Meier survival curves were calculated and analyzed using the log-rank univariate test. Multivariate regression analysis was conducted using Cox's regression model. Univariate regression analysis indicated that the pathologic types, number of bone metastases, clinical stage, ECOG scores, and serum ALP levels were significantly correlated with survival ( $P < 0.05$ ). Multivariate regression analysis indicated that the number of bone metastases, clinical stage, and serum ALP levels were significantly correlated with prognosis ( $P < 0.05$ ). The risk associated with multiple bone metastases was 1.72 times of that of single bone metastasis ( $P = 0.029$ ); the risk associated with advanced clinical stage was 1.49 times of that of early clinical stage ( $P = 0.001$ ); and the risk associated with a high serum ALP level was 1.75 times of that of the low serum ALP level ( $P = 0.006$ ). Pathologic types, number of bone metastases, clinical stage, ECOG scores, and serum ALP levels were the prognostic factors for bone metastases from lung cancer. Wang *et al.* (2019) focused on retrospective analysis of data from 14,528 lung cancer patients with multiple primary malignant neoplasm (MPMN). Multivariate analysis showed that SMPMN, LCF and the age of the primary cancer diagnosed first ( $\geq 60$  years) and NSCLC staging  $> II$  were significant independent factors for inferior prognosis of patients.

## **2.6 Relationship Between Patients' Survival and Covariate of Cervical Cancer**

According to Aklilu (2023) the covariate of Cervical Cancer which affects survival time include age, marital status, employment status, family history, smoking status, comorbidity, cancer grade, staging of the disease, and treatment plan. The study conducted by Miura *et al.* (2016) revealed a significant correlation between advancing age and reduced survival time among individuals diagnosed with cervical cancer. There exists a correlation between advancing age and decreased survival time among

individuals diagnosed with cervical cancer. The 5-year relative survival rate for individuals diagnosed with invasive cervical cancer is 92% when identified at an early stage. However, this rate declines to 59% if the cancer has metastasized to adjacent tissues or organs and regional lymph nodes. Furthermore, the survival rate further decreases to 17% if the cancer has spread to a distant anatomical site.

Research suggests that unmarried individuals diagnosed with cervical cancer tend to have shorter survival times compared to their married counterparts. According to Wong et al. (2018), there is a tendency for individuals who are not married to have a shorter survival time. The independent prognostic significance of marital status has been observed in relation to various significant outcomes of cervical cancer. According to a study conducted by Ding, Yu, Li, and Ding (2021), there is a positive correlation between marital status and enhanced survival rates among individuals diagnosed with cervical cancer. Furthermore, it has been determined that marital status serves as an autonomous indicator for the likelihood of undergoing cervical cancer screening. Research studies have indicated that unmarried female individuals who are diagnosed with cancer, including those specifically with cervical cancer, tend to face a heightened likelihood of experiencing delayed diagnosis and unfavourable prognosis when compared to their married counterparts.

The employment status of individuals diagnosed with cervical cancer was found to be a significant positive predictor of the risk of mortality. The study found that patients employed in the formal sector had a longer survival time than unemployed patients. The survival time of patients who were employed was longer compared to those who were unemployed. This finding aligns with a study conducted by Kashyap et al. (2019), which demonstrated that employment status serves as a prognostic factor for the survival



duration of cervical cancer. Specifically, the study revealed that individuals with lower income levels face an elevated risk of mortality associated with cervical cancer. Norström et al. (2019) emphasize that secure employment in safe working environments encompasses more than just financial compensation. Such employment can offer various advantages that are crucial for maintaining optimal health. The occurrence of job displacement and the subsequent state of unemployment have been found to correlate with a range of adverse health consequences. Employees with higher salaries are more likely to be provided with insurance coverage. Additionally, individuals with lower income levels exhibit a reduced likelihood of utilizing preventive healthcare services that may be covered by insurance, such as screenings for blood pressure and cholesterol.

The presence of a familial history of cervical cancer is a notable determinant that strongly correlates with the prognosis of individuals affected by the disease. According to the findings of Waggoner et al. (2010), there exists an increased susceptibility to cervical cancer among women who have a familial history of the disease, specifically those with a mother or sister who have been diagnosed with cervical cancer, as compared to women who do not have any familial history of cervical cancer.

The survival time of cervical cancer patients is significantly reduced among individuals who engage in smoking, as compared to those who abstain from smoking. Individuals who did not smoke exhibited a greater duration of survival in comparison to those who engaged in smoking. The present study aligns with previous research by Gurmu (2018), which observed that individuals who smoke exhibited shorter survival durations than those who do not smoke.

Rajamaki et al. (2021) observed that a previous medical history of comorbidities is linked to decreased survival rates and an increased likelihood of mortality. The presence of comorbidities has been found to have a negative impact on survival rates. Consequently, the effective management of these comorbidities can potentially influence both the survival outcomes and overall well-being of this susceptible population.

Tshewang et al. (2021) indicate that the initial phases of the illness exhibit a more favourable prognosis. Specifically, the study reports that the five-year survival rates for individuals diagnosed with stage I disease surpass 90%. In contrast, females afflicted with a severe ailment exhibit a significantly bleaker prognosis, as less than 10% of individuals manage to survive stage IV illness. Stage IV cervical malignancy is characterized by the spread of cancer to adjacent structures, such as the bladder or rectum, as well as distant organs. At this stage, the cancer has reached the metastasis phase.

According to Yfantis et al. (2020), individuals who underwent chemotherapy exhibited a markedly diminished quality of life in comparison to those who did not undergo this treatment. Moreover, the impact of chemotherapy on the quality of life is contingent upon the duration of time that has elapsed since the surgical procedure.

## **CHAPTER THREE: METHODOLOGY**

### **3.1 Introduction**

The chapter entails the research methodology and research approaches which the researcher relied on while conducting this study. It specifically evaluates the research design used in the study, target population, data collection, data processing and analysis.

### **3.2 Study Design**

The study was a retrospective cohort study design using data from the cervical cancer patient's treatment at MTRH. It involved the use of available information from medical records on patients treated for cervical cancer at MTRH.

### **3.3 Study Site**

The study was conducted at MTRH, which is in Eldoret town, Uasin Gishu County, about 300km west of Nairobi, Kenya. As one of Kenya's two public referral hospitals, MTRH serves a population of approximately 24 million people from western Kenya and neighbouring countries. It is where medical students and residents/interns undertake their medical practical's and obtain hands-on experience. The MTRH campus includes the AMPATH Centre and several speciality care buildings, including: Chandaria Centre for Cancer and Chronic Diseases, Riley Mother Baby Hospital, Shoe4Africa Children's Hospital, Rafiki Center for Excellence in Adolescent Health and Majaliwa Surgical Center.

### **3.4 Study Population**

The population for this study comprised of all cervical cancer patients aged 20–70 years who had been registered at MTRH, Oncology center, from January 1, 2014 to December 31, 2014 and followed up for 5 years. All data were carefully reviewed from the registration log book and patients' registration card; if any inadequate information was

countered it was checked from the file and excluded from analysis if proven to be inadequate. A total of 175 women with cervical cancer were considered.

### **3.5 Eligibility Criteria**

#### **3.5.1 Inclusion Criteria**

- Data for women patients aged 20-70 years diagnosed with cervical cancer between January 1, 2014 to December 31, 2014.

#### **3.5.2 Exclusion Criteria**

- Women diagnosed with cervical cancer aged younger than 20 years or older than 70 years.
- Women diagnosed with cervical cancers but records of their data not available at the CCCDC.

### **3.6 Data Collection**

A letter of permission was obtained from the Institutional Research and Ethics Committee (IREC) of the College of Health Sciences / Moi Teaching & Referral Hospital (MTRH). After permission was granted, an appointment was booked with the CCCDC authorities to know the appropriate time for data extraction. The investigator visited CCCDC at MTRH and individually went through patient case sheets for available information of cervical cancer patients. All the collected information were kept confidential. A pretested data extraction sheet aimed at collecting information in relation to patient details (see “Study variables” below). The data were extracted from the patient records kept at the Medical Records Department (MRD) of CCCDC at MTRH.

### **3.7 Study Variables**

The following study variables were extracted from the patients' medical records; age category, marital status, insurance cover, employment status, menopause, contraceptives, family history, smoking status, comorbidity, HIV/AIDS status, HPV infections, cancer grade, staging of the disease and treatment plan.

### **3.8 Data Analysis**

Extracted data for this study were entered into Microsoft Excel and analyzed using R software. Descriptive statistics such as mean or median for continuous variables and frequencies and percentages for categorical variables were computed. Kaplan Meier survival functions was used to estimate the median survival time among cervical cancer patients. The Cox regression model was used to explore the relationship between patients' survival and individual/clinical predictors. To deal with loss to follow up and missing data, the study employed multiple regression imputation. With regression imputation the information of other variables was used to predict the missing values in a variable by using a regression model. First the regression model was estimated in the observed data and subsequently using the regression weights the missing values were predicted and replaced.

### **3.9 Ethical Consideration**

Ethical approval was granted by the Institutional Research and Ethics Committee (IREC) of the College of Health Sciences / Moi Teaching & Referral Hospital (MTRH) prior to starting the study. The researcher ensured that confidentiality was maintained throughout the study. To safeguard the identity of the patients, unique patient identifiers were generated during data extraction, hence avoiding the use of patient's names.

### 3.10 Statistical Model

This section describes the models used to achieve each of the three objectives; Objective one was achieved using Kaplan-Meier estimator to estimate the median survival time. Cox proportional hazard regression model was used to achieve objective two and three.

#### 3.10.1 Kaplan-Meier Estimator

The Kaplan-Meier estimator is said to be non-parametric or distribution-free since they do not require a specific assumption to be made about the underlying distribution of the survival times. For this study, random right censoring and independent censoring were applied. Kaplan–Meier estimator was used to incorporate information from all of the predictors of survival after a diagnosis of cervical cancer available, both censored and uncensored, by considering any point in time as a series of steps defined by the observed survival and censored times (Morris *et al.*, 2019). On the other hand, when there is no censoring, the estimator is simply the sample proportion of observations with event times greater than  $t$ .

If we assume we have a sample of  $n$  ( $n=175$ ) independent observations, their survival times denoted by  $t_1, t_2, \dots, t_p$  ( $p=5$  years) and indicator of censoring by  $\delta_1, \delta_2, \dots, \delta_q$  where  $\delta_i = 1$ , event/death and where  $\delta_i = 0$  for censored observations. The survival data are denoted by  $(t_i, \delta_i)$ ,  $i= 1, 2 \dots 5$ . The first step in obtaining the Kaplan-Meier estimator of the survival function is to order the survival times as  $t_{(1)} < t_{(2)} < \dots < t_{(5)}$  respectively. Thus, suppose that among the  $n$  observations, there are  $m \leq n$  failures that occurred at distinct  $m$  times.

Where

$n$ : The number of independent observations in the sample, which is 175.

$t_1, t_2, \dots, t_p$ : The survival times of the observations, where  $p$  is 5 years.

$\delta_1, \delta_2, \dots, \delta_q$ : The indicator of censoring for each observation, where  $\delta_i = 1$  indicates an event/death and  $\delta_i = 0$  indicates a censored observation.

$(t_i, \delta_i)$ : The survival data for each observation, where  $i = 1, 2, \dots, 5$ .

$t_{(1)} < t_{(2)} < \dots < t_{(5)}$ : The survival times ordered in ascending order.

$m$ : The number of failures that occurred at distinct  $m$  times among the  $n$  observations.

$m \leq n$ : This indicates that there are at most  $m$  failures (i.e., events) in the sample of  $n$  observations.

According to Kaplan-Meier (1958), the product limit estimator of survival function at time  $t$  can thus be: -

$$\hat{S}_{(t)} = \left(1 - \frac{d_{(1)}}{N_{(1)}}\right) \left(1 - \frac{d_{(2)}}{N_{(2)}}\right) \dots \left(1 - \frac{d_{(j-1)}}{N_{(j-1)}}\right) = \prod_{t_{(j)} < t}^k \left(1 - \frac{d_{(j)}}{N_{(j)}}\right) \text{ for } t_{(k)} \leq t < t_{(k+1)}, k = 1, 2, 3, \dots, m \dots \dots \dots (3.1)$$

When

$\hat{S}_{(t)}$ : This is the survival function at time  $t$ . It represents the probability that an individual will survive beyond time  $t$ , given that they have survived up to time  $t$ .

$(1 - )$ : This represents the probability of not experiencing the event of interest (e.g., death) in a given time interval.

$(1 - )... (1 - )$ : This is a product of probabilities, which represents the probability of not experiencing the event of interest in multiple time intervals.

$\prod_{t(j) < t}^k (1 - \frac{d(j)}{N(j)})$ : This is a product of conditional probabilities, which represents the probability of not experiencing the event of interest in each of the m time intervals, given that the individual has survived up to each time interval.

$t(j)$ : This represents the jth distinct time at which a failure occurred.

$k$ : This represents the number of distinct times at which failures have occurred.

$d_{(j)}$ : This represents the number of failures that occurred at time  $t(j)$ .

$N(j)$ : This represents the number of individuals who were still at risk at time  $t(j)$ .

$\leq t < P$ : This indicates that the equation is valid for all values of t that are greater than or equal to the smallest distinct time at which a failure occurred and less than the follow-up period P.

$k = 1, 2, 3, \dots, m$ : This indicates that the product is evaluated m times, once for each of the m distinct times at which a failure occurred.

$t = 0, S(0) = 1$ , this means that all subjects are alive at time 0.

The variance of the Kaplan-Meier estimator of the survival function which is known as the greenwood formula is given as:

$$\text{var}(\hat{S}(t)) = \left[ \hat{S}(t) \right]^2 \sum_{t(i) \leq t} \frac{d_i}{n_i(n_i - d_i)} \dots \dots \dots (3.2)$$



Where:

$\left[ \hat{s}(t) \right]^2$  represents the variance estimate for the Kaplan-Meier estimator at time  $t$ .

$\hat{\text{var}}(S(t))$  is the estimated survival probability at time  $t$ .

$t_{(i)}$  are the distinct failure times.

$d_i$  is the number of events at time  $(t_{(i)})$ .

$(n_i)$  is the number at risk just prior to time  $(t_{(i)})$ .

The  $(1-\alpha)$  \*95% confidence interval for the survival function  $(S_{(t)})$  at time  $t$  is:

$$\hat{S}_{(t)} \pm z_{\alpha/2} \text{S.e}(\hat{S}_{(t)}) \dots \dots \dots (3.3)$$

Where

$\hat{S}_{(t)}$  is the Kaplan-Meier estimate of the survival function at time  $t$

$\text{S.e}(\hat{S}_{(t)})$  is the standard error of the Kaplan-Meier estimate of the survival function at time  $t$

$z_{\alpha/2}$  is the critical value from the standard normal distribution corresponding to a significance level of  $\alpha/2$

$\alpha$  is the level of significance, which is typically set to 0.05 for a 95% confidence interval

The survival function changes only at failure times. That means decreasing step function takes a jump at failure times and also for censored times the conditional probability of

survival is always 1.00. As a result of this, the survival probability is unchanged from the previous survival probability.

Further, Kaplan-Meier Estimator was used to estimate the median survival time. Suppose that T is a failure time (survival time, lifetime) non-negative-valued random variable. The value of T for this study is the time from the start of treatment up to an event (i.e. death or censored) occurs (Shebeshi, 2011).

The median survival time was estimated by;

If there are no censored observations (...) the median survival time is

$$M = \begin{cases} t_{\frac{(n+1)}{2}} & \text{if } n \text{ odd; or otherwise} \dots\dots\dots (3.4) \\ \frac{1}{2} [t_{\frac{n}{2}} + t_{\frac{n}{2}+1}] & \end{cases}$$

Where

M: Represents the median survival time.

$t_{\frac{(n+1)}{2}}$ : Denotes the survival time at the midpoint when the number of observations (n) is odd.

$t_{\frac{n}{2}}$  and  $t_{\frac{n}{2}+1}$ : Represent the survival times at the two midpoints when the number of observations (n) is even.

n: The total number of observations.

In the presence of censored survival times the median survival is estimated by first calculating the Kaplan-Meier survival curve, then finding the value of M that satisfies the equation  $S(M)=0.5$ .

$$S(t_{median})=0.5, t_{median}=S^{-1}(0.5)\dots\dots\dots (3.5)$$

Where

The median survival time (M) is defined as the time point at which half of the individuals in the study have experienced the event of interest or censored, and the other half have survived beyond that time point.

The symbol "S" typically represents the survival function, which gives the probability of surviving past a certain time point. In the given context, "S = 0.5" likely represents the event of interest occurring with a probability of 0.5, which is used to estimate the median survival time. The expression " $t = S(0.5)$ " may refer to finding the time point at which the survival function equals 0.5, which is used to estimate the median survival time.

### 3.10.2 Fitting a Cox Proportional Hazard Regression Model

A Cox regression model was used to assess the predictors of survival after cervical cancer diagnosis. According to Cox (1972) the Cox model is written as

$$h_i(t) = \exp(\beta_1 X_{1i} + \beta_2 X_{2i} + \dots + \beta_p X_{pi}) h_0(t) \dots \dots \dots (3.6)$$

$$h_i(t) = h_0(t) \exp\{X_i \beta\} \dots \dots \dots (3.7)$$

Where

t denotes the survival time which in this study was 5 years

$h_0(t)$  denotes the baseline cumulative hazard function.

h(t) denotes the hazard due to the effects of predictor variables (predictors of survival after a diagnosis of cervical cancer)

$x_i$   $i=1,2,\dots,p$  are the predictor variables (Age category, marital status, insurance cover, employment status, menopause, contraceptives, family history, smoking status,

comorbidity, HIV/AIDS status, HPV infections, cancer grade, staging of the disease and treatment plan)

$\beta_i$   $i=1,2,\dots,p$  are the coefficients measuring the effect size of the predictor variables (predictors of survival after a diagnosis of cervical cancer)

The values  $e^{\beta_i}$  are the hazard ratios comparing hazard  $h(t)$  due to a given predictor variable (predictors of survival after a diagnosis of cervical cancer) at a given time point with baseline hazard  $h_0(t)$ .

If  $\beta_i$  is greater than zero then this means that the hazard ratio is greater than one, implying that the hazard increases as the  $i^{\text{th}}$  predictor variable increases, and consequently the survival time reduces.

If  $\beta_i$  is less than zero then this means that the hazard ratio is less than one. This then means that the hazard decreases as  $i^{\text{th}}$  predictor variable decreases implying that the length of the survival time increases.

If value of  $\beta_i$  is equal to zero. This means that the hazard ratio is equal to one. This then means that there is no effect on hazard for the  $i^{\text{th}}$  predictor. Data analysis were performed using the survival package in R.

## **CHAPTER FOUR: RESULTS AND DISCUSSIONS**

### **4.1 Introduction**

This chapter presents the results of the study for each specific objective

### **4.2 Characteristics of Study Participants**

The study sought to determine the socio-demographic and clinical characteristics of study participants.

#### **4.2.1 Socio-Demographic Characteristics of Study Participants**

The study sought to determine the general information of the study participants which included age category, marital status, insurance cover, employment status, menopause, contraceptives use, family history of cervical cancer and smoking status. General information helps the study to understand well about the study participants. The results are presented in Table 4.1.

**Table 4.1 Socio-Demographic Characteristics**

<b>Socio-demographic characteristics</b>	<b>Categories</b>	<b>Frequency (n=175)</b>	<b>Percent</b>
<b>Age Category</b>	20-34 Years	22	12.6
	35-49 Years	51	29.1
	50-64 Years	47	26.9
	65-70 Years	55	31.4
<b>Marital Status</b>	Married	91	52
	Single	29	16.6
	Previously married	55	31.4
<b>Insurance Cover</b>	None	123	70.3
	NHIF	52	29.7
<b>Employment Status</b>	Employee	21	12
	Casual Labourer	129	73.7
	Self-employed	17	9.7
	Farmer	8	4.6
<b>Menopause</b>	No	71	40.6
	Yes	104	59.4
<b>Contraceptives use</b>	None	113	64.6
	Yes	62	35.4
<b>Family History of Cervical cancer</b>	No	102	58.3
	Yes	73	41.7
<b>Smoking Status</b>	Smoker	53	30.3
	Non-Smoker	122	69.7

The study findings in Table 4.1 revealed that the majority of women diagnosed with cervical cancer were aged between 65-70 years represented by 55(31.4%). The majority, 91(52%) of the women diagnosed with cervical cancer, were married. It was also revealed that the majority 123(70.3%), had no medical insurance cover. The study findings further

revealed that 129(73.7%) of the women were casual labourers, and 104(59.4%) of them had reached the menopause stage. It was further revealed that 113(64.6%) of the women do not use contraceptives. Concerning the family history of cervical cancer 73(41.7%) had a history of the disease. Lastly, 53(30.3%) of the women were smokers.

#### 4.2.2 Clinical Characteristics of Study Participants

The study sought to determine the clinical characteristics of study participants which included comorbidity, HIV status, HPV infections, cancer grade, staging of the disease, treatment plan and survival period. The study findings are presented in Table 4.2.

**Table 4.2 Clinical Characteristics**

<b>Clinical characteristics</b>	<b>Categories</b>	<b>Frequency (n=175)</b>	<b>Percent</b>
<b>Comorbidity</b>	No	55	31.4
	Yes	120	68.6
<b>HIV Status</b>	Negative	110	62.9
	Positive	65	37.1
<b>HPV infections</b>	Not done	171	97.7
	Negative	4	2.3
<b>Cancer Grade</b>	Grade 1	35	20.0
	Grade 2	59	33.7
	Grade 3	81	46.3
<b>Staging of the Disease</b>	Stage I	30	17.1
	Stage II	38	21.7
	Stage III	77	44.0
	Stage IV	30	17.1
<b>Treatment Plan</b>	Hospice care	14	8.0
	Chemo	45	25.7
	Follow-up	24	13.7
	Palliative Chemo	32	18.3
	Chemo/Surgery	21	12.0
	Radiation	39	22.3
<b>Survival period</b>	1 year	40	22.9
	2 years	80	45.7
	3 years	19	10.9
	4 years	5	2.9
	5 years	31	17.7
	Total	175	100.0

The study findings revealed that majority 120(68.6%) of women diagnosed with cervical cancer had other comorbidities. The women who were HIV positive were 65(37.1%) while those who have not be screen for HPV infections were 171(97.7%). Cervical cancer women who were in grade 3 of the disease were 81(46.3%). In terms of cervical cancer stage majority 77(44.0%) were diagnosed in stage 3. The women who underwent chemotherapy alone were 45(25.7%). The study results lastly revealed that 31(17.7%) of cervical cancer patients survived beyond 5 years.

### 4.3 Survival Time Among Cervical Cancer Patients

The study first determined the cervical cancer cases and the survival rate per year. The study findings are presented in Table 4.3.

**Table 4.3 Cervical Cancer Cases by Year**

Year	Cases	Died, n (%)	Censored, n (%)	Lost to follow up n (%)
2014	175	21(12)	154(88)	
2015	154	80(45.7)	58(33.1)	16(9.1)
2016	58	9(5.1)	44(25.1)	5(2.9)
2017	44	12(6.9)	32(18.3)	
2018	32	1(0.6)	31(17.7)	

The study findings in Table 4.3 revealed that the number of cervical cancer cases reported in the Moi Teaching and Referral Hospital in the year 2014 were 175 at the beginning of the study, which was the baseline for this study. However, 21(12%) died before the year ended, and 154 were censored. In 2015, 154 of the previous patients were recorded; 80(45.7%) died before the year ended, and 58(33.1%) were censored. In the year 2016, 58 of the previous patients who survived were recorded. However, 9(5.1%) died,



44(25.1%) were censored, and 5(2.9%) were lost to follow up. At the beginning of 2017, 44 of the previous patients who survived were recorded. However, 12(6.9%) died before the year ended, and 32(18.3%) were censored. In the last year of study, that is, 2018, 32 of the previous cases were recorded. The study, however, noted that 31(17.7%) survived cervical cancer. The study findings however revealed that the 21 cervical cancer patients who were lost to follow up during study period, after imputation they were considered to experience the event of interest (censored at the lost to follow up time). The overall median survival time was two years.

#### **4.3.1 Survival Percentages of Cervical Cancer Patients Based on Socio-Demographic Characteristics**

The study findings on survival percentages of cervical cancer patients based on socio-demographic characteristic are presented in Table 4.4.

**Table 4.4 Survival Percentages based on Socio-Demographic Characteristics**

<b>Covariates</b>	<b>Number of patients, n (%)</b>	<b>Died, n (%)</b>	<b>Censored, n (%)</b>
<b>Age category</b>			
20-34 Years	22(12.6)	8(36.4)	14(63.6)
35-49 Years	51(29.1)	41(80.4)	10(19.6)
50-64 Years	47(26.9)	41(87.2)	6(12.8)
65-70 Years	55(31.4)	54(98.2)	1(1.8)
<b>Marital Status</b>			
Married	91(52.0)	73(80.2)	18(19.8)
Single	29(16.6)	27(93.1)	2(6.9)
Previously married	55(31.4)	44(80.0)	11(20.0)
<b>Insurance Cover</b>			
None	123(70.3)	104(84.6)	19(15.4)
NHIF	52(29.7)	40(76.9)	12(23.1)
<b>Employment Status</b>			
Employee	21(12.0)	3(14.3)	18(85.7)
Casual Labourer	129(73.7)	125(96.9)	4(3.1)
Self-employed	17(9.7)	9(52.9)	8(47.1)
Farmer	8(4.6)	7(87.5)	1(12.5)
<b>Menopause</b>			
No	71(40.6)	55(77.5)	16(22.5)
Yes	104(59.4)	89(85.6)	15(14.4)
<b>Contraceptives</b>			
None	113(64.6)	92(81.4)	21(18.6)
Yes	62(25.4)	52(83.9)	10(16.1)
<b>Family History of cervical cancer</b>			
No	102(58.3)	72(70.6)	30(29.4)
Yes	73(41.7)	72(98.6)	1(1.4)
<b>Smoking Status</b>			
Smoker	53(30.3)	51(96.2)	2(3.8)
Non-Smoker	122(69.7)	93(76.2)	29(23.8)
<b>Overall</b>	<b>175(100.0)</b>	<b>144(82.3)</b>	<b>31(17.7%)</b>

The study findings in Table 4.4 revealed that out of 175(100%) patients whose records were extracted, 144(82.3%) died within five years, while 31(17.7%) survived across all the age categories. The majority, 55(31.4%) of the cervical cancer patients, were of age 65+ years old at the beginning of the study. The study revealed that 54(98.2%) of cervical cancer patients aged 65+ died within 5 years. The study on marital status revealed that 27(93.1%) single patients died.

The study findings further revealed that 104(84.6%) died out of the total patients with no health insurance coverage. The study findings on the employment status of the patients revealed that 125(96.9%) of casual labourers died. The study showed that 89(85.6%) of cervical cancer patients who had reached Menopause died. The study findings on the use of contraceptives noted that 52(83.9%) of the patients who used the contraceptives died. On family history, 72(98.6%) of the cervical cancer patients who had a family history of cervical cancer died. The study findings revealed that 53(30.3%) of the patients were smokers, and 122(69.7%) were non-smokers. However, 51(96.2%) of the smokers died within 5 years period.

#### **4.3.2 Survival Percentages of Cervical Cancer Patients Based on Clinical Characteristics**

The study findings on survival percentages of cervical cancer patients based on clinical characteristics are presented in Table 4.5.

**Table 4.5 Survival Percentages Clinical Characteristics**

<b>Covariates</b>	<b>Number of patients, n (%)</b>	<b>Died, n (%)</b>	<b>Censored, n (%)</b>
<b>Comorbidity</b>			
No	55(31.4)	33(60.0)	22(40.0)
Yes	120(68.6)	111(92.5)	9(7.5)
<b>HIV Status</b>			
Negative	110(62.9)	86(78.2)	24(21.8)
Positive	65(37.1)	58(89.2)	7(10.8)
<b>HPV infections</b>			
Not done	172(98.3)	141(82.0)	31(18.0)
Negative	3(1.7)	3(100.0)	0(0.0)
<b>Cancer Grade</b>			
Grade 1	35(20.0)	9(25.7)	26(74.3)
Grade 2	59(33.7)	55(93.2)	4(6.8)
Grade 3	81(46.3)	80(98.8)	1(1.2)
<b>Staging of the Disease</b>			
Stage I	30(17.1)	10(33.3)	20(66.7)
Stage II	38(21.7)	31(81.6)	7(18.4)
Stage III	77(44.0)	73(94.8)	4(5.2)
Stage IV	30(17.1)	30(100.0)	0(0.0)
<b>Treatment Plan</b>			
Radiation	39(22.3)	22(56.4)	17(43.6)
Chemo	45(25.7)	44(97.8)	1(2.2)
Follow-up	24(13.7)	21(87.5)	3(12.5)
Palliative Chemo	32(18.3)	27(84.4)	5(15.6)
Chemo/Surgery	21(12.0)	17(81.0)	4(19.0)
Hospice Care	14(8.0)	13(92.9)	1(7.1)
<b>Overall</b>	<b>175(100.0)</b>	<b>144(82.3)</b>	<b>31(17.7)</b>

The study findings in Table 4.5 revealed that of the patients with comorbidities, 111(92.5%) died. Also, of the patients who had no comorbidities, 33(60.0%) died, and 31(47.5%) were censored. The study findings revealed that 58(89.2%) of HIV positive patients died within 5 years period. The study findings on cancer grades of the patients revealed that 35(20.0%) of the patients had cancer grade one, 59(33.7%) had cancer grade

two, and 81(46.3%) had cancer grade three. Of the total patients with cancer grade three, 80(98.8%) died.

The study findings revealed that 30(17.1%) patients were diagnosed with stage one cervical cancer. Also, 38(21.7%) of the patients were diagnosed with stage two of cervical cancer, 77(44.0%) of the patients were diagnosed with stage three of cervical cancer, and finally, 30(17.1%) were diagnosed with stage four of cervical cancer. Of the patients diagnosed with stage one of cervical cancer, 10(33.3%) died. Also, of the total patients diagnosed with stage two of cervical cancer, 31(81.6%) died. Out of those diagnosed in stage three, 73(94.8%) died. Finally, all patients diagnosed with stage four died within the five-year study period.

The study findings revealed that 39(22.3%) of the patients underwent radiation as a treatment method, while 45(25.7%) underwent chemotherapy. Furthermore, 21(12.0%) of the patients underwent chemo-surgery. Further, 32(18.3%) of the patients underwent palliative chemo. Also, doctors followed up on 24(13.7%) of the patients. Finally, 14(8.0%) of the patients underwent hospice care. Of the patients who underwent radiation, 22(56.4%) died.

### 4.3.3 Kaplan Meier Survival Results

The Kaplan-Meier survival analysis was used to model cervical cancer patients survival time. This method estimates the probability of survival over time, taking into account censored data, which occurs when the event of interest has not occurred for some subjects by the end of the study.

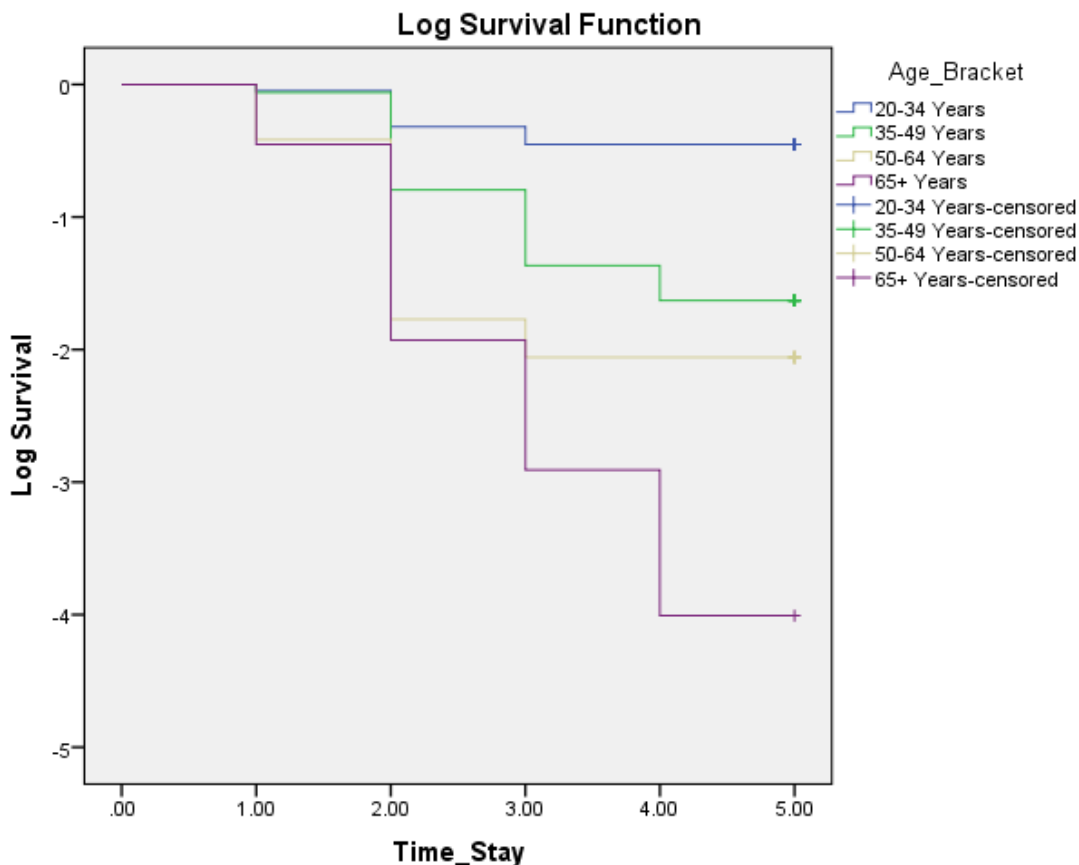
**Table 4.6 Survival Distributions For The Different Levels of Age Category**

	<b>Chi-Square</b>	<b>df</b>	<b>Sig.</b>
Log Rank (Mantel-Cox)	44.166	3	.000

The study findings in Table 4.6 Revealed that the Chi-Square statistic of 44.166 with 3 degrees of freedom and a significance level of .000 suggests a strong association between the age category and survival time for cervical cancer patients. This implies that there is a significant difference in survival times among different age category of cervical cancer

The study findings agreed with Drokow et al. (2022) who indicated that the survival rates for cervical cancer patients vary widely. For example, the one-year survival rate was reported to be 77.5%, and the three-year survival rate was 52.8% in a study involving 16,122 cervical cancer patients.

The following is the Kaplan Meier Survival Curve generated for age category.



**Figure 4.1 Survival Function for Age Category**

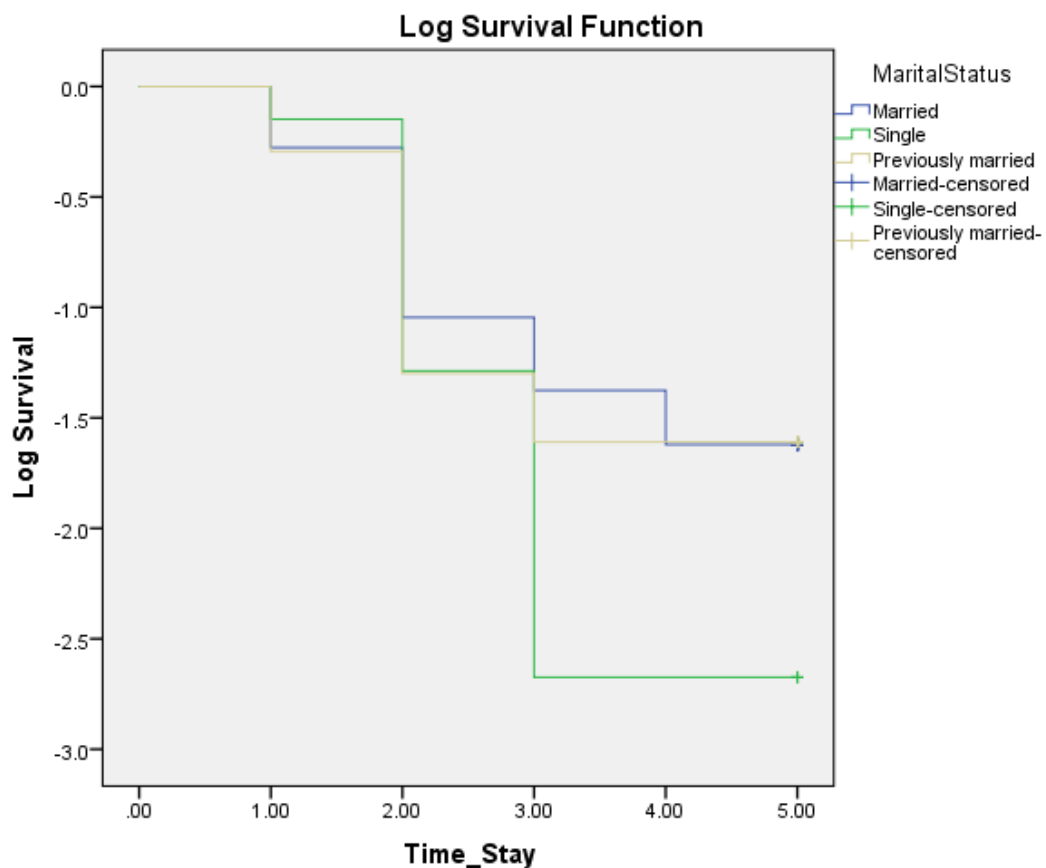
The study findings in Figure 4.1 revealed that the survival proportion appears to be much higher in the women aged between 20 to 34 years compared to the women aged 35 years and above. Although the women aged 65 years and above appear to have a small advantage in survival, fewer participants survived beyond the 5 years. It would appear that cervical cancer patients aged between 20 to 34 years significantly prolong the time until death compared to those above 34 years.

**Table 4.7 Survival Distributions for the Different Levels of Marital Status.**

	<b>Chi-Square</b>	<b>df</b>	<b>Sig.</b>
Log Rank (Mantel-Cox)	.688	2	.009

Table 4.7 provided Log Rank (Mantel-Cox) test result of 0.688 with 2 degrees of freedom and a significance level of 0.009. This indicates that there is a statistically significant difference in survival distributions for the different levels of marital status among cervical cancer patients. This suggests that marital status may have a notable impact on the survival time of cervical cancer patients.

The study findings agreed with Machida et al. (2017) who reported that marriage is associated with improved survival among cancer patients. Cervical cancer patients with husbands had a higher cumulative survival rate compared to those who were not married, divorced, or widowed.



**Figure 4.2 Survival Function for marital status**

The study findings in Figure 4.2 revealed that the survival proportion appears to be much lower in single women compared to the women who are married and those who were

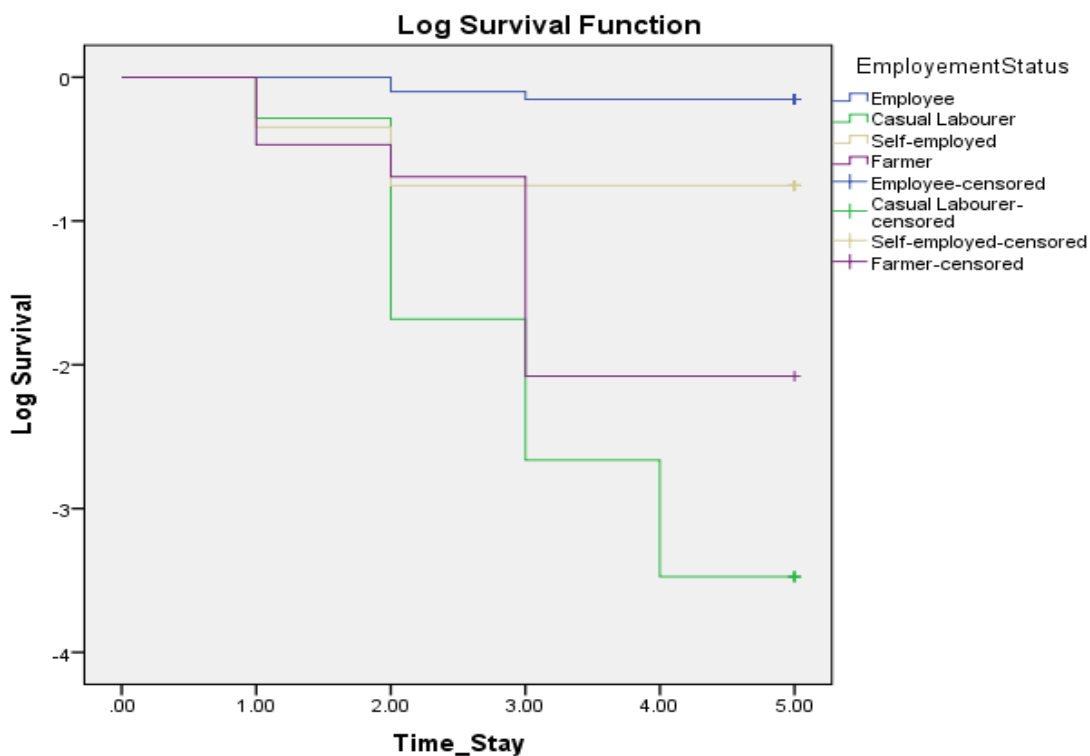


previously married. This implied that single women were more likely to die within 5 years.

**Table 4.8 Survival Distributions for the Different Levels of Employment Status**

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	60.619	3	.000

The Log Rank (Mantel-Cox) test result of 60.619 with 3 degrees of freedom and a significance level of 0.000 indicates a statistically significant difference in survival distributions for the different levels of employment status among cervical cancer patients. This suggests that employment status may have a notable impact on the survival time of cervical cancer patients. The study findings agreed with Mebratie et al. (2022) who noted that employment status, along with other factors, may play a role in influencing the survival time of cervical cancer patients.



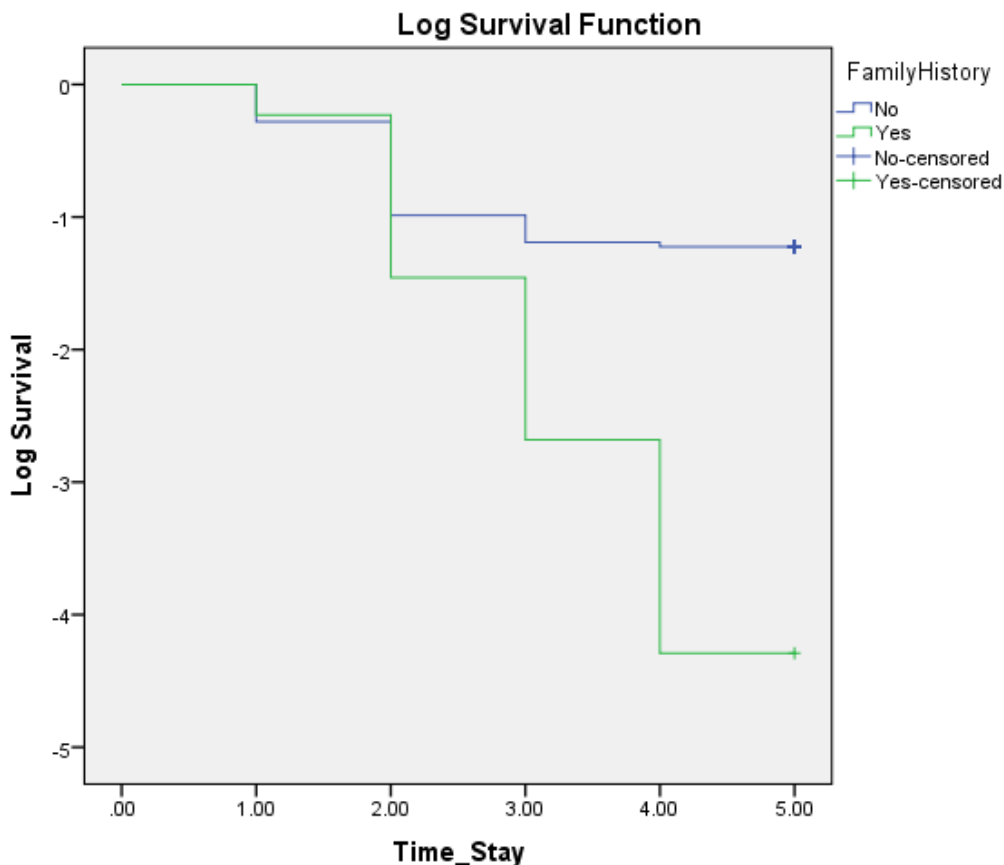
**Figure 4.3 Survival Function for employment status**

The study findings in Figure 4.3 revealed that the survival proportion appears to be much higher in the employed group compared to casual labourers, self-employed and farmers groups, which do not appear to differ considerably (although the casual labourers appear to have a small advantage on survival; that is, fewer participants survived beyond the 5 years. It would appear that employment significantly prolongs the time until participants die compared to the other source of income.

**Table 4.9 Survival Distributions For Family History of cervical cancer .**

	<b>Chi-Square</b>	<b>df</b>	<b>Sig.</b>
Log Rank (Mantel-Cox)	10.979	1	0.001

The Log Rank (Mantel-Cox) test result revealed that test statistic is 10.979 with 1 degree of freedom, and the associated p-value is 0.001. This indicates that there is a statistically significant difference in survival distributions for the different levels of Family History of cervical cancer among cervical cancer patients. The survival outcomes for patients with different family histories of cervical cancer are not the same. The study findings concurred with Hemminki, K. (2012) who noted that family history is significantly associated with the survival time of cervical cancer patients. This suggests that the presence of a family history of cervical cancer may have an impact on the survival outcomes of patients.



**Figure 4.4 Survival Function for Family History**

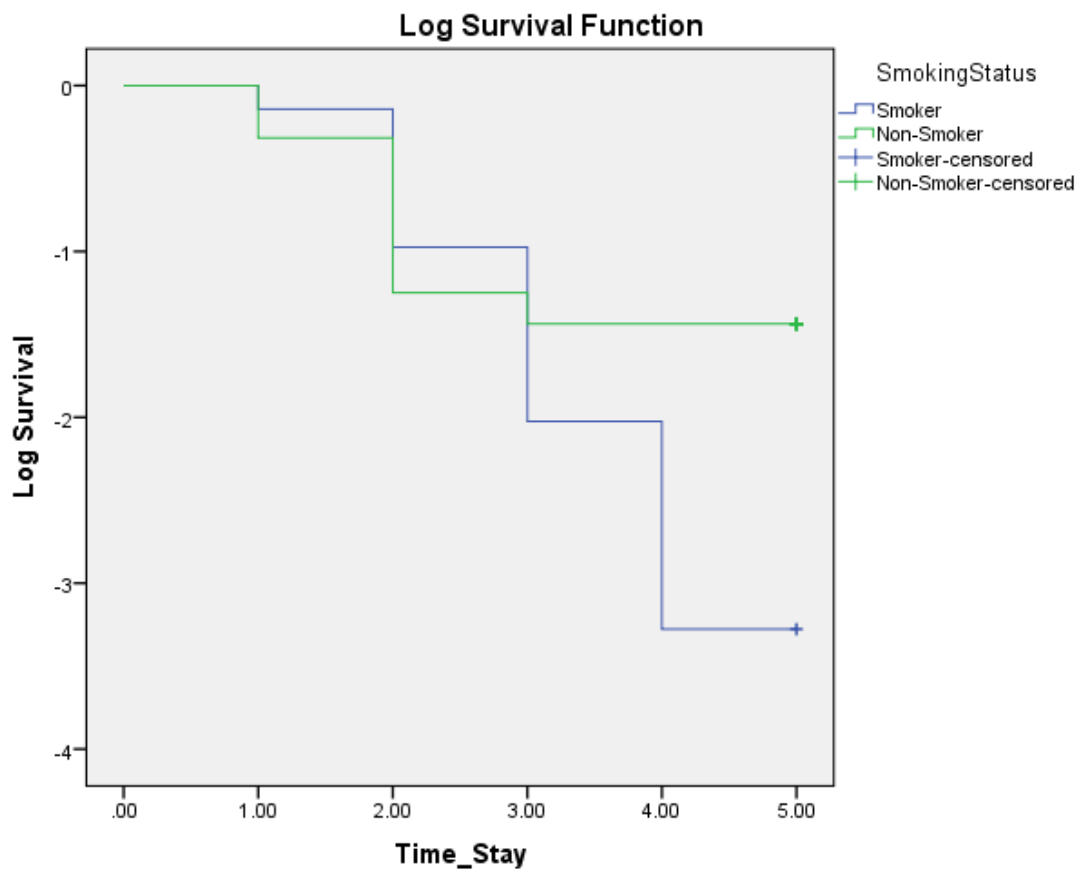
The study findings in Figure 4.4 revealed that the survival proportion appears much higher in women with no family history of cervical cancer than in those with family history. Cervical cancer patients with a family history of cervical cancer appear to have a short survival time.

**Table 4.10 Survival Distributions For The Different Levels Of Smoking Status**

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	0.799	1	0.371

The study results revealed that the Chi-Square value of .799 with 1 degree of freedom and a significance level of .0371 suggests that smoking status have an impact on the survival time of cervical cancer patients. The study findings agreed with Mayadev, Lim,

Durbin-Johnson, Valicenti and Alvarez (2018) who found that smoking decreases survival in cervical cancer patients undergoing definitive treatment with radiation. Additionally, smokers with cervical cancer were found to be more likely to die of the disease, especially if they were also positive for certain types of human papillomavirus (HPV). Furthermore, the current smoking rate for cervical cancer survivors was reported to be higher compared to survivors of other types of cancer, indicating a potential impact on survival rates.



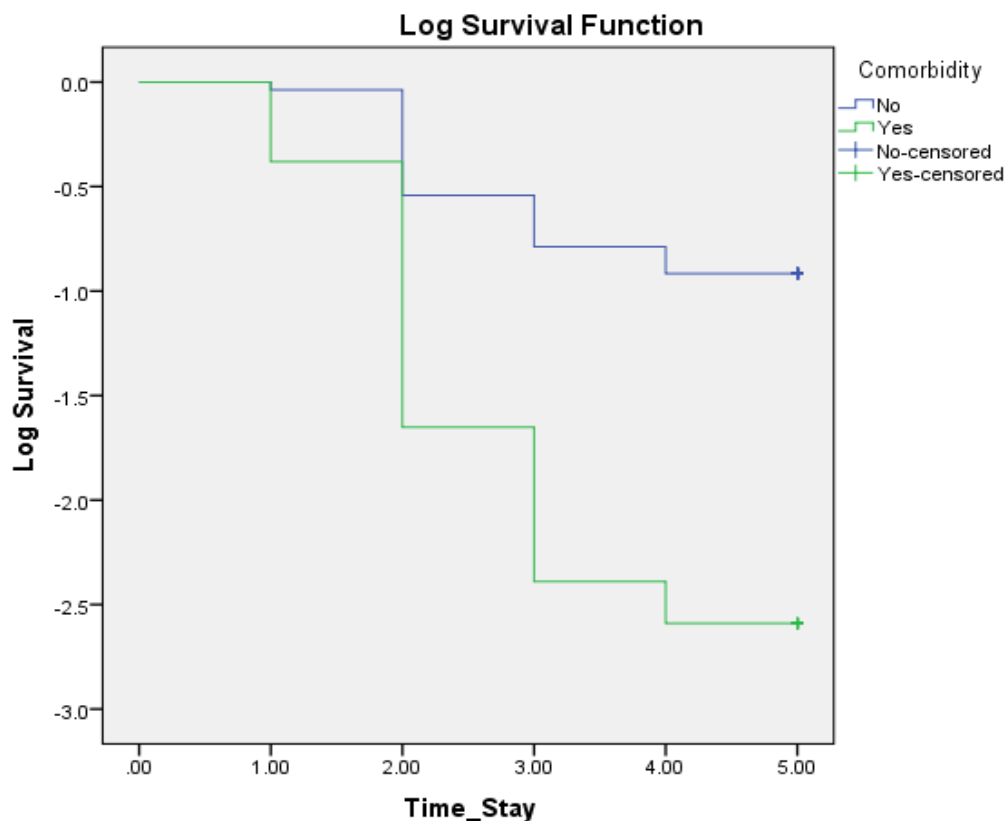
**Figure 4.5 Survival Function for Smoking Status**

The study findings in Figure 4.5 revealed that the survival proportion appears much lower in cervical cancer patients who smoke than non-smokers. Smokers appear to have a small advantage in survival since fewer participants survived beyond the 5 years.

**Table 4.11 Survival Distributions For The Different Levels Of Comorbidity.**

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	35.088	1	0.000

The results show a Chi-Square value of 35.088 with 1 degree of freedom and a significance level of 0.000, indicating a statistically significant difference in survival of cervical cancer patients' distributions between the different levels of comorbidity. The study findings agreed with Castro et al. (2021) who indicated that the presence of comorbidity was a significant predictor of death for cervical cancer patients, emphasizing the importance of treating comorbidities in the early stages of cervical cancer to maximize survival time.

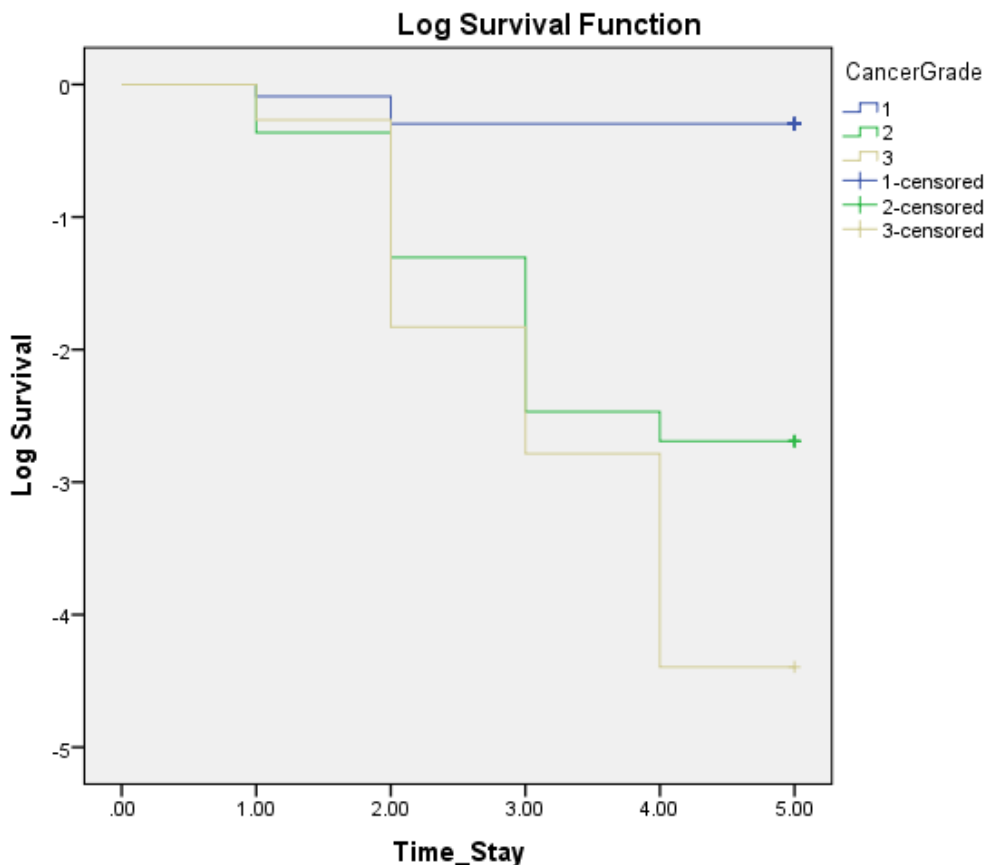
**Figure 4.6 Survival Function for comorbidity**

The study findings in Figure 4.6 revealed that the survival proportion appears to be much higher in cervical cancer patients with no comorbidity than those with underlying comorbidities. It would appear that having no underlying comorbidities significantly prolongs the time until participants die compared to those with underlying comorbidities.

**Table 4.12 Survival Distributions For The Different Levels Of Cancer Grade.**

	<b>Chi-Square</b>	<b>df</b>	<b>Sig.</b>
Log Rank (Mantel-Cox)	62.927	2	0.000

The Chi-Square statistic of 62.927 with 2 degrees of freedom and a p-value of .000 suggests a strong association between cancer grade and survival time for cervical cancer patients. This means that the different levels of cancer grade have a significant impact on the survival time of cervical cancer patients. The study findings concurred with Feng et al. (2021) who found that the expected survival times for patients with different cancer grades varied significantly, with lower survival rates associated with higher cancer grades. Additionally, another study highlighted the significance of cancer stage in relation to the survival time of cervical cancer patients, indicating that lower survival rates were closely correlated with advanced cancer stages.



**Figure 4.7 Survival Function for Cancer Grade**

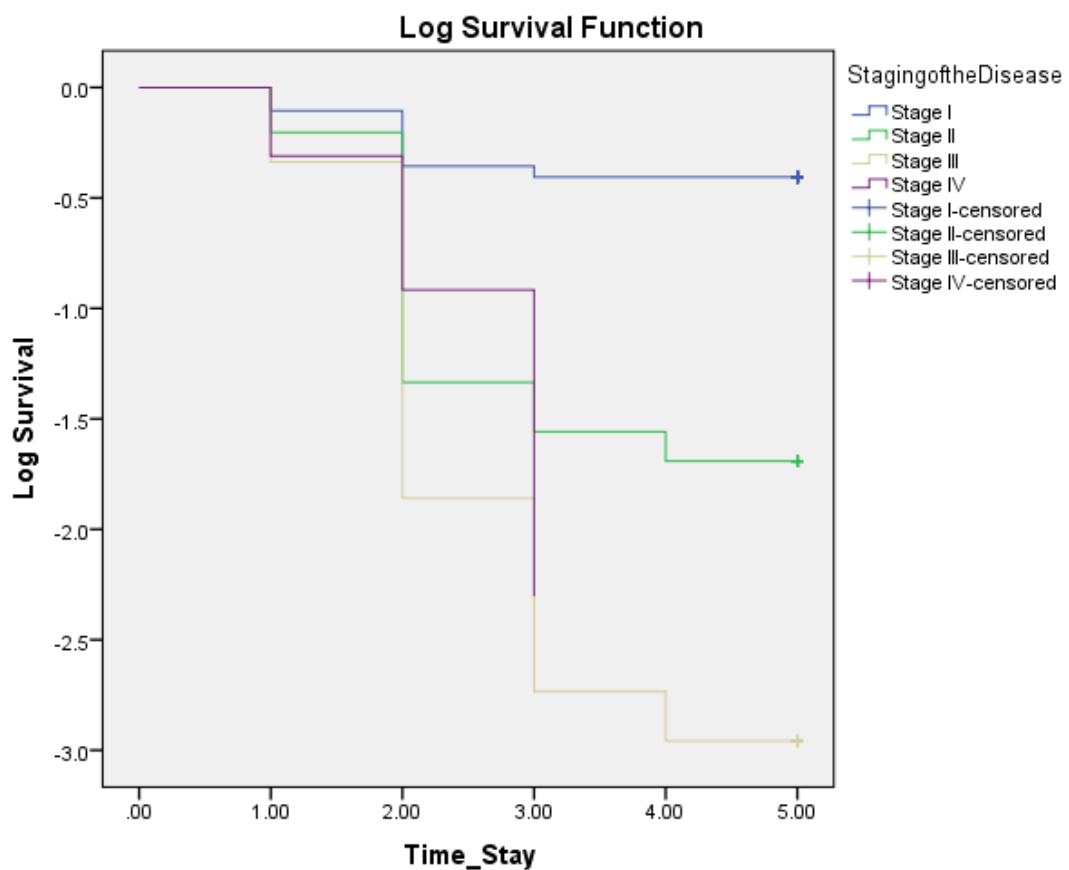
The study findings in Figure 4.7 revealed that the survival proportion appears to be much higher in the cervical cancer patients in grade 1 as compared to those in grades 2 and 3, which do not appear to differ considerably (although the cervical cancer patients with grade 3 cancer appear to have a small advantage on survival; that is, fewer participants survived beyond the 5 years).

**Table 4.13 Survival distributions for the different levels of Staging of the Disease.**

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	43.041	3	0.000

The test resulted in a Chi-Square value of 43.041 with 3 degrees of freedom and a significance level of .000. This implies that the survival time for cervical cancer patients varies depending on the stage of the disease. According to Tshewang, Satiracoo and

Lenbury (2021) study, stage I and II patients have survival rates of 96% and 87% at 1 year, 87% and 60% at 3 years, and 73% and 48% at 5 years, respectively. The 5-year relative survival rate for cervical cancer patients varies depending on the stage of the disease. When cervical cancer is diagnosed at an early stage, the 5-year relative survival rate is 91%. When cervical cancer is diagnosed after it has spread to nearby tissues, organs, or regional lymph nodes, the 5-year relative survival rate is 60%. When cervical cancer is diagnosed after it has spread to a distant part of the body, the 5-year relative survival rate is 19%. The 5-year relative survival rate for all people with cervical cancer is 67%.



**Figure 4.8 Survival Function for staging of the Cervical cancer**

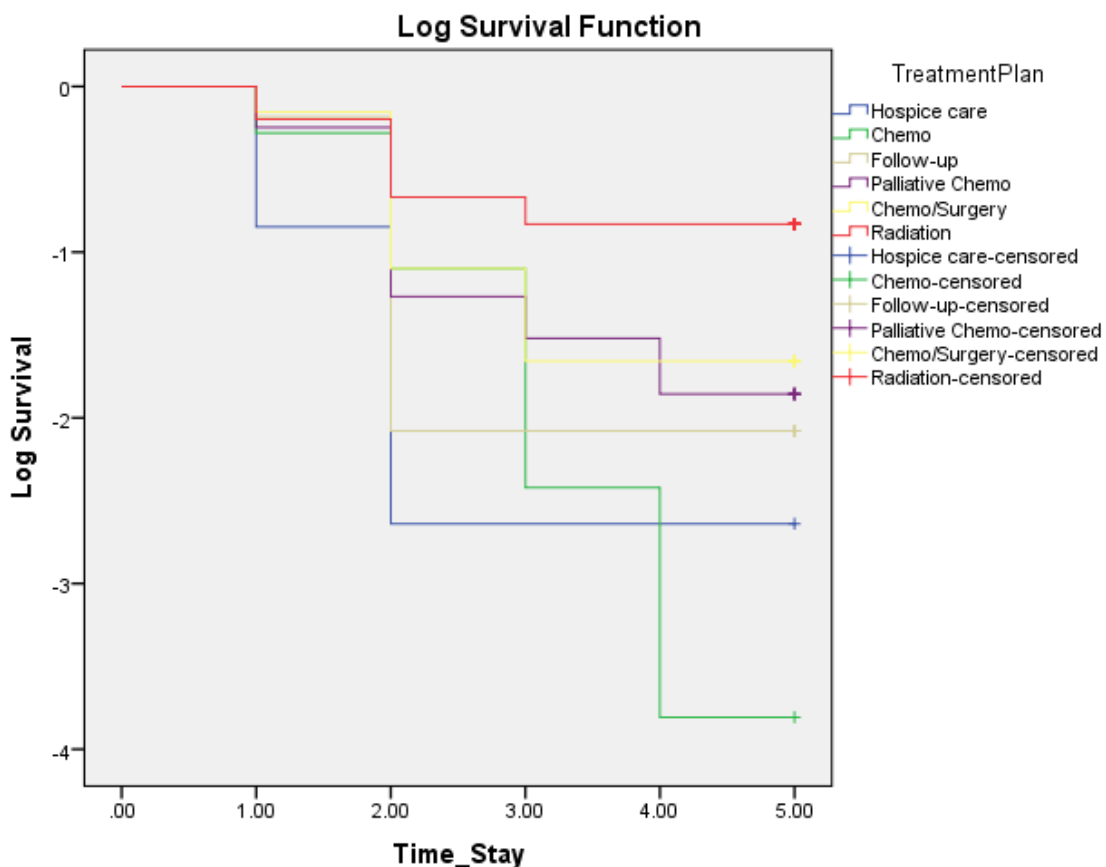


The study findings in Figure 4.8 revealed that the survival proportion appears much higher in cervical cancer patients in stage 1 compared to those in stages 2, 3 and 4 of cancer, which does not appear to differ considerably. Although cervical cancer patients with stage 4 of cancer appear to have a small advantage in survival, none survived beyond the 5 years.

**Table 4.14 Survival Distributions For The Different Levels Of Treatment Plan**

	<b>Chi-Square</b>	<b>df</b>	<b>Sig.</b>
Log Rank (Mantel-Cox)	22.848	5	0.000

The test statistic of 22.848 with 5 degrees of freedom and a p-value of .000 indicates a significant difference in survival distributions among the different treatment plans. This suggests that the survival time for cervical cancer patients varies depending on various factors such as the treatment plan, time interval from diagnosis to treatment, histopathological types, and disease-free survival rate. The study findings concurred with Mwaliko et al. (2023) who found that overall survival was defined as the length of time a patient was alive from the date of diagnosis to 5 years post-diagnosis.



**Figure 4.9 Survival Function for Treatment Plan**

The study findings in Figure 4.9 revealed that the survival proportion appears to be much higher in the radiation as compared to other treatment plans, which do not appear to differ considerably, although those who underwent chemotherapy appear to have a small advantage on survival; that is, fewer participants survived beyond the 5 years.

#### 4.4 Predictors of Survival After a Diagnosis of Cervical Cancer

Cox regression model was fitted to data containing all data (175 cases). Of all 175 cervical cancer patients in the study period, 144(82.3%) died.

##### 4.4.1 Omnibus Tests of Model Coefficients

The study carried out the Omnibus Tests of Model Coefficients to get a likelihood ratio test of the fit of the full model relative to a null (intercept only) model. Statistical

significance suggests the model is a significant improvement in fit relative to the null.

The results are presented in Table 4.15.

**Table 4.15 Omnibus Tests of Model Coefficients**

<b>-2 Log Likelihood</b>	<b>Overall (score)</b>			<b>Change From Previous Step</b>			<b>Change From Previous Block</b>		
	<b>Chi-square</b>	<b>df</b>	<b>Sig.</b>	<b>Chi-square</b>	<b>df</b>	<b>Sig.</b>	<b>Chi-square</b>	<b>df</b>	<b>Sig.</b>
<b>1301.326</b>	68.251	15	.000	84.815	15	.000	84.815	15	.000

The study results in Table 4.15 revealed that the model is a significant [ $\chi^2(15) = 68.251$ ,  $p < 0.05$ ] improvement in fit relative to the null. Omnibus tests of model coefficients provide a score test for simultaneously assessing the effects of the parameters in the model. It was found that the covariates contribute significantly in explaining the variability in the survival of cervical cancer ( $P = 0.00$ ).

#### **4.4.2 Predictors of Survival After a Diagnosis of Cervical Cancer**

Predictors of survival after a diagnosis of cervical cancer was determined by the use of a Cox regression model. The study findings are presented in Table 4.16.

**Table 4.16 Cox Regression Model**

Covariates	B	SE	Sig.	Exp(B)	95.0% CI for Exp(B)	
					Lower	Upper
Age category	.369	.101	.000	1.446	1.186	1.764
Marital Status	-.258	.117	.027	.772	.615	.971
Insurance Cover	.182	.209	.384	1.200	.796	1.809
Employment Status	.328	.161	.042	1.389	1.012	1.905
Menopause	.322	.232	.165	1.380	.876	2.174
Contraceptives	.303	.414	.465	1.353	.601	3.047
Types of Contraceptives	.002	.119	.986	1.002	.793	1.266
Family History	.444	.224	.048	1.559	1.005	2.418
Smoking Status	.807	.254	.002	2.241	1.361	3.688
Comorbidity	.825	.237	.001	2.282	1.433	3.635
HIV Status	-.144	.206	.486	.866	.578	1.298
HPV infections	-.043	.315	.892	.958	.517	1.776
Cancer Grade	.472	.145	.001	1.604	1.208	2.130
Staging of the Disease	.265	.109	.015	1.303	1.052	1.614
Treatment Plan	-.124	.061	.043	.883	.783	.996

Therefore, the cox model was obtained as given below;

$$\ln \{h(t)\} = 0.369X_1 - 0.258X_2 + 0.328X_3 + 0.444X_4 + 0.807X_5 + 0.825X_6 + 0.472X_7 + 0.265X_8 - .124X_9$$

where

$h(t)$  denotes the death due to the effects of predictor variables

$X_1$  represents age category,  $X_2$  represents marital status,  $X_3$  represents employment status,  $X_4$  represents family history,  $X_5$  represents smoking status,  $X_6$  represents comorbidity,  $X_7$  represents cancer grade,  $X_8$  represents staging of the disease and  $X_9$  represents treatment plan.

The study findings in Table 4.16 revealed that age, marital status, employment status, family history, smoking status, comorbidity, cancer grade, staging of the disease and treatment plan were factors that increased the risk of death for cervical cancer patients. The estimated coefficient for age category of the patient being  $\beta = .369$  implies the hazard ratio is  $\exp(\beta) = 1.446$ . This indicates the change of hazard rate for every age increase for patients there is an increase hazard risk of dying (HR=1.446, 95% CI: 1.186-1.764, P=0.000). The study findings concurred with Wang *et al.* (2021) study which revealed that the overall cervical cancer mortality rates generally increased with age of the women. The age effect on mortality rates of cervical cancer was an increase with advancing age. Further, the study findings concurred with Wang, Xue, Wang and Bai (2018) who noted that age has become a contributing factor for cervical cancer death in women over 40 years old. Luo (2017) study findings revealed the decrease survival rate for cervical cancer patients as age increases.

The marital status of the patient was also another risk factor for the survival of cervical cancer. Those patients who were married, the hazard rate of dying of the disease may be lower by 7.7% than those who were single or previously married (HR=0.772, 95%: 0.615-0.971, P= 0.027). Cancer patients who are single are more likely to be diagnosed at a later stage and have a lower chance of living longer than those who are married. In many ways, marriage helps protect women with women's cancer when it comes to their diagnosis and prognosis. The first is how it makes people act. Living with a spouse or partner improves

a woman's way of life and health habits. One reason is that sexually active women often show early signs of some cancers, like cervical cancer, because they bleed after having sex. Also, close partners may notice early signs and tell their wives to go to seek medical care instantly once symptoms develop. Another reason could be that spouses may encourage regular health checks. The study findings concurred with Buja *et al.* (2018), who noted that being married or having a good relationship with a partner is linked to early cancer diagnosis and can help people with cancer live longer. Also, marriage may make people less likely to take risks and put social pressure on things like diet and exercise (Chen *et al.*, 2021).

Also, economic and social support can help people get diagnosed quickly and have a good prognosis. Married women can get help with money from their husbands and other family members, which means they have a better chance of getting good medical care. This was in line with what Buja *et al.* (2018) who found that marriage may offer protection through the help and care from family and larger social support networks. So, marriage is linked to both physical and mental health in a good way. Also, married women with cancer feel more social support from their extended family networks and have better health overall. Also, family members can help share the emotional load, which makes patients less depressed, tired, and anxious.

The patients who were not employed, the hazard rate is 1.389 times higher than those patients who were employed with (HR=0.328, 95% CI: 1.012-1.905, P=0.042). This implied that there is an increased cervical cancer survival rate with employment status since income is a predictive factor of employment status. Unemployed cervical cancer patient has fewer financial resources to comply with their basic needs; they can have reduced access to healthcare. Psychological conditions and stress may also derive from

unemployment and engage the women in poor behaviours that are well-known risk factors for diseases, injuries and death. The study findings agreed with Leuteritz *et al.* (2021), who showed that an average of 89% of employees had returned to work within 2 years after their cervical cancer diagnosis. However, the study findings disagreed with Viseux *et al.* (2022), who noted that employment factors, such as working conditions, work demands and flexibility, may be associated with the low survival rate.

The hazard rate for patients with family history of cervical cancer, is 1.559 times higher than for patients who did not have family history of cervical cancer with (HR=1.559, 95% CI: 1.005-2.418, P=0.048). This implied that patients with a family history of cervical cancer may be genetically predisposed to carcinogenesis. This could affect risk of recurrence, second primary tumors and overall outcomes after treatment of a primary cancer. The study findings contradicted the findings of Lee *et al.* (2014), who discovered that patients with a family history of cancer had greater overall and disease-free survival than patients without a family history of cancer. Morris *et al.* (2013) discovered similar results, observing that patients with a family history of cancer outlived those without a family history of cancer, and that patients with more than one relative with a history of cancer outlived those without a family history of cancer. According to the findings of Isla *et al.* (2016), cancer patients who had a family history of cancer had significantly longer survival than those who did not have a family history of cancer.

The hazard rate of patients who smoke was 2.241 times risk of dying of cervical cancer than those of patients who did not smoke (HR=2.241, 95% CI: 1.361- 3.688, P=0.002). Smoking increases the chance of developing precancerous lesions of the cervix (called moderate or severe dysplasia) and an increase in the chance of developing cervical cancer. Smoking weakens immune system as well as greatly increasing the risk for dysplasia. The

study findings concurred with Min *et al.* (2018) who showed that the relative risks of death due to cervical cancer among current smokers was two times higher compared with non- smokers. Smokers had an increased risk of death due to cervical cancer. Su *et al.* (2018) showed that there is a strong correlation between women with cervical neoplasia and those who currently smoke. Current smoking (even passive smoking) has been linked to increase in the risk of dying.

The patients with comorbidities, the hazard rate of dying of the disease was higher by 22.8% than those who without comorbidities (HR=2.282, 95%: 1.433-3.635, P= 0.001). This implied that increased comorbidity is associated with reduced survival time among women diagnosed with cervical cancer. Comorbidity may form a barrier to participation in cancer screening, which may lead to more advanced disease at diagnosis. Comorbidity may also limit treatment options and increase the risk of treatment complications. The study findings concurred with Sogaard *et al.* (2013) who evaluated that comorbidity is associated with higher mortality from cancer. According to Sarfati, Koczwara and Jackson (2016) findings comorbidity may also limit treatment options and increase the risk of treatment complications.

The patients with cancer grade 3, the hazard rate increase by 1.604 than those in grade 1 with (HR=1.604, 95% CI=1.208-2.130, P=0.001). This implied that cancer grade is a prognostic factor for squamous cervical cancer. The study findings concurred with Matsuo *et al.* (2018) who noted that grade 2–3 reduces the survival time of cervical cancer patients. They found that tumour grade is useful to identify a group of women with decreased survival outcome with current treatments. Similarly, National Comprehensive Cancer Network (2018) found out that women with grade 3 tumors had worse survival outcome as compared to those with grade 1–2 tumors.



The estimated coefficient for staging of the cervical cancer of the patient being  $\beta = .265$  implies the hazard ratio is  $\exp(\beta) = 1.303$ . This indicates the change of hazard rate for every stage increase for patients there is an increase hazard risk of dying (HR=1.303, 95% CI: 1.052-1.614, P=0.015). This implies that if cervical cancer is detected and treated early, while it is still located only in the cervix and uterus, the survival rate is high. If cervical cancer spreads to nearby lymph nodes, or to other organs or other areas of body, the survival rate is lower. One-year relative survival decreased with increasing stage at diagnosis. The risk of distant tumour metastasis grows as the stage advances, resulting in a substantial drop in patients' life expectancy. Patients in the early stages (stages I and II) have a greater life expectancy than those in the latter stages (stage III and IV). Cervical cancer can be treated and has a better chance of survival if detected early. This discovery is consistent with others (Khalkhali *et al.*, 2019).

According to the American Cancer Society, if cervical cancer is detected early, the 5-year survival rate is 92%. Approximately 44% of cervical cancer patients are diagnosed at an early stage. The 5-year survival percentage for cervical cancer that has spread to neighbouring tissues or organs and/or regional lymph nodes is 58%. The 5-year survival rate for cancer that has progressed to a distant portion of the body is 18%.

The estimated coefficient for treatment plan of cervical cancer being  $\beta = -.124$  implies the hazard ratio is  $\exp(\beta) = .883$ . This indicates the change of hazard rate for every treatment plan of the patients there is a decrease hazard risk of dying (HR=.883, 95% CI: .783-.996, P=0.043). This implies that if cervical cancer is diagnosed at the early stages, it can be treated and has a higher survival rate. Cervical cancer is treated in a variety of methods. It is determined by the type of cervical cancer and the extent to which it has spread. Surgery, chemotherapy, and radiation therapy are all options for treatment.

Surgery is the removal of cancer tissue through an operation. Chemotherapy is the use of specific drugs to shrink or destroy cancer. Radiation kills cancer by using high-energy beams (similar to X-rays).

#### 4.5 Relationship Between Patients' Survival and Covariate of Cervical Cancer

A Cox regression model were used to evaluate the relationship between patients' survival and individual/clinical predictors. The study findings are presented in Table 4.17 and 4.18.

**Table 4.17 Patients' Survival and Socio-Demographic Characteristic**

Covariates	Category of covariates	B	SE	Sig.	Exp(B)	95.0% CI for Exp(B)	
						Lower	Upper
<b>Age category</b>	20-34 Years	Ref					
	35-49 Years	.753	.337	.026	2.123	1.096	4.114
	50-64 Years	.995	.343	.004	2.705	1.381	5.295
	65+ Years	.966	.336	.004	2.627	1.360	5.075
<b>Marital status</b>	Married	Ref					
	Single	.942	.426	.027	2.564	1.112	5.912
	Previously married	.976	.428	.023	2.653	1.147	6.137
<b>Insurance Cover</b>	Insurance Cover	-.135	.186	.470	.874	.606	1.259
<b>Employment status</b>	Employee	Ref					
	Casual Labourer	.937	.393	.017	2.552	1.182	5.512
	Self-employed	1.073	.420	.011	2.924	1.283	6.666
	Farmer	1.099	.505	.030	3.000	1.115	8.071
<b>Menopause</b>	Menopause	.303	.172	.078	1.354	.967	1.895
<b>Contraceptives</b>	Contraceptives	-.029	.175	.868	.971	.689	1.369
<b>Family History</b>	Family History	.529	.210	.012	1.697	1.124	2.564
<b>Smoking Status</b>	Smoking Status	.116	.175	.005	1.123	.798	1.582

The study results in Table 4.17 revealed that the significant positive coefficient ( $\beta = .995$ ,  $p = .004$ ) indicates that the hazard rate for death is greater in those who are under the age category of 35 and above years as opposed to those under Age category of 20-34 years. This implied that patients aged 35 and above years have less survival time than cervical cancer patients aged between 20–34 years. Patients treated in old age had a considerably shorter time to death from cervical cancer. This predicted survival duration for cervical cancer patients is greatest in young women and diminishes with age. The current study supports the findings of Miura *et al.* (2016), who discovered that increasing age is associated with a shorter survival duration in cervical cancer patients.

The study further revealed that marital status of cervical cancer patients was negatively predictive of the hazard for death. This indicate that cervical cancer patients who were single ( $\beta = .942$ ,  $p = .027$ ) and previously married ( $\beta = .976$ ,  $p = .023$ ) were more likely to die early than those who were married. This implied that cervical cancer patients who were single and previously married have less survival time than those who were married. Cervical cancer patients who were single had less survival time than those who were married. The study findings concurred with Wong *et al.* (2018), who noted that survival time among single patients in terms of marriage tend to be less. Marital status was an independent risk factor for several important cervical cancer outcomes.

Employment status of cervical cancer patients was a significant positive predictor of the hazard for death. The individuals who were casual labourers ( $\beta = .937$ ,  $p = .017$ ), self-employed ( $\beta = 1.073$ ,  $p = .011$ ) and farmers ( $\beta = 1.099$ ,  $p = .030$ ) were predicted to die early than those who were employed under formal sector. This indicates that patients who were employed under formal sector prolonged the survival time than unemployed patients. Patients who were employed prolonged the survival time than unemployed patients. This

finding is comparable to study conducted by Kashyap *et al.* (2019) who showed that employment status is a predictor of survival time of cervical cancer since less income increase the risk of dying out of cervical cancer. The study results agreed with Norström *et al.* (2019), who noted a steady job in safe working conditions means more than simply a pay check employment can also provide numerous benefits critical to maintaining proper health. Job loss and unemployment are associated with a variety of negative health effects. Insurance coverage is more likely to be offered to employees earning higher salaries. Moreover, those with lower wages are less likely to access preventive care services that insurance may cover, such as screenings for blood pressure and cholesterol.

The survival of time of patients who had a family history of cervical cancer was shorter than those of patients who had no family history ( $\beta = .529$ ,  $p = .012$ ). Family history of cervical cancer is also one factor that significantly predicts the survival of the patients. In this study, family history is significantly associated with survival time for cervical cancer patients. The current study is consistent with other findings Waggoner *et al.* (2010) reported that women who have a mother or sister diagnosed with cervical cancer have a greater risk of developing this cancer than women without any cervical cancer family history.

Cervical cancer patients who smoke shorten the survival time than those who do not smoke ( $\beta = .116$ ,  $p = 0.005$ ). The results of this study suggested that smoking was a significant predictive factor for the survival time of the patients. Non-smokers had a longer survival time than smokers. The current study is consistent with other findings of Gurmu (2018), who noted smokers had shorter survival times than non-smokers.

**Table 4.18 Relationship Between Patients' Survival and Clinical Characteristics**

Covariates	Category of covariates	B	SE	Sig.	Exp(B)	95.0% CI for Exp(B)	
						Lower	Upper
Comorbidity	Comorbidity	.377	.168	.025	1.457	1.050	2.024
HIV/AIDS Status	HIV/AIDS Status	-.277	.171	.105	.758	.543	1.059
HPV infections	Not done	Ref					
	Positive	-.369	.713	.605	.692	.171	2.798
	Negative	-.163	.915	.859	.850	.141	5.108
Cancer Grade	Grade 1	Ref					
	Grade 2	2.221	.410	.000	9.220	4.128	20.593
	Grade 3	2.101	.403	.000	8.170	3.706	18.015
Staging of the disease	Stage I	Ref					
	Stage II	1.516	.367	.000	4.554	2.219	9.348
	Stage III	1.626	.343	.000	5.083	2.596	9.951
	Stage IV	1.672	.377	.000	5.323	2.544	11.138
Treatment plan	Radiation	Ref					
	Chemo	.864	.305	.005	2.372	1.304	4.316
	Follow-up	.340	.336	.312	1.404	.727	2.713
	Palliative	.640	.320	.045	1.896	1.013	3.546
	Chemo						
	Chemo/Surgery	.779	.357	.029	2.178	1.081	4.390
	Hospice Care	1.022	.343	.003	2.780	1.420	5.442

The study findings in Table 4.18 the survival time of cervical cancer patients with comorbidities is shortened than patients without comorbidities ( $\beta = .377$ ,  $p = .025$ ). The study revealed that the survival of cervical cancer patients who had underlying comorbidities is shorter than those who had no comorbidities. The study concurred with Rajamaki *et al.* (2021) noted that a history of comorbidities is associated with shorter survival and a higher risk of death. Comorbidities further decrease survival; therefore, appropriate management of care of these comorbidities might affect not only survival but also the well-being of this vulnerable population.

The study findings further revealed that the grade 1 cervical cancer patients had longer survival time than those patients in grade stage 2 ( $\beta = 2.221$ ,  $p = .000$ ) and grade 3 ( $\beta = 2.101$ ,  $p = .000$ ). The study further revealed that staging of cervical cancer was positively predictive of the hazard for death among patients. This indicates that cervical cancer patients who were in stage II ( $\beta = 1.516$ ,  $p = .000$ ), stage III ( $\beta = 1.626$ ,  $p = .000$ ) and stage IV ( $\beta = 1.672$ ,  $p = .000$ ) were more likely to die early than those who were in stage I. This implies that stage I patients have a longer survival period than stage II, III, and IV patients. As a result, the stage of the disease had a substantial association with the timing of patient survival. Individuals in stages I and II had a longer survival period than patients in stages III and IV. This is because early-stage cervical cancer is easily treatable by modern cancer treatments. This finding is consistent with Tshewang *et al.* (2021) finding that early stages of the disease have a better prognosis; five-year survival rates for stage I disease are greater than 90%. Women with severe disease, on the other hand, have a much worse prognosis, with less than 10% surviving stage IV disease. Cancer has spread to the neighbouring bladder or rectum or more distant organs in Stage IV cervical malignancy, and the cancer is at its metastasis stage.

Treatment plan of cervical cancer patients was a significant positive predictor of the hazard for death. The individual who was under hospice care ( $\beta = 1.022$ ,  $p = .003$ ) were predicted to die early than those who were under radiation. This implied that cervical cancer patients who were in hospice care had a shorter survival time than those who underwent radiation. Women who underwent chemotherapy have a shorter survival time than women who underwent radiation. The study concluded that Yfantis *et al.* (2020) noted that patients who underwent chemotherapy experienced a significantly worse quality of life than those who did not receive chemotherapy. Furthermore, the adverse

chemotherapy effects on the quality of life appear to vary according to the time since surgery.

The study model shows that the most important prognostic factor affecting survival in Cervical cancer patients is the stage at diagnosis. The patients diagnosed when their cancer was already at Stage IV had an almost 5.323 greater risk of dying from cervical cancer than those diagnosed at Stage I. Patients who were active smokers had a greater risk of dying than non-smokers. Patients with comorbidities had a significantly greater risk of dying compared to non- comorbidities patients in the model.

## CHAPTER FIVE: CONCLUSIONS AND RECOMMENDATIONS

### 5.1 Introduction

This section describes the conclusion and recommendations of the study.

### 5.2 Conclusions

In conclusion, cervical cancer remains a significant public health problem in MTRH and in Kenya. The overall probability of survival at 5 years among cervical cancer patients treated in MTRH between 2014 and 2018 is 17.7%, which is significantly low. The overall median survival time was two years.

Risk factors affecting the life expectancy of cervical cancer patients include age, marital status, employment status, family history, smoking status, comorbidity, cancer grade, staging of the disease and treatment plan. Late diagnosis of cervical cancer appears to be mainly associated with a higher risk of dying from cervical cancer.

Patients treated in old age had a significantly shorter time to death from cervical cancer. Survival time for young cervical cancer patients was long and decreased with age. Patients who were employed prolonged the survival time than unemployed patients. Patients with a family history of cervical cancer may be genetically predisposed to carcinogenesis.

Smoking was a significant predictor of the patient's survival time. Non-smokers had a higher chance of survival than smokers. Increased comorbidity was linked to a shorter survival time in women with cervical cancer.

Cervical cancer is treated in a variety of ways. It is determined by the type of cervical cancer and how far it has spread. Surgery, chemotherapy, and radiation therapy are all options for treatment. As a result, the stage of the disease had a significant association



with the timing of patient survival. Patients in stages I and II had longer survival times than patients in stages III and IV. This is due to the fact that available cancer treatments easily cure early-stage cervical cancer.

### **5.3 Recommendation**

The study recommends that in order to increase the median survival rate of cervical cancer patients the ministry of health of the country and policymakers should work on awareness of the cervical cancer so that women would understand risk factors associated with survival time after diagnosis. This can be done by incorporating health education on cervical cancer in the teaching curriculums, carrying out medical camps and community mobilization activities, among other channels that can be used to make people aware. This will encourage women to attend regular screening, increasing the chances of diagnosis at the precancerous stage, which is 100% curable. The study recommends for a collaboration between the Government, private organizations, and local communities is critical in reducing the risk factors associated with survival time after diagnosis of cervical cancer . This includes promoting and developing cervical cancer awareness among the public so that women adopt healthy lifestyles and early screening behaviours.

Since the study found that as the age of cervical cancer patients increases, there is an increasing risk of dying, it is recommended that the ministry of health and health practitioners increase awareness and screening among women above 35 years. This will help in ensuring that the age group are screened early and get treatment. The study recommends that the ministry of health come up with policies for expanding and ensuring health insurance coverage to gather for treatment of unemployed cervical cancer. This will increase access to healthcare when other funding sources, hospital and medical care, become scarcer for an unemployed cervical cancer patient.

The study recommends that the health ministry ensure expanded screening services for early cervical cancer diagnosis at stage 1. Staging cervical cancer is important because it will help the treatment team know which treatments to provide, depending on the stage of the disease. It is recommended that health workers conduct promotions to motivate women at risk for early examination. The study recommends that healthcare systems in MTRH and Kenya should consider investing in highly targeted social support services and interventions that may help reduce the significant survival differences between married and unmarried patients with cancer. More psychological care and social support are needed for single and previously married patients with cervical cancer as they decide on screening and treatments.

The study recommends that health practitioners to pay special attention to treating comorbidities among patients with cervical cancer to reduce the mortality rate. They should regularly check the cervical cancer grade in order to predict the likely outcome of cancer and decide on the best treatment. The study recommends that women with a family history of cervical cancer need to start getting screening tests earlier and get tested more often, with different tests than other people. The study recommends that cervical cancer patients who smoke to quit smoking after a diagnosis of cancer in order to decrease the risk of secondary cancers, alleviate cancer treatment complications, improve survival, general health and quality of life, and decrease mortality from non-cancer tobacco-related diseases.

#### **5.4 Areas for Further Research**

Further research on the time to remission and relapse and treatment should be carried out to give more insight into the burden of the disease and disease management.

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**APPENDIX I: DATA COLLECTION SHEET**

Items	2014	2015	2016	2017	2018
Age					
Marital status	Single [ ] Married [ ] Widowed [ ] Divorced [ ] Separated [ ]				
Insurance Cover	None [ ] NHIF [ ] Others [ ]				
Employment status	Employee [ ] Worker [ ] Self-employed [ ] Other .....				
Menopause					
Contraceptives	Yes [ ] No [ ]				
Family History	Yes [ ] No [ ]				
Smoking status	Non-smoker [ ] Smoker [ ]				
Comorbidity	Yes [ ] No [ ]	Yes [ ] No [ ]	Yes [ ] No [ ]	Yes [ ] No [ ]	Yes [ ] No [ ]
Human papillomavirus (HPV) infection	Not done [ ] Positive [ ] Negative [ ]	Not done [ ] Positive [ ] Negative [ ]	Not done [ ] Positive [ ] Negative [ ]	Not done [ ] Positive [ ] Negative [ ]	Not done [ ] Positive [ ] Negative [ ]
Cancer Grade	Grade 1 [ ]	Grade 1 [ ]	Grade 1 [ ]	Grade 1 [ ]	Grade 1 [ ]

	Grade 2 [ ]	Grade 2 [ ]	Grade 2 [ ]	Grade 2 [ ]	Grade 2 [ ]
	Grade 3 [ ]	Grade 3 [ ]	Grade 3 [ ]	Grade 3 [ ]	Grade 3 [ ]
Staging of the disease	Stage I [ ]	Stage I [ ]	Stage I [ ]	Stage I [ ]	Stage I [ ]
	Stage II [ ]	Stage II [ ]	Stage II [ ]	Stage II [ ]	Stage II [ ]
	Stage III [ ]	Stage III [ ]	Stage III [ ]	Stage III [ ]	Stage III [ ]
	Stage IV [ ]	Stage IV [ ]	Stage IV [ ]	Stage IV [ ]	Stage IV [ ]
Treatment plan	Surgery [ ]	Surgery [ ]	Surgery [ ]	Surgery [ ]	Surgery [ ]
	Chemo [ ]	Chemo [ ]	Chemo [ ]	Chemo [ ]	Chemo [ ]
	Chemo/ Surgery [ ]	Chemo/ Surgery [ ]	Chemo/ Surgery [ ]	Chemo/ Surgery [ ]	Chemo/ Surgery [ ]
	Radiation [ ]	Radiation [ ]	Radiation [ ]	Radiation [ ]	Radiation [ ]
	Follow-up [ ]	Follow-up [ ]	Follow-up [ ]	Follow-up [ ]	Follow-up [ ]
	Palliative chemo [ ]	Palliative chemo [ ]	Palliative chemo [ ]	Palliative chemo [ ]	Palliative chemo [ ]
	Hospice care [ ]	Hospice care [ ]	Hospice care [ ]	Hospice care [ ]	Hospice care [ ]
	Referral [ ]	Referral [ ]	Referral [ ]	Referral [ ]	Referral [ ]
Discharge [ ]	Discharge [ ]	Discharge [ ]	Discharge [ ]	Discharge [ ]	
Outcome	Alive [ ]	Alive [ ]	Alive [ ]	Alive [ ]	Alive [ ]
	Death [ ]	Death [ ]	Death [ ]	Death [ ]	Death [ ]
	Lost to follow up [ ]	Lost to follow up [ ]	Lost to follow up [ ]	Lost to follow up [ ]	Lost to follow up [ ]

## APPENDIX II: IREC APPROVAL



MOI TEACHING AND REFERRAL HOSPITAL  
P.O. BOX 3  
ELDORET  
Tel: 3347102/3

## INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)



MOI UNIVERSITY  
COLLEGE OF HEALTH SCIENCES  
P.O. BOX 4606  
ELDORET  
Tel: 3347102/3  
7<sup>th</sup> April, 2021

Reference: IREC/2020/188

**Approval Number: 0003844**

Wilson Kiptoo,  
Moi University,  
Department of Mathematics, physics & Computing,  
P.O. Box 3900-30100,  
ELDORET-KENYA.

Dear Ms. Kiptoo,

**MODELING SURVIVAL TIME OF CERVICAL CANCER PATIENTS IN MOI TEACHING AND REFERRAL HOSPITAL, KENYA**


This is to inform you that **MTRH/MU-IREC** has reviewed and approved your above research proposal. Your application approval number is **FAN: 0003844**. The approval period is **7<sup>th</sup> April, 2021 – 6<sup>th</sup> April, 2022**.

This approval is subject to compliance with the following requirements;

- i. Only approved documents including (informed consents, study instruments, MTA) will be used.
- ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by **MTRH/MU-IREC**.
- iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to **MTRH/MU-IREC** within 72 hours of notification.
- iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to **MTRH/MU-IREC** within 72 hours.
- v. Clearance for export of biological specimens must be obtained from **MTRH/MU-IREC** for each batch of shipment.
- vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
- vii. Submission of an executive summary report within 90 days upon completion of the study to **MTRH/MU-IREC**.

Prior to commencing your study; you will be required to obtain a research license from the National Commission for Science, Technology and Innovation (NACOSTI) <https://oris.nacosti.go.ke> and other relevant clearances. Further, a written approval from the CEO-MTRH is mandatory for studies to be undertaken within the jurisdiction of Moi Teaching & Referral Hospital (MTRH) which includes 22 Counties in the Western half of Kenya.

Sincerely,

  
**PROF. E. WERE**  
CHAIRMAN



**INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE**

cc	CEO - MTRH	Dean - SOP	Dean - SOM
	Principal - CHS	Dean - SON	Dean - SCD



## APPENDIX III: MTRH APPROVAL



### MOI TEACHING AND REFERRAL HOSPITAL

Telephone : (+254)053-2033471/2/3/4  
 Mobile: 722-201277/0722-209795/0734-800481/0734-683361  
 Fax: 053-2061749  
 Email: [ceo@mtrh.go.ke/directorsoffice@mtrh@gmail.com](mailto:ceo@mtrh.go.ke/directorsoffice@mtrh@gmail.com)

Nandi Road  
 P.O. Box 3 – 30100  
 ELDORET, KENYA

**Ref:** ELD/MTRH/R&P/10/2/V.2/2010

16<sup>th</sup> April, 2021

Wilson Kiptoo  
 Moi University  
 Department of Mathematics, Physics & Computing  
 P.O. Box 3900-30100  
ELDORET-KENYA

MODELING SURVIVAL TIME OF CERVICAL CANCER PATIENTS IN MOI TEACHING AND REFERRAL HOSPITAL, KENYA

In order to conduct research within the jurisdiction of Moi Teaching and Referral Hospital (MTRH) this includes 22 counties in the Western half of Kenya. You are required to strictly adhere to the regulations stated below in order to safeguard the safety and well-being of staff and patients seen at MTRH involved research studies.

- 1 The study shall be under Moi Teaching and Referral Hospital regulation.
- 2 A copy of MU/MTRH-IREC approval shall be provided.
- 3 Studies dealing with collection, storage and transportation of Human Biological Material (HBM) will not be allowed to export the HBM outside the jurisdiction of MTRH.
- 4 For those tests which are unavailable locally the PI is tasked to ensure sourcing of equipment and subsequent training of staff to build their capacity.
- 5 No data collection will be allowed without an approved consent form(s) to participants to sign.
- 6 Take note that **data** collected must be treated with due confidentiality and anonymity.

Permission to conduct research shall only be provided once all the requirements stated above have been met.

*done 16/04/2021*  
 DR. WILSON K. ARUASA, EBS  
 CHIEF EXECUTIVE OFFICER  
 MOI TEACHING AND REFERRAL HOSPITAL



- c.c. - Senior Director, Clinical Services  
 - Director of Nursing Services  
 - HOD, HRISM

*All correspondence should be addressed to the Chief Executive Officer*

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## APPENDIX V: PUBLICATION

European Journal of Mathematics and Statistics  
Vol 4 | Issue 5 | October 2023  
ISSN 2736-5484



RESEARCH ARTICLE

## Predictors of Patient's Survival after a Diagnosis of Cervical Cancer Patients at Moi Teaching and Referral Hospital

Wilson Kiptoo\*, Mathew Stanley Kosgei, and Tum Isaac Kipkosgei

### ABSTRACT

Cervical cancer is one of the most prevalent cancer in women. It is the fourth leading cause of cancer deaths in women worldwide after breast cancer, lung cancer and colorectal cancer. In Kenya, cervical cancer is the leading cause of death in women, and has been shown to have increased by 3 211 in the past 5 years. An increase in cervical cancer in Kenya, has resulted in an economic burden for patients and families. There is an increase in healthcare spending as well as productivity losses due to morbidity and mortality at a productive age. The purpose of the study was to determine the predictors of survival after a diagnosis of cervical cancer. A retrospective cohort design was used in the study. A total of 175 cervical cancer patients were studied over a five-year period, from January 1st to December 31st, 2014. A Cox regression model were used to assess the predictors of survival after cervical cancer diagnosis. The study findings revealed that age, marital status, employment status, family history, smoking status, comorbidity, cancer grade, staging of the disease and treatment plan were factors that increased the risk of death for cervical cancer patients. In conclusion, risk factors affecting the life expectancy of cervical cancer patients include age, marital status, employment status, family history, smoking status, comorbidity, cancer grade, staging of the disease and treatment plan. In an effort for an intervention on factors that increased the risk of death for cervical cancer patients, a collaboration between the Government, private organizations, and local communities is critical. This includes promoting and developing cervical cancer awareness among the public so that women adopt healthy lifestyles and early screening behaviours.

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Published: October 16, 2023

10.24018/ejmath.2023.4.5.264

Moi University, Kenya.

\*Corresponding Author:  
e-mail: kiptoowilson9882@gmail.com

**Keywords:** Cervical cancer, diagnosis, patient's survival, predictors.

### 1. INTRODUCTION

Cervical cancer remains a significant global health concern, particularly in low- and middle-income countries where access to comprehensive treatment options is often limited [1]. Cervical cancer is the fourth most common cancer among women worldwide, and the leading cause of cancer death among women in Africa [2]. The predictors of patient survival after a diagnosis of cervical cancer vary from country to country [3]. However, some of the most common factors include: stage of cancer at diagnosis: The earlier the cancer is detected, the better the chances of survival [4]. In general, the 5-year survival rate for localized cervical cancer is 92%, while the 5-year survival rate for distant metastatic cancer is only 17%. Age is also a factor to survival where younger patients tend to have better survival rates than older patients. Socioeconomic status where women with lower socioeconomic status tend to have worse survival rates for cervical cancer [5]. Comorbidities where women with other chronic health conditions, such as HIV/AIDS, diabetes, or heart disease, tend to have worse survival rates for cervical cancer. Access to care where women who have difficulty accessing care, such as those who live in rural areas or who do not have health insurance, tend to have worse survival rates for cervical cancer.

The type of treatment received can have a significant impact on survival. For example, women who receive surgery and radiation therapy tend to have better survival rates than women who only receive

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## APPENDIX VI: PLAGIARISM REPORT

### MODELLING SURVIVAL TIME OF CERVICAL CANCER PATIENTS IN MOI TEACHING AND REFERRAL HOSPITAL, KENYA

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## APPENDIX VI: R CODES

```

library(tidyverse)
library(readxl)
library(survival)
library(survminer)
dataset <- read_excel("dataset.xlsx", sheet = 'sheet1')
##generalize: create a function to get the frequencies and percentages
cat_fun <- function(data, var) {
  data %>%
    group_by({{ var }}) %>%
    summarise(Frequency = n()) %>%
    mutate(percent = Frequency/sum(Frequency) * 100,
           first_col = {{ var }}) %>%
    relocate(first_col) %>%
    rename('Categories' = {{ var }})
}
cat_fun(dataset, Age_Bracket) %>%
  rbind(cat_fun(dataset, MaritalStatus)) %>%
  rbind(cat_fun(dataset, MaritalStatus)) %>%
  rbind(cat_fun(dataset, InsuranceCover)) %>%
  rbind(cat_fun(dataset, EmploymentStatus)) %>%
  rbind(cat_fun(dataset, Menopause)) %>%
  rbind(cat_fun(dataset, Contraceptives1)) %>%
  rbind(cat_fun(dataset, FamilyHistory)) %>%
  rbind(cat_fun(dataset, SmokingStatus)) %>%
  print(n = 24)
#####clinical characteristics
cat_fun(dataset, Comorbidity) %>%
  rbind(cat_fun(dataset, HIV_Status)) %>%
  rbind(cat_fun(dataset, HPVinfectins)) %>%
  rbind(cat_fun(dataset, CancerGrade)) %>%
  rbind(cat_fun(dataset, StagingoftheDisease)) %>%
  rbind(cat_fun(dataset, TreatmentPlan)) %>%
  print(n = 20)

###survival probabilities
dataset2 %>%
  group_by(Age_Bracket, Event) %>%
  summarise(n = n()) %>%
  spread(Event, n) %>%
  rowwise() %>%
  mutate(no.patients = sum(`0`,`1`))
#####Survival analysis
surv_fit_sex <- survfit(Surv(Time_Stay, Event) ~ Age_Bracket, data = dataset)
survminer::ggsurvplot(
  surv_fit_sex,
  data = dataset,
  conf.int = FALSE, # do not show confidence interval of KM estimates

```

```

surv.scale = "percent", # present probabilities in the y axis in %
xlab = "Time to stay",
ylab = "Survival Probability",
pval = T,                # print p-value of Log-rank test
pval.coord = c(180,.91), # print p-value at these plot coordinates
risk.table = T,          # print the risk table at bottom
legend.title = "Age",    # legend characteristics
legend.labs = c("20-34", "35-49", "50-64", "65-70"),
font.legend = 10,
palette = "Dark2",       # specify color palette
surv.median.line = "hv",
ggtheme = theme_light() # simplify plot background
)
###survival by marital status
surv_fit_sex <- survfit(Surv(Time_Stay, Event) ~ MaritalStatus, data = dataset)
survminer::ggsurvplot(
  surv_fit_sex,
  data = dataset,
  conf.int = FALSE, # do not show confidence interval of KM estimates
  surv.scale = "percent", # present probabilities in the y axis in %
  xlab = "Time to stay",
  ylab = "Survival Probability",
  pval = T,          # print p-value of Log-rank test
  pval.coord = c(180,.91), # print p-value at these plot coordinates
  risk.table = T,    # print the risk table at bottom
  legend.title = "Age", # legend characteristics
  legend.labs = c("Married", "Divorced", "Single"),
  font.legend = 10,
  palette = "Dark2", # specify color palette
  surv.median.line = "hv",
  ggtheme = theme_light() # simplify plot background
)
### survival by employment status
surv_fit_sex <- survfit(Surv(Time_Stay, Event) ~ EmploymentStatus, data = dataset)
survminer::ggsurvplot(
  surv_fit_sex,
  data = dataset,
  conf.int = FALSE, # do not show confidence interval of KM estimates
  surv.scale = "percent", # present probabilities in the y axis in %
  xlab = "Time to stay",
  ylab = "Survival Probability",
  pval = T,          # print p-value of Log-rank test
  pval.coord = c(180,.91), # print p-value at these plot coordinates
  risk.table = T,    # print the risk table at bottom
  legend.title = "Age", # legend characteristics
  legend.labs = c("Employee", "Casual labourer", "Self employed", "Farmer"),
  font.legend = 10,
  palette = "Dark2", # specify color palette
  surv.median.line = "hv",
  ggtheme = theme_light() # simplify plot background
)

```

```
)  
#####COX REGRESSION  
cox_model <- survival::coxph(  
  Surv(Time_Stay, Event) ~ Age_Bracket + MaritalStatus + CancerGrade +  
  FamilyHistory,  
  data = dataset  
)  
#printing the model fitted  
cox_model |>  
  broom::tidy() |>  
  pander::pander(caption = "Cox regression table")
```