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Socio-Demographic determinants of survival from cervical cancer at the Komfo Anokye Teaching Hospital Kumasi, Ghana

By

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KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI, GHANA

SOCIO-DEMOGRAPHIC DETERMINANTS OF SURVIVAL FROM CERVICAL CANCER AT THE KOMFO ANOKYE TEACHING HOSPITAL KUMASI, GHANA

By

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A thesis submitted to the department of population, family and reproductive health, College of Health Sciences, School of Public Health, in partial fulfilment of the requirements for the degree of master in public health in population, Family and Reproductive Health.

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DECLARATION

I hereby declare that except for references to other people's work which have been duly acknowledged, this piece of work is my own composition and neither in whole nor in part has this work been presented for award of a degree in this university or elsewhere.

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DEDICATION

This piece of work is dedicated to God Almighty who made it possible for me to further my education, to my mother Nnomo Felicite, my sweet wife Mbarga Bridget and my brother Betala Jean Francois for their unceasing support and encouragements.

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ACRONYMS

ABC:	ABTINENCE, BE FAITHFUL, USE CONDOM
AIDS:	ACQUIRED IMMUNE DEFFICIENCY SYNDROME
CC:	CERVICAL CANCER
CHRPE:	COMMITTEE ON HUMAN RESEARCH, PUBLICATIONS AND ETHICS
CI:	CONFIDENCE INTERVAL
CIN:	CERVICAL INTRA EPITHELIAL NEOPLASIA
CIS:	CANCER IN SITU
DNA:	DEOXYRIBONUCLEIC ACID
FIGO:	FEDERATION INTERNATIONALE DE GAENECOLOGIE OBSTETRIQUE
HIV:	HUMAN IMMUNODEFICIENCY VIRUS
HPV:	HUMAN PAPILLOMA VIRUS
HR:	HAZARD RATIO
hr-HPV:	HIGH RISK HUMAN PAPILLOMA VIRUS
IARC:	INTERNAIONAL AGENCY FOR RESEARCH ON CANCER
KATH:	KOMFO ANOKYE TEACHING HOSPITAL
KNUST:	KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY
MR:	MORTALITY RATE
MS:	MICROSOFT
OR:	ODD RATIO
Pap :	PAPANICOLAOU SMEAR
P-VALUE:	STATISTICAL PROBABILITY VALUE
32P:	RADIO ACTIVE PHOSPHORUS 32
SE:	STANDARD ERROR
SIL:	SQUAMOUS EPITHELIAL LESION
SR:	SURVIVAL RATE
VIA:	VISION INSPECTION ARRAY
VILI:	VISUAL INSPECTION WITH LUGOL'S IODINE
VLPs:	VIRUS LIKE PARTCLES
WHO:	WORLD HEALTH ORGANISATION
Z-VALUE:	TEST STATISTIC FOR Z-TEST

ABSTRACT

Background

Cervical cancer is the fourth most common cancer among women worldwide. In 2012, an estimated 528000 new cases were reported with the largest burden occurring in less developed countries (around 85%). It accounts for almost 12% of all cancers in females and remains the most common cancer in women in Central and Eastern Africa. In Ghana, approximately 3,000 women are diagnosed annually with cervical cancer with at least 2,000 of them dying from the disease per year. Socio-demographic risks such as education, income, marital status and co-morbidity, seem to significantly contribute to the survival of patients with cervical cancer disease. It is believed that the most vulnerable population affected with cervical cancer is women with low socio-demographic status. However, it is unclear how these factors interact to affect screening, diagnosis and survival in Ghana. This research therefore aimed at assessing the contribution of socio-demographic characteristics such as age, marital status, parity, religion, occupation, education, income, residence (urban and rural), co-morbidity, life style, stage at diagnosis and treatment type on the survival of patients with cervical cancer over a five year period. A retrospective cohort design was employed of all cervical cancer patients who fulfilled the criteria for inclusion, by retrieval of all such data from the folders of the cancer directorate of the KATH. From all such folders variables such as age, marital status, parity, religion, occupation, education, income, residence (urban and rural), co-morbidity, life style, stage at diagnosis and treatment type were extracted using an excel format data set over a five-year period (2004 to 2008). Over the study period, trends in outcomes of health status measures available in patients' records were reviewed and data extracted for analysis based on the socio-demographic variables.

A database was created in MS Access and bio-data of the patients extracted were double-entered and the data were then exported to STATA version 12.0 for analysis. Survival analysis was performed using the Kaplan-Meier method to determine the mean survival time (within the five years period) for patients with cervical cancer. The log-rank method was used to compare the accumulated survival curves between the different socio-demographic variables. The Cox proportional risks multivariate model was used (Hazard ratio) to verify the independent effect of the study variables that present statistical significance in the log-rank test and to also calculate the Cox regression power.

A total of 949 cervical cancer patients' records were reviewed. However, 923 (97.3%) cervical cancer patients' data were used for the analysis. Patients with no records of the initial date of diagnosis were excluded from the analysis as well as those without certain socio-demographic variables such as age, marital status and occupation.

Stage at diagnosis of the disease was associated with survival (outcome) of the patients with cervical cancer (chi=62.60; p=0.00). Nearly half of patients (49.1%) were diagnosed at Stage III of the cervical cancer, 25.1% of them died, 23.8% were alive and 0.2% was lost to follow-up during five year period. The survival at Stage III was estimated to be 48.87%. Majority of the cervical cancer patients (63.5%) underwent radiotherapy while few (4.0%) had both chemotherapy and radiotherapy. However, 23.1% of the patients' treatments statuses were unspecified of which 7.3% of them died, 15.3% were alive and 0.5% censored. Of those patients who received chemotherapy (4.0%), 1.3% of them died while 0.1 % was still alive the end of the analysis. Treatment type was associated with the survival of the patients with cervical cancer (p=0.00).Socio-demographic characteristics such as age, marital status, religion, parity and life style were not associated with survival of cervical cancer patients.

However, patients occupation significantly improve their survival over the period (p=0.00). Patients with co-morbidity (diabetes and hypertension) were 22.5%, of which 11.8% died while 10.6% survived. Co-morbidity was significantly associated with the survival of cervical cancer patients over the period (chi=13.86; p=0.00).The overall rate of mortality for all patients with cervical cancer was 26.46% (CI=23.93–29.26) while the overall survival rate was estimated at SR=41.27% (CI=40.90-42.13).

Conclusion

Socio-demographic characteristics and other patient factors such as stage at diagnosis, treatment, occupation, and co-morbidity were significantly associated with the survival of cervical cancer patients over the five year period. However certain socio-demographic factors such as age, marital status, religion, parity and life style were not significantly associated with survival of the patients' with cervical cancer at KATH.

CHAPTER 1: INTRODUCTION

1.1 Background

Gynaecological cancers have been perpetual public health challenge worldwide. Cancer of the cervix is one the most common cancer among females; it is ranked fourth among cancers in women (Ferlay et al., 2015). It is estimated that 528,000 new cases were reported globally in 2012, with the largest burden occurring in less industrialised countries (around 85% of the global prevalence); and most patients presenting in late stages of the cancer (Rogo et al., 1990). The main challenge in less developed countries is the absence of accurate population and health statistics. This is making it difficult to reliably estimate with exactitude the actual burden of cervical cancer, with relative frequencies obtained from hospitals. Cancer of the cervix is accounting for 12% of all cancers in women. The regions with highest risk of cervical cancer with ASRs (Age Specific Rates) over 30 per 100,000 women include: Eastern Africa (42.7%), Melanesia (33.3%), Southern Africa (31.5%) and Central Africa respectively (Torre et al., 2015).

Worldwide death due to cervical cancer was estimated at 266,000 with almost 87% of death occurring in less developed countries. Mortality varies 18 folds between the different regions the world, with rates ranging less than 2 per 100,000 in West Asia, to 22.2 in the middle of Africa and finally 27.6 in Eastern Africa (Ganesan et al., 2015). In Sub-Saharan Africa, 34.8 new cases of cervical cancer are diagnosed per 100,000 women annually, and 22.5 per 100,000 women die from the disease. These figures compared with 6.6 new cases and2.5 per 100,000 deaths among women, respectively in North America (Assi et al., 2013) show the disparity between the developed and the underdeveloped countries. Cervical cancer remains the most common cancer among women in the Middle and Eastern Africa (Ferlay et al., 2015).

In Ghana, 8.57 women million who are currently above 15 years of age are at risk of developing cervical cancer. While approximately 3,000 women are diagnosed annually with cervical cancer, at least 2,000 of them die from the disease (Broutet, 2013). World Health Organisation (WHO) predicts that by 2025, there will be over 5,000 new cases of cervical cancer annually in Ghana with at least 3,361 of the victims die (Kloku, 2015). Cancer of the cervix is preventable if discovered at a very early stage by screening tools (Dsouza et al., 2013) If the cancer of the cervix is discovered earlier in a patient, she can be handled with an appropriate treatment without difficulty, but it becomes more difficult to manage at an advanced stage (Sawant and Shegokar, 2014). The World Health Survey has indicated very low uptake of cervical cancer screening in rural and urban areas with respective rates estimated at 2.2% and 3.2% (Singh, 2012).

There is also an observed widening inequality in cancer survival rates globally between the rich and the least deprived groups for 19 out of 33 cancer types showing an increasing gap (Rachet et al., 2010). Despite these alarming statistics shown above, the prevention of cervical cancer however in Ghana is not a priority compared to HIV/AIDS, malaria, tuberculosis and breast cancer (Frempong et al., 2014). Although, the Human Papilloma Virus (HPV) vaccine has been licensed for use in Ghana, it is only limited to a few health facilities in the country. This response to the prevention of cervical pre-cancer has already many challenges with its implementation (Castellsague et al., 2007).

1.2 Problem Statement

Annually, Sub-Saharan Africa records high incidence and mortality of cervical cancer per 100,000 women. These incidences and deaths can be attributed to the lack of access to effective screening and services that facilitate early detection and treatment (Sivaram et al.,

2014). Moreover, in Ghana, there is no cervical cancer screening policy or opportunistic screening programs available for women in reproductive age although an estimated 24.3 per 100,000 incidences and 12.4 per100, 000 crude death rates occur annually. The possible underlying factors for this excess mortality are high prevalence of HPV 16 or 18 (Adanu, 2002) and lack of frequent screening leading to advanced disease at diagnosis and underuse of recommended treatment. KATH is a tertiary referral hospital situated in Kumasi, Ghana. The hospital catchment area extends beyond the Ashanti Region, Brong-Ahafo, and the three Northern Regions, as well as some areas of the Western and Central Regions. The catchment population is estimated to be about 10 million people hence providing an ideal environment for study research. Socio-demographic determinants such as education, income, marital status and co-morbidity seem to significantly contribute to survival from cervical cancer disease (Singh et al., 2003). How these factors influence the survival of patients with cervical cancer in Ghana has not been well documented or lacking. Other factors including drinking and smoking (life style), parity, education, diet, physical inactivity, sexual behaviour and use of oral contraceptives are known to impact the progression, from persistent HPV infection to cervical pre-cancer. Therefore assessing the contribution of socio-demographic determinants on the survival of cervical cancer patients is important in understanding the underlying causes of the disease (Merletti et al., 2011). This research attempts to assess the impact of socio-demographic characteristics on the survival of cervical cancer patients, and attempting to elucidate the underlying causes of cervical cancer in Ghana.

1.3 Rationale of the study

It is believed that the most vulnerable population affected with cervical cancer is women with low socio-demographic status (Singh, 2012). However, how these factors interact to influence cervical screening uptake, diagnosis, treatment and survival of cervical cancer

patients is largely unknown. Diagnosis, treatment, and management of cervical cancer are critical for patient's survival as well as patient's factors (life style). A dynamic problem-oriented record can provide a data base for health surveillance and record for subsequent evaluations. The patient's medical records could provide an even wider functional data base for preventive medicine, health education and research into types of patients affected with cervical cancer at KATH. There is also a huge gap in published literature concerning cervical cancer patient's survival in Ghana and probably no documented evidence of cervical cancer survival at KATH. However, to adequately inform policy direction as well as establish the trend of survival of cervical cancer patients presenting at the KATH, collating and analyzing patients' records would help improve managements. This study therefore sought to review and analyze the medical records of patients with cervical cancer to examine their socio-demographic characteristics, stage at diagnosis and treatment type have on their survival for a five year period. The outcome of this study would present up to date associated factors for survival trends which would inform cervical cancer patients' management at KATH and therefore inform policy direction in Ghana.

1.4 Conceptual framework

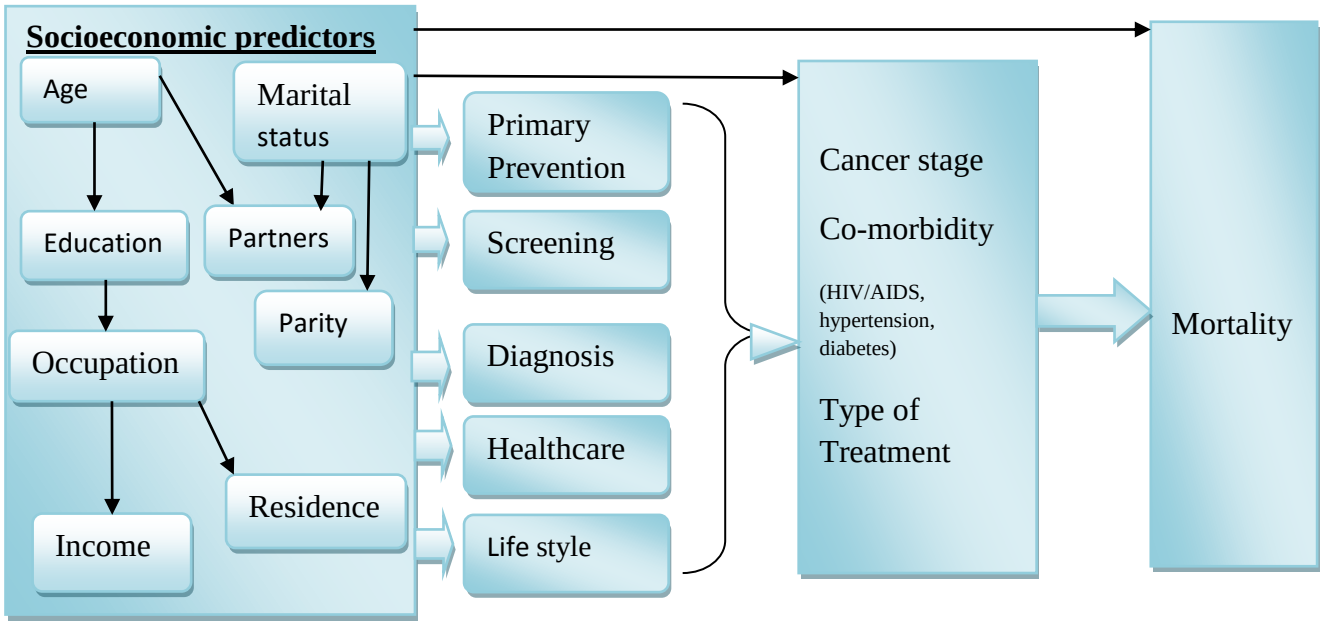


Figure 1: Conceptual Framework showing Socio-economic predictors on the survival of patients with cervical cancer
(*Author's own construct, 2014)*

The figure depicts the causal relationship between socio-demographic factors, cancer prevention, screening, diagnosis, healthcare, lifestyle, cancer stage, co-morbidity and treatment on the survival of cervical cancer patient

1.5 Research questions

This research sought to answer the following questions:

1. How do socio-demographic factors (age, education, occupation, income, marital status, parity, residence) influence on the survival of patients with cervical cancer?
2. How do stage at diagnosis and treatment influence the survival of patients with cervical cancer
3. What is the impact of co-morbidity (Diabetes, HIV/AIDS, and Hypertension) on the survival of patients with cervical cancer?
4. How do patients' factors (alcoholism and smoking of cigarette) influence the survival rate of patients with cervical cancer?
5. What is the mortality rate among patients diagnosed with cervical cancer at KATH?

1.6 Study Objective

The main aim of this study was to determine the relationship between socio-demographic factors on five years survival trends of patients with cervical cancer at KATH.

1.6.1 Specific Objectives

1. To examine the influence of socio-demographic characteristics (e.g. age, marital status, parity, occupation, religion, residence) on the survival of cervical cancer patients.
2. To assess the impact of the stage at diagnosis and treatment on the survival of cervical cancer patients.
3. To examine the impact of co-morbidity (Diabetes, HIV/AIDS, Hypertension) on the survival of patients with cervical cancer.
4. To examine patients' lifestyle factors such as alcoholism and smoking of cigarette influence on the survival of patients with cervical cancer
5. To determine the rate of mortality and its influence on survival of cervical cancer patients over five year period.

Chapter 2: LITERATURE REVIEW

2.1 Cervical Cancer

Cancer is defined as a disease in which the body cells grow out of control and adopt a physiological abnormal behaviour (Saslow et al., 2012). The type of cancer that begins or has an onset in the cervix is known as cervical cancer, though it may spread to the rest of body later by metastasis. Cervical cancer is predominantly caused by the Human Papilloma Virus (HPV). This virus is transmitted sexually and it affects both men and women while it grows without symptoms (asymptomatically). When the infection is not controlled and treated, it persists and the risk of dysplasia as well as further progression to cervical cancer increases (Kuhn et al., 2010). Several studies have established that Human Papilloma Virus (HPV) strains 16 and 18 were identified in 70% of all cervical cancer cases worldwide (Anorlu, 2008).

2.2 Aetiology

2.2.1 Human Papilloma Virus

Human Papilloma Virus (HPV) infections are the most widespread genital infections in the world. They are transmitted by sexual intercourse and develop asymptomatically (Parkin and Bray, 2006). Some women are (known or unknown to them) actual importunate carriers of these viral infections and they are at risk for progression to the pre-cancer stage, cancer in uteri and also, to a low degree, vulva, vaginal and anal cancers (Trottier and Franco, 2006). The main factor in development is the capacity of the Human Papilloma Virus to elude the immune system and create an unrelenting infection. HPV invade the epithelial tissues of the skin and the mucosa of the genitals. More than one hundred strains on HPV have been discovered and eighteen types are well thought out to be connected to cervical cancer, while fifteen types are considered to be of high risk and

three are thought to be moderately infectious. HPV 16 and 18 are predominantly oncogenic worldwide, and account for over 70% of all invasive cervical cancer cases worldwide (Munoz et al., 2003). The pre-cancerous stages and invasive cancer are caused by the high risk type of HPV (hr-HPV). The hr-HPV types have been isolated in up to 99.7% of all cases of cervical carcinomas (Franco et al., 1999). Most women (80%) often contract the HPV infection at a point in their life (Munoz et al., 2003). The transforming and immortalization of cells in cervical cancer are caused by the protein products of the early Human Papilloma Virus genes 6 and 7 (E6 and E7), but in general the virus does not usually produce these protein products. More often there is an interaction between the central molecule in the control of the cell cycle and the viral proteins E6 and E7. The proteins of Human Papilloma Virus E6 prevent the p53 mediated DNA repair and the caspase-mediated cell death response by binding and stirring up the p53 degradation, this therefore enhances the progression of cancerous (tumour) cells. This process is estimated to be the most important event the carcinogenesis associated with Human Papilloma Virus(Scheffner et al., 1990).

2.2.2 Pathophysiology

The uterine cervix or the cervix is the lower part of the uterus. It is connecting the body of the uterus to the vagina. The closest part to the body of the uterus is known as the endocervix. The exocervix is the part of the uterus next to the vagina also called ectocervix. The glandular cells cover the endocervix while squamous cells cover exocervix. The glandular cells and the squamous cells join together and form the transformation zone. It is established that most cervical cancer start in the transformational zone.

The growth of malignant cells in the cervix result into cervical cancer, these malignant cells progressively grow from pre-cancerous cells to become cancerous cells. The precancerous cells are also known as cervical intraepithelial neoplasia (CIN), dysplasia and squamous intraepithelial lesion (SIL) (Schiffman et al., 2007). The two main types of cancers are the squamous cells carcinoma and adenocarcinoma. The squamous cells carcinomas represent about 80% to 90% of cervical cancers. They develop in the squamous cells that cover the exocervix. Most of the rest of cervical cancers are adenocarcinomas. However adenocarcinomas seem to have increased in the last 20 to 30 years. The adenocarcinomas develop from the endocervix in the mucus producing glandular cells. Some cervical cancers which are less commonly encountered portray the characteristics of both squamous cell carcinomas and adenocarcinomas. They are called mixed carcinomas or adenosquamous carcinomas (Creasman et al., 2006).

The process of finding out the extent of the spread of cervical cancer is called staging. The Royal College of Pathologists classified the different stages of cervical cancer after diagnosis. This College of Pathologists studied the characteristics of histopathology to classify the various stages of cervical cancer. To determine the size of a tumour they use information exams and diagnostic tests, which will determine the depth of the tumour in the tissue within and around the cervix, as well as the metastasis (spread to the lymph nodes or distant organs). This process is meaningful considering the fact that the stage of the sickness at diagnosis is the key to choosing the appropriate treatment. The stages are arranged with clinical advice or with epidemiological advice by assigning Romans numerals (I to IV) to the various stages. Some stages have been divided into sub-stages indicated by letters and numbers (Pecorelli et al., 2009).

FIGO staging classification for cervical cancer

Stage 0: Pre-invasive carcinoma also known as carcinoma in situ (CIS). It is part of the intraepithelial neoplasia grade 3 (CIN). The cancerous cells at this stage are exclusively located on the surface of the cervix in the layer of cells lining the cervix. At this point the cells do not invade the inner cervical tissues.

Stage I: The cervical carcinoma is confined to the uterus; extension to uterine corpus is disregarded (no growth out of the uterus). Stage I can further be divided into sub-stages namely stage IA and stage IB in regard to the size and extend of the tumour cells. The cancerous cell mass invasion is not greater than three millimetres in depth and seven millimetres or less in horizontal spread in stage IA. However, with stage IB, lesions are clinically visible (four millimetres) and they are confined to the cervix.

Stage II: The cancer has not spread to the parametria (tissues next to the cervix), it may spread to the upper of the vagina, but it has not grown to the nearby lymph nodes and distant organs. At this level (stage II) the tumour may invade beyond the uterus but not to the pelvic wall or lower third of the vagina. Stage II is equally further divided into Stage IIA and Stage IIB without or with parametria invasion.

Stage III: The tumour extends to the lower part of the vagina wall and/or involves the pelvis. The tumour at this stage can cause hydronephrosis or non-functioning kidney. The cancer may also block the ureters without spreading to the nearby lymph nodes or distant sites. This stage is further divided into two that is: Stage IIIA with the tumour involving the lower third of the vagina without extension to the pelvic wall; Stage IIIB where the tumour extends to the pelvic wall and/or causing hydronephrosis.

Stage IV: This stage is the most advanced stage of the cancer. This stage is further divided into Stage IVA, where the tumour invades the pelvic walls and/or extend beyond the pelvis; Stage IVB including metastasis to distant organs.

2.2.3 Risk factors

The current understanding is that Human Papilloma Virus infection initiates a series of events to cervical cancer development, and that additional somatic alteration with one or more co-factors are necessary to support malignant transformations (Kjellberg et al., 2000). HPV apparently is not sufficient for cervical cancer development, but several possible co-factors have been proposed including exposure to smoking-related carcinogens, alcoholism, contraceptive hormones, multiparity, co-existing microbial/viral infections impaired immune system (Chen et al., 1999).

a) Smoking

Epidemiological studies on cervical cancer that adjusted for sexual risk behaviour, have established that smoking was a risk factor for women in developing cervical cancer (Chen et al., 1999). It was established that the level of substances contained in cigarette such as nicotine and its major metabolite cotinine, increase forty times and four times respectively, this was established with first biological evidence of an etiological role of smoking in cervical neoplasm; this evidence was found in the cervical mucus of women with cervical intraepithelial neoplasia (CIN), compared to serum levels; furthermore benzo-a-pyrene and specific nitrosamines in tobacco were found in the cervical mucus of women who smoke, while these products were not found in women who do not smoke (Trimble et al., 2005). It was also found that smoking was associated with damage of DNA in cervical epithelium irrespective of simultaneous HPV infection (Acladious et al., 2002). When treated with smoke condensate, the immortalized cervical cell lines have

shown to induce cancer. If there is a failure to induce carcinogenesis with smoke condensatein, HPV-infected cells from outside the transformation zone has yielded the evidence of the susceptibility of cells from the transformation zone, taking into consideration that the onset of cervical cancer from the transformation zone, the adenomatous and squamous cell epithelium has been known for many decades (Plummer et al., 2003).

b) Alcoholism

Alcohol has been established as a risk factor for endometrial cancer (Glade, 1999), nevertheless, data on the association of alcohol intake and endometrial cancer are conflicting (Williams and Horm, 1977). Where data are available for an association, low to moderate intake of alcohol is not associated with an increase risk, rather higher intake of alcohol suggest an association with endometrial cancer, results suggest that only alcohol consumption can increase the risk of endometrial cancer in menopausal women, whereas consumption of alcohol in low quantity is unlikely to substantially enhance the risk of endometrial cancer. Alcohol beverages are classified by the International Agency for Research on Cancer (IARC) as the first group of carcinogen (carcinogenic to humans). IARC classifies the consumption of alcoholic beverages as a precursor of cancer at various sites; 3.6% of all cancer cases and 3.5% of cancer deaths worldwide are attributable to alcohol consumption (Boffetta et al., 2006). It has been established that excessive alcohol consumption increases the death toll of cancer patients and facilitating cancer recurrence (Allen et al., 2009). The alcoholic women may be at a higher risk for progression from HPV infections to malignant lesions for life-style related reasons, such as promiscuity and early initiation to sexual intercourse (Group, 1995). Alcoholic women are likely to have smoked more than any other women, consequently women who smoke

have a significant risk increase of cervical cancer than those who do not smoke even when adjusting for HPV infections (Kjellberg et al., 2000)

c) Oral contraceptives

Several studies (epidemiological) have almost homogeneously revealed a significant association between cervical neoplasia and long term (generally varying from 4 to 5 years) oral contraceptive use (Moodley, 2004). The epidemiological correlation between long-term oral contraceptive use and cervical neoplasia was established and oral contraceptives use became broadly acknowledged as a risk factor for cervical cancer in the mid-1980s, when a number of studies were able to control for sexual risk behaviour (Bosch, 2015). An analysis of 24 epidemiologic studies established that the high risk of cervical cancer among women who used oral contraceptives for more than five years declined when they stopped using oral contraceptives regardless of how long they had used these contraceptives before stopping (Appleby et al., 2007). A report by IARC (International Agency for Research on cancer) in 2002 found that, data from eight studies were combined to assess the association between oral contraceptives use and cervical cancer risk among women. There was about three folds an increase in risk among women who use oral contraceptives. The risk was four times higher among women who had used oral contraceptives for more than ten years or longer (Moreno et al., 2002). Apparently all cervical cancers are caused by importunate infections with HPV; however, the association with oral contraceptives may be indirect. Hormones content on oral contraceptives may probably change the susceptibility of cervical cells to HPV infection, affecting the ability of the cells to naturally clear the infection causing the changes that will progress to cancer (Humans et al., 2007)

d) Multiparity

High parity has been associated with cervical cancer in situ (CIS), also women who have had three or more full term pregnancies have an increased risk of developing cervical cancer (Skegg, 2002). A pooled analysis by IARC showed that the odd ratio (OR) for cervical cancer in women who have had seven or more full term pregnancies was four folds higher than that in nulliparous women, even the risk increased linearly with an increasing number of pregnancies (Bosch, 2015). However, the increase in estrogen and progesterone levels induced by pregnancy may alter the immune response to HPV and influence the risk of persistent progression of the cancer (Nobbenhuis et al., 2002). Numerous mechanisms have been recommended to explain the increase risk for precursor lesions or cervical cancer in relation to pregnancy and child birth such as increase in the hormonal levels and impaired immune system (Appleby et al., 2007) It has been shown that the transformation zone of the cervix remains on the ecto-cervix for a longer time in multiparous women facilitating the direct exposure to HPV infections (Autier et al., 1996). There was found an increase risk in relation to childbirths and not to the number of pregnancies indicating that the biological explanation is related to delivery and not really to pregnancy while women who had not/ never given birth according to pregnancy (abortion/ectopic pregnancy) had no increased risk of developing cancer in situ (Jensen et al., 2013). The damage of local tissues during vaginal delivery and oxidative cellular stress may damage the DNA in cervical tissues and cells giving way to HPV integration mechanisms (Williams et al., 2012).

e) Sexual life and infections

First sexual intercourse at a very early age, many sexual partners, or many sexual partners of the spouse are aimed to be at risk of entertaining an HPV infection (Smart et al., 2004). It has been found that previous chlamydial infections correlate with the increase risk of cervical cancer (Munoz et al., 2003). Chlamydia trachomatis is a bacterium that infects

the reproductive system and it is the most common sexually transmitted bacterial infection. It has been found to have an influence on cervical intraepithelial neoplasia grade 2. It has an independent co-factor that facilitates the development of cervical neoplasia. Chlamydial infection does not directly cause cervical cancer, but it is believed to aid its development at early stages (cervical carcinogenesis) (Smith et al., 2002).

f) Impaired immune system

Women, who present an impaired immune defence such as those with human immunodeficiency virus (HIV) and/or stress, are at higher risk of cervical cancer than women with a sound immune system (Goodkin et al., 1993). It is suggested that HPV is more persistent in women with HIV, higher levels of HPV are usually detected in HIV positive women coupled with multiple HPV infections. The incidence rate of cervical cancer is nine times higher in HIV positive women. Women who are treated with Immune-suppressing drugs following a transplant are more likely to develop cervical cancer; cervical intra neoplasia may progress into invasive cancer more rapidly than is usual in natural progressive history of cervical cancer (de Jong et al., 2005).

g) **HPV infection**

The HPV viral infection is transmitted through sexual intercourse, and it is the infection mainly responsible for cervical cancer. More than 100 types of HPV viruses have been identified and 40 of these types affect the uro-genital tract. The HPv viral infection is asymptomatic making it difficult to be identified for HPV testing and check up (Bathula et al., 2015). Virtually 99.7% cervical cancers are caused by unrelenting infection with a high risk type of HPV (hr-HPV). Approximately 15types of hr-HPV or oncogenic HPV have been identified with HPV-16 and HPV-18 being responsible for about 70% of all cervical cancers (Frumovitz, 2014). Infection by a type of HPV is not a protection for a second or more types. Among patients infected with mucosal HPV, approximately 5% to

30% get infected with more than one type of virus simultaneously (Bathula et al., 2015). Although the infection is spread commonly by sexual intercourse, it can also be spread by skin contact with an area of the body infected by HPV (Winer et al., 2003). It estimated that more than half of all sexually active people are infected with one or more HPV types in their life time. However, most of the HPV infections do not lead to cervical cancer because the development of cervical cancer requires a persistent hr-HPV infection (Parkin and Bray, 2006). It is indicated that most of the infections by HPV are transient and up to 90% resolve within a period of 2 to 5 years. In young women diagnosed with HPV infection, it last for an average period of 8 to 13 months (Moscicki et al., 1998). It is established that aging is a common factor for persistent infection with HPV. The rate of persistent hr-HPV infection for women older than 55 years is 50%, compared with 20% in women younger than 25 years of age. Though long term infection is necessary for the development of cervical cancer, a wide majority of women with persistent high risk infection will not develop cervical cancer (Hariri et al.).

h) Multiple partners

A woman who has many sexual partners puts her at high risk of acquiring the HPV infection which is dominant in men. Generally, the risk of a woman to develop cervical cancer depends on her husband's (partners') sexual behaviour. Men are more promiscuous in their reproductive age than women and men are often simple carriers of HPV viruses. They can easily transmit the virus from one person to another or from one partner to another without getting infected themselves. Recently the risk of cervical cancer is carried equally by the two genders due to a new developed risky sexual behaviour. Both sexes equally experiment and adopt new sexual behaviours, which increases the risk of female partners to develop cervical cancer (Castellsagué et al., 2002).

2.2.4 Management and treatment of cervical cancer

Various medical fields or disciplines are required in approaching the treatment and management of cervical cancer hence it is known as multidisciplinary approach. Medical oncologists, gynaecologic oncologists, radiation oncologists may all be needed. Cancer patients often have multifaceted needs that may not be addressed by one specialist. The multidisciplinary team would ensure an equitable approach in planning and managing the disease. The treatment of cervical cancer depends therefore on the stage of the disease. More often surgery will be the treatment of choice for early invasive cervical cancer, while radiotherapy or combined therapy (radiation and chemotherapy) are the contemporary standard of care. Patients treated with chemotherapy or receive palliation of symptoms with radiation therapy, are considered to have the disseminated character of the cancer (Classe et al., 2006). Other different factors can affect the treatment decision such as the location of the cancer within the cervix, the type of cancer (squamous cell or adenocarcinoma), age, the physical condition of the patient and the will of the patient to preserve fertility.

Cervical cancer at **Stage 0** is often considered as CIS (carcinoma in situ) because cancer cells in CIS are located at the surface of the layer of the cervix. The treatment options include cryosurgery, cold knife conisation, loop electro-excision procedure (LEEP/LEEZ), and laser surgery. Adenocarcinoma in situ will require hysterectomy, but a cone biopsy can be applied to women who want to bear children.

Stage I treatment also depends on preserving of fertility by the woman. Treatment with repeated cone biopsy or a radical trachelectomy (cervix and upper vaginal removal) may be preferred if the cancer includes lymphovascular invasion. Radical Hysterectomy may

be applied. If the woman does not want to preserve fertility, radical hysterectomy with removal of pelvis lymph nodes can be applied, brachytherapy or external beam radiation therapy to the pelvis.

Stage II requires surgery, radiation or radiation with chemotherapy (concurrent chemo-radiation). Note that the above options of treatments can also be applied to stage IB. The standard treatment is often a radical hysterectomy with the removal of lymph nodes in the pelvis and/or para-aortic lymph nodes. Radical trachelectomy may be recommended if the patient wants to maintain fertility. A different option can be suggested using both external beam radiation therapy, and concurrent chemoradiation. It has to be noted that Stage IB and stage IIA can be treated with chemotherapy given with radiation therapy (both external beam and bradytherapy), while the chemotherapy may be cisplatin or cisplatin plus fluorouracil. Radical hysterectomy with removal of pelvic lymph nodes, the surgery might be followed by radiation therapy, which often is given with chemotherapy.

Stages IIB, III and IVA require radiation therapy and concurrent chemotherapy. The chemotherapy here may include cisplatin or cisplatin plus fluorouracil (5-FU). The radiation is including both the external radiation and brachytherapy. It is always important to conduct a check up at this level with surgery or an imaging study (MRI,PET/CT). The appearance of the lymph nodes after the imaging study may show over sized lymph nodes. The lymph nodes can be biopsied to confirm any cancer spread.

Stage IVB will always show the spread of the cancer out of the pelvis to other parts of the body. Stage IVB is not usually curable. The treatment options often include radiotherapy to the symptoms of the metastasis to areas near the cervix or distant organs (bones and lungs). Chemotherapy is also recommended (cispatin or carboplastin along with

paclitaxel and gemcitabine). Bevacizumab (Avastin) may also be added (Etter et al., 2012)

2.2.5 Prevention of cervical cancer.

a) Primary prevention

Primary prevention is a way to reduce infection spread. For example the use of condom and the ABC concept (Abstinence, Be faithful, use Condom) used in Uganda are ways that can help in reducing the incidence of hr-HPV (Parikh, 2007)

b) Secondary prevention

Cervical cytology can help in identifying precancerous changes of the cervix which are recognized as cervical intraepithelial neoplasia. Occurrence of abnormal cells in the cervix is a possible presentation of cervical cancer. Screening the population is shown to reduce the incidence of cervical cancer in the world as well as cutting down the proportion of women with advanced disease (Peto et al., 2004). HPV test, VIA, VILI, colposcopy and cytology (Pap smear) are different techniques used in screening programmes for detection of CIN lesions and it precursors in cervical smears. Screening is identified to be the major preventive method for women in their procreative age and even those who are older. The test for HPV as a screening stool for cervical intraepithelial neoplasia has been evaluated during the recent years. The HPV testing or colpocospic diagnosis with inspection of the cervix is performed in some locations lacking resources for cytologic (Pap smear) screening (Appleby et al., 2007). Visual inspections with acetic acid (VIA) have been often implemented together with visual inspection with Lugol's iodine (VILI) (Wright et al., 2005)

c) Prophylactic vaccines

A significant proportion of HPV infections are attributed to four sub-types of the virus, 6, 11, 16 and 18. HPV16 and 18 cause about 70% of cervical cancer cases in the world. HPV (6 and 11) are responsible for genital warts (Wiley et al., 2002).Two HPV vaccines have been developed and they are in use in many countries: Cervarix which is a bivalent exposure to HPV (Kash et al., 2015). The mode of action of these vaccines is the use of virus-like particles that consist of L1 capsid proteins of individual HPV types in order to prevent hr-HPV 16 and 18 that are responsible for inducing precancerous lesions and cancer of the cervix (De Vuyst et al., 2009). The above vaccines against hr-HPV 16 and 18 certainly will decrease the risk of invasive cervical cancer if women shall receive them during adolescence and preferably before the first sexual intercourse. This in turn will provide some immunity against the oncogenic HPV improving its efficiency further; however vaccination cannot completely eradicate cervical cancer knowing that about 18Hr HPV types are known presently (Villa, 2007).

2.2.6 Cervical cancer treatment/management

Current and future treatment of cervical cancer is multi-dimensional including surgery, radiotherapy, chemotherapy, and pharmaceuticals directed towards tumour markers.

2.2.6.1 Surgery

Surgery will preserve the functions of the ovaries and prevent early menopause. Surgery will enable the accurate assessment of the pelvic lymph nodes; it is preferred in young women provided that there are no contraindications. The post-surgery outcome is associated with a number of factors such as the size of the primary tumour, the depth of the stromal invasion (Landoni et al., 1997).

Cryosurgery is a method of surgery that uses extreme cold to destroy abnormal diseased tissues. In cervical cancer treatment uses a metal probe cooled with nitrogen liquid placed on the cervix killing abnormal cells by freezing them (Soutter et al., 1997).

Laser surgery consists of using a focused laser beam directed through the vagina to burn off by vaporizing abnormal cells or to remove a piece of tissue for further study (Roberts et al., 1996). The conization surgery consists of removing a cone-shape tissue from the cervix using a surgical or Laser knife (cold knife biopsy) or using the LEEP/LEETZ which consists of thin wire electrically heated.

Hysterectomy is the surgical removal of the uterus that is the body of the uterus and the cervix, excluding the parametria and uterosacral ligaments which are the structures next to the uterus. The lymph nodes located in the vagina and the pelvis is not removed as well as the fallopian tubes and the ovaries. The hysterectomy process can be abdominal, vaginal or laparoscopic (consisting of a surgical incisions with a laparoscope through the abdomen for the removal of the uterus monitored on a screen).

Radical hysterectomy is the surgical removal of the uterus alongside with the parametria and the utero-sacral ligaments. Trachelectomy is surgical removal of the cervix, lymph nodes and the upper part of the vagina to treat cervical cancer. However the body of the uterus is conserved and an artificial opening of the cervix is created inside the uterine cavity.

Pelvic exenteration is surgical procedure aimed at a total removal of the organs similar to radical hysterectomy. The spread of the cancer in this process will require or not the

removal of the bladder, vagina, rectum, and part of the colon. Early stages of cervical cancer often require treatment with surgery and sometimes in combination with chemotherapy and radiotherapy, while later stages are always treated with radiotherapy and/or concurrent chemotherapy and radiotherapy combination. New surgical operations have been proposed in last two decades such as nerve sparing radical hysterectomy, radical trachelectomy, laparoscopic assisted radical vaginal hysterectomy, laparoscopic lumbo-aortic lymph node dissection, robot assisted laparoscopic radical hysterectomy, and laparoscopic pelvic exenteration (Kenter and Heintz, 2002).

2.2.6.2 Radiation therapy

In radiation therapy high energy x-rays or particles are used to kill the cancerous cells. External beam radiation processes the x-rays at the cancerous cells from outside the body of the patient. It is also known as EBRT (External Beam Radiation Therapy). The treatment procedure with the EBRT takes only a few minutes. The treatment is given for five days week during five to seven weeks. When the radiation therapy is combined with chemotherapy it is called concurrent chemo-radiation (Kenter and Heintz, 2002).

Brachytherapy or internal radiation consists of placing the source of radiation in or near the cancerous cells to kill them. The most used method of Brachytherapy is intracavitary whereby the source of radiation is placed in a device located in the vagina or in the cervix to kill the cancerous cells. It is often used in addition to EBRT as part of cervical cancer main treatment (Pötter et al., 2007).

2.2.6.3 Chemotherapy

Parenteral drugs (injection through vein) and oral drugs (per mouth) are given to patients with cervical cancer for systemic effects. Drugs through the blood stream can reach the various organs of the body making chemotherapy useful in stopping metastatic cells that have spread in other parts of the body. Each period chemotherapy is given to a patient constitutes a cycle and after every cycle there is period of recovery. There is parenteral ministration of cisplatin once weekly four hours before radiation therapy. The patients receive cisplatin 5-fluorouracil once a month during their radiation therapy. Most often in more advanced cases Cisplatin, Carboplatin, Paclitaxel, Topotecan and Gemcitabine are used to treat cervical cancer (Tinker et al., 2005).

Though the higher doses of Cisplatin have yielded higher response rates to treatment, advanced stages of cervical cancer have not shown a significant difference in overall survival from the disease (Cadron et al., 2005). The addition of ifosfamide to cisplatin therapy yielded also no significant difference in the survival of the patients (Omura et al., 1997) The addition of pacltaxel to cisplatin gave way to an increase response of the patients to the treatment and there was an increase in the median progression of the survival of the patients but no change in the overall survival of patients (Moore et al., 2004).

Cervical cancer stage I is micro-invasive and often treated by hysterectomy including the upper vagina. At stage IA2 of the disease the lymph nodes are also ablated. Conization can be applied for the patients who want to preserve their fertility and alternatively trachelectomy can be chosen for treatment. A radical vaginal or abdominal trachelectomy can be performed for patients with stage IB of the disease. Surgery or chemotherapy can

also be applied in patients with early tumours at stage IB and IIA, here the radiation therapy should be given externally to the pelvis or internal (brachytherapy) radiation. The risk of relapse can be reduced in patients who were treated by surgery method showing high risk features pathological examination by giving them a combined therapy (radiotherapy plus chemotherapy). For tumours of stage IB2 and IIA2 treatment, radiation therapy and cisplatin therapy can be combined with hysterectomy (in which case adjuvant radiation therapy will be required), or cisplatin therapy can be followed by hysterectomy. Advanced stages (IIB to IVA) are treated with radiation therapy in combination with chemotherapy. It is always essential to identify the spread of cancerous cells to the lymph nodes surrounding the cervix earlier for a satisfactory choice of treatment. This will help in providing prognostic information. Studies have shown that it is possible to predict the status of the regional lymph nodes through pelvic sentinel node (Sant et al., 2003).

Therapeutic vaccines

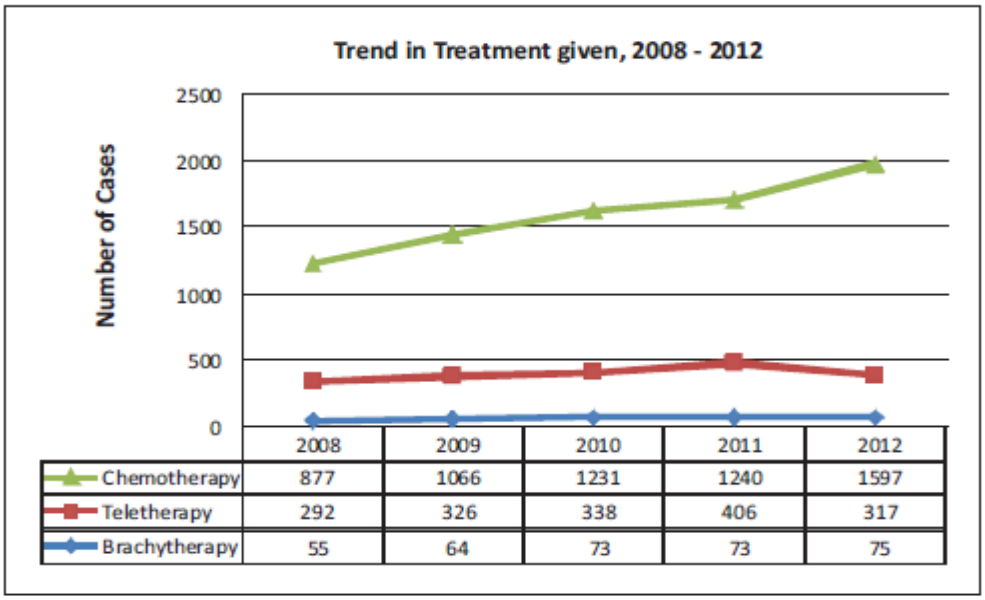
Vaccines that aim to control HPV infections through cell mediated immunity and have shown encouraging results in different clinical and preclinical trials. They include the therapeutic vaccines targeting HPV 6 and HPV 7 (Peng et al., 2004).

Figure 2.Treatment options of cancer at KATH

Treatment Options for Cancer Conditions

The figure below reflects the different treatment options available at the Oncology Directorate.

Figure 61: Trend in Treatment given, 2008-2012.



	2008	2009	2010	2011	2012
Chemotherapy	877	1066	1231	1240	1597
Teletherapy	292	326	338	406	317
Brachytherapy	55	64	73	73	75

The trend indicates marked increases in chemotherapy as well as brachytherapy services from 2008 to 2012. Only cervical cases are put on brachytherapy treatment which recorded 73 in 2011 and 75 in 2012. Only the teletherapy section recorded a decrease of 21.9% in 2012.

(KATH annual report for 2012)

2.3 Global Epidemiology of cervical cancer

2.3.1 Burden and Mortality

a) Burden

The cancer of the cervix is ranked fourth among all cancers encountered in women. Cancer of the cervix is also the seventh most frequent among all cancers encountered in humans. It is estimated that 528,000 new cases were recorded in 2012 worldwide. Around 85% of cervical cancer of the world population burden occurs in regions that are less developed. The disease burden accounts for almost 12% of all cancers in females globally. With Age Standardized rates, the estimation is that high risk regions record over 30 per 100,000. These regions include Central Africa (30.6), Southern Africa (31.5), Melanesia (33.3), and Eastern Africa

(42.7); this pattern is low in Western Asia (4.4) and Australia/New Zealand (5.5) (Ferlay et al., 2015).

b) Mortality

The global estimation number of deaths from cervical cancer in 2012 was 266,000, accounting for 7.5% of all female cancer deaths. Approximately nine out of ten cervical cancer deaths occur in less developed countries for a percentage of 87%. Mortality contrasts 18- fold between different regions of the world, with rates ranging from 27.6 in Eastern Africa, 22.2 in Central Africa, Melanesia 20.6 to 2 per 100,000 in Western Asia, Western Europe and Australia/New Zealand (Ferlay et al., 2015).

2.3.2 Epidemiology

Cancer of the cervix has become a challenge for public health both in developed and developing countries, though it can be prevented with early screening, detection and curable with appropriate and effective treatment in very early stages (Samantha Garbers and Chiasson, 2004). Approximately 528,000 new cases are diagnosed globally every year. The worldwide burden of cervical cancer is the highest in developing countries, and the new cases observed can be 18 times greater in poor countries compared to their developed counterparts (Torre et al., 2015). The available age standardized rates in Africa are the highest in the world. Sub-Saharan African rates vary per 100,000 women from 19.9 in Ibadan (Nigeria) through 35.7 in Bamako (Mali), 41,7 in Kyadondo (Uganda) (Parkin et al., 1999).

Among developing regions, Africa has the largest burden of cervical cancer. Africa also records the highest incidence and mortality from cervical cancer annually (Ferlay et al., 2010). The main precursor of cervical cancer that is HPV infection is globally observed in different levels. Surveys have shown13-fold variation among women who are sexually active.

This infection prevalence varies per 100,000 women from 2.0% in Hanoi (Vietnam), 3.0% in Barcelona (Spain), 14.8% in Colombia, 17.7 in Argentina, and 26.3 in Nigeria (Matos et al., 2003). The Sub-Saharan Africa records 34.8 new cases per 100,000 women diagnosed with cervical cancer annually and 22.5 per 100,000 of these cases die of the disease (Faith-Anthony et al.). Despite the evidence of high rate of incidence and burden in Africa, the situation has been under-reported in many countries making the disease a factor that is unknown in terms of data available, though rural residence was associated with higher mortality rates (Palacio-Mejía et al., 2003). Cancer of the cervix is the largest cause of life lost to cancer in developing countries (Jemal et al., 2010). The incidence and the mortality rates of cervical cancer have substantially declined in industrialized countries following the introduction of the various screening programmes, while these programmes are almost non-existent in developing counties, hence having an effect on women survival (Parkin et al., 1999)

2.4 Cervical Cancer in Ghana

In Ghana, cervical cancer is ranking primary source of cancer in women and the first most widespread female cancer between the ages 15 to 44 (Wiredu and Armah, 2006a). There is an estimated number of 3,052 new cases every year representing a crude incidence rate of 24.3 per 100,000 (Adanu, 2002).

The crude mortality rate is also estimated at 12.4 per 100,000 while 1,556 deaths are recorded annually. Cervical cancer is the foremost reason of female cancer deaths in Ghana and it is the second leading cause of death of cancer in women aged15 to 44 years in Ghana. These rates are swiftly growing in contrast to the declining incidence, burden and mortality in the developed countries where effective screening programmes are implemented (Blumenthal

et al., 2005).The World Health Organization (WHO) projects 5,000 new cases of cervical cancer annually in Ghana by 2025 with a rise of death toll of 3,361 (Williams and Amoateng, 2012). Though cervical cancer is preventable by screening, it is effective when the cancer is detected at a very early stage and can therefore be treated, compared to challenges observed when treating an advanced stage cancer. Countless cases of cancer of cervix seem to occur following the early development of a precursor premalignant condition (Cervical intraepithelial neoplasis), consequently the screening for this condition has become a major strategy for attempting to reduce mortality. The Pap (Papanicolaou) smear test and the VIA (Visual Inspection Array) with acetic acid are currently available in private and public hospitals in the country (William et al., 2014).

2.5 Screening

The Pap smear test as well as the VIA (visual inspection with acetic acid) are the current screening tools available in some hospitals along with private health facilities in Ghana, non-governmental organizations conducted screening proceedings especially in various rural areas in the country (Bosu, 2013). Beside, two vaccines (the bivalent and quadrivalent HPV vaccines) are available for use in the country (Gardasil) (HPV Recombinant, Quadrivalent) were both registered in June 2013. However, the rates of screening in the two settlements (urban and rural areas) of Ghana are particularly low with 3.2% and 2.2% of sexually active women screened respectively every year (Quentin et al., 2011). Previously recognized obstacles to the early exposure of cervical cancer in Ghana, were a low level of knowledge concerning cervical cancer aetiology, pap smear test and cervical cancer screening (Abotchie and Shokar, 2009).

HPV DNA Screening

This screening test aims to identify hr-HPV (16, 18, 31, 33, 35, 45, 51, 52, 56, 59 and 68) type of viruses associated the majority of invasive cervical neoplasia cases. To test human papiloma virus (HPV) the investigators rely on exclusive techniques of molecular biology employing the probes of nucleic acid. Various tests for hr-HPV that use nucleic acid probes were made commercially available since the late 1980s, however the various tests were cumbersome. They involved probes of nucleic acid labelled with (32P) radio-active phosphorus (Poljak et al., 2016). It was observed that the largely polygamous groups in Ghana recorded high prevalence of hr-HPV. Sub-Saharan African counties (not exempting Ghana) female populations who have had their primary sexual intercourse before the age of 18 years, and illiteracy are strongly associated with HPV infections (Attoh et al., 2010). In Western Africa 4.3% of the women population are believed to carry hr-HPV 16 or 18 infections (Thomas et al., 2004). The consequence of this is the extension of the reach of formal education and the design of adolescent–specific health educational programmes for cervical cancer in Ghana (Domfeh et al., 2008).

Liquid based cytology:

This method uses similar collection techniques as the Pap smear with a tool that accumulates cells (cancerous) from the transformational area of the cervix. The device is placed in a vial containing haemolytic and mucolytic agents enabling a better detection of squamous abnormalities (Kitchener et al., 2009).

Visual screening which involves the straight examination of the cervix excluding the taking of samples. The technique uses acetic acid (VIA) which temporarily turns white the precancerous cells for easy identification; or it will involve solution of iodine based which is

used to turn the precancerous tissues or cells into yellow to identify them from the normal cells coloured brown. However, this technique seems to be cost effective in low resource settings (Arbyn et al., 2008).

2.6 Determinants of survival of cervical cancer

It is rather difficult to understand the mechanisms of socio-economic status and the differences in the survival from cervical cancer of the patients, knowing that the outcomes of cervical cancer are influenced by various mechanisms and determinants of the social conditions of cancer patients (Singh, 2012). How socio-demographic status affects an intermediate prognostic determinant is quite often very complex, this is because all the differences in cervical cancer survival between affluent and deprived classes cannot be explained by a single prognostic determinant. There are three groups of possible determinants of association between socio-demographic status and possible determinants of cervical cancer survival: factors associated with patients' particulars, diagnosis and treatment (Brandful et al., 2014). According to some researches, the health care system organization plays an important role in the survival of patients with cancer, but it is not easy to investigate this aspect at a micro-ecological or an individual level (Vercelli et al., 2006).

A primary hypothesis could be based on the fact that deprivation can influence the timely access of the patients to hospital/health care; this could be due to the delay of the patient in quest of medical advice after the early symptoms coupled with the delay observed between the first medical diagnosis and the treatment onset. It has to be considered that the access to health care is often multifaceted notion which can be described as "a timely use of personal health services in order to obtain the best possible health outcomes". The easy access to health care can be negatively affected by various aspects such as: the organization of the

health care system, the resources allocation, waiting lists, difficulties in transportation and a deficient communication process with health care personnel (Dejardin et al., 2014).

Among other factors, the long periods required for chemotherapy or radio-therapy which often can cause the wrong application of the various standard protocols of treatment; the regularity and punctuality associated with medical personnel for frequent prevention or therapy procedures; also important is the frequency of the use of health care centres and facilities in case of emergency. In this logic it is necessary to notice that the procedure of diagnosis and therapy are influenced by the access to health facilities; the immediate consequence of this being the cancer stage at diagnosis. The cancer stage at diagnosis also establishes the choice of the type of treatment (curative or palliative) (Garner, 2003).

2.6.1 Education

The various inequalities observed in mortality rates related to the level of education have been recognized and documented from corner to corner in a variety of countries worldwide. The difference in the style of life and health, behaviours are the main dynamic observed to be able to play a major role in treating many diseases. The quality of treatment is expected to be dependent on personal income when health services are in the open market with a measure of affordability. This option is not observed in egalitarian welfare states like European countries that have developed a system where public health care systems aspire to suggest the same health care access and of high quality to every citizen without considering the socioeconomic status of the patients as well as their location. This is concurrent to the disease diagnosis and care where private solutions are rare. In regard to the description above, it is unexpected that inequalities in education confers a similar mortality among patients of the two settlements, in other words the mortality rates will be different in two systems where patients are taken in charge on one hand and patients are not taken in charge in another hand (Fiva et al., 2014).

The level of education can reveal health knowledge and literacy of a patient or the ability of someone to deal with his/her state of disease (Schillinger et al., 2004). Approximately 1,556 new cervical cancer deaths occur in Ghana every year, and the level of education can be attributed to the life style (behaviour), the conditions of health (morbidity), as well as the access that a patient has to knowledge and resources directly or indirectly related to the survival from cervical cancer. Several influences related to the survival of patients have been listed as follows: screening, stage at diagnosis, health care seeking ability, treatments and time lines assumed for a particular type of cancer (Hussain et al., 2008). It has been established that the level of education below high school education is a risk factor for patients in their early stages of cancer (Robert et al., 2004).

2.6.2 Income

The cancer survival and the income of the patient have been demonstrated to be associated in several studies due to several factors among which the stage at presentation, access to health care services, diet, environmental exposures, and differentials levels of tobacco and alcohol consumption. Cancers have been shown to have worse survival in patients with lower income. People with better or sufficient income usually have better access to care and obtain that of better quality than the people considered to have lesser or poorer income (Siegel et al., 2012). Booth *et al* analyzed the effects of median household income on survival for a number of cancers in Canada and found a substantial gradient in survival between the highest and the lowest income quintiles for all cancers (Booth et al., 2010). Lower neighbourhood socioeconomic status was equally associated significantly with poorer cervical cancer survival, both individual and general survival, the costs associated with cancer vary with various factors; the cervical cancer patients would usually incur a variety of expenses related

to their medical bills as a result of their treatment, the cost associated with travelling to hospital, increase in household bills due to treatment with substantial fall in the income. The decreased in income combined with extra costs of living can have extensive consequences for cervical cancer patients and their families (Chu et al., 2011).

2.6.3 Marital Status

The patients who are not married and diagnosed with cancer present a considerably higher risk of being diagnosed at an advanced stage of the disease, or they can be undertreated and die more probably of the disease. It has been observed that all causes of cancer mortality rates are often higher amongst unmarried patients than the married patients (Kravdal and Syse, 2011). Women who are not married are more likely to suffer from violent death, and consequently they have a considerable excess of mortality emanating from disorders associated with life style. Marriage henceforth is considered to be very important especially when conferring social support to the patient on detecting cancer, treating and surviving from cervical cancer (Patel et al., 2010). Married couples possibly will have a favourable or better access to healthcare and psychological support from their spouses to seek medical attention and to follow a curative treatment when necessary. Patients who are married would likely comply to the various treatments that are prescribed, improving their survival status. Unmarried patients usually display distress, anxiety and depression than their married counterparts after cancer diagnosis, given that a partner will be psychologically supported by the social settings when she undergoes emotional stress and burden. It has been suggested that patients who are not married are likely to change their life style to reduce stress and depression by smoking and/or using alcohol, constituting additional factors that may increase the poor prognosis of the disease and poor survival (Aizer et al., 2013).

It has been shown that marital status influences the prognosis following a cancer diagnosis; this can probably be due to a general poor overall health at the diagnosis time in unmarried patients compared to their married counterparts. Generally, married couples may have better chance to carry out a satisfactory course therapy in comparison to their counterparts who are not married; this may show importance in the difference of treatment regimen received and compliance to such treatment regimen. It is more probable also to married individuals to presenting their tumours at a more early stage of the disease than those who are not married (Kravdal and Syse, 2011).

2.6.4 Co-morbidity (Hypertension, diabetes, HIV/AIDS)

Co-morbidity can be defined as a supplementary clinical entity that has existed or that might occur during the clinical course of a patient who has an index disease under study (Valderas et al., 2009). Several observational studies have established that patients who are found with an additional ailment different from the predominant one present with poorer survival than patients who have no co-morbidity associated with the disease (Irisa et al., 2012). Additional ailments have been proven to affect cancer survival through influence on factors such as screening, treatment regimen and adherence (Geraci et al., 2005). The fact that the difference in morphology, histology, differentiation, and proliferation status are associated with co-morbidity is acceptable, for example cancer risks are higher in patients with obesity; in patients with diabetes and consequently leading to insulin resistance; and in patients with inherited (for example acquired from HIV/AIDS), or induced by drug treatments like treatments with immune-suppression steroids (Sciacca et al., 2013). Co-morbid conditions (infections) in some instances have been proven to be precursors of cervical cancer. Precancerous lesions caused by sexually transmitted diseases such as genital Herpes can lead to cervical cancer. It was established that co-morbid infections generated by human

papilloma viruses that initiate cervical warts can damage the cells lining the cervix and lead to unregulated growth of genetically modified (abnormal) cells (Geraci et al., 2005).

2.7 Cervical Cancer Survival

The survival from cervical cancer is determined by the length of time a patient lives after the first positive diagnosis by screening. The percentage of women who survive at least five years after the disease has been diagnosed for the first time, constitute the five-year survival. It is proven that the stage of cancer establishes the patients' survival after diagnosis. The key indicator for monitoring progress of cancer around the world, that is population-based cancer survival data are not widely available in countries from Africa, Asia and Central America. A research conducted in twelve countries worldwide had shown that a five-year age standardized relative survival (ASRS) and observed survival were defined by the clinical extent of the disease. Cervical cancer survival was shown to be the highest in China, South Korea, Singapore, Turkey and the lowest in Uganda and Gambia. Five-year ASRS ranged between 63-79% worldwide, but it did not exceed 22% in Gambia, or 13% in Uganda (Sankaranarayanan et al., 2010).

The five-year observed survival rate for all stages is 68%. If cancer is screened and detected at an early stage, women with invasive cancer have a survival rate between 90 and 91%. Considering a five-year cervical cancer observed by stage, rates of survival (SR) range as follows: Stage I and IA SR=93%, Stage IB SR=80%, Stage IIA SR=63%, Stage IIB SR=58%, Stage IIIA SR=35%, Stage IIIB SR=32%, Stage IVA SR=16%, Stage IV SR=15% (Benedet et al., 2000).

CHAPTER 3: METHODOLOGY

3.1 INTRODUCTION

This chapter comprises: the study design and type, the study area, the study population, variables, sampling method, sample size, data collection and handling, data analysis, ethical consideration, assumptions and limitations.

3.2 Study Design and type

A retrospective cohort design involving the review of secondary data was used to aggregate data from patients' records who were diagnosed with cervical cancer at KATH (the Komfo Anokye Teaching Hospital) from 2004 to 2008. Over the study period (2004-2008), trends and outcomes of health status measures available in patients' records (folders) at the Oncology Directorate were reviewed and data extracted for analysis base on socio-demographic variables over a five-year period. The study was conducted at KATH where all the women diagnosed with cervical cancer were treated and followed up for a five-year period.

3.3 Profile of the study area

The Komfo Anokye Teaching Hospital (KATH) was established in 1955, and it became a Teaching Hospital for medical students training from KNUST (Kwame Nkrumah University of Science and Technology) in 1975. KATH is a tertiary referral hospital and has an in-patients bed capacity of 1000. KATH is situated in Kumasi, Ghana. The hospital catchment area extends beyond the Ashanti Region, Brong-Ahafo, and the three Northern Regions, as well as some areas of the Western and Central Regions. The catchment population is estimated to be about 10 million people.

3.3.2 Study Site: Oncology Directorate

The Oncology Directorate is specialized in providing comprehensive care to patients and the general public the primary, secondary and tertiary areas of prevention of cancer. Delivery of services include Medical Oncology and Radiation Oncology, Haematology, furthermore records show that, the out-patients department (OPD) recorded 8,371 new cases in 2012 (fig3). Teletherapy, chemotherapy and Brachytherapy treatments are also provided to patients. The Oncology Directorate operates a multi-disciplinary clinic that includes: Oncology-Surgery (Breast) and Oncology-ENT (Head and Neck) clinics. In 2012 a total number of 395 patients were currently being treated and followed up compared to 251 patients in the year 2011. Cancer of the cervix was the first most common cancer reported among women in the year 2012.

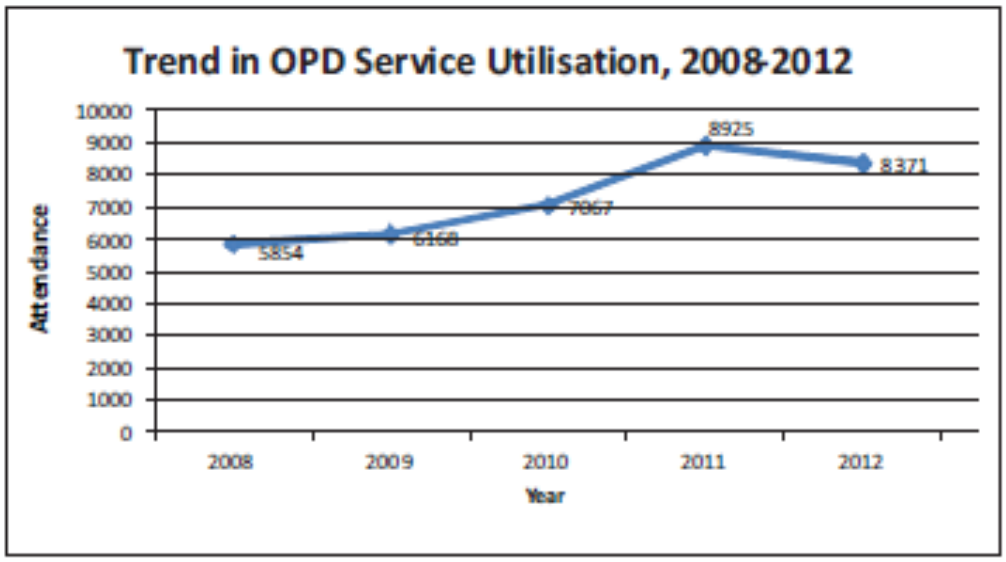
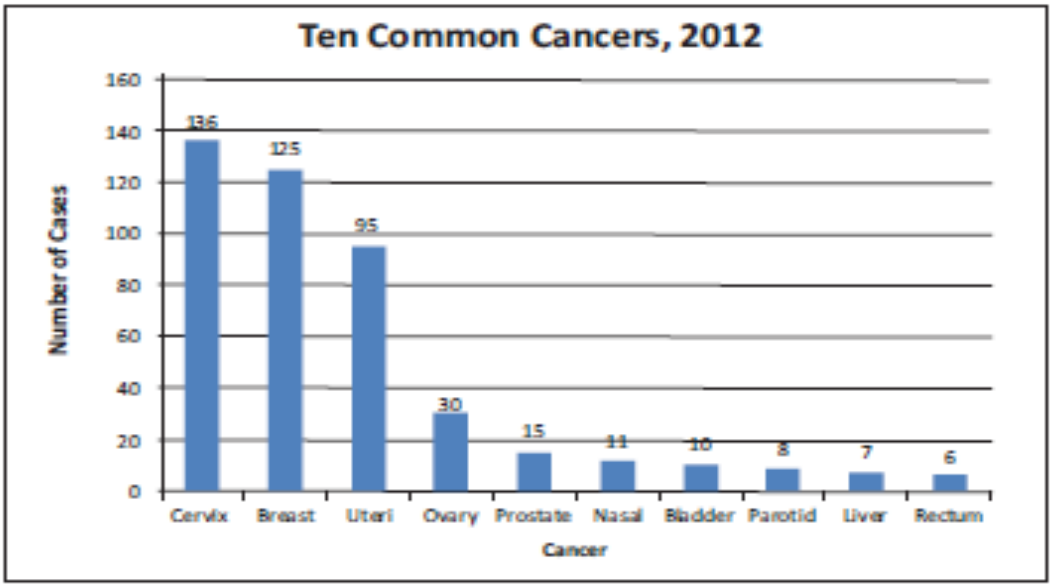


Figure3.1: Trend in OPD Service Utilization for 2008-2012



Majority of the patients reported cervix and breast cancers. Parotid, liver and rectum cancers were among the least cases of cancer reported.

Figure 3.2: Ten common cancers reported for 2012 at KATH (KATH annual report 2012).

3.4 Sample Size.

In the process of reviewing secondary data, the files of every patient with cervical cancer recorded at the Oncology Directorate from 2004 to 2008 were selected. A total number of 949 folders dating from 2004 to 2008 were retrieved from the archives and records rooms of the Oncology Directorate at KATH. 923 folders met the selection criteria for data analysis.

3.5 Sampling of secondary data.

Patients' records available were collected over the period, 2004-2008. Patients with baseline records from 2004 to 2008 were included in the study. The data were aggregated between one to five years intervals for each patient. Completed data capture sheets were checked for completeness, correctness and inconsistencies. The data collected were processed alongside the data collection exercise. A database for quantitative data was created in MS Access.The

data were collated from December 2014 to March 2015 at the Oncology Directorate/Cancer Registry of KATH.

3.6 Sampling Procedures

3.6.1 Inclusion criteria: During the period of data collection and implementation of the study, certain parameters of the patients were selected from the patients' files. To be included, patients' files must have the following details: Age, ethnicity, cancer stage, date of diagnosis, type of treatment, date of death, religion, occupation, parity, status (lost or not to follow up), co-morbidity, life style (drinking and smoking status).

3.6.2 Exclusion criteria: Patients' files excluded from the study were files with one or more missing information such as date of diagnosis, age, type of treatment, parity, occupation, cancer stage etc. Out of 949 patients' files reviewed, 923 files met the inclusion criteria.

3.7 Study variables

Clinical and socio-demographic variables such as age, marital status, parity, occupation, residence, ethnicity, etc. were extracted and analyzed. The clinical variables such as the stage at diagnosis (I, II, III, and IV), co-morbidity, treatment, etc. were included. However educational status and the level of income were never recorded in the patients' files.

3.8Data Collection Tools and Techniques

A review of historical secondary data was collected over the period, 2004-2008. The data were collected from December 2014 to March 2015 at the Oncology Directorate/Cancer Registry of KATH. The following variables, demographic characteristics, medical history, the initial stage at diagnosis, treatment history and outcomes were manually extracted for analysis. Data on survival and death of patients followed up with a minimum of five years

records were extracted for the analysis. All deaths were verified from the death registry of the Oncology Directorate at KATH and all files indicating a lost to follow up were considered to be dead individuals. The survival time was calculated in years, considering the dates at initial diagnosis.

3.9 Data Analysis

A data base was created in MS (Micro-Soft) Access. The data were double-entered in an Excel sheet and statistical analysis was conducted using STATA software version 12.0. The analysis of data was based on the proposed variables. The Kaplan-Meier method was used to perform the survival analysis, to determining a five-year period mean survival of all selected folders of cervical cancer patients. The accumulated survival curves between the different categories of study variables were compared using the log-rank method. To substantiate the effect of independence of the study variables representing a statistical significance in log-rank test, the model of Cox proportional risks multivariate (Hazard ratio) was used, as well as calculating the Cox regression power. The Ethical Clearance was issued by the Committee on Human Research, Publication and Ethics (CHRPE) at KNUST (Kwame Nkrumah University of Science and Technology) and the Komfo Anokye Teaching Hospital (KATH). Permission was obtained from the Medical Director of the Oncology Directorate/ Cancer registry and Administrator/ Medical Director of Komfo Anokye Teaching Hospital (KATH).

3.11 Training of research assistants

Four research assistants were trained for three days on how to extract the relevant data from patients' hospital records to ensure effective data collection, handling and processing.

CHAPTER 4: RESULTS

This chapter includes: the baseline survival of patients, background characteristics of patients, socio-demographic factors (age, marital status, parity, occupation, religion, education, and residence) influence on survival, survival determinants including disease stage at diagnosis and treatment, co-morbidity and survival, and mortality rates of patients with cervical cancer at KATH.

4.1 Background of the patients

Table 4.1 below shows details of the background characteristics of cervical cancer patients. 923 patients data extracted from the records, 44.2% aged between 60 – 79 years, followed by 40 – 59 years (41.9%), and 8.6% were below 40 years. Many of the patients (47.4%) were farmers, 30.3% traders, 1.8% civil/public servants while 14.2% were unemployed. Many patients (46.9%) were married, 25.0% widowed, 23.3% divorced and 3.9% single. In 2006, 18.0% were diagnosed while 36.7% in 2008 and 2009. Out of the 923 patients, 86.3% were Christians, 10.6% Muslims, and 3.1% others religions. Many of the patients were of Asante ethnic group (43.3%), Fante (3.4%), Ga (0.1%), Ewe (1.0%) and 51.2% other ethnic groups. Out of 923 patients, 632 had children of which 18.4% had almost 3 children, 51.1% between 4-6 children while 28.8% had at least 6 children.

Table 4.1: Background of cervical cancer patients

Demographic	Cervical patients N=923 n (%)
Age (years)	
<40	79 (8.6)
40–59	387 (41.9)
60–79	408 (44.2)
≥80	49 (5.3)
Occupation	
Unemployed	131 (14.2)
Civil servant	17 (1.8)
Farmer	437 (47.4)
Trader	280 (30.3)
Student	10 (1.1)
Seamstress	4 (0.4)
Other	44 (4.8)
Marital status	
Married	433 (46.9)
Single	36 (3.9)
Widowed	231 (25.0)
Divorced	215 (23.3)
Not specified	8 (0.9)
Year of diagnosis	
2004	201 (22.24)
2005	155 (17.24)
2006	197 (21.84)
2007	154 (17.14)
2008	194 (21.54)
Religion	
Christian	796 (86.3)
Muslim	98 (10.6)
Other	329 (3.1)
Parity (n=632)	
None	11 (1.7)
1-3	116 (18.4)
4-6	323 (51.1)
> 6	182 (28.8)
Ethnicity	
Asante	400 (43.3)
Fante	31 (3.4)
Ga	1 (0.1)
Ewe	19 (1.0)
Other	482 (52.2)

4.2 Survival of cervical cancer patients.

Figure 4.1 below depicts the Kaplan-Meier estimate of the baseline survival function of patients with cervical cancer. After the first two years (28 months) at diagnosis, at least 50% the patients had survived with the disease. By five years after diagnosis, nearly 40% of the patients with cervical cancer survived. The rate of survival for a five-year period is estimated to be SR= 41.27%.

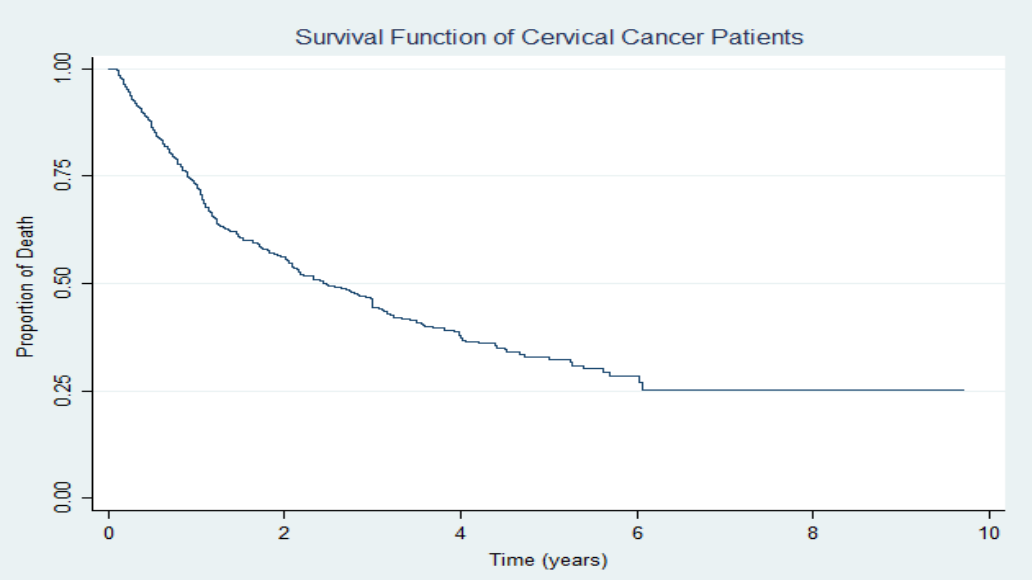


Figure4.1*: Baseline survival function of patients (Kaplan-Meier estimate)*

This figure is a five-year survival curve of patients with cervical cancer showing at least 50% survival at two years and 41.27% at five years after diagnosis.

4.3 Survival and socio-demographic characteristics

Table 4.2 below presents the influence of socio-economic characteristics of patients (age, marital status, religion, occupation and life style) on the survival of cervical cancer patients. There was no association between patients' survival and their age (p=0.96). Marital status was not associated with the survival of patients (p=0.76).There was no association between religious denomination of patients on survival (p=0.10). Parity of patients on survival was

not significant (p=0.62).However there was a significant association between the occupation of patients and their survival (p= 0.01) over the five year period.

Table 4.2: Demographic characteristics and survival of patients

Variable	*HR	*SE	z	p>z	[95%* Cl]
Age	1.01	0.004	0.05	0.96	[0.99, 1.02]
Marital status					
*Single	ref				
Married	0.96	0.110	-0.31	0.76	[0.77, 1.21]
Occupation					
Unemployed	ref				
Employed	0.69	0.096	-2.68	0.01	[0.52, 0.90]
Religion					
Other	Ref				
Christian	0.96	0.168	-0.22	0.83	[0.68, 1.35]
Parity status (n=632)					
Parity	1.01	0.02	0.50	0.62	[0.97, 1.06]

*Single, divorced or widowed *Married or Cohabiting *HR =Hazard Ratio
*SE=Standard Error *CI= Confidence Interval

Figure 4.2 below depicts Kaplan-Meier survival estimate by the religion of patients. The non-parallel plots of religion (Christian or Muslim or other put together) graphically explained the insignificant influence of religious affiliation of patients on the survival of cervical cancer patients.

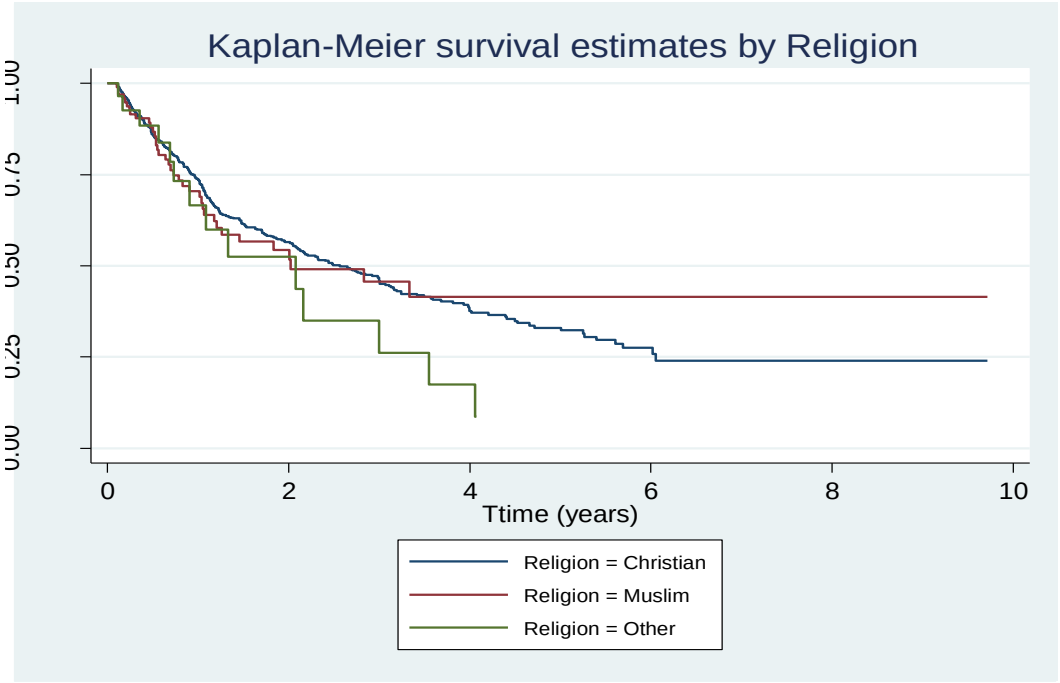


Figure 4.2: Survival by religion (Kaplan-Meier estimate)

The figure depicts Kaplan-Meier survival estimate by the religion of patients with intersections between the survival curve and the religion curves confirming no association between survival and religion

Figure 4.3 below depicts Kaplan-Meier survival estimate by the marital status of patients. The non-parallel plots of either single, divorced on one hand, and widowed or married and cohabiting graphically explained the insignificant influence of marital status on the survival of cervical cancer patients. The hazard ratio (HR) for marital status was 0.69 (0.52, 0.90).

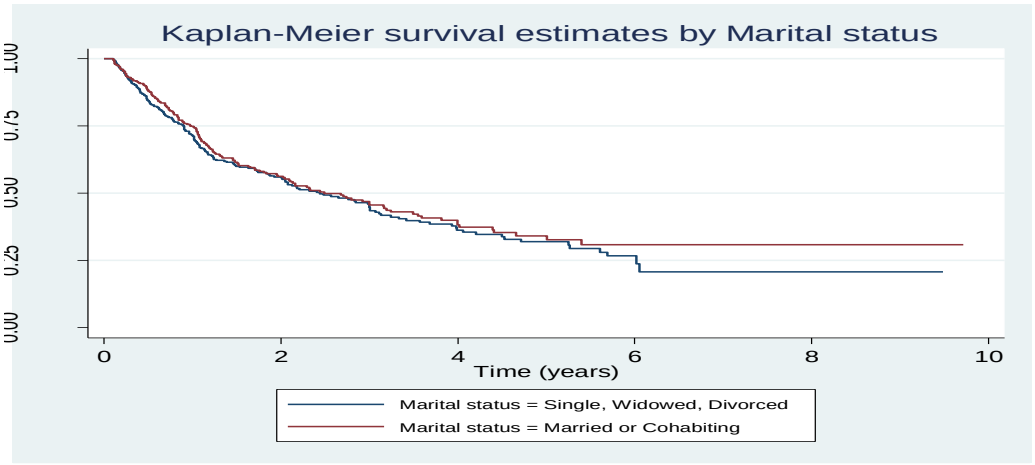


Figure 4.3: Survival by marital status (Kaplan-Meier estimate)

The figure depicts Kaplan-Meier survival estimate by marital status of patients showing no association between marital status and the patient' survival curves

Figure 4.4 below depicts Kaplan-Meier survival estimate by occupation of patients. The parallel plots of occupation (employed or unemployed) graphically explained the significant influence of occupation on the survival of cervical cancer patients. The influence of occupation on the survival of patients was statistically significant (p=0.00).The five year survival rate in respect to occupation was SR=46.34%.

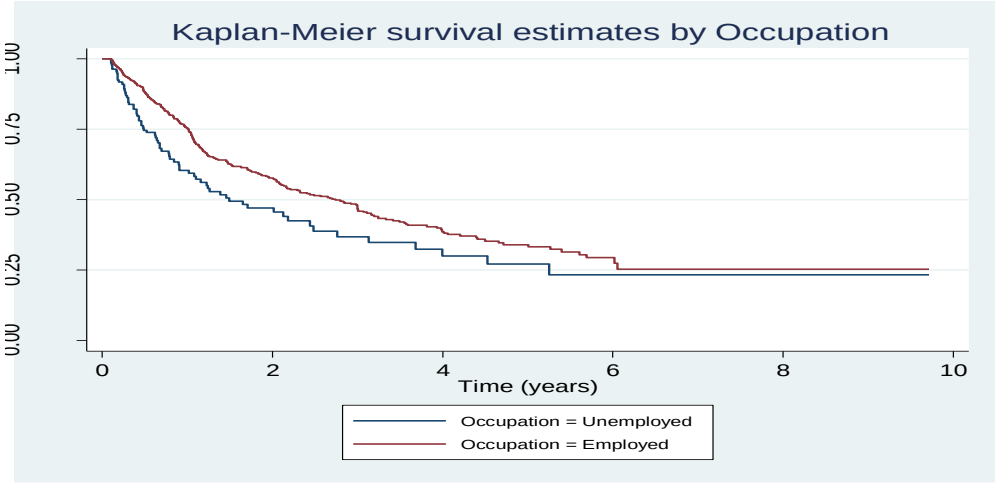


Figure 4.4: Survival by occupation (Kaplan-Meier estimate)

Figure 4.4 depicts Kaplan-Meier survival estimate showing an association between patients' survival and their occupation.

4.4 Factors affecting the survival of patients with cervical cancer

From table 4.3 below, 4.6% of the patients were diagnosed at Stage I, of which 1.0% died and 3.6% survived after five years. At Stage IIB (24.9%), 6.5% died, 18.4% survived. At Stage III (49.1%), 25.1% died, 23.8% survived and 0.2% was lost to follow-up. Patients who ever took alcohol (4.8), 2.4% survived, 1.2% survived who ever smoked cigarette (2.9%), while 10.6% with co-morbidity (22.5%) survived whereas 33.2% survived who were treated using radiotherapy (63.5%).

Table 4.3: Factors affecting the survival status of patients with cervical cancer

Variable	Status of patients during follow-up			F-test	Total
	Dead n(%)	Aliven(%)	Lost n(%)	(P-value)	n(%)
Stage					
I	9 (1.0)	33 (3.6)	0 (0.0)		42 (4.6)
IA	23 (2.5)	10 (1.1)	1 (0.1)	62.60	34 (3.7)
II	60 (6.5)	101 (10.9)	2 (2.2)	(0.00)	163 (17.7)
IIB	57 (6.2)	170 (18.4)	3 (0.3)		230 (24.9)
III	232 (25.1)	220 (23.8)	2 (0.2)		454 (49.1)
Drinking alcohol					
No	359 (38.9)	512 (55.4)	8 (0.9)	1.74	879 (95.2)
Yes	22 (2.4)	22 (2.4)	0 (0.0)	(0.42)	44 (4.8)
Smoking cigarette					
No	366 (39.6)	523 (56.7)	7 (0.8)	5.36	896 (97.1)
Yes	15 (1.6)	11 (1.2)	1 (0.1)	(0.05)	27 (2.9)
Co-morbidity					
None	272 (29.5)	436 (47.2)	7 (0.8)	13.86	715 (77.5)
Yes	109 (11.8)	98 (10.6)	1 (0.1)	(0.00)	208 (22.5)
Type of treatment					
Unknown	67 (7.3)	141 (15.3)	5 (0.5)	33.75	213 (23.1)
Chemotherapy	12 (1.3)	24 (2.6)	1 (0.1)	(0.00)	37 (4.0)
Radiotherapy	278 (30.1)	306 (33.2)	2 (0.2)		586 (63.5)
Chemo+radiotherapy	24 (2.6)	63 (6.8)	0 (0.0)		87 (9.4)

4.5 Survival and mediators using Cox Proportional Model

Table 4.4 below presents mediators' effects on the survival of patients with cervical cancer indicating two Cox Proportional models. Cancer stage diagnosed at IA and III were associated with survival of patients with in Model 1 (p=0.00) and Model 2 (p=0.05) with

hazard ratio of4.23 (1.94-9.22) and 2.93(1.50-5.71) in Model 1 and 1.98 (1.00-6.43) and 1.98(1.02-4.59) in Model 2 respectively. The presence of co-morbidity was associated with survival of patients in both Model 1 and Model 2 (p=0.00) with hazard ratio of1.45 (1.12-1.87) and 1.46 (1.12-1.89) respectively. Smoking and intake of alcohol were not associated with the survival of patients with cervical cancer in both Models 1while in Model 2 smoking of cigarette was associated (p=0.03) with patient survival. A combination of stage at diagnosis and treatment was also associated (p=0.04) with patient survival.

Table 4.4: Survival and mediators (Cox Proportional Model)

	Model1(p=0.00) (Adjustment for age)				Model2(p=0.00) Model 1 + Treatment			
Covariate	***HR**	***z**	***p>z**	**95% *CI**	***HR**	***z**	***p>z**	**95% *CI**
Co-morbidity								
No diseases	Ref.							
With other diseases	1.45	2.83	0.00	1.12-1.87	1.46	2.84	0.00	1.12-1.89
Smoking								
Non-smokers	Ref.							
Smokers	0.61	-1.83	0.07	0.36-1.04	0.55	-2.14	0.03	0.32-0.95
Drinking								
Non-drinkers	Ref.							
Drinkers	1.23	0.92	0.36	0.84-2.14	1.17	0.68	0.49	0.75-1.81
Cancer Stage (Model 1; p=0.02; Model 2; p=0.00)								
IA	4.23	3.63	0.00	1.94-9.22	2.55	1.98	0.05	1.00-6.43
II	1.73	1.54	0.12	0.86-3.51	1.54	1.17	0.24	0.74-3.19
IIB	1.30	0.71	0.48	0.64-2.62	0.72	-0.630	0.53	0.26-2.00
III	2.93	3.15	0.00	1.50-5.71	2.16	1.98	0.05	1.02-4.59
Treatment(Model2; p=0.02)								
Chemotherapy					0.81	-0.58	0.56	0.40-1.65
Radiotherapy					0.77	-0.75	0.45	0.38-1.53
Chemo+Radio					0.41	-1.67	0.09	0.15-1.16
Interaction Effect								
Stage & Treatment					1.10	2.08	0.04	1.00-1.20

**HR =Hazard Ratio *CI= Confidence Interval *z = z value *p>z = p-value ≥0.05*

This table shows Cox Proportional model analysis of patient survival with cervical cancer. In model 1, the Cox Proportional model included co-morbidity, drinking, smoking, and cancer stage at diagnosis and the covariates stratified by age group of patients (<40, 40–59, 60–79 and ≥80) years. In Model 2, the type of treatment for cervical cancer patients was included in to Model 1.

Figure 4.5and **4.6** depict graphical presentations of the proportional hazard and test models for cervical cancer stages at diagnosis. Patients diagnosed at stage I had the higher survival trend while stage IA has high risk of dying followed by patients in stage II, followed by stage IIA and then stage IIB. The survival rate according to the disease stage at diagnosis was SR=40.33%

4.5.1Survival of cervical cancer stages at diagnosis with Hazard and Test Models

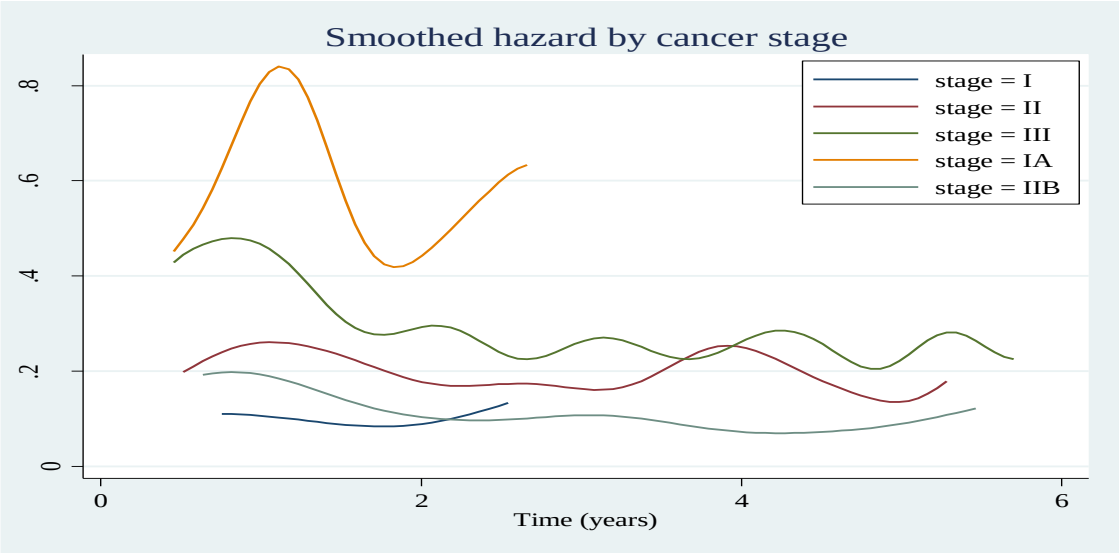


Figure 4.5: Graph or Hazard rate and cervical cancer stage

This shows the proportion and survival trends of patients diagnosed at the different stages with cervical cancer. The smooth graphs represent the different stages at diagnosis and the trend of survival over time.

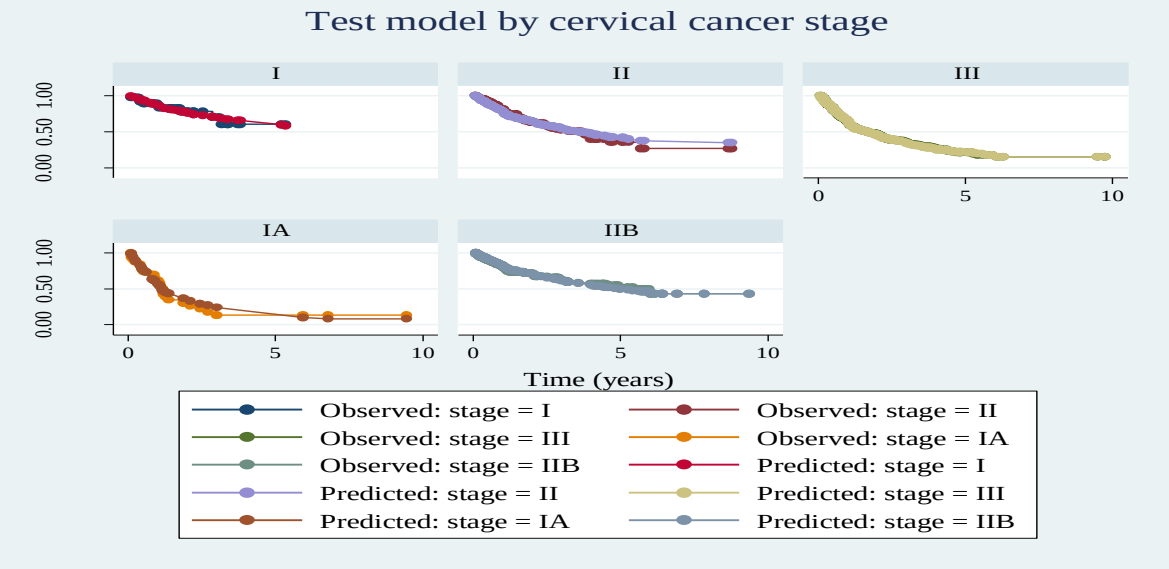


Figure 4.6: Test model by cervical cancer stage

This shows the proportion and survival trends of patients diagnosed at the different stages with cervical cancer. The hazards graphs represent the different stages at diagnosis and the trend of survival over time.

4.6 Treatment and Survival Trends

Figures 4.7and **4.8** depict graphical presentations of hazard and test models for survival trends of cervical cancer patients' treatments over time. Patients treated using radiotherapy

had higher survival trend over time while patients who had chemotherapy had low survival trend with time. Radiotherapy and chemotherapy accounted for 33.2% and2.6% period survival over five years(table 4.2). Patients who had both chemotherapy and radiotherapy had shorter survival trend over time. From figure 4.5 shows the predicted survival probability and observed survival probability for radiotherapy, chemotherapy plus radiotherapy, and unspecified treatments for the test model. The survival rate in respect to treatment was SR=34.72%.

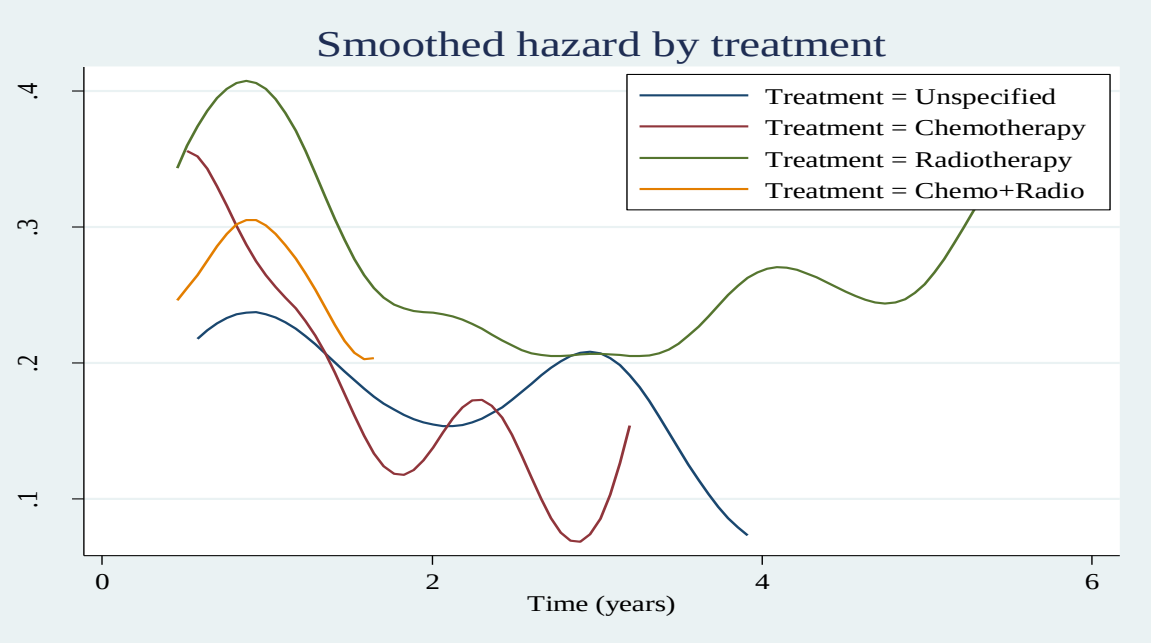


Figure 4.7: Graph of hazard rate and cervical cancer treatment

This shows the proportion and survival trends of patients treated with different using method overtime. The smooth graphs represent the different treatments types and the trend of survival over time

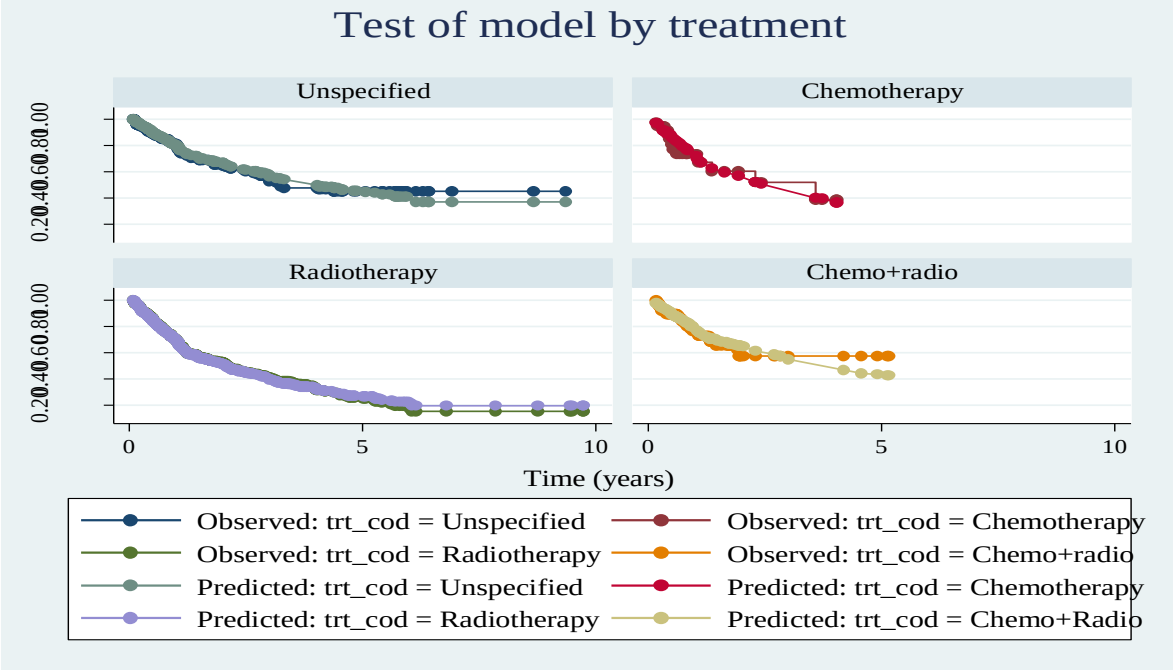


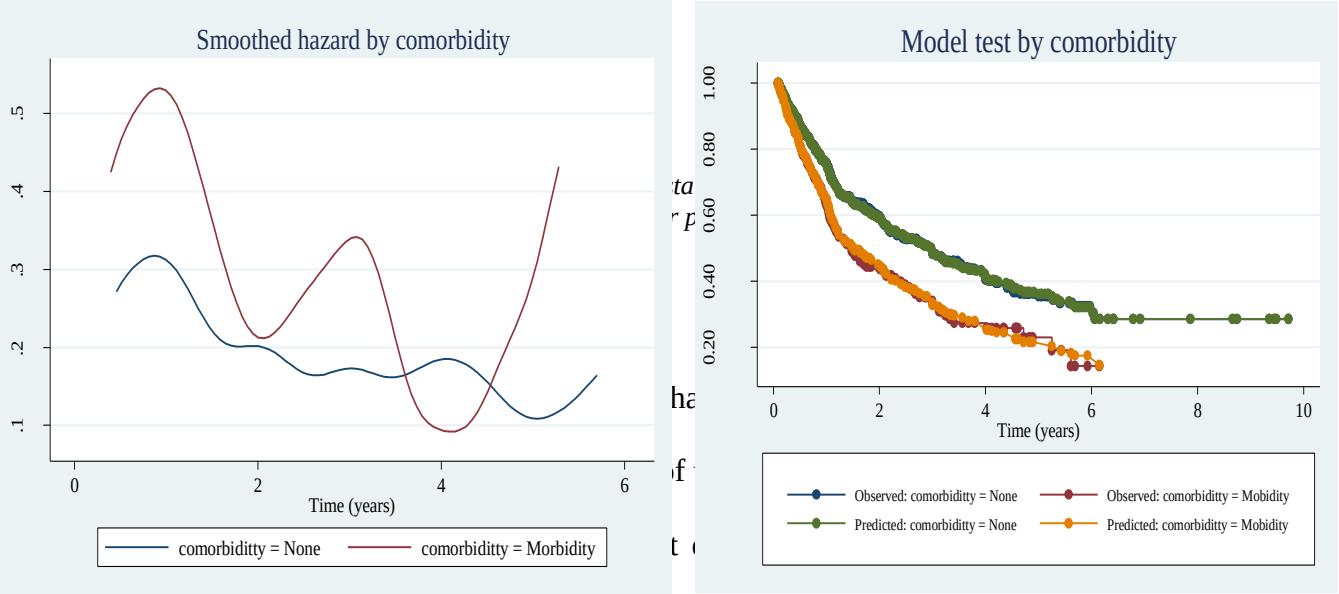
Figure 4.8: Test of model by cervical cancer treatment

This shows the proportion and survival trends of patients treated differently with cervical cancer. The hazards graphs represent the different treatment types and the trend of survival over time

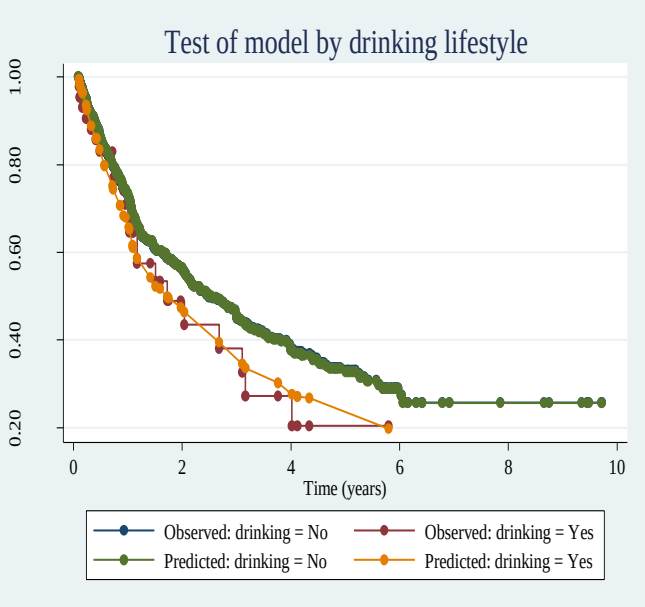
4.7 Survival and co-morbidity (Hypertension, Diabetes and HIV/AIDS)

Figure 4.11 below shows that, the risk of dying with cervical cancer with no other diseases was relatively low compared to patients with co-morbidity. Figure 4.12 shows the level of significance of co-morbidity and the survival of cervical cancer patients. Both the predicted and the observed survival probability curves are closely aligned for co-morbidity and no co-morbidity. From table 4.3; 77.5% of the patients had no record of diseases other than cervical cancer while 22.5% had other diseases (Diabetes, Hypertension and HIV/AIDS). Of the patients with no record of co-morbidity, 47.2% survived, 29.5% died and 0.8% was censored. Cervical cancer patients with co-morbidity, 11.8% died during the study period, 10.6% survived and 0.1% was censored. Co-morbidity was associated (p=0.00) with the survival of the patients. Five-year survival rate in respect to co-morbidity was SR=45.22%.

Figure 4.9: Graph of Hazard rate and co-morbidity



association between patients' survival with alcohol intake (chi=1.74; p=0.42). Drinking habit was not associated with the survival of cervical patients (Table 4.2).Of the patients who ever smoke cigarette (2.9%), 1.3% of them survived. Smoking was not associated with patients' survival (Table 4.2).The test for proportional hazard model figure shows intersection between the cigarette smoking and the survival curves, the cigarette smoking curve was not marginally closer to the observed survival probability and this displayed the smoking factor being not significant in the model.



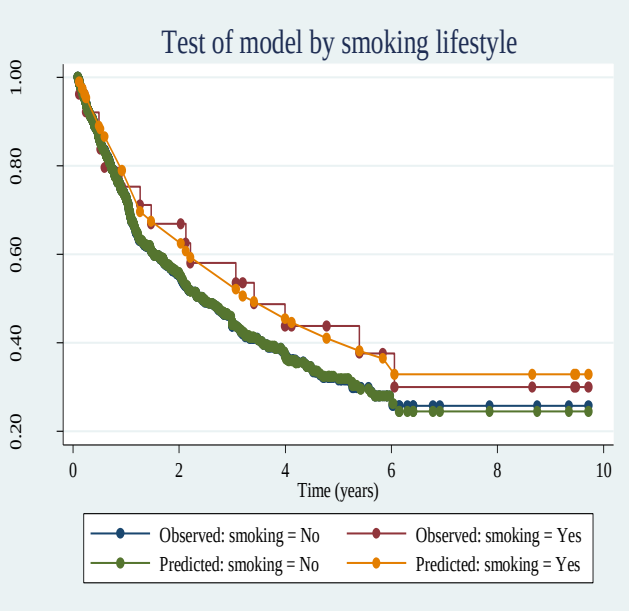


Figure 4.11: Test of model by drinking alcohol **Figure 4.12: Test of model by smoking**

The test for proportional hazard model crossed with drinking and smoking statuses curves proving that drinking and smoking factors were not significant in both models.

4.9 Mortality Rate

Mortality rates in table 4.5below were estimated as per 1000 population. The total person-time at risk of dying for the 923 cervical cancer patients was 1439.68 years with 381 failures and the rate of mortality for all cervical cancer patients was 264.64 (239.36–292.60) per 1000 person. The mortality rate was higher in aged cancer patients (≥80 years) which was 354.67 (233.54–538.65) per 1000 and lower in age group 40–59 years representing 242.84 (207.04–284.84) per 1000. Unemployed patients had higher mortality rate of 358.55 (283.67–453.19) per 1000 whilst employed patients had lower mortality rate of 249.91 (223.62–279.29) per 1000 and longer survival times (1244.45) years.

Patients with other related diseases (co-morbidity) had higher mortality rate of 373.96 (309.96–451.19) per 1000 while those with no diseases other than cervical cancer had lower mortality rate of 236.89 (210.35–266.78) per 1000 and longer survival times (1148.21) years.

In terms of disease stages, the mortality rates increased from stage I to stage IA. Patients with cancer stage I had the lowest mortality rate of 122.36 (63.67–235.17) per 1000 person followed those with stage IIB which represent 151.75 (117.06–196.74) per 1000 person. Patient with cancer stage IA had higher death rate of 442.26 (293.89–665.53) per 1000 person. Cervical cancer patients undergoing radiotherapy and chemotherapy treatment had higher mortality rate of 308.32 (274.12–346.77) per 1000 person and 280.53 (159.32–493.97) per 1000 person respectively.

Table 4.2: Mortality rate (incident rate) per 1000 cervical cancer patients

Factors	Person-time	Failure	Rate/1000	95% *CI
Cohort	1439.7	381	264.64	239.36–292.60
Age				
<40	122.97	34	276.49	197.56–386.95
40–59	621.80	151	242.84	207.04–284.84
60–79	632.88	174	274.93	236.97–318.97
≥80	62.03	22	354.67	233.54–538.65
Occupation				
Unemployed	195.23	70	358.55	283.67–453.19
Employed	1244.45	311	249.91	223.62–279.29
Co-morbidity				
No	1148.21	272	236.89	210.35–266.78
Yes	291.47	109	373.96	309.96–451.19
Cervical Cancer Stage				
I	73.55	9	122.36	63.67–235.17
IA	52.01	23	442.26	293.89–665.53
II	295.12	60	203.31	157.86–261.84
IIB	375.61	57	151.75	117.06–196.74
III	643.39	232	360.59	317.05–410.10
Treatment Type				
Unspecified	384.15	67	174.41	137.27–221.60
Chemotherapy	42.78	12	280.53	159.32–493.97
Radiotherapy	901.67	278	308.32	274.12–346.77
Chemo+Radio	111.08	24	216.06	144.82–322.35

CI= Confidence Interval

CHAPTER 5: DISCUSSION

5.0 Introduction

This chapter discusses the major findings on the influence of socio-demographic determinants on the survival of cervical cancer patients examined at KATH from 2004 to 2008. These characteristics examined include: the disease stage at diagnosis, treatment, age, marital status, parity, education, religion, occupation, lifestyle, co-morbidity and mortality.

5.1 Summary of the key findings

Many patients (44.20%) were aged between 60 and 79 years old and the survival rate according to age was SR=42.49%, however age was not associated to survival of patients.

Majority of the patients were diagnosed at stages IIB (24.9%) and III (49.1%), the survival rate in respect to disease stage was SR=40.33% as disease stage was associated to the patients' survival.

Majority of the cervical cancer patients (63.5%) at KATH were treated using radiotherapy while few were under Chemotherapy treatment. The survival rate in respect to treatment was SR=34.72%.

The cervical cancer patients with co-morbidity had high mortality (MR=39.39%) rate compared to patients without co morbidity (MR=23.68%). The survival rate in respect to co-morbidity was SR=45.22%.

The total person-time at risk of dying for the 923 cervical cancer patients was found to be 1439.68 years with 381 failures and the rate of mortality for all cervical cancer patients was MR= 26.46%.

The mortality was higher among unemployed patients (MR=35.85%). Co-morbid patients also died in larger numbers than those who reported with cervical cancer only. The mortality rate among the co-morbid patients was MR=39.39% (309.96–451.19). Patients with a

combined therapy had a lower mortality rate compared to those who underwent a single therapy owing probably to the synergetic effect of the combined treatment. The mortality rate among patients with a combined therapy was MR=21.60% (144.82–322.35).

5.2 Socio-demographic characteristics on the survival of cervical cancer patients

5.2.1 Age

It is known that women below 20 years of age are extremely rare to be diagnosed with the cancer of the cervix; the median age of diagnosis is 48 years. Cervical cancer diagnosis reveals about half proportion of patients ranging between the ages of 35 to 54 years. The diagnoses of cervical cancer among women over 65 years of age are about 20%, it is predominant with women who did not receive cancer screening since their younger age in regular bases (Ferlay et al., 2015). In this study, majority of the patients (44.2%) aged between 60 – 79 years followed by those aged between 40 – 59 years. Nearly 9.0% of the patients were below 40years. In this study, it was observed that stage at diagnosis was often in the advanced stage. This could be a plausible reason for which majority of the patients in this study were well advanced in age when they were diagnosed with the condition since many of them failed to report early with the early stage of the cancer while they were younger.

In a study conducted in England between 2007 and 2011, a five-year survival for cervical cancer was found to be highest in the younger women and decreased with increasing age. A five-year net survival for patients who were diagnosed with cervical cancer ranged from 90% in patients between 15 and 39 years old to 25% in those aged from 80 to 99 years old (Coleman et al., 2011). However in this study, the survival of cervical cancer patients with age was not significant. However, the net survival of patients in respect to age was

SR=42.39%. This may be a consequence of late screening among patients who are sexually active and in their reproductive age in the country as a great number of patients were diagnosed at the advanced stage and age, pattern that is not observed in more advanced countries.

5.2.2 Marital Status

(Waite LJ, 2003) observed that mortality rates of cancer were higher among women who were never married, than those married. This could be indicative of the importance of marriage, a social support for spouse for early screening and exposure (detection), management and survival of the disease. Women who are married could have financial support to have access to medical care and also they could have encouragement from their partners while undergoing curative therapy, and support from their spouses leading to an improvement and subsequence survival. Patients not married would likely suffer distress, depression, and anxiety after being diagnosed with cancer, and lack an intimate partner to share their emotional burden and appropriate social support. It has been established that survival of cancer patients following a positive cancer diagnosis, can be influenced by the marital status of the patient given that unmarried people generally have poor overall health compared to the married couples (Kravdal, 2001). However, in this study it was observed that marital status of the patients was not associated with the survival of cervical cancer patients. This may be probably due to the low proportion of patients who were never married (3.9%) in this study to show a difference.

5.2.3 Parity

It has been found that cervical cancer and cancer in situ had a significant association with parity (Bayo et al., 2002). Cervical cancer patients who have had three full term pregnancies

or more had a higher risk of developing cancer than those who had not given birth (Moreno et al., 2002). It was found by the IARC (International Agency for Research on Cancer) in a pooled analysis, that cervical cancer patients with seven or more full term pregnancies presented odds ratio four times higher than women who never gave birth (nulliparous women), even as there was a linear progression of the risk of getting cervical cancer with the increase number of pregnancies (Munoz et al., 2006). In a study conducted in 2006 in New York by McCarthy it was observed that, the tendency for cervical patients who were multiparous (more than 4 deliveries) to survive was relatively shorter than that of patients who had less children (Dolecek et al., 2010)In the current study it was observed that there was no association between parity and cervical cancer survival. Women with low parity have no longer survival compared to those of high parity. This may be a result of decrease in fertility rates in Ghana over the years and/or unrevealed full term pregnancies.

5.2.4 Education

The level of education may be a sign of health literacy or the ability of a person to manage a disease without assistance (Goldman and Smith, 2002). With approximately 1,556 new cervical cancer deaths occurred in Ghana every year, it has been observed that the level of education could be associated with patients' health conditions, behaviour, or access to resources and knowledge that can impact indirectly or directly on the survival from cervical cancer (Wiredu and Armah, 2006b). In a study conducted in Kenya it was observed that the level of education is one of the main contributing factors to the low survival rates recorded among cervical cancer patients in Kenya (Maranga et al., 2013). In the current study, there was no data on patients' educational status and could therefore not be analyzed to determine the influence of survival with educational status. However, educational status is generally low among Ghanaian women.

5.2.5 Religion

The cultural values and beliefs derived from religious model of disease have consequences on the perceptions related to ailment, health seeking, treatment, and health outcomes. It has been established that there was a difference among diverse ethnic groups concerning attitudes, beliefs, and values that are related to health seeking behaviours. Therefore, cervical cancer is not an exception because cultural values and beliefs are known as important determinants not only for cancer prevention and behavioural control, but also of the outcomes of psychology and behaviours following cancer diagnosis and treatment (Wiredu and Armah, 2006b). A study conducted in Lebanon supported that an important contributor to psychological outcome of coping with cancer, was perceived in an agent of support related to religious/spiritual beliefs (Daher, 2012). It was perceived that religious/spiritual beliefs acted as a principal source of support, although they seemed not to have a particular social outcome (Daher, 2012). In this present study, the Kaplan-Meier survival estimate indicated that religion (Christian, Muslim or others put together) had no significant influence on the patients' survival with cervical cancer. This may be attributed to the fact most of the study patients were Christians with a small proportions from other religions and hence the direct influence on patients' survival was not significant.

5.2.6 Occupation

There exist a close association between occupation and income. The cost associated with cervical cancer is relatively expensive beyond the reach on the average patient. There are varied costs that can be incurred ranging from medically-related expenses like treatment, cost associated with travelling to and from the hospital, increase in household bills due to special meals and support. As a consequence of decreased income and extra costs incurred, while occupation and income remained the same, this further compounded the burden of cancer

patients and their families (Taskila-Åbrandt et al., 2004). Financial considerations is vital in uptake of treatment and medication, a study conducted in Nigeria revealed that for 95 cervical cancer patients referred to undergo radiotherapy treatment, 19% of them actually underwent the process meanwhile 81% did not undergo the process for lack on financial assistance. It seemed important to note that all patients who underwent radiotherapy were classified to belong to higher social class compared to those who did not attend; also patients who underwent this radiotherapy spent approximately 30% of their annual income to ensure their treatment (Nairn and Merluzzi, 2003).

The influence of occupation of the cervical cancer patients on their survival in the present study was statistically significant as depicted by the Kaplan-Meier survival estimate by the occupation of patients. The survival rate in respect to occupation was SR=46.34%. Cervical cancer patients who were gainfully employed lived longer than those who were unemployed. The mortality rate (MR= 35.85%)was also higher among patients who were unemployed compared to those who were employed (MR=24.99%). The finding in this present study further support other studies that occupation plays a vital role in patients' access to health services and timely diagnosis, follow-up and a longer survival.

5.3 Stage at diagnosis of cervical cancer, treatment and survival of patients at KATH.

The clinical stage at which a patient is diagnosed with cervical cancer is key to the survival of the patients (Woods et al., 2006). The cervical cancer patient stage at diagnosis and the type of treatment have influence on their survival (Booth et al., 2010). In this study, it was found that the stage at diagnosis was significantly associated with patients' survival. Patients diagnosed at Stage IA and Stage III were more likely to die of the disease even following treatment compared with other stages of the disease. The risk of patients dying (44.2%) from

cervical cancer diagnosed at Stage IA was high and could not survive beyond 3 years contrary to published literature.

While patients diagnosed at stage I had the highest survival rate (88.8%). Other studies (Woods, Rachet *et al*. 2006) have established that the early stage at diagnosis of patients with cervical cancer, the greater their survival. A related study in America found that patients diagnosed at Stage IA had 93% survival rate beyond five years (Saslow et al., 2012). These patients were probably misclassified and grouped under Stage IA or they received an inappropriate treatment, considering that many patients (23.1%) treatments were unknown. These patients could possibly had confounding factors such as co-morbidity, inappropriate treatment or other unknown underlying causes that had contributed significantly to their poor survival. However, the other stages were fairly similar to other studies conducted in Africa (Wiredu and Armah, 2006a) and in the Americans (McCarthy et al., 2010). In this present study, it has been observed that nearly 50% of the patients were diagnosed with the advanced stage (III) of the disease. Der and colleagues (Der et al., 2015) in a related study showed that majority of cervical cancer patients or patients presented with ovarian carcinoma often were diagnosed with advanced stages of the disease.

Cervical cancer treatment requires a multi-disciplinary approach and expertise. This includes gynaecologic oncologist, radiation oncologist, and medical oncologist. It has been proven to be necessary because the treatment of cervical cancer depends on the stage at diagnosis of the disease. Considering the example of an early invasive cancer, surgery is the treatment of choice and in more advanced cases, radiation combined with chemotherapy is proven to be the current standard of care. Meanwhile patients with disseminated disease may require chemotherapy or radiation to provide symptom palliation (Peiretti et al., 2012). Patient's

income plays an important role in the quality of treatment offered since cancer diseases are not insured in the NHIS in Ghana. Cancer treatment is inevitably not an exception to the rule where there are virtually no private alternatives for special services and quality of care (Fiva et al., 2014).

In this study, it has been found that 63.5% of the cervical cancer patients at KATH were under Radiotherapy treatment while few were under Chemotherapy treatment. This should be an indication that most of the patients reported with an advanced stage of the disease. Cervical cancer patients undergoing radiotherapy and chemotherapy treatment mortality rates were 30.8% and 28.0%respectively whiles patients under both chemotherapy and radiotherapy was 21.6%.This means that patients undergoing the combination therapies had the highest chance of survival relative to the other treatment options. It has to be noted that there were no surgeries reported currently. This could be due to the late stage at diagnosis and the most plausible explanation is that only early invasive cancer would require surgery. For the advanced cases, the choices of treatment would be radiation, chemotherapy or combination of both. Late stage at diagnosis influences the survival of patients with cervical cancer reducing their life expectancy. The type of treatment would determine survival of patient. Mono-therapy is said to have short survival rate for advanced stage of the disease compared with to a combined treatment (Tewari et al., 2014).

5.3.1 Co-morbidity

Any additional entities that existed or may occur during the clinical course of a patient with an index disease under study have been found to exert a poorer survival on the patient. Thus, patients with cervical cancer with other co-morbidities had shorter survival than those without any additional illness (Irisa et al., 2012). It was observed in this study that co-

morbidity (Diabetes and Hypertension) was significantly associated with the survival of patients and-patients with co-morbidity have shorter survival rate relative to those without it. This could be linked to further health deterioration impacted on patients already vulnerable to the cancer and would succumb to the actual cervical cancer. The risk of dying for cervical cancer patients was relatively low in patients without co-morbidity (MR=23.68%) compared to those with a co-morbidity (MR=37.39%). Co-morbidity directly contribute to worsen the survival of patients even after treatment (Geraci et al., 2005). In another study (Geraci, 2005) co-morbid illness was significantly reducing cancer patients' survival. This same finding was observed in this study and confirmed that co-morbidity influences the survival of cervical cancer patients by reducing the patients' five-year life expectancy. The survival rate in respect to co-morbidity is SR=45.22%.

5.3.2 Life Style

5.3.2.1 Smoking cigarette

Epidemiological studies that adjusted for sexual risk behaviour have established smoking as a risk factor for cervical cancer (Rajkumar et al., 2006). In a study by Ann L. Cocker (Coker et al., 2009), it was found that the survival of the cervical cancer patients who smoke was strongly reduced compared with the survival of patients who did not smoke. It was observed in this study that the patients who did not smoke and died represented 39.6% while 55.4% were still alive. Patients who smoke and died were 1.6% and 1.2% of these patients survived. We found no association between smoking and cervical cancer survival. This could be due to the fact that only few numbers of patients reported ever smoked cigarette and the effect could therefore not have direct influence on patients' survival. The finding in this study contrasts with other findings that suggest that tobacco use has influence in reducing patients' survival (Weiderpass et al., 2001).

5.3.2.2 Drinking (Alcohol)

Excessive alcohol intake has been observed to increase the death toll of cancer patients worldwide and facilitating cancer recurrence (Mayadev et al., 2015). Another study showed that 3.6% of all cancer cases were due to alcohol consumption, meanwhile 3.5% deaths due to cancer in the world are attributable to alcohol consumption (Boffetta et al., 2006). In the present research, it has been observed that, 95.2%of patients did not drink alcohol while only 4.8% ever reported taking alcohol. There was found no association between patients' survival and their intake of alcohol. Only a small proportion ever drunk alcohol and may not influence on patients survival, contrary to previous findings that showed that alcohol intake increases the death toll among cervical cancer patients (Mayadev et al., 2015).

5.4 Mortality Rates and Cancer survival factors

In this study, the overall mortality rate was 26.5% while it was reported that 7.5% of all female cancer deaths worldwide in 2012. The rates reported in this present study was four times the global value, twice in western Africa, 18.5% and fairly similar the rates in Central Africa (22.2%) and of Eastern Africa (27.6%). The rates of mortality depict the effect of cervical cancer management over a period of time and years via the impact of early stage detection, improved screening and diagnosis. There was a general decline of cervical cancer mortality rates in most European countries within the period between 2000 and 2010 (Ferlay et al., 2015). Cervical cancer mortality rates of patients are affected by their age, cancer stage, occupation, co-morbidity, and type of treatment.

5.4.1 Mortality and Age

It was observed in a study conducted in USA that the rates of overall incidence of cervical cancer increases with age (Rositch et al., 2014) and consequently mortality increases. In the

current study it is observed that the mortality rate was higher among older cancer patients (MR= 35.46%) and decreases with younger patients (40–59; MR= 24.28%). This could probably be explained as the inability older patients to fight the disease due to general health deterioration compared to their young counterparts.

5.4.2 Mortality rate and occupation

In this study, unemployed patients had higher mortality rate (MR=35.85%) compared to patients employed (MR=24.99%). Patients employed would have more resources and can afford health care services, and choose the appropriate treatment than those without employment. A similar pattern was observed in a study published in 2010 (Booth et al., 2010). When median household income on survival for cancers was analyzed there was found a substantial gradient in survival between the highest and the lowest income quintiles, with a subsequent higher mortality rate among unemployed patients compared to those who were workers (Booth et al., 2010).

5.4.3 Mortality rate and stage at diagnosis

Mortality rates increase with advance stage of cancer and decreases with early stage of the condition. In this study stage I recorded the lowest mortality rate suggesting low gravity of cancer at this stage compared to stage V with the highest mortality rate (Bleyer and Welch, 2012).

a) Stage I

In this study, patients with cancer at stage I had the lowest mortality rate of (12.23%) while patients with cancer at stage IA had higher death rate (MR=44.22%). It was expected that at stage 1A mortality should be minimal. However, the rate reported contradicts with previous studies (Singh, 2003). In this study it is suspected that patients classified under stage 1A

could possibly be misclassification of the stage, inappropriate treatment of patients. Stage I cervical cancer is early stage affecting only the cervix and more than 95% would survive for over 5 years after diagnosis (Landoni et al., 1997).

b) Stage II

Cervical cancer is said to be in Stage II when the cancer has spread to tissue close to the cervix. And more than 50% of women with stage II cervical cancer would survive for over 5 years after diagnosis. Stage IIA cervical cancer, is slightly better than stage IIB cervical cancer. In this study, mortality rate at stage IIB was 15.17% relatively low than pattern reported by some literature (Singh, 2003).

c) Stage III

Cervical cancer at Stage III present the spread of the cancer to the lower vagina or the side of the pelvis and chance of survival is 40%.However, in this study survival rate was 36% fairly similar to the literature (Pecorelli, 2009).

d) Stage IV and Stage V

The cancer at Stages IV and V has spread to distant organs other the cervix or the uterus such as the bladder and the bowel; this provides a 5% survival to the patient. In this study, there was no data or incomplete data of patients and were not analyzed.

5.4.4 Mortality rate and Treatment

In this study, cervical cancer patients who underwent radiotherapy treatment had higher mortality rate (MR=30.83%) compared to chemotherapy (MR=28.05%). It has been established that patients diagnosed at an early stage of the disease could be treated with radiation therapy and/or with chemotherapy, while later stages require chemotherapy or both. In this study, only a few patients were diagnosed at the early stages. However, majority of the patients (63.5%) were treated using radiotherapy although majority of them were diagnosed

at advanced stages requiring chemotherapy or combined therapy. This could possible explain the high mortality among them. It is worthy of note that only a few patients were treated using chemotherapy. In this study, mono-therapy was not the best choice for treatment. However, either the physicians were mistreating their patients or patients could not probably afford for a combined therapy. The combined therapy in this present study however has a relatively low mortality rate compared to the single therapies; chemotherapy and radiotherapy. Combined therapy had a synergetic action on the disease thereby either prolonging the survival of the patient. The survival from cancer is inclined to be poorer in developing countries than it is in industrialized countries, this is probably attributed to a combined set of factors such as delayed screening, late stage diagnosis as well as limitation to standard and timely treatment. It is known that proper application of appropriate cancer control measures can prevent a substantial proportion of the burden of cancer (Singh, 2012).

5.4.5 Mortality rate and co-morbidity

It has been reported that co-morbidity has a significant influence on cervical cancer patients' survival. However, the cervical cancer patient real cause of death might not always be established either due to the secondary disease or cervical cancer (Søgaard et al., 2013). In this study, it is observed that patients with co-morbidity had higher mortality rate (MR=37.39%) relative to patients without co-morbid (MR=236.89). This observation confirms the trend suggested (Søgaard, 2013) for which co-morbidity increases mortality and reduces survival of cervical cancer patients.

5.4.6 Limitations and scope of the study

This study was based on review of secondary data from records of patients' folders and certain vital variables were missing such as educational level of the patients, residence

(urban/rural) as well as their level of income. Also, follow-up of patients concerning death records and relocation were missing. This study was limited by the data contained in and or missing in the files. However systemic bias was controlled for during data analysis. Many vital variables were missing from the records and could probably lead to weak empirical evidence. The scope of this study covered a period January 1st 2004 to December 31st 2008.

CHAPTER 6: CONCLUSION AND RECOMMENDATIONS

The main aim of this study was to determine the contribution of socio-economic determinants on five years survival trends of patients with cervical cancer at KATH. The contributions of socio-economic determinants on five year survival are explained in different categories of these factors which were: age, stage, occupation, co-morbidity, and the type of treatment.

6.2 Conclusion

In this study, age was stratified. Patients' socio-demographic variables such as, marital status, parity, and religion were not associated with the survival of cervical cancer patients. However, occupation of patients with cervical cancer was significantly associated with their survival (P=0.00). It was found that patients who had an employment had a higher survival rate SR=53.43% compared to patients who were unemployed. The survival rate of patients without occupation was SR=38.04%. The stage at diagnosis of patients with cervical cancer at KATH ranged from stage I to stage III according to FIGO classification. Most patients (49.1%) were diagnosed at stage III. This suggested late diagnosis. Stage at diagnosis was significantly associated with the survival of patients (P=0.00). However the mortality rate was higher in patients diagnosed with stage IA (MR=44.22%) contrary to published literature that suggests higher mortality among patients of later stages (stages III, IV, and V) of the disease. The type of treatment was significantly associated to the survival of patients with cervical cancer (P=0.00).While majority of the patients (63.5%) received radio-therapy suggesting late stage treatment or inappropriate treatment. Many patients received undocumented treatment (23.1%). The survival rate was SR=34.72% in respect to the type of treatment. In this study the type of treatment either improved or shortened the survival of the patients. Also, 22.5% of Patients had a co-morbid condition (Hypertension or Diabetes). Co-morbidity was significantly associated to the survival of the patients (P=0.00).Co-morbidity

reduced the survival of cervical cancer patients. The survival rate in respect to co-morbidity was SR=45.22%.

The patient's factors (drinking alcohol and smoking cigarette) were not significantly associated to the survival of the patients. The overall survival rate for all cervical cancer patients was 41.7%. However, the mortality rate of patients with cervical cancer at KATH was estimated at 26.46%. Cervical cancer patients' variables such as age, cancer stage at diagnosis, occupation, co-morbidity, and type of treatment determined the variation of different mortality rates. The survival rates were proportional to mortality rates.

6.3 Recommendation

A number of recommendations are suggested to the Ministry of Health, the Ghana Health Service, and the Oncology Directorate of KATH. Further recommendations for further studies have also been stated below.

The Ghana Health Service and the Ministry of Health

- Awareness, educational campaigns and promotion on cervical cancer screening should be included as part of the antenatal and maternal care services
- Opportunistic screenings programmes should be organized to promote early uptake for cervical cancer screening
- Screening for Human Papilloma Virus (HPV) infections services should be expanded to all district hospitals
- Provision of vaccine for HPV services targeting at high risk HPV
- Policy for cervical cancer registry and screening should be put in place facilitate case detection and management

KATH and the Oncology Directorate

There were some data gaps including key variables such as patients' income, educational level, and residential area (urban/rural) that were not captured in patients' folders/records. Hence, it will be recommended that

- Physicians should be trained and informed to capture all patients' demographical characteristics to assist in determining risk associated with developing the disease.
- Stage at diagnosis should also be appropriately documented
- Database of patients should be developed and linked to the national cancer registry to enhance cancer reporting and documentation.

Recommendations for further studies

- Hospital based survey study should be conducted on cervical cancer across the major health facility to determine the cervical cancer burden in the country.
- Population based study on HPV should be study conducted to screen for the prevalence high risk genotype in the country to facilitate appropriate vaccine usage.
- Cohort of cervical cancer patients at diagnosis should be followed in a longitudinal study to fully understand dynamics of the socio-demographic characteristics on the survival of patients.

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APPENDICES

A- QUESTIONNAIRE

	Socioeconomic determinants of survival from cervical cancer at KATH		
NO	**QUESTIONS AND FILTERS**	**CODING CATEGORIES**	**SKIP**
SOCIO-DEMOGRAPHIC CHARACTERISTICS			
Q1	age	|__|__| age (completed years) Don't know 88	
Q2	Marital status	Married ..... 1 Single ..... 2 Divorced ..... 3 Widow 4	
Q3	Religious affiliation	Christian..... 1 Muslim..... 2 Traditionalist..... 3 Don't know 88	
Q4	Ethnicity	Akan..... 1 Ga/Dangme ..... 2 Ewe ..... 3 Guan..... 4 Mole-Dagbani ..... 5 Grussi..... 6 Gruma ..... 7 Hausa ..... 8 Other 9	
Q5	Educational status	No education..... 1 Primary ..... 2 Secondary ..... 3 Tertiary 4	
Q6	Occupation	Agricultural worker…….....1 Salaried employment…….....2 Petty trader /marketing ……....3 Domestic activities……....4 Student…….....5 Unemployed…….....6 Retired…….....7 Other…….....8 Don't know 88	
Q7	Income per month	≤Gh¢50 ..... 1 Gh¢100 ..... 2 Gh¢150-500 ..... 3 Gh¢550-1000 ..... 4 Gh¢1050-2000 ..... 5 ≥Gh¢2050 6	
Q8	Residence	Rural ..... 1 urban 2	

Risk factors			
Q9	Parity	Nulliparous ..... 1 Uniparous..... 2 Two children..... 3 Other……...4	
Q10	Number of partners	One ……1 Two…….2 Other……...3 Don't know..... 88	
Q11	Smoking	Yes ……1 No……...2 Don't know……88	
Q12	Alcohol intake	Yes ……1 No……...2 Don't know……88	
Q13	Contraceptive use	Yes..... 1 No ..... 2 Don't know..... 88	
Q14	Weight	|__|__||__|__ (kg) Don't know..... 88	
Q15	Height	|__|__||__|__ (m) Don't know..... 88	
Q16	HIV status	Yes..... 1 No 2	
Q17	STI status	Yes..... 1 No ..... 2 Don't know..... 88	→ **Q18** →**Q18**
Q17a	Specify STI infection		
Q18	Other infections	Yes..... 1 No ..... 2 Don't know..... 88	→ **Q19** → **Q19**
Q18a	Specify infections	1…… 2…….. 3…….	
Q19	Other diseases	Yes..... 1 No ..... 2 Don't know..... 88	→ **Q20** → **Q20**
Q19a	Specify the diseases	1…… 2…….. 3…….	
Q20	Date diagnosed	|__|__||__|__|__|__||__| ddmmyy	
Q21	Stage diagnosed	Stage I..... 1 Stage II..... 2 Stage III 1	

		Stage IV ..... 2 Don’t know 88	
Q22	Start date of treatment	|__|__||__|__|__|__||__| dd/mm/yy	
Q23	Treatment types	Surgery..... 1 Chemotherapy..... 2 Radiotherapy..... 3 Others..... 4 Don’t know 88	
Q24	Outcome	Alive ..... 1 Dead..... 2 Don’t know 88	

B- DATA EXCEL SPREAD SHEET

ID	AddressOne	HRegion	Date at diagnosis	Date Treatment Started	DateCompleted	smoking	drinking	comorbidity	age	parity	occupation

screening	Date of First Diagnosis	Year first diagnosis	Follow Update First	Follow Update Last	status 1	Death date	stage	religion	ethnicity	Marital status	Treatmenttype