KWAME NKRUMAH UNIVERSITY OF SCIENCE & TECHNOLOGY,

KUMASI.

CLINICOPATHOLOGICAL PATTERNS AND QUALITY OF LIFE OF COLORECTAL CANCER PATIENTS AT KOMFO ANOKYE TEACHING HOSPITAL, KUMASI GHANA

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By

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DECLARATION

With the exception of references and quotations from other sources which have all been credited, I hereby declare that this piece of work is the original research work of my very good self and that no part of it has been presented elsewhere.

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ABSTRACT

Colorectal cancer is a major cause of morbidity and mortality throughout the world and the incidence of colorectal cancer is increasing in developing countries including Sub Sahara Africa. The aim of this study was to elucidate the incidence, five years survival rate and the quality of life of colorectal cancer patients, as well as to identify the prognostic factors among diagnosed and treated patients at Komfo Anokye Teaching Hospital (KATH)**.** A retrospective cross sectional study where all colorectal cancer cases from 2009 to 2015 presented to the Surgical and Oncological Department of KATH were reviewed. The records of subjects were analysed for information on their demographics, clinical and pathological parameters. Survival analysis was done, and the survival time was defined as the time between the date of first diagnosis and the date of last follow-up or death. Quality of life of patients was assessed using the European Organisation for Research and Treatment of Cancer (EORTC) standard questionnaire for cancer patients and the colorectal cancer specific model EORTC CR 29. The EORTC questionnaire was filled through telephone interviews with the study subjects. In all, 221 cases of colorectal cancer were identified. The mean age of the study participants was 54 ± 16.8 and ranged from 16 to 90 years. Fifty (50) of the participants (22.6%) were less than 40 years. Majority were females 127 (57.5%), 16 (7.24%) showed records of family history of cancer and the prevalence of comorbidities was (24.89%). The major clinical symptoms presented; were weight loss (44.80%), bleeding per rectum (39.82%), abdominal pain (38.91%) constipation (31.67%) Hematochezia (28.96%) change in bowel habit (20.81%), anorexia (20.36%), and anaemia (15.84%). Majority of the patients presented with rectal cancer cases 108(48.87%). The rectum 96(43.40%) was the most common anatomical site for colorectal cancer, followed by the caecum 35 (15.80%) and sigmoid colon 22 (10.00%) among the study participants. Adenocarcinoma was the commonest histopathological tumour in 151 (68.33%) of the studied subjects. Majority of the tumours showed moderately differentiation 104 (47.10%). According to the Tumour Node Metastasis (TNM) staging of cancer, majority of the patients 89(40.27%) were in late stage (TNM Stage III) of the cancer and only 13 (5.98%) were in stage 1. The overall crude annual incidence of colorectal cancer at KATH was 4.62 per 100,000 population. The age specific standardized incidence rate using WHO world population as standard was 7.93 per 100,000 population. The five years survival rate was recorded at 16%. Family history, Chemotherapy, BMI and both chemotherapy and radiotherapy were significant ($p< 0.05$) clinical prognostic factors. TNM tumour stage, depth of tumour invasion, lymph node metastasis, and distance metastasis had worse significant association with overall survival. The global health status had a mean score of 64.15±24.58, signifying moderate quality of life among the patients. Colon cancer patients (72.8±21.7) had a significantly ($p=0.039$) better quality of life compared to rectal cancer patients (56.9±20.7) Overall, the function scales assessment was good among the patients with physical function having the highest scores of 84.61±24.58 and emotional function having the least score 66.36±26.32. With the exception of financial difficulty 33.0 (0.0100), pain 17.0 (0.0-33.0) and fatigue 22.0 (0.0-33.0), the symptom scale assessment was good among the patients. With the CRC specific questionnaire, body image had the highest score (85.25± 22.35) on the functional scale and a comparison between colon and rectal cancer patients showed a significant difference ($p=0.0261$). In the symptom scale, flatulence was the most common symptom with the highest score 33(0.0-67.0). Overall, patients had good symptom score. Our study has established that, there is a progressive but

steady increase in the incidence of colorectal cancer in our setting and that the observed trend is similar to that of most African countries. Late staged presentations, high mortality and hence low survival rate are the hallmarks of the disease in this region and pose a great challenge in the management and clinical outcome of these patients.

DEDICATION

I dedicate this work to my whole family especially my Mum and Dad, Mr Joseph Batu and Mrs Mary Bio Batu, to my brothers and sisters, Samuel,

Albert, Jacob, Catherine, Theresa and Martha for their constant prayers and support and to my motivator, Emmanuel Acheampong.

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Finally, I say a big Thank You to the entire staff of the Records Unit at both the Surgery and Oncology department of Komfo Anokye Teaching Hospital. God richly bless you all.

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ABBREVIATIONS

AJCC	American Joint Committee on Cancer
APC	Adenomatous Polyposis Coli
BMI	Body Mass Index
CD	Crohns Disease
CEA	Carcinoembryonic Antigen
CHRPE	Committee on Human Research, Publication and Ethics
CIN	Chromosomal Instability
CRC	Colorectal Cancer
CSS	Cancer specific survival
EORTC	European Organisation for research and Treatment of Cancer
EPIC	European Prospective Investigation into Cancer and Nutrition
FACT-C	Functional Assessment of cancer Therapy
FAP	Familial Adenomatous Polyposis
GIT	Gastrointestinal Tract
HNPCC	Hereditary Non-Polyposis Colorectal Cancer
IARC	International Agency for Research on Cancer
KATH	Komfo Anokye Teaching Hospital
MIS	Microsatellite Instability
MMR	Mismatch Repair
MSI	Microsatellite Instability
NSAIDS	Non-steroidal anti-inflammatory drugs
OS	Overall Survival
pM	Distant Metastasis
pN	Lymph Node metastasis
pT	Depth of tumour Invasion
QoL	Quality of life
TNM	Tumour Node Metastasis
UC	Ulcerative Colitis

CHAPTER ONE

1.0 INTRODUCTION

Colorectal cancer (CRC), also referred to as cancer of the colon or rectum is one of the major causes of cancer deaths worldwide (IARC, 2002). Global Cancer Statistics in 2008, stated that colorectal cancer is the second most common cancer in females and third in males and (Jemal *et al.*, 2011; Fang *et al.*, 2013) with over 1.2 million new cases and 608,700 deaths estimated to have occurred. Incidence and mortality rates are considerably higher in males than in females (Siegel *et al.*, 2012). Common symptoms include abdominal pain, rectal bleeding, altered bowel habits, and involuntary weight loss. Symptoms depend on cancer location, cancer size, and presence of metastases (Bond, 2000). Globally, the incidence of colorectal cancer varies widely by over 10-fold, with the highest incidence rates in Australia and New Zealand, Europe and North America, and the lowest rates in Africa and Asia (Jemal *et. al.*, 2009; Center *et. al.*, 2011). These geographic differences appear to be attributable to differences in dietary and environmental exposures (Center *et al.*, 2009).

Several factors have been shown to put individuals at risk to CRC and these include age, the presence of polyps, inflammatory bowel disease, lifestyle, genetic background and family medical history (IARC, 2011). Environmental factors such as obesity, physical inactivity, poor diet, smoking and heavy alcohol consumption account for approximately 80% of all colorectal cancer cases (Haggar and Boushey, 2009). Genetic susceptibility is associated with familial adenomatous polyposis (FAP) and Lynch Syndrome (hereditary non-polyposis colorectal cancer (HNPCC) which accounts for 10% of all colorectal cancer cases. Individuals who have these diseases have an increased lifetime risk of CRC of up to 80% (Haggar and Boushey, 2009).

In most African studies, colorectal cancer represents 3%-6% of all malignant tumours thereby apparently making it a rare disease, but this is no longer the case (Adesanya and

Darocha-Afodu, 2000). The uncommonness of this disease in black Africans may be due to the young age of the population, shorter transit time of faeces, high fibre diet and infrequency of precancerous conditions such as Familial Adenomatosis polyposis, ulcerative colitis and Crohns disease (Popoola *et al.*, 2013). Recent studies show that the incidence of colorectal cancer in the developed world is declining, but increasing in subSaharan Africa (Siegel *et al.,* 2011; Soliman *et al.,* 2001). Colorectal cancer mostly presents at young age among Africans. On the average, patients tend to be between 10 15 years younger and one-third of the patients aged around 40 years and below (Adesanya and Darocha-Afodu 2000).

In Accra, Ghana, cancer of the colon and rectum is the third most common malignancy diagnosed (Biritwum *et al.,* 2000) and the 10th cause of cancer deaths. It represents the 8th and the 9th cause of cancer deaths in males and females respectively (Wiredu and Armah, 2006). According to Naaeder and Acheampong, (1994) the rise in the incidence of adenocarcinoma of the colon and rectum in Ghana is due to an increase in the life expectancy of the population and modest improvements in diagnosis. Dakubo *et al.,* (2010), concluded that the incidence of colorectal cancer has increased over the last four decades in tandem with an aging population of Accra with adenocarcinoma as the predominant histological type.

The survival of colorectal cancer greatly rely on the stage of the disease at diagnosis and typically ranges from a 90% 5-year survival rate for cancers detected at the localized stage; 70% for regional; to 10% for people diagnosed for distant metastatic cancer (Jemal *et al.* 2004; Ries *et al.,* 2008). Since the 1960s, survival for colorectal cancer at all stages has increased substantially and has been better in countries with high life-expectancy and good access to modern specialized health care. However, enormous disparities in colorectal cancer survival exist globally and even within regions (Jackson-Thompson *et al.,* 2006;

Boyle, 2000). This variation is not easily explained, but most of the marked global and regional disparity in survival is likely due to differences in access to diagnostic and treatment services (Boyle and Langman, 2000). Approximately 80% of patients now survive the first year after diagnosis, and approximately 62% survive 5 years and more. Besides disease-free and overall survival time, quality of life (QoL) has become an important outcome measure for colorectal cancer patients (Arndt *et al.*, 2004). Quality of life (QoL) is a dynamic, subjective and centered on patient construct, comprising physical, functional, emotional, and social/family well-being (Marventano *et al.*, 2013). Therefore, QoL is an important outcome for evaluating the full impact of the disease on the individuals, their family and their community (Marventano *et al.*, 2013). In cancer surveillance, prognostic factors are utilized by clinicians to predict the probable course of disease in patients and the likely outcome of the disease. Clinical and pathological prognostic factors can facilitate clinical decision-making and appropriate treatment (Siegel *et al*, 2010).

1.1 PROBLEM STATEMENT

Colorectal cancer is a major cause of morbidity and mortality throughout the world (IARC 2002). Though colorectal cancer has become a major source of morbidity and mortality globally, few countries in Sub Saharan Africa have data on its incidence (Calys-Tagoe *et al.*, 2012). Kamangar *et al.*, 2006

Colorectal cancer constitutes a major public health issue globally with an estimated 1.2 million new cases and over 630,000 deaths per year with almost 8% of all cancer deaths (Kamangar *et al.*, 2006; Jemal *et al.*, 2011). Worldwide, there has been growing evidence that, not only is the incidence of colorectal cancer changing, but also its distribution patterns seem to be changing (Singh *et al.*, 2010). Recent studies show that the incidence of colorectal cancer is increasing in sub-Saharan Africa, especially in the urban centers

(Siegel *et al.*, 2011). In Nigeria, Ibadan, 81% increase in incidence of colorectal cancer was recorded over a period of two decade (Iliyasu *et al.,* 1996) accounting for approximately 10%-50% of all gastrointestinal (GIT) malignancies.

In Africa, colorectal cancer tends to present at a younger age with advanced aggressive features associated with poor prognosis (Sule and Mandong 1999; Seleye-Fubara and Gbobo, 2005). Recent studies from Nigeria and Ghana has shown that colorectal cancer in West Africa has a distinctive pattern with young age of onset and predominantly leftsided tumours (Dakubo *et al*., 2010; Irabor and Adedeji, 2009). Current studies have also shown that colorectal cancer is no longer uncommon among the indigenous people of Ghana and that patients mostly present with late stage cancers that are mostly incurable (Dakubo *et al.,* 2010). This has been shown to result in poor outcome of treatment for colorectal cancers. According to Chalya *et al.*, (2013), late presentation is partly due to lack of local data on the current trends of colorectal cancer and community unawareness of the importance of early reporting to the hospital for early diagnosis and treatment. Furthermore, colorectal cancer and its management can have an adverse effect on population social functioning, including work and productive life. Patients with colorectal cancer, both stoma and non-stoma patients, are troubled by frequent or irregular bowel movements, diarrhea, flatulence, and fatigue, and often have to follow dietary restrictions (Arndt *et al.,* 2004). Less is known however, about how colorectal cancer patients in Ghana rate their overall Quality of life (QoL) and how they cope with the awareness of living with a chronic and potentially life-threatening disease. This therefore creates the need for an investigation of the current trend of colorectal cancer among patients in Ghana. In essence, this is the core objective of this work.

1.3 HYPOTHESIS

1. There is no increase in the incidence of colorectal cancer in our population

2. There is no association between the clinic-pathological factors and overall survival.

1.4 RATIONALE OF THE STUDY

Colorectal cancer is one of the most common cancers worldwide and its incidence is reported to be increasing in resource limited countries probably due to acquisition of western lifestyles (Chalya *et al.,* 2013). According to Dakubo *et al.,* (2010), the trend of colorectal cancer in Accra has crude incidence rate of 12.53 for males, 9.87 for females and 11.18 per 100, 000 population. Information on incidence will inform health policy makers on where to direct resources for effective management and clinical outcome of the disease in Ghana. Globally, there is enormous disparity in colorectal cancer survival which has mostly been attributed to differences in access to diagnostic and treatment services. Thus information on survival analysis will help improve the current treatment regimens for better survival of patients.

Furthermore, recent studies have shown that the anatomical distribution of colorectal cancer has shifted from the common left sided distal colon cancers to proximal right ward shift (Cheng *et al.,* 2001). These proximal cancers have their own biological and clinical differences from distal cancers. Recognizing the dynamic shift of CRC in the general population will likely affect national CRC prevention and management plan.

Information of these distribution patterns will therefore be important and likely help to influence early colorectal cancer screening strategies (Singh *et al.,* 2010: Zauber *et al.,* 2012).

It has been established by surveillance studies that, prognostic factors are utilized by clinicians to predict the probable course of the disease and its likely outcome (Siegel *et al,* 2010).

Additionally, assessment of QoL in patients with colorectal cancer may improve the understanding of how the cancer and its therapy influence patients' lives and thus help to adapt pragmatic treatment strategies.

Updated knowledge on colorectal cancer incidence, survival rate, pattern and distribution as well as quality of life among different age groups and gender would ultimately influence colorectal cancer diagnosis and improve public health strategies in the management of the disease in Ghana.

1.5 MAIN OBJECTIVE OF STUDY

The aim of this study is to elucidate the incidence and the five years survival rate of colorectal cancer, and to identify prognostic factors among diagnosed and treated patients at Komfo Anokye Teaching Hospital.

1.6 SPECIFIC OBJECTIVES

1. To determine the clinico-pathological patterns of colorectal cancer at KATH
2. To estimate the age standardized incidence and five year survival rate of colorectal cancer from 2009 to 2015.
3. To evaluate the relationship between social, clinical and pathological parameters and overall survival (OS) in colorectal cancer patients
4. To assess the quality of life of the treated colorectal cancer patients

CHAPTER TWO

2.0 LITERATURE REVIEW 2.1 ANATOMICAL AND MICROSCOPIC FEATURES OF THE LARGE INTESTINE

The large intestine is the final section of the alimentary canal which extends from the terminal ileum to the anal canal (Macfarlane and Macfarlane, 2003). The colon is a tubular structure approximately 1.5 meters long in adults and constitute of the cecum, the

ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon and the sigmoid colon. The rectum, 12 cm in length in the adult, begins at the peritoneal reflexion and follows the curve of the sacrum ending at the anal canal. The rectum serves primarily as a storage reservoir and tumours in the rectum are less than 16 cm from the anal verge and located at least partially within the supply of the superior rectal artery (Scanlon and Sanders, 2014).

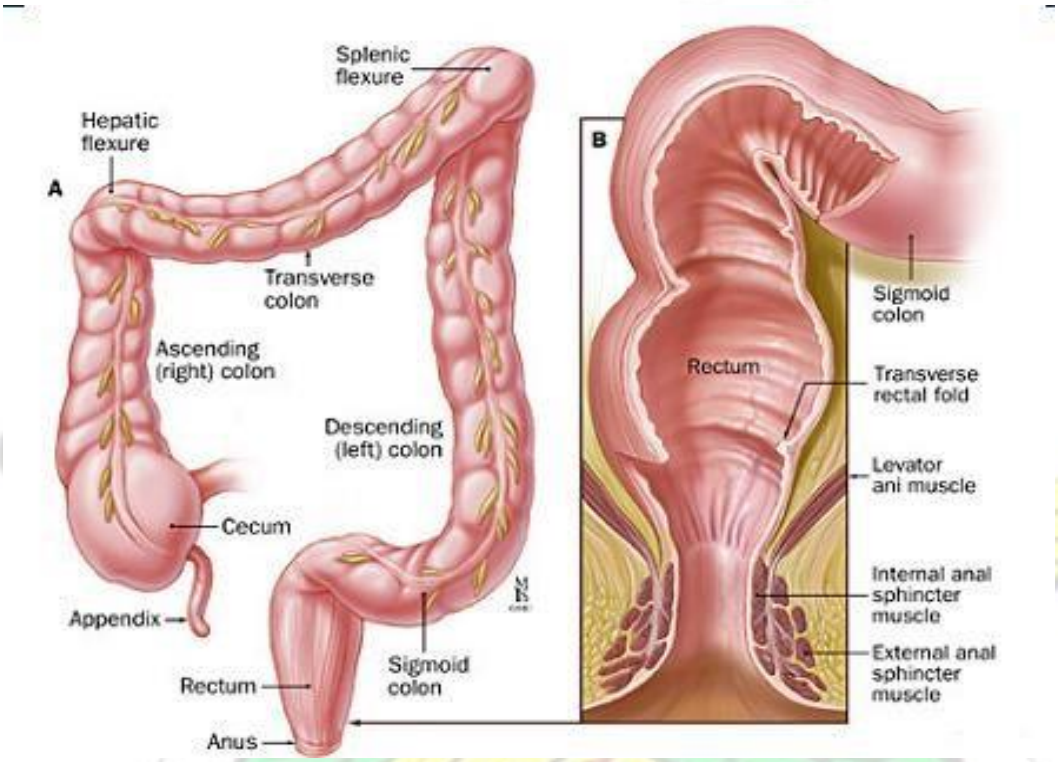

Figure 2.1: Normal colorectal anatomy; A, Anatomy of the colon B, Anatomy of the rectum Source: (www.jhmicall.org, 2010)

Histological and microscopic structural assessment of colon shows four layers; the mucosa, the sub mucosa, the muscularis externa/ propria (containing circular and smooth muscle layers) and the serosa (Yeatman, 2001). Earliest genetic changes mostly occur in the mucosa cells due to continuous cell division of the normal cells to replenish those that are shed from the bowel wall into the lumen. The rectal mucosa is similar to that of colon except for more numerous goblet cells (Araki *et al.*, 1996)**.** The sub mucosa layer contains blood vessels, lymphatics and terminal nerve fibres. It is an important layer with regards

to the genesis of cancer because once a tumour has invaded into this region of the bowel wall it can gain entrance to the blood supply and lymphatic system, permitting distant spread throughout the body (Yeatman, 2001).

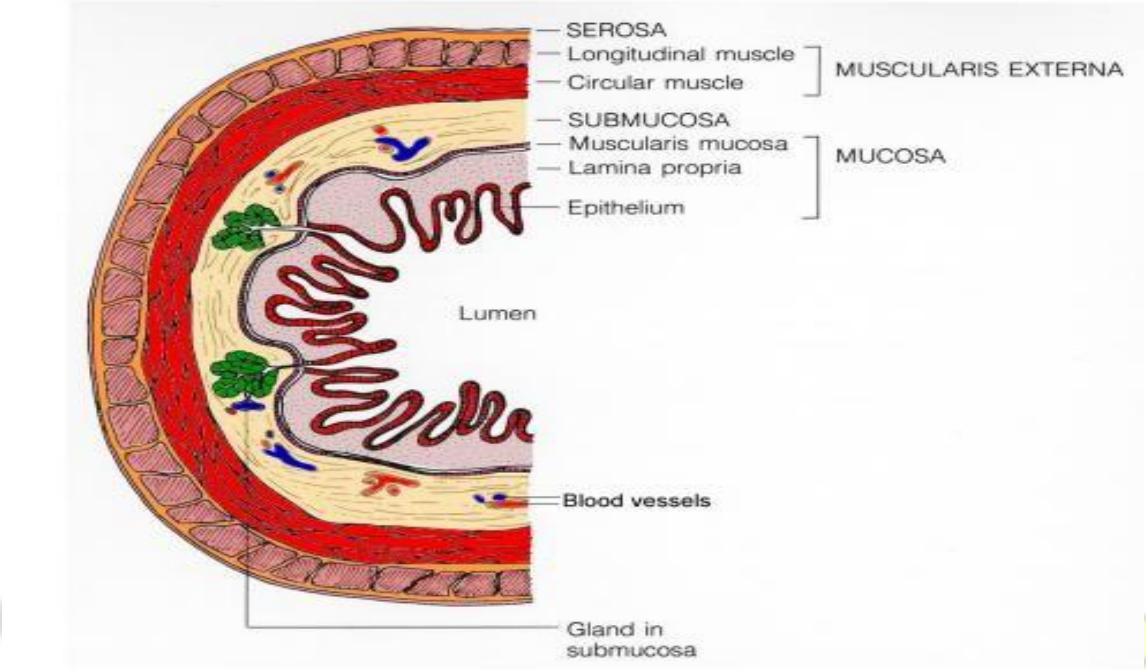

Figure 2.2: Layers of the colon. Source: (www.cancerquest.org, 2012)

2.2 COLORECTAL CANCER

Colonic and rectal cancer is jointly referred to as a single disease called colorectal cancer (Iversen, 2012). Colorectal cancer is characterised by malignant growth which occurs in the large bowel and occasionally, confined locally for a comparatively long period before metastasis through the bowel wall to lymph nodes and other parts of the body (Potter, 1995; Campbell, 1999). Colon cancer ranges from the caecum to the sigmoid (approximately 15 cm above the anal verge), and rectal cancer, from the recto-sigmoid to the anus (de Heer, 2007).

2.3 EPIDEMIOLOGY OF COLORECTAL CANCER

2.3.1 Worldwide burden, incidence and morality of colorectal cancer

Colorectal cancer is the third most commonly diagnosed cancer worldwide with an incidence of 1.23 million new cases per year. Among men, it is the third most frequently diagnosed cancer after prostate and lung cancer (663,000 cases, 10.0%), and the second most common cancer type after breast cancer in women (570,000 cases, 9.4%) (Ferlay *et al.*, 2010). The estimated death rate of colorectal cancer in 2008 was 608 000 which represented 8% of all cancer deaths. This therefore renders CRC as the fourth most common cause of cancer deaths (Ferlay *et al.*, 2010). Africa, Asia and South America have the lowest incidence of colorectal cancer with North America, Australia/New Zealand and Western Europe having the highest incidence (Center and ME, 2011). Australia/Zealand has the highest estimated rates of (44.8 and 32.2 per 100,000 in men and women respectively), and Western Africa. Has the lowest rate of (4.5 and 3.8 per 100,000) (Fazeli and Keramati, 2015). Incidence rates are substantially higher in men than in women (overall sex ratio of the ASRs 1.4:1) (Ferlay *et al.*, 2010). Approximately, half of the patients diagnosed with colorectal cancer die from the disease within five years. In the western world, the lifetime risk of developing colorectal cancer is 4-5% (Sjo, 2012). Nevertheless, the incidence of colorectal cancer is increasing in developing countries which now add a little over a third of new cases of CRC to the annual worldwide incidence (GLOBOCAN, 2008).

2.3.2 African Burden

In Sub Saharan Africa, among males and females, colorectal cancer is the 5th and 4th most commonly diagnosed cancer and the 6th and 5th most common cause of cancer death respectively (Jemal *et al.*, 2012). In 2008, 26,816 cases and 20,889 deaths were projected in sub- Saharan Africa (Cancer, 2014) which is far lower than the 1.2 million new cases and 608,700 deaths world estimates (Jemal *et. al.*, 2009).

Colorectal cancer has been shown to be a rare disease in African where it represents 2-6% of all malignant tumours (Holcombe and Babayo, 1990; Okobia and Aligbe, 2005; Sighoko *et al.*, 2011). For both sexes the crude incidence of colorectal cancer in Sub-Sahara Africa was estimated to be 4.04 per 100 000 population, 4.38 for men and 3.69 for women (Graham *et al.*, 2012). Information obtained from most cancer registries in Africa also supports the perception that colorectal cancer is rare in Africa (Cancer, 2003). In Gambia and Zimbabwe, the age standardised incidence per 100,000 population ranges from as low as 1.5 in males and 2.5 in females to 8.5 in males and 7.1 in females respectively (Katsidzira *et al.*, 2015). Current studies from Sub Sahara Africa indicate that the incidence of colorectal cancer is increasing especially in the urban centers (Soliman *et al.*, 2001; Siegel *et al.*, 2010). In West Africa, the incidence of colorectal cancer is increasing although, slowly. The incidence rate of CRC are increasing quickly in numerous African countries traditionally recognized as low risk countries, including Nigeria ((Abdulkareem *et al.*, 2008; Irabor *et al.*, 2010), Ghana (Dakubo *et al.*, 2010a), Tunisia, (Missaoui *et al.*, 2011) and Egypt (Soliman *et al.*, 1997; Abou-Zeid *et al.*, 2002). In these areas, CRC now represents about 10- 50% of all malignant tumours. These current unfavourable trends are assumed to be reflective of combination of risk factors, such as changes in dietary patterns, obesity and smoking (de Kok *et al.*, 2008; Center *et al.*, 2009b). Studies from Nigeria and Ghana indicate that colorectal cancer in West Africa has a characteristic unique pattern with young-age onset and mostly left-sided tumours (Irabor and Adedeji, 2009; Dakubo *et al.*, 2010b). Hospital- based data in Ghana and Nigeria depict the crude incidence rates of CRC to be 11.18 per 100,000 population and 3.4 per 100,000 population respectively (Dakubo *et al.*, 2010a; Irabor *et al.*, 2010). These rates are far lower than the incidence rates of over 40 per 100,000 populations reported in Western nations (Haggar and Boushey, 2009). In Nigeria, CRC is the fourth most common malignant neoplasm which recorded an increase of 81% in incidence over a period of two decades in

Ibadan. (Iliyasu *et al.*, 1996; Irabor *et al.*, 2010). It also accounted for 10%-50% of all gastrointestinal (GIT) malignancies (Obafunwa, 1990; Elesha and Owonikoko, 1998). The crude incidence of CRC in Nigeria has been assessed at 3.4 per 100,000 populations (Sack and Rothman, 2000). Thirty three (33) years ago, about 18 patients were seen annually (1980) hence evoking the view that the incidence of CRC is increasing in Nigeria (Irabor and Adedeji, 2009; Irabor *et al.*, 2010).

In Ghana, the number of new cases of colorectal cancer has increased by 8- fold per year from an average of 4.1 new cases in 1960s to an average of 32.6 new cases currently (Badoe, 1966; Dakubo *et al.*, 2010a). After cancer of the breast and the liver, colorectal cancer is now the 3rd most common malignant disease (Biritwum *et al.*, 2000). It is the 10th cause of overall cancer death and 8th and 9th cause of cancer deaths in males and females respectively(Wiredu and Armah, 2006). Over the past two or three decades, there have been improvements in the life expectancy of Ghanaians which mean that a large portion of the population has entered the colorectal cancer age group (Society, 2008).

About 6.7% of Ghanaians were 50 years or older in 1960. In 1990, this figure had risen to 10% and presently is 12.1 %. In consonance with the ageing population, the number of new cases of colorectal cancer has increased progressively over the same period. On the average, 33 new cases are seen yearly at the Korle-Bu Teaching Hospital and the population at risk most is in the age group 50–75 years (Dakubo *et al.*, 2010a). The predominant risk factor is helicobacter pylori infection, the dietary component of red meat – beef, lamb, pork and veal and its processed varieties. Its highest incidence is in the seventh decade in both develop and developing countries (McArdle *et al.*, 1990; Naaeder and Archampong, 1994; Dakubo *et al.*, 2010a) 13). A study by Raskin *et al.* (2012) on the molecular characterisation of colorectal cancer in Ghana showed a very high occurrence of MSI-high colorectal tumours (41.4%). The frequency of KRAS mutations in African

Americans is similar to the mutations found in the Ghanaian population, but there was absence of BRAF mutations (Raskin *et al.*, 2012).

2.4 AETIOLOGY AND RISK FACTORS

Colorectal cancer aetiology is very complex and involves interactions between environmental factors and inherited susceptibility (Wallin, 2011). Colorectal cancer occurs in two major forms: sporadic colorectal cancer and inherited colorectal cancer. Approximately two thirds (70%-75%) of new cases of CRC are sporadic (i.e., occurs in people who have no family history of the disease) (Kang *et al.*, 2011). In these sporadic cases, the necessary genetic changes occurs de novo, caused by etiologic factors such as age, lifestyle factors and environmental exposures.

2.4.1 Age

The risk of developing CRC increases with age although it affects all ages. The age related exponential increase in CRC incidence is explained by the accumulating genetic events in ageing tissues (DePinho, 2000). After the age of 40, the probability of being diagnosed with CRC increases gradually, rising sharply after age 50 (Food, 2007; Ries *et al.*, 2008). Over 90% of colorectal cancer cases are diagnosed in people aged 50 or older (Ries *et al.*, 2008). The incidence rate is over 50 times higher in individuals aged 60 to 79 years than in those younger than 40 years (Society, 2005; Ries *et al.*, 2008). However, colorectal cancer seems to be increasing among younger people (O'Connell *et al.*, 2003; O'Connell *et al.*, 2004). In the United States, colorectal cancer is now one of the 10 most commonly diagnosed cancers among men and women aged 20 to 49 years (Fairley *et al.*, 2006). Colorectal cancer diagnosed in patients younger than 45 years i.e. the early onset CRC is relatively rare, accounting for 2-8% of all large bowel cancers (Parramore *et al.*, 1998; Turkiewicz *et al.*, 2001) .

2.4.2 Behavioural and Lifestyle factors for colorectal cancer

Diet as a possible risk factor for colorectal cancer has been widely studied over the years. Terry *et al.* (2001), showed an association between low fruit and vegetable intake and increased risk of colorectal cancer. It is hypothesized that the fibre, antioxidant vitamin, folic acid, micronutrient, or phytochemical (flavone) content in vegetables and fruits may exert a protective effect. The difference in dietary fibre intake has been proposed as a reason for the geographical difference in CRC incidence rate with the underlying basis being that increased intake of dietary fibre may increase faecal bulk and reduce colonic transit time (Food, 2007; Haggar and Boushey, 2009) Furthermore, some observational studies have noted an inverse relationship between dietary fibre consumption and risk of colorectal adenomas and or CRC (Negri *et al.*, 1998; Lin, 2009).

Some studies have also suggested that a diet high in red meat, animal fat, or cholesterol content may be associated with CRC development, especially in the left colon (Willett *et al.*, 1990; Chao *et al.*, 2005). A possible etiological factor for this is that, typical western diet favour's the development of bacterial flora which is capable of degrading bile salts to potentially carcinogenic N-nitroso compounds (Larsson and Wolk, 2006). For red meat, the mechanism has been attributed to the presence of heme iron in red meat (Kabat *et al.*, 2007; Santarelli *et al.*, 2008). In addition, some meat cooked at high temperatures result in the production of heterocyclic amines and aromatic hydrocarbons which are believed to have carcinogenic properties (Sinha, 2002; Santarelli *et al.*, 2008).

The role of exercise in reducing the risk of colorectal cancer is now well established (Fung and Brown, 2013). In 2009, a meta-analysis concluded that regular exercise reduced the risk of colon cancer by almost 25% in both men and women (Wolin *et al.*, 2007). Various mechanisms have been put forward to explain the positive effect of exercise in reducing CRC. These include lowering levels of prostaglandins, decreasing gut transit time and

improving immune function (Samad *et al.*, 2005). Obesity is now a well-established risk factor for colorectal cancer. A meta-analysis by Moghaddam *et al.*,

(2007) estimated that individuals with a Body Mass Index (BMI) ≥30kg/m2 had a 20% greater risk of developing CRC compared to normal weight controls (Moghaddam *et al.*, 2007).

Hypertension, elevated blood glucose, hyperinsulinemia and Type-2 diabetes are metabolic abnormalities associated with insulin resistance syndrome that are also independently associated with colorectal cancer (Giovannucci, 2007). The findings of a recent meta-analysis (Larsson *et al.*, 2005) suggested that Type 2 diabetes increases the risk of colorectal cancer by thirty percent (30%). The underlying mechanisms linking insulin resistance syndrome with colorectal cancer are not fully understood, but the available evidence suggests that hyperinsulinemia is the likeliest cause (Calle and Kaaks, 2004). Long term cigarette smoking has been shown to be associated with colorectal cancer. Tobacco smoke is known to contain carcinogens such as heterocyclic amine, nitrosamines, and polycyclic hydrocarbons which has been shown in studies to increase cancer growth in the colon and rectum, and increase the risk of being diagnosed with CRC (Haggar and Boushey, 2009). Cigarette smoking is important to both the formation and growth rate of adenomatous polyps which are precursor lesions for CRC (Zisman *et al.*, 2006; Botteri *et al.*, 2008). Studies have also shown that cigarette smokers have an earlier average age of onset of incidence of CRC

((Zisman *et al.*, 2006; Tsong *et al.*, 2007). The EPIC trail investigated the impart of alcohol consumption on a cohort of almost half a million subjects over a 6 year period concluded that both lifetime and baseline alcohol intake increased the risk of colon and rectal cancer (Ferrari *et al.*, 2007). Furthermore, a pooled analysis of fourteen separate studies suggested that a high alcohol intake defined as more than 100g/week was associated with a 19%

increase in the risk of colon cancer in men and women (Moskal *et al.*, 2007). A direct effect of acetaldehyde, a compound known to alter DNA has been implicated in the mechanism by which alcohol influences tumour development (Toriola *et al.*, 2008).

In 1999, a large meta-analysis reported that the risk of colorectal cancer was significantly lower in postmenopausal women who are on Hormone Replacement Therapy (HRT) compared to those who had never received such treatment (Grodstein *et al.*, 1999). The reason being that, oestrogen decreases the production of bile acids which have been implicated in initiating and promoting malignant change of colonic epithelium (McMichael and Potter, 1980). Also oestrogen decreases serum levels of insulin like growth factors (IGF-1), an important mitogen required for cellular proliferation and subsequent transformation into cancerous cells (Campagnoli *et al.*, 2009). There is good evidence that patient taking non-steroidal anti-inflammatory drugs (NSAIDs) reduce their risk of developing colorectal cancer. In 2003, a randomised controlled trial of over 1000 patients concluded that daily aspirin reduced the risk of colorectal adenoma formation in patients with a history of polyps (Baron *et al.*, 2003) These findings are supported by epidemiological data which suggests that NSAIDs not only reduce the incidence of adenomas (Arber, 2000) but also reduce the risk of progression to adenocarcinoma (Peleg *et al.*, 1994).

2.4.3 Environmental and Western lifestyle

Studies among migrates and their offspring provides evidence of environmental risk of CRC. Incidence rates of CRC tends to increase among migrants from low-risk to high risk countries (Janout and Kollárová, 2001). Apart from migration, other environmental factors influencing CRC incidence is urban residence. Urban residents have higher incidence of colorectal cancer. This higher incidence in urban areas is more evident among men than

women and for colon cancer than for rectal cancer (Boyle and Langman, 2000). The highest rates of colorectal cancer are found in Western countries and up to15-fold differences in age-standardised incidence rates are observed between different geographical locations across the world (Muir and Parkin, 1985).

Table 2.1 Environmental and host factors associated with the development of sporadic colorectal cancer Environmental Factors

Western lifestyle	diet smoking alcohol sedentary lifestyle
Diet	red meat fruits and vegetables vitamins and anti-oxidants
Drugs	Aspirin (Reduced risk) NSAID's (reduced risk) HRT(Reduced risk)
Host factors	
Host physiology	age comorbidity cardiovascular disease obesity
Inflammatory Response	Systemic Local

NSAID: non-steroidal anti-inflammatory drugs, HRT: Hormone replacement therapy

Source: (Richards, 2014)

2.5 NON-SPORADIC COLORECTAL CANCER

Inherited colorectal cancer accounts for 5%- 10%, about one third of all colorectal cancers cases. Inherited CRC tend to occur in families, so that first degree relatives of patients with newly diagnosed adenomas or invasive CRCs are at increased risk. While many of these familial clusters are associated with common behaviours or environmental exposures among family members, some are also linked to germ line mutations in specific genes (Cherry, 2011). The most common genetic syndromes are familial adenomatous polyposis

(FAP) syndrome and hereditary non polyposis colorectal cancer (HNPCC) syndrome, also known as Lynch syndrome (Segelman, 2012). These

syndromes often lead to cancers that occur at younger age. Other less common syndrome and conditions include Gardener's syndrome, Turcot's syndrome, oldfield's syndrome Peutz-Jeghers disease, juvenile polyposis, and Cowden disease (Scott, 2003). Patients with inflammatory bowel disease, namely Crohn‟s disease CD or ulcerative colitis UC, have an increased risk of developing colorectal cancer. The risk of CRC in patients with

UC is related to the duration of symptoms and is estimated at 2% after 10 years, 8% after 20 years and 18% after 30 years (Eaden *et al.*, 2001).

2.6 COLORECTAL CARCINOGENESIS

Carcinogenesis is a process that involves a combination of mutations in oncogenes, tumour suppressor genes or epigenetic changes in DNA such as methylation. A genetic model that depicts the switch from healthy colonic epithelia through increasingly dysplastic adenoma to malignant cancer has been proposed. This model recognizes a number of vital oncogenes and tumour suppressor genes, which drives the adenoma to carcinoma transition (Vogelstein *et al.*, 1988). Adenomatous polyposis coli (APC) and the DNA mismatch repair (MMR) genes are some of the genes identified in this pathway (Fearon and Vogelstein, 1990; Groden *et al.*, 1991). For a cell to progress from adenoma to carcinoma, it has been proposed that as many as seven distinct genetic changes are required(Kinzler and Vogelstein, 1996).Of the genes identified to date, inactivation of the tumour suppressor genes APC and p53 and activation of the oncogene Kirsten-ras (Kras) are vital determinants of tumour initiation and progression (Fearon and Vogelstein,

1990). The p53 gene, localized on the short arm of chromosome 17, is mutated in up to 70% of colorectal cancers (Baker *et al.*, 1990).

2.6.1 Patterns of Genetic Instability in Colorectal Cancer

The development of colorectal cancer can be attributed to at least three patterns of instability. Typically, one type will predominate in a specific cancer (Cherry, 2011). Chromosome instability (CIN), which results in genetic deletions, duplications, and rearrangements, is one of the commonest patterns prominent in at least 50% of colorectal cancer cases. CRCs with CIN are distinguished by aneuploid tumor cells. Chromosome instability results in genetic defects in genes such as *APC, KRAS, TGF-β, PIK3CA, EGFR, BRAF, TP53* and other genes(Pino and Chung, 2010). A second pattern of instability in the development of colorectal cancer is microsatellite instability (MSI), which arises in about 15% of CRCs. Microsatellites are simple repetitive DNA sequences

1 to 6 base pairs in length that occur many times through the genome. Inactivation of the DNA mismatch repair (MMR) system brings about MSI which results in sequences that amass errors and become unusually long or short. In some instances, frame shift mutation in a gene, such as a tumour suppressor gene occurs. MSI accounts for more than 90% of the CRCs due to Lynch syndrome. An epigenetic change that requires the methylation of promoters of human genes especially within the CpG islands gene is the third pattern of instability seen in colorectal cancer. These epigenetic changes can lead to the silencing of certain tumour suppressor genes in CRC.(Cherry, 2011)

2.7 MANAGEMENT PRINCIPLES IN COLORECTAL CANCER

2.7.1 Clinical Presentation of Colorectal Cancer

The presentation of colorectal cancer is dependent on the site of tumour and extent of disease. Patients with early cancers are mostly asymptomatic and diagnosis is mostly made through population screening. Common symptoms associated with colorectal cancer include abdominal pain, rectal bleeding, altered bowel habit and involuntary weight loss (Thompson *et al.*, 2007). Proximal cancers rarely cause gross rectal bleeding because the blood tends to mix with the stool and degrade during colonic transit. This occult blood loss

means such patients often present with iron deficiency anaemia (Richards, 2014). In contrast, distal rectal tumours may present with fresh rectal bleeding, pelvic pain or tenesmus (Cappell, 2005). Tumours of the transverse colon and on the left side of the half usually invade the colonic wall in a ring-shaped pattern mainly producing symptoms of the obstructive nature (cramping pain after meal, and change in stool form, occasional sudden ileus development and even bowel perforation). Symptoms of tumours confined to the recto sigmoid portion are most often false and/or painful urge to defecate (tenesmus), narrow stool and hematochezia (Wactawski-Wende *et al.*, 2006). In a few cases, patients without recent symptoms present as an emergency with intestinal obstruction, fistulation or perforation (Bass *et al.*, 2009) (Up to 20–25% of colon cancer cases present as emergencies; in contrast, only a small number of rectal cancer cases present as emergencies (Sjo *et al.*, 2009; Gainant, 2012). In the case of rectal cancer, a palpable mass may be detected in digital rectal examination in over 50% of the cases (Avoranta, 2013).

2.7.2 Diagnosis of Colorectal Cancer

The diagnostic work up for colorectal cancer depends on the mode of presentation. If a patient presents as an emergency with symptoms and signs of peritonitis, a diagnosis of colorectal cancer may only be made incidentally during operative intervention. However, in the elective setting CRCs are usually diagnosed either by direct endoscopic visualization or by a radiological investigation (Barium enema, computerized tomography (CT) or CT colonography). For the majority of cases, histological confirmation is obtained through endoscopic biopsy. A histological diagnosis should be made and the disease fully staged before treatment is commenced.

2.7.3 Diagnostic modalities of Colorectal Cancer

There are several aspects of the colorectal cancer patient evaluation. First, a diagnosis must be established; second, the extent of the disease must be established; and third, the patient's

fitness for treatment must be determined (Rosman and Korsten, 2007). The patient with suspicion of colorectal cancer should undergo a complete physical examination which must include digital rectal examination. In a large number of patients, the digital rectal examination already shows a hard lump inside the rectum, bleeding on touch. Colonoscopy is a procedure for visualizing colonic mucosa and obtaining samples for pathohistological analysis (Thompson *et al.*, 2008). Colonoscopy is the gold standard for detecting colorectal cancer. If for technical difficulties colonoscopy cannot be done, double-contrast irrigography may be considered although only 70-80% of lesions are detected by this method. Virtual colonoscopy and MR colonoscopy are also more and more often used. For rectal cancer, in addition to colonoscopy, clinical examination (Digital palpation and rigid proctoscopy) is of the greatest importance for correctly interpreting modern imaging results. Flexible sigmoidoscopy, examining only the distal colon, is an alternative to colonoscopy and is effective in diagnosing the majority of colorectal tumours (Thompson *et al.*, 2008).

2.7.4 Treatment Strategies of Colorectal Cancer

Treatment for colorectal cancer depends on the extent of cancer spread. The only curative strategy in the treatment of colorectal cancer is, and so far remains, complete surgical resection. Despite the fact that approximately 70–80% of patients are eligible for curative surgical resection at the time of diagnosis (Abulafi and Williams, 1994), five year overall survival is only 50–60%(Gatta *et al.*, 1998; Kleihues and Stewart, 2003). Two out of three patients who undergo curative resection will experience local recurrence or distant metastases. In 85%, relapse is diagnosed within the first 2.5 years after surgery (Gill *et al.*, 2004). From diagnosis of metastatic disease, patients with advanced colorectal cancer have a median survival rate of only six months. During this period many patients will suffer from severe physical and psychological tumour associated symptoms that detract from

their quality of life (Seymour *et al.*, 1997). Therefore, systemic treatment of colorectal cancer seek to prevent local recurrence or metastatic disease after complete surgical resection—adjuvant therapy. Also, systemic treatment seeks to prolong survival, control symptoms, and improve quality of life in patients with metastatic disease— palliative therapy and lastly to increase relapse free survival through preoperative treatment—neoadjuvant therapy.

For invasive colorectal cancer, surgical resection of the tumour with adequate margins, plus removal of the regional lymph nodes, and restoration of the continuity of the gastrointestinal tract by anastomosis is the mainstay of treatment. A permanent colostomy is required for cases of low rectal cancer, while temporary defunctioning colostomy may protect against leakage of a low colorectal anastomosis (Mahmoud *et al.*, 2004). Treatment maybe directed at either cure or palliation, the latter being carried out to alleviate pain, obstruction and blood loss (Roberts, 2008).

Depending on the site and stage of the tumour, surgical treatment may be supplemented by adjuvant chemotherapy and/or radiotherapy (the latter is primarily indicated for cancer of the rectum). A number of chemotherapeutic options are available for the treatment of colorectal cancer, including fluorouracil, irinotecan, capecitabine, oxaliplatin, and cetuxima (Foubert *et al.*, 2014).

Adjuvant chemotherapy aims to destroy micro metastases following surgery, and neoadjuvant chemotherapy is aimed at reducing the tumour mass to allow surgery for either the primary tumour or distant metastases (usually to the liver or lungs) (Brkić and Grgić, 2006; Wactawski-Wende *et al.*, 2006).

Therapy of rectal cancer includes adjuvant chemotherapy combined with radiation therapy (Orbell and West, 2010). Despite huge advances in diagnostic and surgery and despite global and national programs of prevention, about 50% of colorectal carcinomas are

diagnosed in advanced stage **(Dobrila-Dintinjana *et al.*)** Advanced disease is largely refractory to conventional therapy and 5 years survival is still poor. Patients with advanced disease suffer from many stress symptoms (pain, vomiting, diarrhoea anorexiacachexia syndrome, and etc.) and the therapeutic goal for them is maintenance of quality of life (QoL) (Dobrila Dintinjana *et al.*, 2008). Many of those symptoms have implications for diagnostic and therapeutic procedures and can heavily disturb the process of chemo immunotherapy and radiotherapy (Dobrila Dintinjana *et al.*, 2008).

2.7.5 Laboratory abnormalities of Colorectal Cancer

Patients with suspected colon cancer should have routine blood tests including a hemogram with platelet count determination, serum electrolytes and glucose determination, evaluation of routine serum biochemical parameters of liver function (LFT), and a routine coagulation profile. About half of patients with colon cancer are anemic (Cappell and Goldberg, 1992). Anemia, however, is very common, so that only a small minority of patients with anemia have colon cancer. Iron deficiency anemia of undetermined etiology, however, warrants evaluation for colon cancer, particularly in the elderly (Ioannou *et al.*, 2002). Hypoalbuminemia is uncommon, but not rare, in colon cancer. It usually indicates poor nutritional status from advanced cancer (Spratt and Spjut, 1967). Routine serum biochemical parameters of liver function are usually within normal limits in patients with colon cancer. Abnormalities, particularly elevation of the alkaline phosphatase level, often indicate hepatic metastases (Jönsson *et al.*, 1983). The serum lactate dehydrogenase level may increase with colon cancer.

2.8 PROGNOSTIC FACTORS IN COLORECTAL CANCER

The prognosis of CRC differs widely among patients, and depends on a number of factors. Knowledge about prognosis is important for two main reasons; firstly, to identify patients in stage I-II at high risk of recurrence who might benefit of Adjuvant Treatment, and to

identify patients in stage III with low risk of recurrence, who should not be overtreated with Adjuvant Treatment. Secondly, to decide structure and intensity of follow up programs; this should be based on calculated risk of recurrence inthe individual patient to avoid unnecessary and costly examinations (Sjo, 2012). Currently, the gold standard of prognostication is the clinicopathological staging based on the TNM classification system. Stage of the disease at presentation has profound effect on the prognosis. However, prognosis also differs between patients within the same TNM stage, and many clinical, histopathological and biomolecular markers have potential impact on outcome (Sjo, 2012).

2.8.1 Tumour Factors and Colorectal Cancer Prognosis

A large number of tumour characteristics have been described as having prognostic value in colorectal cancer. These range from gross pathological features such as evidence of lymph node involvement right through to the presence or absence of specific molecular markers or genetic mutations. The following summarises those tumour factors reported to influence disease progression and survival in colorectal cancer.

2.8.1.1 Pathological stage as a prognostic factor in colorectal cancer

The pathological stage of the tumour is widely regarded as the single biggest determinant of outcome in colorectal cancer. The staging systems most commonly employed is the Dukes and TNM classifications

The staging of colorectal cancer quantifies the extent of disease and provides a framework for selecting the appropriate treatment. A number of staging systems exist but across the world the most common is the Tumour, Node Metastases (TNM) system produced by the American Joint Committee on Cancer (AJCC). Using this system, the stage of colorectal cancer has three components, the primary tumour (T), the regional lymph nodes (N) and the presence of metastatic disease (M), which are combined to form stage groupings (Fleming, 1997). In patients with newly diagnosed colorectal cancer, abdominal, pelvic

and chest CT is used to define the extent of local tumour extension and establish the presence or absence of regional lymphatic spread and distant metastases. Accurate staging of the rectum is important for decision-making regarding the provision of neo-adjuvant treatment in rectal cancer (Brown, 2014).

The depth of tumour invasion (pT), the lymph node metastasis (pN) and the presence of distant metastases (pM are independent prognostic factors. There is also a strong correlation between these three factors. Tumour (pT) stage: Advanced T-stage is associated with reduced long term outcome (Compton *et al.*, 2000b). Patients with stage II tumours (pT3-4, pN0, pM0) experience recurrence in about 20-30% of the cases (Andre *et al.*, 2006; Park *et al.*, 2008). Lymph node metastases (pN) : The presence of lymph node metastases is associated with reduced survival, and prognosis worsens with an increasing number of metastatic nodes (Chen and Bilchik, 2006). Tumours presenting with distant metastases have the poorest prognosis, which is obvious and well documented.

Table 2.2: TNM Staging of Colorectal Carcinoma

Stage	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1,T2	N0	M0
Stage II	T3,T4	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage III	Any T	N1,N2	M0
Stage IIIA	T1, T2	N1	M0
Stage IIIB	T3, T4	N1	M0
Stage IIIC	Any T	N2	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

Source:(O'Connell *et al.*, 2004)

2.8.1.2 Tumour site/ location as a prognostic factor in colorectal cancer

According to their macroscopic appearance, colorectal cancers are divided into exophytic, ulcerative and stenosing tumors (Dobrila-Dintinjana *et al.*). Exophytic tumors are most often located in the right half of the colon, while stenosing tumours are mostly found in its left half. The majority (up to 75%) of colorectal cancer occur within the descending colon, sigmoid colon and rectum, 15% of cases are located in the cecum and ascending colon, and only 10% in the transverse colon (Astin *et al.*, 2011; Cervera and Fléjou, 2011). Adenocarcinoma accounts for more than 95% of colorectal cancer cases. The prognosis of the disease is associated with the depth of tumour invasion through the colonic wall, peripheral lymph node involvement and absence or presence of distant metastases (Kyriakos, 1985; Arbman *et al.*, 1996). The site of the tumour has been investigated as a possible prognostic factor. Patients with colon cancer are considered to have a better survival than those with rectal cancer. In previous studies distal location and advanced stage of tumour were determined as independent prognostic factors for survival of patients with colorectal cancer. While the incidence of colon cancer is evenly distributed in both sexes; there are considerable differences in distribution according to sex for rectal cancer. For unknown reasons, rectal cancer occurs about 50% more often in men than in women(Nedrebø, 2013).

2.8.1.3 Tumour grade as a prognostic factor in colorectal cancer

Tumour grade describes how well the tumour is differentiated and is reported subjectively by the pathologist examining the specimen. Colorectal tumours are generally categorized as low grade (well or moderately differentiated) or high grade (poorly differentiated). A number of

60 studies have suggested that tumour grade is a prognostic factor in colorectal cancer.

For example in a study of over 100,000 patients, O'Connell and colleagues reported reduced survival in patients with high grade tumours compared to low grade tumours in stage I I– IV colon cancer (O'Connell *et al.*, 2004).

Lower differentiation grade is associated with poorer outcome. Similar results have been reported in rectal cancer with poorly differentiated tumours displaying an increased risk of local recurrence and reduced 5 year survival (McDermott *et al.*, 1984). However, there remains concern that the histological grading of tumours in this way is subject to significant inter -observer variability (Thomas *et al.*, 1983). There is evidence that tumour grade influences survival in colorectal cancer although its effect appears to be small and is not likely to apply to stage I disease.

2.8.1.4 Histologic subtype as a prognostic factor in colorectal cancer

The prognosis of CRC is most favourable in adenocarcinomas and worst in small cell carcinomas (Singh *et al.*, 1987; Compton *et al.*, 2000a). In adenocarcinomas, tumours with extracellular mucin in more than 50% of the tumour volume are classified as mucinous. These are most prevalent in men and in the right colon, and patients with mucinous tumours have reduced survival (Papadopoulos *et al.*, 2004).

2.8.2 Clinical Prognostic Factors of Colorectal Cancer

2.8.2.1 Emergency presentation as a prognostic factor in colorectal cancer

Postoperative mortality (10-25%) (Garcia-Valdecasas *et al.*, 1991; Anderson *et al.*, 1992), and morbidity (>50%) are increased in patients who have undergone emergency operation (Öhman, 1982; Jestin *et al.*, 2005). Since the early eighties, patients operated for obstruction have been reported with poor long term survival, (Öhman, 1982; Umpleby *et al.*, 1984; Chapuis *et al.*, 1985), In a German multi-centre study from 1994 (Hermanek *et al.*, 1994) overall survival was 33% and 51%, respectively in emergency versus elective patients. Patients admitted emergently have more advanced tumours and consequently the

rate of curative resection is lower,(Garcia-Valdecasas *et al.*, 1991; McArdle and Hole, 2004) However, even after curative resection five year survival is lower than following elective operation (Mella *et al.*, 1997; Jestin *et al.*, 2005). In 2006, McArdle et al. reported poor outcome in emergency patients presenting with the symptoms blood loss, obstruction or perforation (McArdle *et al.*, 2006).

2.8.2.2 Age as a prognostic factor in colorectal cancer

The incidence of CRC increases with age, as well as the morbidity and mortality from other causes than cancer. Overall survival is therefore decreased in older patients with CRC. The impact of age on cancer specific survival or relative survival varies in reported studies. An independent impact of age has been reported by some (Chapuis *et al.*, 1985; Angell-Andersen *et al.*, 2004), whereas others describe no impact on survival or local recurrence (Wiggers *et al.*, 1988b; Jagoditsch *et al.*, 2000).

2.8.2.3 Symptom duration predicts prognosis in colorectal cancer

In 1981, McDermott et al. reported that patients with symptom duration less than 3 months had lower Cancer Specific Survival (CSS) than the other patients (McDermott *et al.*, 1981). Several other series during the eighties showed significantly shorter duration of symptoms in more advanced stages (Stubbs and Long, 1986) and better prognosis with long duration of symptoms 138, 144, (Pescatori *et al.*, 1982). In the last two decades, few studies have included this variable, most likely because of the difficulties in defining and registration symptom duration.

2.8.3 Molecular markers of colorectal cancer

A large number of molecular markers have been proposed as prognostic indicators in colorectal cancer. The majority of these molecules are confined to experimental studies

and only a small number, such as carcinoembryonic antigen and K-ras, are ever used in clinical practice (Dickinson *et al.*, 2015).

2.8.3.1 Carcinoembryonic antigen (CEA) as a prognostic marker in colorectal cancer

CEA has been proposed for roles in both the diagnosis and prognosis of colorectal cancer. In terms of the prognostic value of CEA in patients with known colorectal cancer, the evidence has been conflicting. A number of studies have shown that patients with high preoperative concentration of CEA have a worse outcome than those with low levels (Grande *et al.*, 2008) Preoperative elevation of CEA, and the degree of elevation, is associated with increased risk of recurrence and decreased long term survival (Wiggers *et al.*, 1988a; Harrison *et al.*, 1997) with the highest level of evidence (Compton *et al.*, 2000b) Also when analysing subsets of patients (stage I/II), preoperative CEA is reported to be a significant prognostic factor (Harrison *et al.*, 1997). Following potentially curative resection, CEA may rise if recurrence occur, and the reported sensitivity and specificity are 64% and 91%, respectively (Tan *et al.*, 2009). Even when normal preoperative, it will rise in at least 50% of patients with recurrent disease (Grossmann *et al.*, 2007), making it useful in routine follow up programmes. Currently, CEA is most often measured postoperatively as a means of detecting disease recurrence or monitoring response to treatment (Hurwitz *et al.*, 2004).

2.9 QUALITY OF LIFE ASSESMENT IN COLORECTAL CANCR PATIENTS

2.9.1 Quality of life: definition and assessment

QoL is a, dynamic, subjective and centered on patient construct, comprising physical, functional, emotional, and social/family well-being (Marventano *et al.*, 2013) Therefore, QoL is an important outcome for evaluating the full impact of the disease on the individuals, their family and their community (Marventano *et al.*, 2013). Quality of life,

being a subjective, patient-rated concept, is difficult to quantify. To assess QoL the use of patient-reported questionnaires has become a standard practice.

2.9.2 Relationship of QoL to colorectal cancer survival

QoL is also known to be an independent predictor of survival and response to therapy in cancer patients (Maisey *et al.*, 2002; Roychowdhury *et al.*, 2003). Assessment of QoL in patients with cancer may improve our understanding of how cancer and its therapy influence the patients' lives and how to adapt appropriate treatment strategies (Arndt *et al.*, 2004). Quality of life is generally measured by structured questionnaires that can be scored and quantified (DeCosse and Cennerazzo, 1997). There are now two quality of life assessment tools available for colorectal cancer patients: the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) (Ward *et al.*, 1999) and the European Organization for Research and Treatment of Cancer Quality of Life Module-Colorectal Cancer EORTC QLQ-CR 29 (Palmer *et al.*, 2008). Both of these tools could be used for colorectal cancer patient with a range of disease stages and different treatments. EORTC QLQ-CR29 is designed to be used together with EORTC QLQ-C30 which is reliable and valid measure of the quality of life of cancer patients in multicultural clinical research settings (Aaronson *et al.*, 1993a)

Broun *et al.*, (2011) found that a 10-point increase in baseline global QoL scores (using EORTC QLQ-C30) was associated with a 7% decreased risk of death (Braun *et al.*, 2011). Moreover, a recent 18-month trial suggested that baseline QoL influenced CRC patient's survival (Grosso *et al.*, 2012).

CHAPTER THREE

3.0 METHODOLOGY

3.1 STUDY DESIGN

The study was a retrospective cross sectional one where all colorectal cancer cases presenting to the Surgical and Oncological Department of Komfo Anokye Teaching Hospital (KATH) were reviewed. The medical records of all CRC patients managed at the Hospital from 2009 to 2015 were retrieved from the Medical records unit of the Surgery and Oncology Department. The records were analysed for information on demographics, clinical and pathological variables including anatomical distribution, clinical presentations, tumour stage based on the TNM, histological type, grade of tumour, symptom duration, date of diagnosis, duration of clinical features, tumour location, the type of surgery performed, endoscopy findings, laboratory findings, histological findings and surgical notes were extracted. The type of treatment including chemotherapy and radiotherapy, and follow-ups were also analysed. Survival analysis was carried out, with survival defined as the time between the date of diagnosis and the date of last follow-up or death. Quality of life and general wellbeing of subjects were assessed using the EORTC QLQ 30 standard questionnaire for cancer patients and colorectal cancer specific model EORTC QLQ-CR29.

3.2 STUDY SITE/SETTING

The study was conducted at the Komfo Anokye Teaching Hospital at the surgical and oncological Units. Komfo Anokye Teaching Hospital (KATH) is a tertiary referral teaching hospital located in Kumasi, the Regional capital of the Ashanti Region in Ghana with a total projected population of 4,780,380 **(Ghana Statistical Service, 2010).** It is the second largest Hospital in Ghana.

3.3 TARGETED POPULATION OF STUDY

The subjects of this study included all clinically and histologically confirmed colorectal cancer patients who presented to Komfo Anokye Teaching Hospital (KATH) during the study period from 2009 to 2015

3.4 SAMPLE SIZE

In all, a total of 221 cases were identified from both the surgery and oncology units. The surgery unit recorded 113 cases whereas 108 cases were identified from the oncology unit.

3.5 INCLUSION CRITERIA

a. Patients who consented to participate in the study.
b. All colorectal cancer cases seen at KATH in 2009 to 2015 were considered eligible for inclusion.
c. Colorectal cancer cases with complete clinical examination, indicating the presence of malignant tumors in the large bowel.

3.6 EXCLUSION CRITERIA

- Patients with large bowel conditions other than CRC and histopathologically confirmed non-malignant tumours were excluded.

3.7 QUALITY OF LIFE (QOL) QUESTIONNAIRE

The validated QoL instruments included in this study were the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and the EORTC QLQ-CR29.

The QLQ-C30 is general cancer instrument which consists of 30-items that evaluate global QOL, 5 functional scales, (physical, role, cognitive, emotional, and social), and 9 symptom scales (fatigue, nausea/vomiting, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhoea, and financial impact) (Aaronson *et al.*, 1993b). The EORTC QLQ-

CR29 contains 29-items that evaluate 3 functional QOL items (body image, anxiety, weight) and 14 symptom items (urinary frequency, blood and mucus in stool, stool frequency, urinary incontinence, dysuria, abdominal pain, buttock pain, bloated feeling, dry mouth, hair loss, trouble with taste, flatulence, fecal incontinence, sore skin) that are associated with colorectal cancer and its treatment (Whistance *et al.*, 2009). There are different scales for patients with or without stoma, and different questions to evaluate sexual function for men and women (Whistance *et al.*, 2009). For both QLQ-C30 and QLQ-CR29, the responses were scored on a Likert scale of 4 response categories. Higher functional and global QOL domain scores indicated increased function and better QOL, and higher symptom scores represent worse symptoms. The time frame for all scales in the questionnaire was in reference to the last/previous week.

3.7.1 Procedure for data collection

From the retrospective data, all patients who fell within the study period were contacted using their respective phone numbers or that of their relatives. The EORTC questionnaire was filled through telephone interviews with the study subjects. The objectives of the study were explained to them and informed consent was sought from the subjects. They were made to know that their participation was entirely voluntary.

3.7.2 Scoring of the EORTC Questionnaires

Using EORTC scoring methodology, the responses to the QOL questionnaires were linearly transformed to produce a semi continuous 0 to 100 score.

3.8 ETHICAL CONSIDERATION

Ethical clearance for commencement of the study was sought from the Committee on Human Research, Publication and Ethics (CHRPE), Kwame Nkrumah University of Science and Technology, School of Medical Sciences (KNUST-SMS) & Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana.

3.9 DATA ANALYSIS AND MANAGEMENT

Data was entered in Excel spread sheet for window and analysed using SPSS version 22 and Stata version 12. Data for continuous variables between two groups were compared with t-test and presented as mean ± SD standard deviation. Categorical variable were presented as frequency (n) and percentage (%). Significance was defined as a P value of <0.05. Incidence rate was calculate using the GSS 2010 population data for Kumasi. Survival analysis was carried out with survival defined as the time between the date of first diagnosis and the date of last follow-up or death. Survival data was obtained by telephone interview of the patients or in the case of the deceased, their relatives. Univariate and Multivariate Cox regression analysis was used to determine predictor variables that were associated with outcome. Difference between survival was tested using log rank test.The overall survival as well as the survival rate at different stages of the disease was estimated using the Kaplan Meier method. The primary efficacy endpoint was Overall Survival among the patients.

CHAPTER FOUR

4.0 RESULTS

From this retrospective study, 221 cases of colorectal cancer were identified. The mean age of the study participants was 54 ± 16.8 which ranged from 16 to 90 years. Fifty 50 (22.6%) of the participants were less than 40 years and the majority 58 (26.2%) fell within the age group of 51-60. The majority of the participants 127(57.5%) were females and more than half 133 60% were in the informal occupation sector. Most of them were married 140(63.30%) and Christians 187(84.60%). For the lifestyle characteristics, the prevalence of comorbidities was 55(24.89%). Eighteen 18 (8.14%) of the participants were diabetics, 44(19.91%) were hypertensive and 11(4.07%) had both DM/HPT. A few of the participants 9 (4.07%) had other comorbidities such as asthma, HIV, hepatitis B, sickle cell disease and

fibroid. Of the 221 cases, 16(7.24%) had family history of cancer, 21(9.50%) were alcoholics, 11(4.98%) were smokers and 9(4.07%) were both alcoholics and smokers.

Table 4.1: Socio-demographic and lifestyle characteristics of study participants

Variable	Frequency(n (%)	Variable	Frequency n (%)
Age (Mean, SD)	**54 ± 16.8**	**Presence of Comorbidities**	
≤40	50(22.60%)	Yes	55(24.89%)
41-50	31(14.00%)	No	166(75.11%)
51-60	58(26.20%)	**Family History**	
61-70	43(19.50%)	Yes	16(7.24%)
>70	39(17.60%)	No	205(92.76%)
Gender		**Diabetes**	
Male	94(42.50%)	Yes	18(8.14%)
Female	127(57.50%)	No	203(91.86%)
Occupation		**Hypertension**	
Formal	29(13.10%)	Yes	44(19.91%)
Informal	133(60.20%)	No	177(80.09%)
Student	11(5.00%)	**Both DM/HPT**	11(4.98%)
Retired	32(14.50%)	**Others**	9(4.07%)
Unemployed	16(7.20%)	**Alcoholic**	
Marital Status		Yes	21(9.50%)
Single	27(12.20%)	No	200(90.50%)
Married	140(63.30%)	**Smoker**	
Divorced	21(9.50%)	Yes	11(4.98%)
Widowed	33(14.90%)	No	210(95.02%)
Religion		**Both Alcool/Smoker**	9(4.07%)
Christian	187(84.60%)		
Muslim	32(14.50%)		
Traditional	2(0.90%)		

Table 4.2 shows the clinical parameters of the study participants. The year 2015 had the highest frequency (44) of colorectal cancer diagnosis at KATH (19.90%). The duration of symptoms ranged from > 1month to 7 years with a median duration of 6 months with majority of the participants presenting with >6month duration. The major clinical symptoms presented were weight loss (44.80%), bleeding per rectum (39.82%), abdominal

pain (38.91%) constipation (31.67%) Hematochezia (28.96%) change in bowel habit (20.81%), anorexia (20.36%), and anaemia (15.84%) and the patients presented with more than one symptom as show Table 4.2. Out of the 221 patients, 145 (65.61%) underwent surgical procedures for colorectal cancer. Of these 145 patients, 96 (66.21%) were operated electively and the remaining 49 (33.79%) were operated on an emergency basis. The most frequent type of surgical procedure performed was colostomy 63(43.45%) followed by right hemi colectomy 26 (17.93%). One hundred and three 103(46.61%) of the patients received chemotherapy, 55 (24.89%) had radiotherapy and 43(19.46%) had both chemo and radiotherapy. The patients' anthropometrics measurement showed that majority 90 (40.72%) had normal weight with a mean weight of 21.36± 5.77. At the end of the study, 33 (14.93%) were alive, 103(46.61%) were dead and 85(38.46%) were lost to follow up.

Table 4.2: Clinical parameters of the study participant

Variable	Frequency n (%)	Variable	Frequency n (%)
Year of Diagnosis		**Chemotherapy**	
2009	19(8.60%)	Yes	103(46.61%)
2010	24(10.90%)	No	118(53.39%)
2011	27(12.20%)	**Radiotherapy**	
2012	30(13.60%)	Yes	55(24.89%)
2013	43(19.50%)	No	166(75.11%)
2014	34(15.40%)	**Both Chemo and Radio therapy**	43(19.46%)
2015	44(19.90%)	**Types of surgical operation Performed**	
Duration of Symptoms (months)	Median 6(3-12)	Right Hemi colectomy	26(17.93%)
<6	95(42.99%)	Left Hemi colectomy	3(2.07%)
6 to 12	85(38.46%)	Sigmoid colectomy	14(9.66%)
>12	41(18.55%)	Transverse Colectomy	1(0.07%)
Clinical presentations		Low Anterior Resection (LAR)	16(11.03%)
Abdominal Pain	86(38.91%)	Abdominal Peritoneal Resection (APR)	6(4.14%)
Constipation	70(31.67%)	Colostomy	63(43.45%)
Anorexia	45(20.36%)	Hartman's Procedure	13(8.97%)
Weight loss	99(44.80%)	Others	3(2.07%)
Change in bowel habit	46(20.81%)	**Anthropometric Measures**	
Bleeding per rectum	88(39.82%)	Body Mass Index(BMI) (X^2**± SD)**	**21.36± 5.77**
Hematochezia	64(28.96%)	Underweight	77(34.84%)
Anaemia	35(15.84%)	Normal	90(40.72%)
Treatment Modalities		Overweight	32(14.48%)
Surgery		Obese	22(9.95%)
Yes	145(65.61%)	**Patient Status**	
No	76(34.39%)	Alive	33(14.93%)
Nature of operation		Dead	103(46.61%)
Emergency	49(33.79%)	Lost to follow up	85(38.46%)
Elective	96(66.21%)		

Majority of the patients presented with rectal cancer cases 108(48.87%), followed by colon 75(33.94%), and 7(3.17%) had tumours in more than one site. The rectum 96(43.40%) was the most frequent site for colorectal cancer, followed by the caecum 35 (15.80%) and sigmoid colon 22(10.00%). Microscopically, adenocarcinoma was the most common histopathological tumour in 151(68.33%) patients and majority of the tumours were moderately differentiated 104 (47.10%). According to the TNM staging of cancer, majority

of the patients 89(40.27%) were identified as being in late stage (TNM Stage III) and only 13 (5.98%) were in stage 1 as shown in Table 4.3.

Table 4.3: Pathological features of colorectal cancer at KATH

Variable	Frequency n (%)	Variable	Frequency n (%)
Tumour Location		**Histological Type of Cancers**	
Colon	75(33.94%)	Adenocarcinoma	151(68.33%)
Rectal	108(48.87%)	Mucinous Adenocarcinoma	26(11.76%)
Anorectal	18(8.14%)	Signet Ring Cell carcinoma	8(3.62%)
Anal	13(5.88%)	Squamous Cell Carcinoma	14(6.33%)
Multiple sites	7(3.17%)	Neuroendocrine Carcinoma	3(1.36%)
Histological Grade		Non Hodgkin Lymphoma	1(0.45%)
Well differentiated	51(23.1%)	Rhabdomyosarcoma	1(0.45%)
Moderately differentiated	104(47.10%)	Others	4(1.81%)
Poorly differentiated	25(11.30%)	Not Stated/Unknown	13(5.88%)
Undifferentiated	24(10.90%)	**Anatomical Site of Tumour**	
unknown	17(7.70%)	Caecum	35(15.80%)
Tumour Stage		Ascending Colon	10(4.50%)
stage I	13(5.98%)	Transverse Colon	1(0.50%)
stage II	64(28.96%)	Descending Colon	3(1.40%)
Stage III	89(40.27%)	Sigmoid Colon	22(10.00%)
Stage IV	36(16.29%)	Rectosigmoid	12(5.40%)
Blank	19(8.59%)	Rectum	96(43.40%)
		Anorectum	18(8.10%)
		Anus	13(5.90%)
		More than 1 site	11(5.00%)

Age and gender distribution among the colorectal cancer patients showed that majority 59(26.7%) fell within the age group of 50-59 years with 36(61.0%) being females and 23(39.0%) being males.

Table 4.4: Age and Gender distribution of colorectal cancers

Variable	N (%)	Males (%)	Females (%)
0-9	0 (0%)	0	0
10-19	8 (3.6%)	3(37.5%)	5(62.5%)
20-29	11(5.0%)	7(63.6%)	4(36.4%)

30-39	27(12.2%)	12(44.4%)	15(55.6%)
40-49	26(11.8%)	11(42.3%)	15(57.7%)
50-59	59 (26.7%)	23(39.0%)	36(61.0%)
60-69	46(20.8%)	20(43.5%)	26(56.5%)
70-79	34(15.4%)	14(41.2%)	20(58.8%)
80-89	9(4.1%)	4(44.4%)	5(55.6%)
90-99	1(0.5%)	0(0%)	1(100%)

Figure 1 shows the incidence rate of colorectal cancer at KATH from 2009 to 2015. The annual incidence rate of colorectal cancer increased steadily from 2009 to 2012 (0.4, 0.5, 0.56 and 0.63 per 100,000 population). From 2012, there was a sharp increase incidence followed by a sharp decrease in incidence in 2014 to 0.71 per 100,000 populations. Then in 2015 the incidence increased to 0.92 per 100,000 populations. The overall crude annual incidence of colorectal cancer at KATH was 4.62 per 100,000 populations.

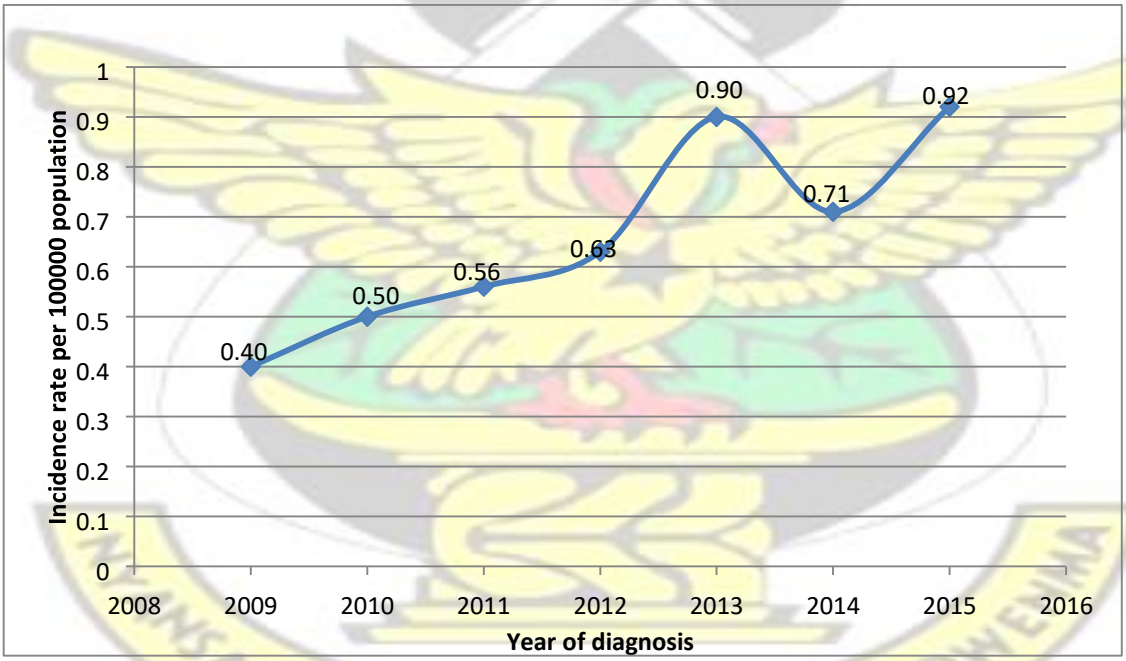

Figure 4.1: Annual incidence rate of colorectal cancer at KATH from 2009 to 2015

Table 4.5 shows the yearly crude incidence rate of colorectal cancer between males and females. Overall crude incidence rate was higher in females (5.15 per 100,000 populations per annum) than in males (4.06 per 100,000 populations).

Table 4.5: Yearly Incidence Rate of colorectal cancer between males and females at KATH

Year	Frequency	Crude Incidence Males	Crude Incidence Females	Crude Incidence Both sexes
2009	19	0.35	0.45	0.4
2010	24	0.35	0.65	0.5
2011	27	0.3	0.81	0.56
2012	30	0.52	0.73	0.63
2013	43	0.73	1.06	0.9
2014	34	0.78	0.65	0.71
2015	44	1.04	0.81	0.92
Overall	**221**	**4.06**	**5.15**	**4.62**

Table 4.6 shows the age specific incidence and age standardized incidence rate of colorectal cancer at KATH. The overall crude incidence was 4.62 per 100,000 populations per annum. Females had an incidence of 5.15 and that of males was 4.06 per 100,000 populations. Within the age groupings, females within the age group of 60-69 and males within the age group70-79 had the highest incidence of (36.89) and (33.46) respectively. For both sexes, the highest incidence (34.42) was within the age groups of 60-69 and 70-79. The age specific standardized incidence rate using WHO world population as standard was 7.93 per 100,000 population

Table 4.6: Age specific incidence and age standardised incidence rate of colorectal cancer at KATH.

Age Grouping(years)	Age specific crude incidence rate per 100, 000 population			Age standardised incidence rate
	Male	Female	Both sexes	Both sexes
0-9	0	0	0	0.00
10-19	0.55	0.91	0.73	0.12
20-29	1.7	0.84	1.24	0.20
30-39	4.08	4.6	4.36	0.64
40-49	5.52	7.09	6.33	0.80
50-59	18.81	26.65	22.92	2.27
60-69	31.65	36.89	34.42	2.30
70-79	33.46	35.09	34.4	1.28
80-89	26.42	19.66	22.18	0.30
90-99	0	3.93	7.35	0.01
Overall	**4.06**	**5.15**	**4.62**	**7.93**

Table 4.7 shows the clinical symptoms of colorectal cancer and their association with tumour location. Abdominal pain, constipation, anorexia, change in bowel habit, bleeding per rectum and anaemia had statistically significant associations ($p< 0.05$) in both univariate and multivariate analysis. Abdominal pain had significant increased odds of association (OR=4.61 and OR=8.58) with tumours located in the colon in both univariate and multivariate analysis respectively. Weight loss and passage of bloody stool had no significant association ($p> 0.05$) with specific tumour locations.

Table 4.7: Association of clinical presentation with tumour located in the colon

	Univariate analysis			Multivariate analysis		
Symptoms	**OR**	**95% CI**	**P Value**	**OR**	**95% CI** (3.701	**P Value**
Abdominal Pain	4.61	(2.54 - 8.35)	**0.0001**	8.58	- 19.876)	**0.0001**
constipation	0.51	(0.27 - 0.97)	**0.041**	0.35	(0.149 - 0.803)	**0.013**
Anorexia	0.35	(0.155 - 0.801)	**0.013**	0.26	(0.086 - 0.784)	**0.017**
Weight loss	0.58	(0.326 - 1.025)	0.061	0.85	(0.359 - 2.007)	0.71
Change in bowel habit	0.34	(0.149 - 0 .771)	**0.01**	0.35	(0.133 - 0.901)	**0.03**
Bleeding per rectum	0.13	(0.064-0.281)	**0.0001**	0.16	(0.071- 0.381)	**0.0001**
Passage of bloody stool	0.55	(0.289- 1.062)	0.075	0.83	(0.376 -1.853)	0.656
Anaemia	0.35	(0.139- 0.887)	**0.027**	0.24	(0.071 - 0.790)	**0.019**

Table 4.8 shows the association of clinical presentations with late stage tumours. Of all the symptoms, weight loss had the highest odds (1.775 and 2.077) of association with late stage tumours in both univariate and multivariate analysis and the association was statistically significant ($p=0.039$). Anorexia (1.104), Bleeding per rectum (1.141), Passage of bloody stool (1.287**)** and anemia (1.438), though were not statistically significant, had increased odds of association in univariate analysis with passage of bloody stool and anemia having increasing odds in multivariate analysis as well. **Table 4.8: Association of clinical Presentation with Late Stage Tumour**

	Univariate Analysis			Multivariate analysis		
Symptoms	**OR**	**95% CI**	**P Value**	**OR**	**95% CI**	**P Value**

Abdominal Pain	0.978	(0.548-1.744)	0.939	0.831	(0.44-1.57)	0.569
Constipation	0.961	(0.537-1.805)	0.985	0.897	(0.469- 1.716)	0.743
Anorexia	**1.104**	(0.544-2.241)	0.784	0.755	(0.33-1.729)	0.507
Weight loss	**1.775**	(1.001-3.150)	0.05	**2.077**	(1.036-4.164)	**0.039**
Change in bowel habit	0.838	(0.415-1.694)	0.623	0.75	(0.361- 1.562)	0.443
Bleeding per rectum	**1.141**	(0.639-2.036)	0.656	0.943	(0.504- 1.763)	0.853
Passage of bloody stool	**1.287**	(0.693-2.389)	0.424	**1.274**	(0.657- 2.471)	0.473
Anaemia	**1.438**	(0.677-3.054)	0.344	**1.204**	(0.536- 2.702)	0.653

Figure 4.2 shows the overall survival curve for colorectal cancer patients at KATH. From the graph 1, 2, 3, 4 and 5 years survival rates were 64%, 40%, 21% 16% and 16% respectively. The median survival time was 15 months with a confidence interval of (11.79-18.21)

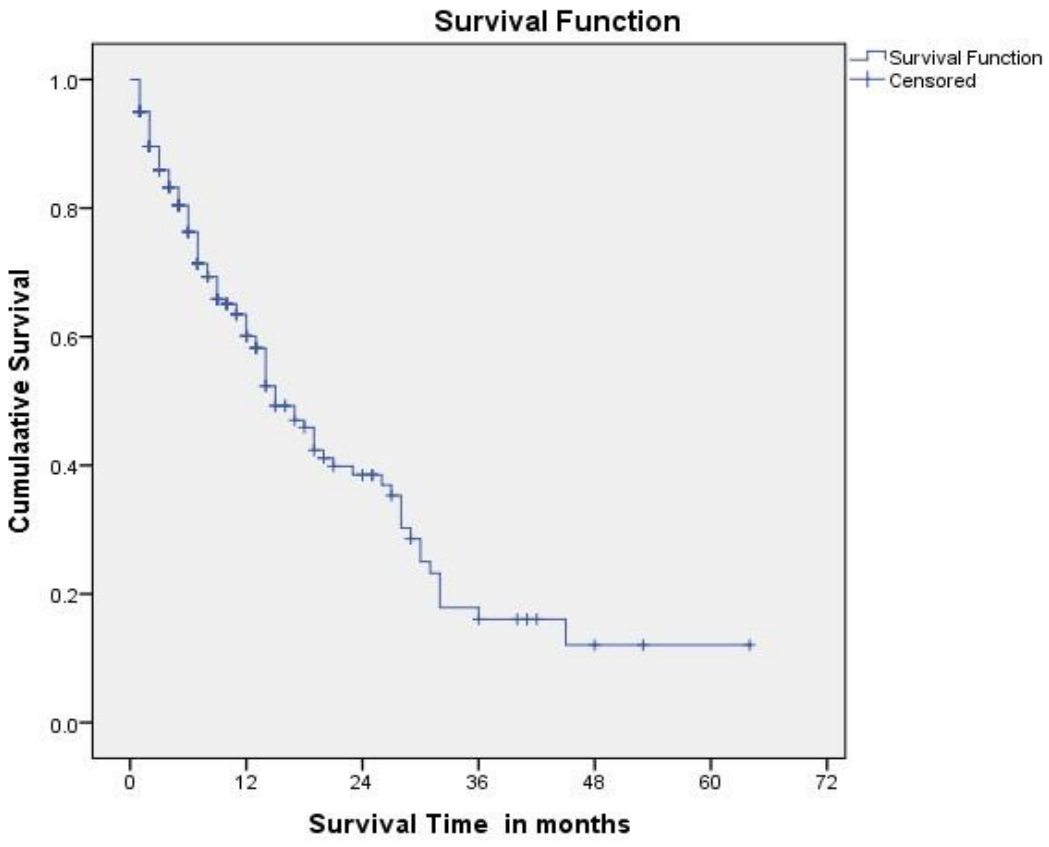

Figure 4.2: Overall 5 years survival function curve in colorectal cancer patients at KATH.

Figure 4.3 shows the cumulative survival of colorectal cancer based on the cancer stage. From the graph, the survival rate for stage I was 90%, stage II (34%), stage III (12%) and stage 4 (0%). The difference in survival among the different cancer stages using log rank test was statistically significant (p=0.0001)

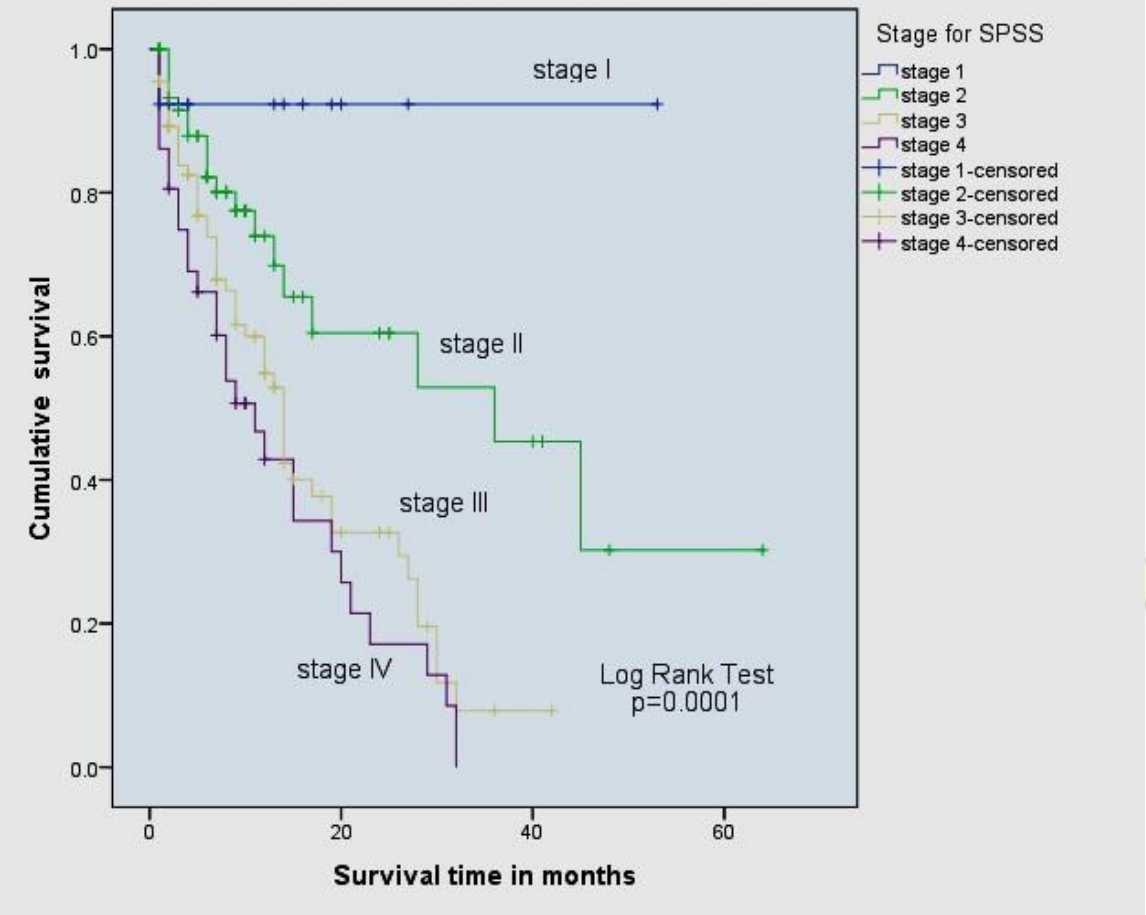

Figure 4.3: Survival Curves for different stages of colorectal cancer.

There was no statistically significant association between the socio-demographics such as age, gender and marital status with survival (p >0.05). With the lifestyle characteristics, family history was significantly associated with survival (p=0.036). Other lifestyle parameters such as presence of comorbidities, Hypertension, diabetes, alcohol intake and smoking showed no statistically significant association with survival (p >0.05) as shown in Table 4.9.

Table 4.9: Association of socio-demographic and lifestyle characteristics with survival using log rank test

Variable	Median(OS)	P Value
Age		0.241
< 40	28	
40-49	17	
50-59	14	
60-69	14	
≥70	20	
Gender		0.996
Female	15	
Male	14	
Marital Status		0.464
Married	28	
Single	14	
Divorced	19	
Widowed	15	
Family History		**0.036**
No	15	
Yes	--	
Presence of Comorbidities		0.25
No	15	
Yes	15	
Hypertension		0.232
No	17	
Yes	14	
Diabetes		0.588
No	15	
Yes	28	
Alcoholic		0.717
No	15	
Yes	21	
Smoked No		
	15	0.696
Yes	13	

Table 4.10 shows the association of clinical and pathological parameters with colorectal cancer survival. Among the clinical parameters, chemotherapy as a treatment modality was significantly related to survival (p=0.0001). The median survival time of patient who underwent chemotherapy was higher (30 months) compared to those without chemotherapy (11) Table 4.10a. Body mass index (BMI) was also significantly associated

with survival (P= 0.036) with underweight patients having the least median survival time (11). For the pathological parameters, there were significant differences in the stage of tumour, lymph node metastasis and distance metastasis with survival ($p< 0.05$). Late staged tumours had low median survival time (14, 11months) compared to early staged tumours (36). Other parameters such as histological grade, depth of tumour invasion and tumour location were statistically not associated with survival.

Table 4.10a: Association of clinical and pathological parameters with survival using log rank test

Variable	Median(OS)	P Value
Duration of Symptoms		0.567
< 6	19	
6 to 12	14	
> 12	14	
Surgery		0.64
No	15	
Yes	14	
Nature of Operation		0.741
Emergency	14	
Elective	19	
Chemotherapy		**0.0001**
No	11	
Yes	30	
Radiotherapy		0.402
No	14	
Yes	17	
Both Chemo and Radiotherapy		0.587
No	15	

Yes	15	

Table 4.10b: Association of clinical and pathological parameters with survival using log rank test

Variable	Median (OS)	**P value**
BM1 Categories		**0.036**
Underweight	11	
Normal	18	
Overweight	26	
Obese	23	
Pathological Tumour Location		0.405
Colon	14	
Rectum	17	
Anorectum	18	
Anal	12	
More than one site	19	
Histological Grade		0.332
Well differentiated	14	
Moderately differentiated	15	
Poorly differentiated	30	
Undifferentiated	18	
Tumour Stage		**0.0001**
Stage 1 Stage II	36	
Stage III	14	
Stage IV	11	
Depth of Tumour Invasion		0.07
T2	28	
T3	14	

T4	14	
Lymph Node Metastasis		**0.0001**
N0	36	
N1	12	
N2	15	
Distant Metastasis		**0.0001**
M0	19	
M1	11	

OS= Overall Survival

Table 4.11 shows the association of socio-demographic and lifestyle characteristics with survival. Using cox regression analysis, family history was the only variable that had statistically significant association with survival in both univariate and multivariate analysis ($p<0.05$). Age, gender, marital status and the lifestyle characteristics were statistically not associated with survival ($p>0.05$). As age increases, the odds of surviving decreases as shown in the hazard ratios but was statistically not significant. Male gender (HR: 1.00(0.67-1.49), being widowed (HR: 1.37(0.80- 2.33), presence of comorbidities (HR: 1.27(0.84-1.94) and having hypertension (HR: 1.31 (0.83- 2.08) had higher hazard ratios in both univariate and multivariate analysis, meaning the odds of survival in these parameters are low but statistically not significant.

Table 4.11a: Association of socio-demographics and lifestyle characteristics with survival using Cox regression analysis

	Univariate Analysis			Multivariate Analysis		
Variable	**HR**	**95% CI**	**P Value**	**HR**	**95% CI**	**P Value**
Age <						
40	1 (ref)					
40-49	0.51	(0.20-1.30)	0.16	0.49	(0.18-1.34)	0.159
50-59	**1.28**	(0.71-2.33)	0.424	1.27	(0.63-2.54)	0.52
60-69	**1.30**	(0.71-2.37)	0.399	1.36	(0.63-2.92)	0.465
≥70	**1.16**	(0.61-2.21)	0.655	0.97	(0.42-2.20)	0.909

Gender						
Female	1 (ref)					
Male	1.00	(0.67-1.49)	0.996	1.11	(0.71-1.74)	0.626
Marital Status						
Married	1 (ref)					
Single	0.91	(0.46-1.84)	0.799	0.94	(0.40-2.21)	0.877
Divorced	0.75	(0.37-1.51)	0.423	0.90	(0.43-1.89)	0.781
Widowed	**1.37**	(0.80- 2.33)	0.25	**1.27**	(0.68-2.37)	0.439
Family History						
No	1 (ref)					
Yes	0.37	(0.14 -0.99)	**0.049**	3.44	(0.09- 0.88)	**0.029**

Table 4.11b: Association of socio-demographics and lifestyle characteristics with survival using Cox regression analysis

	Univariate Analysis			**Multivariate Analysis**		
Variable	**HR**	**95% CI**	**P Value**	**HR**	**95% CI**	**P Value**
Presence of Comorbidities						
No	1 (ref)					
Yes	**1.27**	(0.84- 1.94)	0.262	**1.29**	(0.74-2.26)	0.734
Hypertension						
No	1 (ref)					
Yes	**1.31**	(0.83- 2.08)	0.244	**1.11**	(0.45-2.75)	0.734
Diabetes No	1 (ref)					
Yes	**1.17**	(0.65-2.10)	0.597	0.74	(0.35-1.55)	0.512
Alcoholic						
No	1 (ref)					
Yes	0.88	(0.42-1.81)	0.722	0.65	(0.25- 1.69)	0.401
Smoked No	1 (ref)					
Yes	0.84	(0.34-2.06)	0.703	1.40	(0.42-4.69)	0.607

In both univariate and multivariate analysis, clinical parameters in the cox regression model showed, chemotherapy (p=0.0001), and being underweight (p< 0.05) as well as having both chemo and radiotherapy (p=0.042) in only multivariate analysis as significant prognostic factors in colorectal cancer survival. Chemotherapy was associated with high odds of survival (HR: 0.38 (0.25- 0.57) whereas having chemo radiotherapy (HR:

3.63(1.05-12.59) and being underweight (HR: 1.74(1.11-2.72) were associated with decrease odds of surviving. Duration of symptoms, surgery, nature of operation and having radiotherapy were statistically not associated with survival (p> 0.05) as shown in table 4.12

Table 4.12: Association of Clinical parameters with survival using Cox regression analysis

	Univariate Analysis			Multivariate Analysis		
Variable	**HR**	**95% CI**	**P Value**	**HR**	**95% CI**	**P Value**
Duration of Symptoms						
< 6	1 (ref)					
6 to 12	1.18	(0.671- 2.057)	0.573	1.23	(0.78-1.93)	0.38
> 12	1.34	(0.759- 2.379)	0.311	1.23	(0.62-2.26)	0.491
Surgery						
No	1 (ref)					
Yes	1.11	(0.72 - 1.69)	0.648	3.82	(0.16-91.51)	0.408
Nature of Operation						
Emergency	0.99	(0.63-1.58)	0.985	3.41	(0.14-82.49)	0.451
Elective	1 (ref)					
Chemotherapy No	1 (ref)					
Yes	0.38	(0.25- 0.57)	**0.0001**	0.23	(0.13-0.41)	**<0.0001**
Radiotherapy No	1 (ref)					
Yes	0.82	(0.51- 1.32)	0.413	0.56	(0.20-1.60)	0.282
Both Chemo and Radiotherapy No	1 (ref)					
Yes	0.87	(0.52-1.46)	0.596	3.63	(1.05-12.59)	**0.042**
BM1 Categories						
Normal	1 (ref)					
Underweight	1.74	(1.11-2.72)	**0.016**	1.78	(1.11-2.86)	**0.017**
Overweight	0.95	(0.51-1.75)	0.86	0.93	(0.48-1.78)	0.817
Obese	0.94	(0.46- 1.89)	0.852	0.95	(0.46-1.98)	0.894

Table 4.13 shows the association of pathological parameters with survival using cox regression analysis. Stage of tumour, depth of tumour invasion, lymph node metastasis and distant metastasis were significant prognostic factors in univariate analysis (P< 0.05). Late stage tumours (Stage III (HR: 9.41(1.29- 68.58), p=0.027 and stage IV (HR: 12.89 (1.74-95.24), P=0.012) were associated with worse survival. Similarly T stage (T3 (HR: 3.42(1.05-11.11) P=0.041 and T4 (HR: 3.51(1.09-11.33) P=0.036), N stage (N1 (HR: 2.65(1.58-4.43), P=0.0001 and N2 (HR: 2.42(1.24-4.73), P=0.009) and M1 (HR: 12.16(1.37-3.40) P=0.001) were associated with lower odds of survival. Other parameters such as tumour location and histological grade were statistically not significant.

Table 4.13 Association of pathological parameters with survival using Cox regression analysis

	Univariate Analysis			Multivariate Analysis		
Variable	**HR**	**95% CI**	**P Value**	**HR**	**95% CI**	**P Value**
Tumour Location						
Colon	1 ref					
Rectum	0.99	(0.64 -1.53)	0.965	0.86	(0.50- 1.48)	0.592
Anorectum	0.41	(0.14 -1.14)	0.088	0.40	(0.12-1.37)	0.144
Anal	1.12	(0.49 -2.5)	0.79	2.15	(0.69-6.62)	0.183
More than one site	1.28	(0.49-3.28)	0.612	0.76	(0.22-2.64)	0.66
Histological Grade						
Well differentiated	1 ref					
Moderately differentiated	1.62	(0.94 -2.80)	0.085	1.33	(0.70-2.52)	0.377
Poorly differentiated	1.58	(0.77-3.55)	0.229	1.01	(0.35-2.91)	0.986
Undifferentiated	1.66	(0.75-3.33)	0.193	1.56	(0.63-3.85)	0.338
Tumour Stage						
Stage 1	1 ref					
Stage II	4.12	(0.55-30.84)	0.168	2.00	(0.16- 25.79)	0.595
Stage III	9.41	(1.29- 68.58)	**0.027**	4.97	(0.28-87.64)	0.274
Stage IV	12.89	(1.74-95.24)	**0.012**	13.34	(0.49-359.01)	0.123
Depth of Tumour Invasion						
T2	1 ref					
T3	3.42	(1.05-11.11)	**0.041**	1.67	(0.37-7.61)	0.508
T4	3.51	(1.09-11.33)	**0.036**	1.93	(0.43 -8.59)	0.389

Lymph Node Metastasis						
N0	1 ref					
N1	2.65	(1.58-4.43)	**0.0001**	1.01	(0.25-4.08)	0.991
N2	2.42	(1.24-4.73)	**0.009**	0.71	(0.17- 2.95)	0.641
Distant Metastasis						
M0	1 ref					
M1	2.16	(1.37- 3.40)	**0.001**	0.49	(0.11-2.18)	0.352

Table 4.14 shows the association between Carcinoembryonic antigen (CEA) levels and liver function test with survival. The levels of CEA and all parameters considered under the liver function test were statistically not significant in both univariate and multivariate analysis ($p>0.05$) hence no association with survival. In both Univariate and multivariate analysis, level of survival was lower in relation to elevated levels of ALT (HR: 1.76 (0.61-5.08), Total protein (HR: 2.69 (0.35-20.33), and Globulin (HR: 1.08 (0.51-2.29) but their association with survival was statistically not significant ($p>0.05$). Also the hazard ratios were higher in low level of albumin (HR: 1.06 (0.52-2.16), elevated levels of CEA (HR: 1.04 (0.53-2.04), AST (HR: 1.33 (0.47-3.79), and ALP (HR: 1.07(0.52-1.99) meaning the odds of survival was lower in these parameters in univariate analysis.

Table 4.14: Association between CEA and Liver function with Survival using Cox regression analysis

	Univariate Analysis			Multivariate Analysis		
Variable	**HR**	**95% CI**	**P Value**	**HR**	**95% CI**	**P Value**
CEA						
Normal	1 ref					
Elevated	1.04	(0.53-2.04)	0.919	0.81	(0.39-1.71)	0.586
AST Normal						
	1 ref					
Elevated	1.33	(0.47-3.79)	0.596	0.36	(0.02-7.06)	0.505
ALT Normal						
	1 ref					
Elevated	1.76	(0.61-5.08)	0.293	5.97	(0.29-121.04)	0.244
ALP						
Normal	1 ref					
Elevated	1.07	(0.52-1.99)	0.968	0.81	(0.37-1.74)	0.583
GGT						
Normal	1 ref					
Elevated	0.94	(0.29-3.08)	0.917	0.65	(0.14-2.92)	0.571
Total protein						
Normal	1 ref					
Low	0.99	(0.41-2.41)	0.991	1.54	(0.42-5.57)	0.512
Elevated	2.69	(0.35-20.33)	0.339	2.76	(0.31-24.36)	0.36
Albumin						
Normal	1 ref					
Low	1.06	(0.52-2.16)	0.88	0.97	(0.33-2.88)	0.956
Globulin						
Normal	1 ref					
Low	0.29	(0.04- 2.14)	0.223	0.14	(0.01-1.49)	0.104
Elevated	1.08	(0.51-2.29)	0.831	1.27	(0.43-3.69)	0.665

HR; Harzard Ratio, CEA; carcinoembryonic antigen, AST; Aspartate aminotransferase, ALT; Alanine aminotransferase, ALP; Alkaline phosphatase, GGT; Gama-Glutamyl transferase

Table 4.15 shows the association between haematological parameters and colorectal cancer survival. Low levels of RBC (HR: 59.4(6.28-262.77), P<0.001) was significantly associated with worse survival in multivariate analysis. Also low MCV was significantly associated with worse survival in both univariate (HR: 2.15 (1.08-4.28), P=0.029) and multivariate analysis (HR: 57.1(4.19-376.19) P=0.002). Lastly, there was a statistically significant association between RDW-SD and survival (p= 0.0001) in multivariate analysis. Low RDW-SD was associated with worse prognosis in colorectal cancer survival

(HR: 74.78 (5.51-401.32). All other parameters showed no statistically significant association with survival (p>0.05).

Table 4.15a: Haematological parameters as prognostic factors in colorectal cancer using Cox regression analysis

	Univariate Analysis			Multivariate Analysis		
Variable	**HR**	**95% CI**	**P Value**	**HR**	**95% CI**	**P Value**
WBC						
Normal	ref 1					
Elevated	1.91	(0.78-4.67)	0.157	0.15	(0.02-1.0)	0.05
RBC						
Normal	ref 1					
Low	1.52	(0.68-3.43)	0.31	59.4	(6.28-262.77)	**<0.001**
Elevated	0.67	(0.18-2.55)	0.556	2.15	(0.26-17.10)	0.478
HgB						
Normal	ref 1					
Low	1.76	(0.76-4.10)	0.189	2.86	(0.27-29.74)	0.379
Elevated	1.31	(0.27-6.37)	0.736	0.21	(0.006-7.06)	0.383
HCT						
Normal	ref 1					
low	1.85	(0.72-4.79)	0.203	0.08	(0.005-1.32)	0.078
MCV						
Normal	ref 1					
Low	2.15	(1.08-4.28)	**0.029**	57.1	(4.19-376.19)	**0.002**
Elevated	--	----------	-------	------	----------	--------
MCH						
Normal	ref 1					
Low	1.24	(0.54-2.283)	0.614	1.06	(0.24-4.73)	0.938
Elevated	0.41	(0.12-1.19)	0.100	0.39	(0.06-2.50)	0.326

WBC; White blood cells, RBC; Red blood cells, HgB; Haemoglobin, HCT; Haematocrit MCV; Mean Corpuscular Volume, MCH; Mean Corpuscular hemoglobin

Table 4.15b: Haematological parameters as prognostic factors in colorectal cancer using Cox regression analysis

	Univariate Analysis			**Multivariate Analysis**		
Variable	HR	**95% CI**	**P Value**	**HR**	**95% CI**	**P Value**
MCHC						
Normal	ref 1					
Low	1.84	(0.70- 4.82)	0.217	1.35	(0.12-15.43)	0.811
Elevated	0.73	(0.17-3.17)	0.672	0.99	(0.07-14.47)	0.997
PLT						
Normal	ref 1					

Low	0.82	(0.23-2.36)	0.709	1.11	(0.18-6.69)	0.91
Elevated	1.02	(0.39-2.68)	0.961	0.32	(0.03-3.19)	0.338
RDW-SD						
Normal	ref 1					
Low	1.5	(0.44-5.07)	0.515	74.78	(5.51-401.32	**0.0001**
Elevated	1.51	(0.72-3.16)	0.279	0.48	(0.09-2.51)	0.382
PWD						
Normal	ref 1					
Low	1.33	(0.50-3.54)	0.561	0.4	(0.07-2.41)	0.332
Elevated	0.61	(0.23-1.60)	0.316	0.62	(0.12-3.25)	0.576
MPV						
Normal	ref 1					
Low	1.17	(0.52-2.61)	0.701	0.8	(0.17-3.9)	0.786
Elevated	0.61	(0.14-2.69)	0.517	0.76	(0.13-4.64)	0.768
P-LCR						
Normal	ref 1					
Low	1.15	(0.40-3.27)	0.717	0.52	(0.03-10.32)	0.668
Elevated	----------	----------	---------	----------	----------	--------
PCT						
Normal	ref 1					
Low	1	(0.33-3.00)	0.995	4.33	(0.73-25.56)	0.105
Elevated	0.855	(0.42-1.76)	0.67	2.29	(0.45-11.65)	0.318

MCHC; Mean Corpuscular Hemoglobin, PLT; Platelet Count, RDW-SD; Red Blood Cell distribution Width, PWD; Platelet Distribution Width, MPV; Mean Platelet Volume, P-LCR; Platelet large cell ratio, PCT; Plateletcrit.

Table 4.15c: Haematological parameters as prognostic factors in colorectal cancer using Cox regression analysis

	Univariate	Analysis		Multivariate	Analysis	
Variable	HR	95%CL	p value	HR	95%CL	P value
Neut%						
Normal	ref 1					
Low	------	----------	------	-------	----------	-------
Elevated	1.11	(0.39-3.19)	0.848	2.29	(0.44-11.85)	0.32
Lymph%						
Normal	ref 1					
Low	1.54	(0.76-3.15)	0.231	1.64	(0.47-5.68)	0.433
Elevated	3.26	(0.93-11.35)	0.064	13.8	(1.28-148.67)	**0.03**
Mono%						
Normal	ref 1					
Low	------	----------	---------	---------	----------	-------
Elevated	1.5	(0.76-2.94)	0.241	1.69	(0.43-6.72)	0.455
Eosin%						
Normal	ref 1					

Low	1.93	(0.81-4.62)	0.136	2.81	(0.43-8.46)	0.283
Elevated	9.74	(2.11-44.86)	**0.003**	1.65	(0.03-80.244)	0.801
Baso%						
Normal	ref 1					
Elevated	1.41	(0.66-3.04)	0.373	2.82	(0.75-10.59)	0.124

Neut: Neutrophil, Lymph; Lymphocyte, Mono; Monocyte, Eosin; Eosinophil, Baso; Basophil

Table 4.16 shows the overall quality of life of colorectal cancer patients and a comparison between colon and rectal cancer patients using the EORTC QLQ-C30. The global health status which assess the overall quality of life had a mean score of 64.15±24.58 hence the overall quality of life among the patients was moderate. Colon cancer patients (72.8±21.7) had a better quality of life compared to rectal cancer patients (56.9±20.7) and the difference in the quality of life was statistically significant (p=0.039). Overall, the function scales assessment was good among the patients with physical function having the highest scores of 84.61±24.58 and emotional function having the least score 66.36±26.32. Between colon and rectal cancer patients, there was a statistically significant difference in the cognitive function (p=0.0134) with colon cancer patients (88.9±13.5) having better cognitive function than rectal cancer patients (75.0±16.3). With the exception of financial difficulty 33.0(0.0-100), pain 17.0(0.0-33.0) and fatigue (22.0(0.0-33.0), the symptom scale assessment was good among the patients. Comparison of the symptoms score between colon and rectal cancer cases showed a significant difference in constipation (p=0.0337) with rectal cancer patients experiencing worse symptoms than colon cancer patients. Overall few patients experienced financial difficulty (33.0(0.0-100).

Table 4.16: Comparison of Quality of life between Colon and Rectal cancer patients using the EORTC QLQ C30

Variable	Overall Mean ± SD	Rectal Mean± SD)	Colon Mean± SD)	P value
Global Health Status/QOL	64.15±24.58	56.9±20.7	72.8±21.7	**0.0399**
C30 Functional Scales				

Physical functioning	84.61 ±24.58	79.6±30.2	90.6±14.3	0.2058
Role functioning	81.82 ±25.41	77.8±29.6	86.7±19.1	0.3247
Emotional functioning	66.36 ±26.32	58.3±29.1	76.1±19.2	0.0516
Cognitive functioning	81.30 ±16.45	75.0±16.3	88.9±13.5	**0.0134**
Social functioning	79.27 ± 26.66	75.9±26.9	83.3±26.7	0.4332
C30 Symptom Scales	Median IQR			
Fatigue	22.0(0.0-33.0)	8.25(0.0-22)	0.0(0.0-11)	0.1887
Nausea/Vomiting	0.0(0.0- 17.0)	17(0.0-21)	0.0(0.0-17)	0.1496
Pain	17.0(0.0-33.0)	17(12.8-50)	17(0.0-33)	0.8362
Dyspnea	0.0(0.0-33.0)	0.0(0.0-33)	0.0(0.0-33)	0.9673
Insomnia	0.0(0.0-33.0)	0.0(0.0-67)	0.0(0.0-0)	0.1763
Appetite loss	0.0(0.0-33.0)	0.0(0.0-67)	0.0(0.0-33)	0.3151
Constipation	0.0(0.0-33.0)	16.5(0.0-67)	0.0(0.0-0)	**0.0337**
Diarrhea	0.0(0.0-33.0)	0.0(0.0-75.3)	0.0(0.0-0.0)	0.0684
Financial difficulties	33.0(0.0-100)	33(0.0-100)	33(0.0-100)	0.7514

Scores ranges from 0 to 100. In the functional scale higher score = good quality of life, lower score = poor In symptom scale, higher score=poor quality of life, lower =good, SD= standard deviation

Table 4.17 shows the quality of life between colon and rectal cancer patients using the EORTC CR 29 Colorectal cancer specific questionnaire. In the functional scale, body image had the highest score (85.25± 22.35) and a comparison between colon and rectal cancer patients showed a significant difference (p=0.0261). In the symptom scale, flatulence was the most common symptom with the highest score (33(0.0-67.0). Overall, patients had good symptom score. With the exception of bloating pain which was statistically significant (p=0.0427) between colon and rectal cancer patients, all other symptom parameters were statistically not significant. Among the cancer patients, 7 (21.21%) had stoma and majority of the rectal cancer patients had stoma care problems (67(16.5-67).

Table 4.17: EORTC CR 29 Colorectal cancer specific questionnaire for assessment of quality of life between colon and rectal cancer patients

Variable	Overall Mean ± SD	Rectal Mean ± SD	Colon Mean ± SD	P value
CR29 Functional Scale				
Body Image	85.25± 22.35	78.4±26.1	93.4±13.7	**0.0261**

Anxiety	67(33-100)	67(33-100)	67(33-100)	0.6165
Weight	76.82± 30.63)	76±29.8	77.8±32.6	0.8696
CR29 Symptom Scale				
Urinary Frequency	17(0.0-58.50)	8.50(0.0-54.3)	17(0.0-67.0)	0.5949
Blood and Mucus in stool	0.0(0.0-0.0)	0.0(0.0-4.25)	0.0(0.0-0)	0.6068
Stool Frequency	17(0.0-33.0)	17(0.0-37.3)	17(0-33.0)	0.4339
Urinary Incontinence	0.0(0.0-33.0)	0.0(0.0-33)	0.0(0-33)	0.7063
Dysuria	0.0(0.0-0.0)	0.0(0.0-33)	0.0(0.0 -0)	0.4953
Abdominal Pain	0.0(0.0-67.0)	16.5(0.0-100)	0.0(0-33)	0.4128
Buttock Pain	0.0(0.0-33.0)	0.0(0.0-33)	0.0(0.0-33)	0.2124
Bloating Pain	0.0(0.0-33.0)	0.0(0.0-0.0)	0.0(0.0-33)	**0.0427**
Dry Mouth	0.0(0.0-16.50)	0.0(0.0-8.25)	0.0(0.0-33)	0.6146
Hair Loss	0.0(0.0-33.0)	0.0(0.0-8.25)	0.0(0.0-67)	0.5856
Taste	0.0(0.0-33.0)	0.0(0.0-33)	0.0(0.0-33)	0.6343
Flatulence	33(0.0-67.0)	33(0.0-67)	33(0.0-67)	0.8388
Faecal Incontinence	0.0(0.0-0.0)	0.0(0.0-8.25)	0.0(0.0-0.0)	0.999
Sore Skin	0.0(0.0-33.0)	0.0(0.0-33)	0.0(0.0-0.0)	0.3855
Embarrassment	0.0(0.0-33.0)	0.0(0.0-41.5)	0.0(0.0-33)	0.2299
Presence of Stoma				0.4134
Yes	7 (21.21%)	5(71.43%)	2(28.57%)	
No	26 (78.79%)	13(50%)	13(50%)	
Stoma Care Problems	33(0.0-67.0)	67(16.5-67)	0.0(0.0-24.8)	0.111

Scores ranges from 0 to 100. In the functional scale higher score = good quality of life, lower score = poor
In symptom scale, higher score=poor quality of life, lower, SD= standard deviation

CHAPTER FIVE

5.0 DISCCUSION

5.1 CLINICAL PATTERNS AND PRESENTATIONS OF COLORECTAL CANCER AT KATH

The clinicopathological patterns of colorectal cancer have been reported to vary in different geographical regions. In the western world, colorectal cancer is a disease of older patients, with most being diagnosed after the age of 50 years (Center *et al.*, 2009a) whereas colorectal cancer in African population tends to present at a young age with advanced aggressive disease and associated poor prognosis (Sule and Mandong, 1999). In this retrospective study, we review the clinicopathological patterns and presentations of colorectal cancer at Komfo Anokye Teaching Hospital. The mean age of participants (54 ±16.8) years (Table 4.1) reported in this study is similar to findings in other African studies

which reported mean ages of 53 year in Nigeria (Akinola and Arigbabu, 1994) , 58.8 years in Tunisia (Missaoui *et al.*, 2010), 58 years in Ghana (Dakubo *et al.*, 2014), 50 years in Central sudan(Taha *et al.*, 2015) and 50.8 years in Burundi(Ntagirabiri *et al.*, 2016). Most studies in Africa show average ages between 43 and 46 years (Abou-Zeid *et al.*, 2002; Irabor and Adedeji, 2009; Chalya *et al.*, 2013b). However, the mean age described in this study is younger than the age described in most developed countries (Koo *et al.*, 2008; Altekruse *et al.*, 2010). In the United States, from 2003-2007, the median age at diagnosis was 70 years (Koo *et al.*, 2008). The peak age of presentation in this study was in the age range 51-60 years (26.2%) which coincides with a retrospective study by Abdalla *et al.* (2007) and Irabor *et al.* (2014).

The probability of being diagnosed with colorectal cancer increases after 40 years of age, rises progressively from 40, and sharply after age 50 (Food, 2007; Ries *et al.*, 2008). Studies have shown that, more than 90% of colorectal cancer cases occur in people aged 50 or older (Ries *et al.*, 2008). In Africa, colorectal cancer mostly affect the young (<40 years). Colorectal cancer incidence among the young (age less than 40 years) in this study was 22% (Table 4.1) which is similar to findings in Egypt by Gado *et al.* (2014) where 25% of CRC occurred in patients aged less than 40 years. Higher incidence was reported by Abdalla *et al.* (2007) in Khartoum hospital where 35.4% of patients were 40 years or less. In Saudi Arabia and Iran, incidence in patients below 40 years ranges from 17-36% (Al-Ahwal and Al-Ghamdi, 2005; Pahlavan and Kanthan, 2006) whereas in the western countries, the incidence is about 2-6% (Cascinu *et al.*, 1996; Cusack *et al.*, 1996; Mitry *et al.*, 2001). All these data reflects that, colorectal cancer in Middle East and Africa is more common in the young than in Western countries. Colorectal cancer in the younger age group has been shown to present a diagnostic and therapeutic problem and prognosis tends to be less favorable (Sule and Mandong, 1999). The increasing incidence of CRC in the young in low-risk communities necessitates family screening for genetic mutations

(HNPCC) since genetic factors may play an important role in the development of this disease. This makes early detection and management an important measure in order to reduce incidence and mortality. On the other hand, it may be related to improvements in medical interventions and or to dietary factors since the young Africans tend to live more Westernized life-style.

Contrary to prevoius studies in Ghana (Dakubo *et al.*, 2010a; Dakubo *et al.*, 2014), and other african countries (Ojo *et al.*, 1991; Boytchev *et al.*, 1999; Seleye-Fubara and Gbobo, 2004) the gender prevalence of CRC in our study (Table 4.1) was in favour of females, with male: female ratio of 1:1.3 as compared to other studies which reported higher prevalence in males. Globally, incidence rates are considerably higher in males than in females (Siegel *et al.*, 2012). This has been attributed to the higher adoption of certain risk behaviors associated with colorectal cancer such as: smoking, heavy alcohol consumption and obesity in men (Center *et al.*, 2009a; Missaoui *et al.*, 2010). The decreased incidence of colorectal cancer in women and female animals has been linked to a role of female hormones. In vitro evidence has demonstrated that estrogen regulates the cell growth of colonic mucosa and inhibits cell proliferation of colonic tumors through binding to estrogen receptors (Issa *et al.*, 1994; Campbell-Thompson *et al.*, 2001). The current findings of higher prevalence of CRC in females could be attributed to high partronage of hospital attendance by females compared to males in our local setting since females are more conscoius of their health and hence report to hospital for the least discomfort they expericence.

The prevalence of comorbidities among colorectal cancer patients in this current study was 24.9% (Table 4.1). A retrospective study by Van Leersum *et al.* (2013) in south of Netherlands recorded an increase prevalence rate from 47% to 62%. Other findings from Van Leersum studies indicated that hypertension and cardiovascular diseases were most

prevalent comorbidities and this supports results from our current study where hypertension (19.9%) was the most prevalent comorbidity among the CRC patients.

Risk of developing colorectal cancer is high for patients with a positive family history or underlying predisposing condition like ulcerative colitis. In this study, a family history of colorectal cancer was reported in 16 (7.2%) of cases, a figure which is higher than 5.4% and 4.3% reported by (Chalya *et al.*, 2013b) in Tunisia and (Azadeh *et al.*, 2007) in Iran but similar to findings by Kumar *et al.* (2015) in Oman who recorded 8.6%. This suggests that genetic factors may be playing an important role in the development of this disease in our country.

The majority of patients presented with symptoms of weight loss 44.8%, bleeding per rectum 39.8% and abdominal pain 38.9%. In a study by (Dakubo *et al.*, 2010a) in Accra, Ghana, bleeding per rectum was the commonest symptom which concurs with studies in other developing countries (Yawe *et al.*, 2007). According to Giordano and Jatoi (2004), the prevalence of weight loss is higher in patients with late stage cancers. Tisdale (2009) explained that tumor and host factors are responsible for the progressive attrophy of adipose tissue and skeletal muscle that results in weight loss in about 50% cancer of patients. The overall mortality rate in the present study was 46.6%, a figure which is higher than 6.1% reported by Dakubo *et al.* (2010a) in Ghana and 10.% reported by Chalya *et al.* (2013a) The high mortality rate in our study may be attributed to the fact that most patients presented with late staged cancers.

Findings from this study (Table 4.3) also shows that the major anatomical site of CRC was the rectum (43.4%), followed by the caecum (15.8%) and sigmoid colon (10%). This trend is supported by findings from a systematic review by (Graham *et al.*, 2012) who found that the major anatomical site of CRC in sub saharan Africa was the rectum (in 46% of cases), followed by the caecum (17%).This trend is also similar to findings in a

retrospective study by Abdalla *et al.* (2007) in Sudan but contrasts with the right-side preponderance (proximal shift) reported (Guraya and Eltinay, 2006) in Saudi Arabia and in developed countries (Takada *et al.*, 2002). Majority of the patients presented with late stage cancers (Stage III, 40.3%). Adenocarcinoma was the most common histological type (68.3%) with moderately differenciatiated tumours accounting for (47.8%) of the cases. These findings are in agreement with studies by (Missaoui *et al.*, 2010; Chalya *et al.*, 2013a) who reported similar histopathological patterns. Many reasons have been ascribed to the late presentation of patients with CRC. In our local settings, the reason could be that warning symptoms may be taken for granted by many patients who may not relate them to serious disease and so be ignored. Other reasons could be ignorance with misconception on the cause of CRC, lack of awareness of the disease, low standard of education, insufficient diagnostic and therapeutic equipment and lack of screening programs in this region (Chalya *et al.*, 2013a).

5.2 INCIDENCE RATE OF COLORECTAL CANCER

Cancers of the colon and rectum are the 5th leading cancers diagnosed in West Africa after cervical, breast, prostate, and liver cancers, with an age_standardized incidence rate of 4.9 per 100,000 persons per year (GLOBOCAN, 2008). There is a marked variation in the incidence of colorectal cancer worldwide, with western countries having a high rate compared to Africa (Center *et al.*, 2009a; Jemal *et al.*, 2011). However, a rising incidence of colorectal cancer has been reported from various parts of Africa which were considered low incidence areas (Adesanya and da Rocha-Afodu, 2000; Seleye-Fubara and Gbobo, 2004). Findings from this study show that(Table 4.5), the overall crude annual incidence of colorectal cancer at KATH was 4.62 per 100000 populations. Overall crude incidence rate was higher in females (5.15 per 100,000 populations per annum) than in males (4.06 per 100,000 populations). For both sexes, the highest incidence (34.42) was within the age groups of 60-69 and 70-79. The age specific standardized incidence rate using WHO world

population as standard was 7.93 per 100,000 populations. These findings are comparatively lower than results by Dakubo *et al.* (2010a) in Accra, Ghana where the number of new cases seen annually was 32.8 in a population of about 3,000,000 18. The crude incidence rate was 11.18 per 100,000 population in both sexes. According to a study by Laryea *et al.* (2014), on cancer incidence in Ghana, using the population based cancer registry in Kumasi, the estimates for crude incidence and age standardized incidence of colorectal cancer was in the range of 0.1 to 0.3 per 100,000. Compared to our current estimates, there have been a drastic increase in the incidence of colorectal cancer over the years, although not as high as reported in the developed countries. This could be due to adoptation of western diets, which are mostly high in fat and less in fiber, resulting in obesity which is a risk factor for CRC. Incidence rates reported in other developing countries are similar to our current findings. The age standardized incidence rate for colorectal cancer in United Arab

Emirates was 6.8/ 100,000 person per year, which is similar to our current estimate. Previous studies have shown incidence reports of 1.7 cases per 100,000 person per year in some Western African countries to 51.7 cases per 100,000 person per year in North America (Al-Shamsi *et al.*, 2011).

5.3 ASSOCIATION OF CLINICAL PRESENTATION WITH TUMOUR LOCATION AND STAGE

In this hospital based retrospective study, we were able to prove that there are significant differences in the clinical presentations of the patients depending on tumour location and stage. Finding from this study (Table 4.7) shows that, abdominal pain is significantly associated with colon cancers where as constipation, anorexia, change in bowel habit, bleeding per rectum and anaemia are more prevalent in non colon cancers (rectum, anorectum and anal cancers) in both univariate and multivariate analysis. This agrees with results from (Peedikayil *et al.*, 2009) in India who reported bleeding per rectum and

constipation to be associted with distal CRC and abdominal pain with proximal CRC. Studies by (Vanek *et al.*, 1986; Alexiusdottir *et al.*, 2012), reported that, colon cancers were associated with higher incidence of anaemia.

A study by Ben-Ishay *et al.* (2013) indicated that patients in the late TNM stages presented with significantly more weight loss (P= 0.04) . This is supported by findings from this current study which showed that, weight loss was significantly associated with late TNM stage cancers (Table 4.8). Other studies have also reported change in bowel habit and abdominal pain to be associated with late TNM stage tumours, and bleeding per rectum with early TNM stage (Cappell and Goldberg, 1992; Alexiusdottir *et al.*, 2012), however this trend was not observed in this current study.

5.4 SOCIAL, CLINICAL AND PATHOLOGICAL PARAMETERS AS PROGNOSTIC FACTORS IN COLORECTAL CANCER.

Globally,colorectal cancer survival has improved in the last few decades, due partly to earlier detection and more effective treatments (Faivre-Finn *et al.*, 2002). However, CRC is still one of the major causes of cancer deaths in developing countries. In developing Asian countries, the five-year survival rates range from 28% to 42% (McMichael *et al.*, 1980; Sankaranarayanan *et al.*, 2011) compared with more than 60% in the US, Japan and Switzerland (Gelboin, 1980; Vargas and Thompson, 2012). In this study, the overall five years survival rates was 16%,(Figure 4.2) which is extremely lower than the typically reported survival rates in developed countries. The 1, 2, 3 and 4 years survival rates were 64%, 40%, 21% and 16% respectively (Figure 4.1). A population-based study by Sankaranarayanan *et al.* (2011) on Cancer survival in Africa, Asia, and Central America reported that, survival for colorectal (large bowel) cancer varied from 4% in the Gambia to 60 % in Seoul, Republic of Korea. The survival figures were less than 8% in the sub-Saharan African countries of the Gambia and Uganda and less than 30% in Harare, Zimbabwe, all of which have poorly-developed cancer health care infrastructure and

limited availability of and accessibility to curative treatments for most patients. In China, the overall 5-year post-operative survival rate was 60.8% in colorectal cancer patients. Other research studies from Iran have indicated 5-year survival rates of colorectal cancer 27.2% and 61% (Mehrabani *et al.*, 2012).

CRC survival largely depends upon the stage of the disease at diagnosis. Five-year survival rates for CRC typically range from 90% for localized cancers, 70% for regional cancers, to 10% for distant metastatic cancers (Haggar and Boushey, 2009). In this study, the overall survival rates based on CRC stage were 90%, for stage I, 34% for stage II, 12% for stage III and 0% for stage 4 (Figure 4.3). The difference in survival among the different cancer stages using log rank test was statistically significant (p=0.0001). Al-Ahwal *et al.* (2013) in Saudi Arabia recorded 63.3% for patients with localized disease, 50.2% for those with regional disease, and 14.7% for patients with metastatic disease. The lower survival rates in this study can be due to lack of cancerpreventing and screening programs, accessibility to specialized centers, and lack of efficient diagnostic techniques to improve diagnosis, prognosis, and hence survival.

Prognosis in patients with CRC is determined by the tumour itself as well as certain patient-related factors. Knowing the prognostic factors could therefore help the physicians to improve prognosis (Alici *et al.*, 2006). Findings from this present study indicates that, socio-demographics such as age, gender and marital status were statistically not associated with survival. Family history was significantly associated with improved survival (p=0.036) in both the log rank test and the cox regression model (Table 4.9 and Table 4.11). This is in agreement with findings from (Zell *et al.*, 2008) who reported that CRC cases with family history of the disease have improved overall survival compared with sporadic CRC cases. Patient gender has been extensively evaluated although in the majority of studies this was of no significance in predicting survival independently of other factors

(Moghimi-Dehkordi *et al.*, 2008; Rosenberg *et al.*, 2008; Saha *et al.*, 2011) and thus, in line with findings from our current study. In literature, results concerning patients age are even more diverse. In a number of studies (Gharbi *et al.*, 2010; Zhang *et al.*, 2010; Moghimi-Dehkordi and Safaee, 2012), this parameter was not found to be an independent prognostic variable. However, in other reports (Moghimi-Dehkordi *et al.*, 2008; Rosenberg *et al.*, 2008; Mehrkhani *et al.*, 2009), age did seem to play a role, predicting a poorer survival rate for older patients than younger ones. In keeping up with Akhoond *et al.* (2011) study, our study could not prove a significant relationship between survival rate and marital status.

Among the clinical parameters (Table 4.), chemotherapy as a treatment modality was significantly related to improved survival (p=0.0001) whereas having both chemoradiotherapy and being underweight (BMI) were associated with worse survival. Kumar *et al.* (2015), in Oman reported BMI and Chemotherapy as independent risk factors of colorectal cancer which supports findings from our current study. A retrospective study by Tsang *et al.* (2016) also reported that underweight was an adverse prognostic factor and was associated with a higher risk of death whereas overweight and obesity are favourable prognostic factors for overall survival in metastatic cancer patients.

Many patients with stage III disease receive chemotherapy in addition to surgery (Ragnhammar *et al.*, 2001). Such "adjuvant" therapy increases the chances for a complete cure by destroying microscopic accumulations of cancer cells before they have an opportunity to grow to larger tumours. The effect of the treatment at a group level is documented to improve survival by 15-20% (Glimelius *et al.*, 2011). According to Boyle *et al.* (2013) being overweight or obese was associated with poorer survival in colorectal cancer patients. It has been proposed that obesity may influence colorectal cancer survival

by increasing insulin resistance and increasing the levels of insulin and insulinlike growth factors(Vrieling and Kampman, 2010).

Pathological evaluation is a critical component in the management of patients with colorectal cancer. In the present study, the stage of tumor was correlated to worse survival. Several studies have demonstrated that advanced disease stage was prognostic factor associated with poor prognosis in patients with CRC (Bufalari *et al.*, 2006; Ghazali *et al.*, 2010). In the present study, the state of regional lymph node metastasis was a highly significant independent prognostic factor (Table 4.13) which concurs with results from other studies (Compton *et al.*, 2000b; Liang *et al.*, 2004). Cox proportional hazard model in this current study revealed that, distant metastasis was a significant factor predicting poor survival. There are many reports that confirm our findings (He *et al.*, 2002; Oya *et al.*, 2003). Many studies have indicated a relationship between the extent of wall penetration and prognosis (He *et al.*, 2002; Safaee *et al.*, 2012), and this trend was also observed in our current study. The survival prospects of patients with large bowel cancer is clearly related to the degree of penetration of the tumour through the intestinal wall, the presence or absence of regional lymph nodal involvement, and the presence or absence of distant metastases. These three characteristics form the basis for staging and treatment options for this cancer (Compton and Greene, 2004).

Serum carcinoembryonic antigen (CEA) is widely accepted as a clinically significant prognostic indicator of recurrence and therapeutic benefit in colorectal cancer (Wanebo *et al.*, 1978; McNally *et al.*, 2015). Increased early postoperative CEA levels are often a sign of remaining cancer tissue, while a later increase is suggestive for cancer recurrence. Both, early and late increased postoperative CEA levels are associated with decreased survival (Yakabe *et al.*, 2010; Lin *et al.*, 2011). The assessment of association between biochemical parameters (CEA, liver function and haematological parameters in this study revealed that,

the elevated levels of CEA and the liver function test parameters were statistically not significant in both univariate and multivariate analysis ($p>0.05$) hence no association with survival. Other studies have also failed to identify a significant survival disadvantage of a raised CEA level preoperatively (Charnsangavej *et al.*, 2006; Kishi *et al.*, 2009). Although routine blood test is commonly included in many follow-up strategies, recurrent disease is rarely identified by an isolated abnormality in serum haemoglobin (Graffner *et al.*, 1985). Similarly, very few recurrences are identified on the basis of abnormal liver function tests, which are typically a late finding occurring well after hepatic metastases have been discovered by other test or imaging study (Fantini and DeCosse, 1990). Hence serum haemoglobin and liver function tests have been demonstrated to be ineffective indicators of disease recurrence or improved survival in colorectal cancer (McArdle, 2000; Anthony *et al.*, 2004; Jeffery *et al.*, 2007).

Finding from the study shows that (Table 4.15), low levels of RBC, MCV and RDW-SD were significant prognostic factors associated with worse survival in multivariate analysis. Köhne *et al.* (2002) identified platelets > or = 400 x 10(9)/l, alkaline phosphatase > or = 300 U/l, white blood cell (WBC) count > or = 10 x 10(9)/l and haemoglobin < 11 x 10(9)/l, as variables associated with worse prognostic outcome in colorectal cancer patients being treated with 5-FU based therapy which differs from our current findings. In multivariate analysis, MCV increase was independently associated with favourable survival outcomes (Cokmert *et al.*, 2014). This is in agreement with findings from our current study where low level of MCV was associated with worse survival. Anaemia has been shown to be a negative prognostic marker of survival, independent of tumour stage in a wide range of malignant diseases including CRC (Knight *et al.*, 2004; Clarke and Pallister, 2005). Overall anaemia in patients presenting with cancer is associated with reduced survival (Caro *et al.*, 2001) and reduced quality of life (Demetri, 2001; Ludwig *et al.*, 2004). Several mechanisms cause anaemia in colorectal cancer (CRC), including gastrointestinal

haemorrhage, bone marrow infiltration, haemolysis, myelosuppression secondary to therapy and cancer-related anaemia (CRA) (Clarke and Pallister, 2005). Many lower gastrointestinal tumours present as iron deficiency anaemia (Goodman and Irvin, 1993). Cancer-related anaemia is characterised by normochromic and normocytic red cell indices, a form of anaemia seen in chronic illness (anaemia of chronic inflammation) (Clarke and Pallister, 2005). In this study, the low levels of RBC, MCV and RDW-SD could suggest possible anaemia among the colorectal cancer patients (Table 4.15).

5.5 QUALITY OF LIFE OF COLORECTAL CANCER PATIENTS AT KATH

QoL refers to "global well-being," including physical, emotional, mental, social, and behavioral components (Heydarnejad *et al.*, 2011). Health-related quality of life (HRQL) is a subjective evaluation based on a patient's level of psychological, social, and physical ability. It has become an important concern for cancer patients, and it is linked to their capacity to derive benefits from therapy (Mhaidat *et al.*, 2014).

The quality of life assessment using the EORTC revealed that, the overall quality of life was moderate among the colorectal cancer patients with a mean score of 64.15±24 which is similar to findings by (Almutairi *et al.*, 2016) in Saudi Arabia who reported a mean score of 67.1. Colon cancer patients had a better quality of life compared to rectal cancer patients and the difference was statistically significant (p=0.039). Overall, the function scales assessment was good among the patients with physical function having the highest scores of 84.61±24.58 and emotional function having the least score 66.36±26.32. Among the symptoms score, the worst symptom was financial difficulty followed by fatigue and pain. Constipation was significantly higher in rectal cancer patients than colon cancer patients. A study by (Hokkam *et al.*, 2013) showed that the most preserved functional scale was the social function. Among symptom scales, the worst symptom was the financial difficulties followed by insomnia and fatigue. In this study, the EORTC CR 29 Colorectal

cancer specific questionnaire revealed that patients had good body image of themselves and a comparison between colon and rectal cancer patients showed a significant difference (p=0.0261) with colon patients having a higher score than rectal cancer patients (Table 4.17). In the symptom scale, flatulence was the most common symptom. Overall, patients had good symptom score. In all bloating pain was significantly higher in colon than rectal cancer patients. However, (Hokkam *et al.*, 2013) revealed that the most annoying symptom affecting the quality of life was bloating feeling which was significantly more with non-stoma patients.

Studies from other countries have shown that most colorectal cancer patients report good health,(Sprangers *et al.*, 1995) but colorectal cancer patients may suffer long-lasting pain and reductions in functional and social well-being (Ramsey *et al.*, 2000).

It is well established that colorectal cancer is one of those cancers that can largely be prevented by the early detection and removal of adenomatous polyps (Levin *et al.*, 2008; Fatemi *et al.*, 2010), and survival is therefore significantly better when colorectal cancer is diagnosed while still localized. Screening strategies are needed for early detection of adenomas and colorectal cancer.

CHAPTER SIX

6.0 CONCLUSIONS

- The clinico-pathological patterns and presentations of colorectal cancer in our setting are similar to that of most African and developing countries. These aspects include predominance of rectal cancers, high incidence in the younger people and delayed presentation of the disease in an advanced stage. Peculiar to our setting was the predominance of females, majority with symptom of weight loss and moderately differentiated adenocarcinomas.

- The estimated annual incidence rates of colorectal cancer at KATH were much lower compared to rates in developed countries, but higher than values reported at KATH in 2012, hence signifying an increase in the rate of colorectal cancer in our setting.

- The survival rate of colorectal cancer in Kumasi, Ghana is very low (16%). This is due to late stage presentations resulting in high mortality rate.

- Significant clinical and pathological prognostic factors identified in our study included, Family history, only chemotherapy, Both chemotherapy and radiotherapy, BMI, TNM tumour stage, Depth of tumour invasion, Lymp node metastasis, distance metastasis, Mean Corpuscular Volume (MCV), Red Blood cell (RBC) and Red cell distribution width (RDW).

- The overall quality of life of the colorectal cancer patients was moderate. In both, QoL instruments used, the symptom score was good. However, deficits in emotional and social functioning and specific limitations like fatigue, pain, flatulence, urine frequency stool frequency and financial difficulties represent the main factors that hampered the Quality of life (QOL) among colorectal cancer patients in our study.

6.1 RECOMMENDATIONS

- Government should build the capacity of health care providers in Ghana by providing the much needed diagnostic tools for early diagnosis and referral of colorectal cancer cases. National screening programmes should be implemented for early detection and prevention of the disease.

- We highlight the significance of health education to create awareness among communities through different media in other to increase care seeking behaviour for improved clinical outcome.

- Proper documentation of data on CRC at all levels should be enforced so as enable its usage for future research, advocacy purpose and also to inform policy makers.

- Further research should be pursued to identify the risk factors of colorectal cancer in our setting especially the genetic and environmental risk factors.

- Further studies to investigate the molecular characteristics of colorectal cancer and to profile specific genetic mutations for identification of predictive markers for effective therapeutic interventions in our population is strongly recommended.

6.2 STUDY LIMITATIONS

Information about some patients were incomplete in view of the retrospective nature of the study. This might have introduced some bias in our findings. The study included only patients who were evaluated and treated at a single institution, which may not reflect the whole population in this region, although almost all oncologic patients in the Northen and Central sector of Ghana are refererd to KATH to be managed. However, despite this limitation, the study has provided useful data that can help healthcare providers in the management of patients with colorectal cancer.

REFERENCES

Aaronson N.K., Ahmedzai S., Bergman B., Bullinger M., Cull A., Duez N.J., Filiberti A., Flechtner H., Fleishman S.B. and de Haes J.C. (1993a) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute* 85(5), 365-376.

Aaronson N.K., Ahmedzai S., Bergman B., Bullinger M., Cull A., Duez N.J., Filiberti A., Flechtner H., Fleishman S.B., de Haes J.C. and et al. (1993b) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 85(5), 365-376.

Abdalla A.A., MI M.T.M. and Khair R.Z.A.M. (2007) Presentation of Colorectal Cancer in Khartoum Teaching Hospital Ahmed A Abdalla1, Mohamed Toum Musa MI 2, Randa Zaki AR M Khair3.

Abdulkareem F.B., Abudu E.K., Awolola N.A., Elesha S.O., Rotimi O., Akinde O.R., Atoyebi A.O., Adesanya A.A., Daramola A.O. and Banjo A.A.F. (2008) Colorectal carcinoma in Lagos and Sagamu, Southwest Nigeria: a histopathological review. *World J Gastroenterol* 14(42), 6531-6535.

Abou-Zeid A.A., Khafagy W., Marzouk D.M., Alaa A., Mostafa I. and Ela M.A. (2002) Colorectal cancer in Egypt. *Diseases of the colon & rectum* 45(9), 1255-1260.

Abulafi A. and Williams N. (1994) Local recurrence of colorectal cancer: the problem, mechanisms, management and adjuvant therapy. *British journal of surgery* 81(1), 7-19.

Adesanya A. and da Rocha-Afodu J. (2000) Colorectal cancer in Lagos: a critical review of 100 cases. *The Nigerian postgraduate medical journal* 7(3), 129-136.

Akhoond M., Kazemnejad A., Hajizadeh E., Fatemi S. and Motlagh A. (2011) Investigation of Influential Factors Affecting Survival Rate of Patients with Colorectal Cancer using Copula Function. *Iranian Journal of Epidemiology* 6(4), 40-49.

Akinola D.O. and Arigbabu A.O. (1994) Pattern and presentation of large bowel neoplasms in Nigerians. *Cent Afr J Med* 40(4), 98-102.

Al-Ahwal M.S. and Al-Ghamdi A.A. (2005) Pattern of colorectal cancer at two hospitals in the western region of Saudi Arabia. *Saudi Journal of Gastroenterology* 11(3), 164.

Al-Ahwal M.S., Shafik Y.H. and Al-Ahwal H.M. (2013) First national survival data for colorectal cancer among Saudis between 1994 and 2004: what's next? *BMC public health* 13(1), 1.

Al-Shamsi S.R., Bener A., Al-Sharhan M., Al-Mansoor T.M., Azab I.A., Rashed A., Kakil R.I. and Amiri K.M. (2011) Clinicopathological pattern of colorectal cancer in the United Arab Emirates. *QNRS Repository* 2011(1), 1816.

Alexiusdottir K.K., Möller P.H., Snaebjornsson P., Jonasson L., Olafsdottir E.J., Björnsson E.S., Tryggvadottir L. and Jonasson J.G. (2012) Association of symptoms of colon cancer patients with tumor location and TNM tumor stage. *Scandinavian Journal of Gastroenterology* 47(7), 795-801.

Alici S., Kaya S., Izmirli M., Tuncer I., Ozbek H. and Sayarlioglu H. (2006) Analysis of survival factors in patients with advanced-stage gastric adenocarcinoma. *Medical science monitor* 12(5), CR221-CR229.

Almutairi K., Alhelih E., Al-Ajlan A. and Vinluan J. (2016) A cross-sectional assessment of quality of life of colorectal cancer patients in Saudi Arabia. *Clinical and Translational Oncology* 18(2), 144-152.

Altekruse S., Kosary C., Krapcho M., Neyman N., Aminou R., Waldron W., Ruhl J., Howlader N., Tatalovich Z. and Cho H. (2010) SEER cancer statistics review, 1975-2007. *Bethesda, MD: National Cancer Institute* 7.

Anderson J., Hole D. and McArdle C. (1992) Elective versus emergency surgery for patients with colorectal cancer. *British journal of surgery* 79(7), 706-709.

Andre T., Sargent D., Tabernero J., O'Connell M., Buyse M., Sobrero A., Misset J.-L., Boni C. and De Gramont A. (2006) Current issues in adjuvant treatment of stage II colon cancer. *Annals of surgical oncology* 13(6), 887-898.

Angell-Andersen E., Tretli S., Coleman M., Langmark F. and Grotmol T. (2004) Colorectal cancer survival trends in Norway 1958–1997. *European Journal of Cancer* 40(5), 734-742.

Anthony T., Simmang C., Hyman N., Buie D., Kim D., Cataldo P., Orsay C., Church J., Otchy D. and Cohen J. (2004) Practice parameters for the surveillance and follow-up of patients with colon and rectal cancer. *Diseases of the colon & rectum* 47(6), 807-817.

Araki K., Furuya Y., Kobayashi M., Matsuura K., Ogata T. and Isozaki H. (1996) Comparison of mucosal microvasculature between the proximal and distal human colon. *Journal of electron microscopy* 45(3), 202-206.

Arber N. (2000) Do NSAIDs prevent colorectal cancer? *Canadian journal of gastroenterology= Journal canadien de gastroenterologie* 14(4), 299-307.

Arbman G., Nilsson E., Hallböök O. and Sjödahl R. (1996) Local recurrence following total mesorectal excision for rectal cancer. *British journal of surgery* 83(3), 375379.

Arndt V., Merx H., Stegmaier C., Ziegler H. and Brenner H. (2004) Quality of life in patients with colorectal cancer 1 year after diagnosis compared with the general population: a population-based study. *Journal of clinical oncology* 22(23), 48294836.

Astin M., Griffin T., Neal R.D., Rose P. and Hamilton W. (2011) The diagnostic value of symptoms for colorectal cancer in primary care: a systematic review. *Br J Gen Pract* 61(586), e231-e243.

Avoranta T. (2013) The prognostic and predictive value of selected biomarkers in colorectal cancer.

Azadeh S., Moghimi-Dehkordi B., Fatem S., Pourhoseingholi M., Ghiasi S. and Zali M. (2007) Colorectal cancer in Iran: an epidemiological study. *Asian Pacific journal of cancer prevention: APJCP* 9(1), 123-126.

Badoe E. (1966) Malignant disease of gastrointestinal tract in Korle Bu Hospital, Accra, Ghana, 1956-65. *The West African medical journal* 15(5), 181.

Baker S., Presinger A., Jessup J. and Parakeva C. (1990) Marko witz S, Wilson JKV, Hamilton S, Vogelstein B: p53 gene mutations occur in combination with 17p allelic deletion as late events in colorectal tumorigenesis. *Cancer Res* 5077177722.

Baron J.A., Cole B.F., Sandler R.S., Haile R.W., Ahnen D., Bresalier R., McKeownEyssen G., Summers R.W., Rothstein R. and Burke C.A. (2003) A randomized trial of

aspirin to prevent colorectal adenomas. *New England Journal of Medicine* 348(10), 891-899.

Bass G., Fleming C., Conneely J., Martin Z. and Mealy K. (2009) Emergency first presentation of colorectal cancer predicts significantly poorer outcomes: a review of 356 consecutive Irish patients. *Diseases of the colon & rectum* 52(4), 678-684.

Ben-Ishay O., Peled Z., Othman A., Brauner E. and Kluger Y. (2013) Clinical presentation predicts the outcome of patients with colon cancer. *World J Gastrointest Surg* 5(4), 104-109.

Biritwum R., Gulaid J. and Amaning A. (2000) Pattern of diseases or conditions leading to hospitalization at Korle Bu Teaching Hospital, Ghana in 1996. *Ghana Med J* 34(4), 197-205.

Botteri E., Iodice S., Raimondi S., Maisonneuve P. and Lowenfels A.B. (2008) Cigarette smoking and adenomatous polyps: a meta-analysis. *Gastroenterology* 134(2), 388-395. e383.

Boyle P. and Langman J. (2000) ABC of colorectal cancer: Epidemiology. *BMJ: British Medical Journal* 321(7264), 805.

Boyle T., Fritschi L., Platell C. and Heyworth J. (2013) Lifestyle factors associated with survival after colorectal cancer diagnosis. *British journal of cancer* 109(3), 814822.

Boytchev H., Marcovic S. and Oettle G. (1999) The characteristics of large bowel cancer in the low-risk black population of the Witwatersrand. *Journal of the Royal College of Surgeons of Edinburgh* 44(6), 366-370.

Braun D.P., Gupta D., Grutsch J.F. and Staren E.D. (2011) Can changes in health related quality of life scores predict survival in stages III and IV colorectal cancer? *Health and quality of life outcomes* 9(1), 1.

Brkić T. and Grgić M. (2006) Kolorektalni karcinom. *Medicus* 15(1_Gastroenterologija), 89-97.

Brown G. (2014) Thin section MRI in multidisciplinary pre-operative decision making for patients with rectal cancer. *The British journal of radiology*.

Bufalari A., Giustozzi G., Burattini M.F., Servili S., Bussotti C., Lucaroni E., Ricci E. and Sciannameo F. (2006) Rectal cancer surgery in the elderly: a multivariate analysis of outcome risk factors. *Journal of surgical oncology* 93(3), 173-180.

Calle E.E. and Kaaks R. (2004) Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. *Nature Reviews Cancer* 4(8), 579-591.

Campagnoli C., Biglia N., Altare F., Lanza M., Lesca L., Cantamessa C., Peris C., Fiorucci G. and Sismondi P. (2009) Differential effects of oral conjugated estrogens and transdermal estradiol on insulin-like growth factor 1, growth hormone and sex hormone binding globulin serum levels. *Gynecological Endocrinology*.

Campbell-Thompson M., Lynch I.J. and Bhardwaj B. (2001) Expression of estrogen receptor (ER) subtypes and ERβ isoforms in colon cancer. *Cancer research* 61(2), 632-640.

Campbell T. (1999) Colorectal cancer. Part 1: Epidemiology, aetiology, screening and diagnosis. *Professional nurse (London, England)* 14(12), 869-874.

Cancer I.A.f.R.o. (2003) Cancer in Africa: epidemiology and prevention. *IARC scientific Publications*(153), 1.

Cancer I.A.f.R.o. (2014) The GLOBOCAN project: cancer incidence and mortality worldwide in 2012. *URL: http://globocan. iarc. fr/(дата обращения: 13.01. 2010)*.

Cappell M.S. (2005) The pathophysiology, clinical presentation, and diagnosis of colon cancer and adenomatous polyps. *Medical Clinics of North America* 89(1), 1-42.

Cappell M.S. and Goldberg E.S. (1992) The Relationship Between the Clinical Presentation and Spread of Colon Cancer in 315 Consecutive Patients: A Significant Trend of Earlier Cancer Detection From 1982 Through 1988 at a University Hospital. *Journal of clinical gastroenterology* 14(3), 227-235.

Caro J.J., Salas M., Ward A. and Goss G. (2001) Anemia as an independent prognostic factor for survival in patients with cancer. *Cancer* 91(12), 2214-2221.

Cascinu S., Ferro E.D., Grianti C., Ligi M. and Catalano G. (1996) S phase fraction and tumor aneuploidy in colorectal carcinoma of young patients. *Cancer* 78(9), 18571860.

Center M.M., Jemal A., Smith R.A. and Ward E. (2009a) Worldwide variations in colorectal cancer. *CA: a cancer journal for clinicians* 59(6), 366-378.

Center M.M., Jemal A. and Ward E. (2009b) International trends in colorectal cancer incidence rates. *Cancer Epidemiology Biomarkers & Prevention* 18(6), 16881694.

Center M.M. and ME J.F. (2011) Global cancer statistics. *CA: a cancer journal for clinicians* 61(2), 69.

Cervera P. and Fléjou J.-F. (2011) Changing pathology with changing drugs: tumors of the gastrointestinal tract. *Pathobiology* 78(2), 76-89.

Chalya P.L., Mchembe M.D., Mabula J.B., Rambau P.F., Jaka H., Koy M., Mkongo E. and Masalu N. (2013a) Clinicopathological patterns and challenges of management of colorectal cancer in a resource-limited setting: a Tanzanian experience. *World J Surg Oncol* 11(2).

Chalya P.L., Mchembe M.D., Mabula J.B., Rambau P.F., Jaka H., Koy M., Mkongo E. and Masalu N. (2013b) Clinicopathological patterns and challenges of management of colorectal cancer in a resource-limited setting: a Tanzanian experience. *World journal of surgical oncology* 11(1), 1.

Chao A., Thun M.J., Connell C.J., McCullough M.L., Jacobs E.J., Flanders W.D., Rodriguez C., Sinha R. and Calle E.E. (2005) Meat consumption and risk of colorectal cancer. *Jama* 293(2), 172-182.

Chapuis P., Dent O., Fisher R., Newland R., Pheils M., Smyth E. and Colquhoun K. (1985) A multivariate analysis of clinical and pathological variables in prognosis after resection of large bowel cancer. *British journal of surgery* 72(9), 698-702.

Charnsangavej C., Clary B., Fong Y., Grothey A., Pawlik T.M. and Choti M.A. (2006) Selection of patients for resection of hepatic colorectal metastases: expert consensus statement. *Annals of surgical oncology* 13(10), 1261-1268.

Chen S.L. and Bilchik A.J. (2006) More extensive nodal dissection improves survival for stages I to III of colon cancer: a population-based study. *Annals of surgery* 244(4), 602-610.

Cherry L.M. (2011) The genetic etiology of familial and nonfamilial colorectal cancer. *Proceedings (Baylor University. Medical Center)* 24(2), 139.

Clarke H. and Pallister C. (2005) The impact of anaemia on outcome in cancer. *Clinical & Laboratory Haematology* 27(1), 1-13.

Cokmert S., Demir L., Can A., Akyol M., Vedat Bayoglu I., Dirican A., Kucukzeybek Y., Erten C. and Oktay Tarhan M. (2014) Capecitabine-related increased mean corpuscular volume of red blood cell may be a predictive marker of treatment response and survival in patients with metastatic colorectal cancer. *J buon* 19(1), 75-82.

Compton C., Fenoglio‐Preiser C.M., Pettigrew N. and Fielding L.P. (2000a) American Joint Committee on Cancer prognostic factors consensus conference. *Cancer* 88(7), 1739-1757.

Compton C.C., Fielding L.P., Burgart L.J., Conley B., Cooper H.S., Hamilton S.R., Hammond M.E.H., Henson D.E., Hutter R.V. and Nagle R.B. (2000b) Prognostic factors in colorectal cancer: College of American Pathologists consensus statement 1999. *Archives of pathology & laboratory medicine* 124(7), 979-994.

Compton C.C. and Greene F.L. (2004) The staging of colorectal cancer: 2004 and beyond. *CA: a cancer journal for clinicians* 54(6), 295-308.

Cusack J.C., Giacco G.G., Cleary K., Davidson B.S., Izzo F., Skibber J., Yen J. and Curley S.A. (1996) Survival factors in 186 patients younger than 40 years old with colorectal adenocarcinoma. *Journal of the American College of Surgeons* 183(2), 105-112.

Dakubo J., Naaeder S., Tettey Y. and Gyasi R. (2010a) Colorectal carcinoma: an update of current trends in Accra. *West African journal of medicine* 29(3).

Dakubo J., Naaeder S., Tettey Y. and Gyasi R. (2010b) Colorectal carcinoma: An update of current trends in Accra.[Carcinome colorectal: Une mise à jour des tendances actuelles de Accra].

Dakubo J.C., Naaeder S.S. and Gyasi R.K. (2014) Clinicopathological aspects of adenocarcinoma of the large bowel in a low incidence population. *Journal of surgical oncology* 109(3), 245-249.

de Heer P. (2007) *Molecular and biological interactions in colorectal cancer*: Department of Surgery, Faculty of Medicine, Leiden University Medical Center (LUMC), Leiden University.

de Kok I.M., Wong C.S., Chia K.S., Sim X., Tan C.S., Kiemeney L.A. and Verkooijen H.M. (2008) Gender differences in the trend of colorectal cancer incidence in Singapore, 1968–2002. *International journal of colorectal disease* 23(5), 461467.

DeCosse J.J. and Cennerazzo W.J. (1997) Quality_of_life management of patients with colorectal cancer. *CA: a cancer journal for clinicians* 47(4), 198-206.

Demetri G. (2001) Anaemia and its functional consequences in cancer patients: current challenges in management and prospects for improving therapy. *British journal of cancer* 84(Suppl 1), 31.

DePinho R.A. (2000) The age of cancer. *Nature* 408(6809), 248-254.

Dickinson B.T., Kisiel J., Ahlquist D.A. and Grady W.M. (2015) Molecular markers for colorectal cancer screening. *Gut*gutjnl-2014-308075.

Dobrila-Dintinjana R., Trivanović D., Dintinjana M., Vukelić J. and Vanis N. Effects of Dietary Counseling on Patients with Colorectal Cancer. *Colorectal Cancer—From Prevention to Patient Care, InTech, Rijeka*211-226.

Dobrila Dintinjana R., Guina T., Krznarić Ž., Radić M. and Dintinjana M. (2008) Effects of nutritional support in patients with colorectal cancer during chemotherapy. *Collegium antropologicum* 32(3), 737-740.

Eaden J., Abrams K. and Mayberry J. (2001) The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut* 48(4), 526-535.

Elesha S. and Owonikoko T. (1998) Colorectal neoplasms: a retrospective study. *East African medical journal* 75(12), 718-723.

Fairley T.L., Cardinez C.J., Martin J., Alley L., Friedman C., Edwards B. and Jamison P. (2006) Colorectal cancer in US adults younger than 50 years of age, 1998–2001. *Cancer* 107(S5), 1153-1161.

Faivre-Finn C., Bouvier-Benhamiche A., Phelip J., Manfredi S., Dancourt V. and Faivre J. (2002) Colon cancer in France: evidence for improvement in management and survival. *Gut* 51(1), 60-64.

Fang Y.-J., Wu X.-J., Zhao Q., Li L.-R., Lu Z.-H., Ding P.-R., Zhang R.-X., Kong L.-H., Wang F.-L. and Lin J.-Z. (2013) Hospital-based colorectal cancer survival trend of different tumor locations from 1960s to 2000s.

Fantini G. and DeCosse J. (1990) Surveillance strategies after resection of carcinoma of the colon and rectum. *Surgery, gynecology & obstetrics* 171(3), 267-273.

Fatemi S.R., Shivarani S., Malek F.N., Vahedi M., Maserat E., Iranpour Y. and Zali M.R. (2010) Colonoscopy screening results in at risk Iranian population. *Asian Pac j cancer prev* 11(6), 1801-1804.

Fazeli M.S. and Keramati M.R. (2015) Rectal cancer: a review. *Medical Journal of The Islamic Republic of Iran (MJIRI)* 29171-170.

Fearon E.R. and Vogelstein B. (1990) A genetic model for colorectal tumorigenesis. *Cell* 61(5), 759-767.

Ferlay J., Shin H.R., Bray F., Forman D., Mathers C. and Parkin D.M. (2010) Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International Journal of Cancer* 127(12), 2893-2917.

Ferrari P., Jenab M., Norat T., Moskal A., Slimani N., Olsen A., Tjønneland A., Overvad K., Jensen M.K. and Boutron_Ruault M.C. (2007) Lifetime and baseline alcohol intake and risk of colon and rectal cancers in the European prospective investigation into cancer and nutrition (EPIC). *International Journal of Cancer* 121(9), 2065-2072.

Fleming I. (1997) Kidney Flemimg ID Cooper JS Henson DE Hutter RVP Kennedy BJ Murphy GP O'Sullivan B. Sobin LH Yarbro JW eds.. Kidney. AJCC Cancer Staging Manual. American Joint Committee on Cancer. Manual for Staging of Cancer, 231-239: Lippincott-Raven Publishers Philadelphia.

Food N. (2007) Physical Activity, and the Prevention of Cancer: A Global Perspective World Cancer Research Fund and American Institute for Cancer Research Washington DC. *WA, USA*.

Foubert F., Matysiak-Budnik T. and Touchefeu Y. (2014) Options for metastatic colorectal cancer beyond the second line of treatment. *Digestive and Liver Disease* 46(2), 105-112.

Fung T.T. and Brown L.S. (2013) Dietary patterns and the risk of colorectal cancer. *Current nutrition reports* 2(1), 48-55.

Gado A., Ebeid B., Abdelmohsen A. and Axon A. (2014) Colorectal cancer in Egypt is commoner in young people: Is this cause for alarm? *Alexandria Journal of Medicine* 50(3), 197-201.

Gainant A. (2012) Emergency management of acute colonic cancer obstruction. *Journal of visceral surgery* 149(1), e3-e10.

Garcia-Valdecasas J., Llovera J., Reverter J., Grande L., Fuster J., Cugat E., Visa J. and Pera C. (1991) Obstructing colorectal carcinomas. *Diseases of the colon & rectum* 34(9), 759-762.

Gatta G., Faivre J., Capocaccia R., de Leon M.P. and Group E.W. (1998) Survival of colorectal cancer patients in Europe during the period 1978–1989. *European Journal of Cancer* 34(14), 2176-2183.

Gelboin H.V. (1980) *Genetic and environmental factors in experimental and human cancer: proceedings of the 10th international symposium of the Princess Takamatsu Cancer Research Fund, Tokyo, 1979*: Japan Scientific Societies Press.

Gharbi O., Chabchoub I., Limam S., Hochlef M., Ben F.L., Landolsi A., Gahbiche S., Braham A., Mokni M. and Ajmi S. (2010) [Prognostic factors and survival of metastatic colorectal cancer in the Sousse University Hospital (Tunisia): comparative study of two treatment period of 200 patients]. *Bulletin du cancer* 97(4), 445-451.

Ghazali A.K., Musa K.I., Naing N.N. and Mahmood Z. (2010) Prognostic factors in patients with colorectal cancer at Hospital Universiti Sains Malaysia. *Asian Journal of Surgery* 33(3), 127-133.

Gill S., Loprinzi C.L., Sargent D.J., Thomé S.D., Alberts S.R., Haller D.G., Benedetti J., Francini G., Shepherd L.E. and Seitz J.F. (2004) Pooled analysis of fluorouracilbased adjuvant therapy for stage II and III colon cancer: who benefits and by how much? *Journal of clinical oncology* 22(10), 1797-1806.

Giordano K.F. and Jatoi A. (2004) A synopsis of cancer-related anorexia and weight loss. *Business Briefing: US Oncology Review*1-5.

Giovannucci E. (2007) Metabolic syndrome, hyperinsulinemia, and colon cancer: a review. *The American journal of clinical nutrition* 86(3), 836S-842S.

Glimelius B., Dahl O., Cedermark B., Jakobsen A., Bentzen S.M., Starkhammar H., Grönberg H., Hultborn R., Albertsson M. and Påhlman L. (2011) Adjuvant chemotherapy in colorectal cancer: a joint analysis of randomised trials by the Nordic Gastrointestinal Tumour Adjuvant Therapy Group. *Acta oncologica*.

GLOBOCAN (2008) Cancer Fact Sheet. Colorectal cancer incidence and mortality worldwide in 2008. *Summary IARC*.

Goodman D. and Irvin T. (1993) Delay in the diagnosis and prognosis of carcinoma of the right colon. *British journal of surgery* 80(10), 1327-1329.

Graffner H., Hultberg B., Johansson B., Müller T. and Petersson B. (1985) Detection of recurrent cancer of the colon and rectum. *Journal of surgical oncology* 28(2), 156-159.

Graham A., Davies Adeloye L.G., Theodoratou E. and Campbell H. (2012) Estimating the incidence of colorectal cancer in Sub–Saharan Africa: A systematic analysis. *Journal of global health* 2(2).

Grande M., Milito G., Attinà G.M., Cadeddu F., Muzi M.G., Nigro C., Rulli F. and Farinon A.M. (2008) Evaluation of clinical, laboratory and morphologic prognostic factors in colon cancer. *World journal of surgical oncology* 6(1), 1.

Groden J., Thliveris A., Samowitz W., Carlson M., Gelbert L., Albertsen H., Joslyn G., Stevens J., Spirio L. and Robertson M. (1991) Identification and characterization of the familial adenomatous polyposis coli gene. *Cell* 66(3), 589-600.

Grodstein F., Newcomb P.A. and Stampfer M.J. (1999) Postmenopausal hormone therapy and the risk of colorectal cancer: a review and meta-analysis. *The American journal of medicine* 106(5), 574-582.

Grossmann I., De Bock G., Kranenbarg W.M.-K., van de Velde C. and Wiggers T. (2007) Carcinoembryonic antigen (CEA) measurement during follow-up for rectal carcinoma is useful even if normal levels exist before surgery. A retrospective study of CEA values in the TME trial. *European Journal of Surgical Oncology (EJSO)* 33(2), 183-187.

Grosso G., Biondi A., Marventano S., Mistretta A., Calabrese G. and Basile F. (2012) Major postoperative complications and survival for colon cancer elderly patients. *BMC surgery* 12(Suppl 1), S20.

Guraya S.Y. and Eltinay O.E. (2006) Higher prevalence in young population and rightward shift of colorectal carcinoma. *Saudi medical journal* 27(9), 1391-1393.

Haggar F.A. and Boushey R.P. (2009) Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clinics in colon and rectal surgery* 22(4), 191.

Harrison L.E., Guillem J.G., Paty P. and Cohen A.M. (1997) Preoperative carcinoembryonic antigen predicts outcomes in node-negative colon cancer patients: a multivariate analysis of 572 patients. *Journal of the American College of Surgeons* 185(1), 55-59.

He W., Wang L., Hu H., Kang S., Qian H. and Xu F. (2002) [Correlation of invasion, metastasis, and prognosis in low and middle rectal cancer]. *Ai zheng= Aizheng= Chinese journal of cancer* 21(11), 1222-1225.

Hermanek P., Wiebelt H., Riedl S.u. and Staimmer D. (1994) Studiengruppe Kolorektales Karzinom Langzeilergebnisse der chirurgischen Therapie des Coloncarcinoms. *Chirurg* 65(4), 287-287.

Heydarnejad M., Hassanpour D.A. and Solati D.K. (2011) Factors affecting quality of life in cancer patients undergoing chemotherapy. *Afr Health Sci* 11(2).

Hokkam M., Farrag M. and El Kammash M. (2013) Assessment of quality of life of colorectal carcinoma patients after surgery. *World Journal of Colorectal Surgery* 3(1), 4.

Holcombe C. and Babayo U. (1990) The pattern of malignant disease in north east Nigeria. *Tropical and geographical medicine* 43(1-2), 189-192.

Hurwitz H., Fehrenbacher L., Novotny W., Cartwright T., Hainsworth J., Heim W., Berlin J., Baron A., Griffing S. and Holmgren E. (2004) Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. *New England Journal of Medicine* 350(23), 2335-2342.

Iliyasu Y., Ladipo J., Akang E., Adebamowo C., Ajao O. and Aghadiuno P. (1996) A twenty-year review of malignant colorectal neoplasms at University College Hospital, Ibadan, Nigeria. *Diseases of the colon & rectum* 39(5), 536-540.

Ioannou G.N., Rockey D.C., Bryson C.L. and Weiss N.S. (2002) Iron deficiency and gastrointestinal malignancy: a population-based cohort study. *The American journal of medicine* 113(4), 276-280.

Irabor D. and Adedeji O. (2009) Colorectal cancer in Nigeria: 40 years on. A review. *European journal of cancer care* 18(2), 110-115.

Irabor D., Arowolo A. and Afolabi A. (2010) Colon and rectal cancer in Ibadan, Nigeria: an update. *Colorectal Disease* 12(7Online), e43-e49.

Irabor D.O., Afuwape O.O. and Ayandipo O.O. (2014) The present status of the management of colon and rectal cancer in Nigeria. *Journal of Cancer Research* 2014.

Issa J.-P.J., Ottaviano Y.L., Celano P., Hamilton S.R., Davidson N.E. and Baylin S.B. (1994) Methylation of the oestrogen receptor CpG island links ageing and neoplasia in human colon. *Nature genetics* 7(4), 536-540.

Iversen L.H. (2012) Aspects of survival from colorectal cancer in Denmark. *Danish medical journal* 59(4), B4428-B4428.

Jagoditsch M., Lisborg P.H., Jatzko G.R., Wette V., Kropfitsch G., Denk H., Klimpfinger M. and Stettner H.M. (2000) Long-term prognosis for colon cancer related to consistent radical surgery: multivariate analysis of clinical, surgical, and pathologic variables. *World journal of surgery* 24(10), 1264-1270.

Janout V. and Kollárová H. (2001) Epidemiology of colorectal cancer. *ACTA-UNIVERSITATIS PALACKIANAE OLOMUCENSIS FACULTATIS MEDICAE*5-10.

Jeffery M., Hickey B.E. and Hider P.N. (2007) Follow_up strategies for patients treated for non_metastatic colorectal cancer. *The Cochrane Library*.

Jemal A., Bray F., Center M.M., Ferlay J., Ward E. and Forman D. (2011) Global cancer statistics. *CA: a cancer journal for clinicians* 61(2), 69-90.

Jemal A., Bray F., Forman D., O'Brien M., Ferlay J., Center M. and Parkin D.M. (2012) Cancer burden in Africa and opportunities for prevention. *Cancer* 118(18), 43724384.

Jestin P., Nilsson J., Heurgren M., Påhlman L., Glimelius B. and Gunnarsson U. (2005) Emergency surgery for colonic cancer in a defined population. *British journal of surgery* 92(1), 94-100.

Jönsson P., Bengtsson G., Carlsson G., Jonson G. and Tryding N. (1983) Value of serum5-nucleotidase, alkaline phosphatase and gamma-glutamyl transferase for prediction of liver metastases preoperatively in colorectal cancer. *Acta chirurgica scandinavica* 150(5), 419-423.

Kabat G., Miller A., Jain M. and Rohan T. (2007) A cohort study of dietary iron and heme iron intake and risk of colorectal cancer in women. *British journal of cancer* 97(1), 118-122.

Kamangar F., Dores G.M. and Anderson W.F. (2006) Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. *Journal of clinical oncology* 24(14), 2137-2150.

Kang W., Lee S., Jeon E., Yun Y.-R., Kim K.-H. and Jang J.-H. (2011) Emerging role of vitamin D in colorectal cancer. *World journal of gastrointestinal oncology* 3(8), 123.

Katsidzira L., Gangaidzo I.T., Mapingure M.P. and Matenga J.A. (2015) Retrospective study of colorectal cancer in Zimbabwe: Colonoscopic and clinical correlates. *World journal of gastroenterology: WJG* 21(8), 2374.

Kinzler K.W. and Vogelstein B. (1996) Lessons from hereditary colorectal cancer. *Cell* 87(2), 159-170.

Kishi Y., Kopetz S., Chun Y.S., Palavecino M., Abdalla E.K. and Vauthey J.-N. (2009) Blood neutrophil-to-lymphocyte ratio predicts survival in patients with colorectal liver metastases treated with systemic chemotherapy. *Annals of surgical oncology* 16(3), 614-622.

Kleihues P. and Stewart B.W. (2003) World cancer report.

Knight K., Wade S. and Balducci L. (2004) Prevalence and outcomes of anemia in cancer: a systematic review of the literature. *The American journal of medicine* 116(7), 11-26.

Köhne C.-H., Cunningham D., Di Costanzo F., Glimelius B., Blijham G., Aranda E., Scheithauer W., Rougier P., Palmer M. and Wils J. (2002) Clinical determinants of survival in patients with 5-fluorouracil-based treatment for metastatic colorectal cancer: results of a multivariate analysis of 3825 patients. *Annals of Oncology* 13(2), 308-317.

Koo J.H., Wong S.K.C., Jalaludin B., Kneebone A., Connor S.J. and Leong R.W. (2008) Clinical and pathologic outcomes of colorectal cancer in a multi-ethnic population. *Clinical Gastroenterology and Hepatology* 6(9), 1016-1021.

Kumar S., Burney I.A., Zahid K.F., Souza P.C.D., Belushi M.A., Meki T.D.M.W.A., Furrukh M. and Mansour S. (2015) Colorectal cancer patient characteristics, treatment and survival in Oman—a single center study. *Asian Pac j cancer prev* 164853-4858.

Kyriakos M. (1985) The President's cancer, the Dukes classification, and confusion. *Archives of pathology & laboratory medicine* 109(12), 1063-1066.

Larsson S.C., Orsini N. and Wolk A. (2005) Diabetes mellitus and risk of colorectal cancer: a meta-analysis. *Journal of the National Cancer Institute* 97(22), 16791687.

Larsson S.C. and Wolk A. (2006) Meat consumption and risk of colorectal cancer: a meta-analysis of prospective studies. *International Journal of Cancer* 119(11), 2657-2664.

Laryea D.O., Awuah B., Amoako Y.A., Osei-Bonsu E., Dogbe J., Larsen-Reindorf R., Ansong D., Yeboah-Awudzi K., Oppong J.K. and Konney T.O. (2014) Cancer incidence in Ghana, 2012: evidence from a population-based cancer registry. *BMC cancer* 14(1), 1.

Levin B., Lieberman D.A., McFarland B., Smith R.A., Brooks D., Andrews K.S., Dash C., Giardiello F.M., Glick S. and Levin T.R. (2008) Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi‐Society Task Force on Colorectal Cancer, and the American College of Radiology*†. *CA: a cancer journal for clinicians* 58(3), 130-160.

Liang J., Wan D., Pan Z., Zhou Z., Chen G., Li L., Lu Z. and Wu X. (2004) [Multivariate regression analysis of recurrence following curative surgery for colorectal cancer]. *Ai zheng= Aizheng= Chinese journal of cancer* 23(5), 564-567.

Lin J.-K., Lin C.-C., Yang S.-H., Wang H.-S., Jiang J.-K., Lan Y.-T., Lin T.-C., Li A.F.Y., Chen W.-S. and Chang S.-C. (2011) Early postoperative CEA level is a better prognostic indicator than is preoperative CEA level in predicting prognosis of patients with curable colorectal cancer. *International journal of colorectal disease* 26(9), 1135-1141.

Lin O.S. (2009) Acquired risk factors for colorectal cancer. *Cancer Epidemiology: Modifiable Factors*361-372.

Ludwig H., Van Belle S., Barrett-Lee P., Birgegård G., Bokemeyer C., Gascon P., Kosmidis P., Krzakowski M., Nortier J. and Olmi P. (2004) The European Cancer Anaemia Survey (ECAS): a large, multinational, prospective survey defining the prevalence, incidence, and treatment of anaemia in cancer patients. *European Journal of Cancer* 40(15), 2293-2306.

Macfarlane S. and Macfarlane G. (2003) Food and the large intestine. In *Gut flora, nutrition, immunity and health*, pp. 24-51: Blackwell Publishing Oxford.

Mahmoud N., Rombeau J., Ross H.M. and Fry R.D. (2004) Colon and rectum. *Sabiston textbook of surgery*.

Maisey N., Norman A., Watson M., Allen M., Hill M. and Cunningham D. (2002) Baseline quality of life predicts survival in patients with advanced colorectal cancer. *European Journal of Cancer* 38(10), 1351-1357.

Marventano S., Forjaz M.J., Grosso G., Mistretta A., Giorgianni G., Platania A., Gangi S., Basile F. and Biondi A. (2013) Health related quality of life in colorectal cancer patients: state of the art. *BMC surgery* 13(Suppl 2), S15.

McArdle C. (2000) ABC of colorectal cancer: effectiveness of follow up. *British Medical Journal* 321(7272), 1332.

McArdle C. and Hole D. (2004) Emergency presentation of colorectal cancer is associated with poor 5‐year survival. *British journal of surgery* 91(5), 605-609.

McArdle C., Hole D., Hansell D., Blumgart L. and Wood C. (1990) Prospective study of colorectal cancer in the West of Scotland: 10_year follow_up. *British journal of surgery* 77(3), 280-282.

McArdle C., McMillan D. and Hole D. (2006) The impact of blood loss, obstruction and perforation on survival in patients undergoing curative resection for colon cancer. *British journal of surgery* 93(4), 483-488.

McDermott F., Hughes E., Pihl E., Milne B. and Price A. (1981) Prognosis in relation to symptom duration in colon cancer. *British journal of surgery* 68(12), 846-849.

McDermott F., Hughes E., Pihl E., Milne B. and Price A. (1984) Influence of tumour differentiation on survival after resection for rectal cancer in a series of 1296 patients. *Australian and New Zealand Journal of Surgery* 54(1), 53-58.

McMichael A., McCall M., Hartshore J. and Woodings T. (1980) Patterns of gastro _ intestinal cancer in european migrants to Australia: The role of dietary change. *International Journal of Cancer* 25(4), 431-437.

McMichael A.J. and Potter J.D. (1980) Reproduction, endogenous and exogenous sex hormones, and colon cancer: a review and hypothesis.

McNally G.E., Lloyd D.M. and Grondona J.P. (2015) Carcinoembryonic Antigen as a Prognostic Factor in Colorectal Cancer with Liver Metastases. *Journal of Cancer Therapy* 6(12), 1035.

Mehrabani D., Almasi-Hashiani A., Moshfeghi K. and Khedmati E. (2012) Survival rate and its predictors in colorectal cancer patients, Southern Iran. *Middle East J Sci Res* 12(8), 1072-1077.

Mehrkhani F., Nasiri S., Donboli K., Meysamie A. and Hedayat A. (2009) Prognostic factors in survival of colorectal cancer patients after surgery. *Colorectal Disease* 11(2), 157-161.

Mella J., Biffin A., Radcliffe A., Stamataki J. and Steele R. (1997) Population_based audit of colorectal cancer management in two UK health regions. *British journal of surgery* 84(12), 1731-1736.

Mhaidat N.M., Al-Wedyan T.J., Alzoubi K.H., Al-Efan Q.M., Al-Azzam S.I., Balas Q.A. and Bataineh Z.A. (2014) Measuring Quality of Life among Colorectal Cancer Patients in Jordan. *Journal of palliative care* 30(3), 133-140.

Missaoui N., Jaidaine L., Abdelkader A.B., Trabelsi A., Mokni M. and Hmissa S. (2011) Colorectal cancer in central Tunisia: increasing incidence trends over a 15-year period. *Asian Pac j cancer prev* 121073-1076.

Missaoui N., Jaidaine L., Ben Abdelkader A., Beizig N., Anjorin A., Yaacoubi M.T. and Hmissa S. (2010) Clinicopathological patterns of colorectal cancer in Tunisia. *Asian Pacific J Cancer Prev* 111719-1722.

Mitry E., Benhamiche A.-M., Jouve J.-L., Clinard F., Finn-Faivre C. and Faivre J. (2001) Colorectal adenocarcinoma in patients under 45 years of age: comparison with

older patients in a well-defined French population. *Diseases of the colon & rectum* 44(3), 380-387.

Moghaddam A.A., Woodward M. and Huxley R. (2007) Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. *Cancer Epidemiology Biomarkers & Prevention* 16(12), 2533-2547.

Moghimi-Dehkordi B. and Safaee A. (2012) An overview of colorectal cancer survival rates and prognosis in Asia. *World J Gastrointest Oncol* 4(4), 71-75.

Moghimi-Dehkordi B., Safaee A. and Zali M.R. (2008) Prognostic factors in 1,138 Iranian colorectal cancer patients. *International journal of colorectal disease* 23(7), 683-688.

Moskal A., Norat T., Ferrari P. and Riboli E. (2007) Alcohol intake and colorectal cancer risk: A dose–response meta_analysis of published cohort studies. *International Journal of Cancer* 120(3), 664-671.

Muir C. and Parkin D. (1985) The world cancer burden: prevent or perish. *British medical journal (Clinical research ed.)* 290(6461), 5.

Naaeder S. and Archampong E. (1994) Cancer of the colon and rectum in Ghana: A 5 _year prospective study. *British journal of surgery* 81(3), 456-459.

Nedrebø B.S.O. (2013) Colorectal Cancer in Norway. National Treatment Guidelines and Outcomes.

Negri E., Franceschi S., Parpinel M. and La Vecchia C. (1998) Fiber intake and risk of colorectal cancer. *Cancer Epidemiology Biomarkers & Prevention* 7(8), 667-671.

Ntagirabiri R., Karayuba R., Ndayisaba G., Niyonkuru S. and Amani M. (2016) Colorectal Cancer: Epidemiological, Clinical and Histopathological Aspects in Burundi. *Open Journal of Gastroenterology* 6(03), 83.

O'Connell J.B., Maggard M.A., Liu J.H. and Etzioni D.A. (2003) Rates of colon and rectal cancers are increasing in young adults. *The American surgeon* 69(10), 866.

O'Connell J.B., Maggard M.A., Livingston E.H. and Cifford K.Y. (2004) Colorectal cancer in the young. *The American journal of surgery* 187(3), 343-348.

O'Connell J.B., Maggard M.A. and Ko C.Y. (2004) Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. *Journal of the National Cancer Institute* 96(19), 1420-1425.

Obafunwa J. (1990) Pattern of alimentary tract tumours in Plateau State: a middle belt area of Nigeria. *The Journal of tropical medicine and hygiene* 93(5), 351-354.

Öhman U. (1982) Prognosis in patients with obstructing colorectal carcinoma. *The American journal of surgery* 143(6), 742-747.

Ojo O., Odesanmi W. and Akinola O. (1991) The surgical pathology of colorectal carcinomas in Nigerians. *Tropical gastroenterology: official journal of the Digestive Diseases Foundation* 13(2), 64-69.

Okobia M. and Aligbe J. (2005) Pattern of malignant diseases at the University of Benin Teaching Hospital. *Tropical doctor* 35(2), 91-91.

Orbell J. and West N.J. (2010) Improving detection of colorectal cancer. *The Practitioner* 254(1733), 17-22.

Oya M., Takahashi S., Okuyama T., Yamaguchi M. and Ueda Y. (2003) Synchronous colorectal carcinoma: clinico-pathological features and prognosis. *Japanese journal of clinical oncology* 33(1), 38-43.

Pahlavan P.S. and Kanthan R. (2006) The epidemiology and clinical findings of colorectal cancer in Iran. *Women* 8643.40.

Palmer G., Martling A., Lagergren P., Cedermark B. and Holm T. (2008) Quality of life after potentially curative treatment for locally advanced rectal cancer. *Annals of surgical oncology* 15(11), 3109-3117.

Papadopoulos V., Michalopoulos A., Netta S., Basdanis G., Paramythiotis D., Zatagias A., Berovalis P. and Harlaftis N. (2004) Prognostic significance of mucinous component in colorectal carcinoma. *Techniques in coloproctology* 8(1), s123s125.

Park S.J., Lee K.Y. and Kim S.Y. (2008) Clinical significance of lymph node micrometastasis in stage I and II colon cancer. *Cancer Research and Treatment* 40(2), 75-80.

Parramore J.B., Wei J.P., Yeh K.A. and Fink A.S. (1998) Colorectal cancer in patients under forty: Presentation and outcome/Discussion. *The American surgeon* 64(6), 563.

Peedikayil M.C., Nair P., Seena S., Radhakrishnan L., Sadasivan S., Naryanan V. and Balakrishnan V. (2009) Colorectal cancer distribution in 220 Indian patients undergoing colonoscopy. *Indian Journal of Gastroenterology* 28(6), 212-215.

Peleg I.I., Maibach H.T., Brown S.H. and Wilcox C.M. (1994) Aspirin and nonsteroidal anti-inflammatory drug use and the risk of subsequent colorectal cancer. *Archives of internal medicine* 154(4), 394-400.

Pescatori M., Maria G., Beltrani B. and Mattana C. (1982) Site, emergency, and duration of symptoms in the prognosis of colorectal cancer. *Diseases of the colon & rectum* 25(1), 33-40.

Pino M.S. and Chung D.C. (2010) The chromosomal instability pathway in colon cancer. *Gastroenterology* 138(6), 2059-2072.

Popoola, Omodele F., Oludara M., NA I., AI I. and SBL M. (2013) Prevalence and Pattern of Cancers among Adults Attending a Tertiary Health Institution in Lagos, Nigeria. *Journal of Dental and Medical Sciences* 6(3), 68-73.

Potter J. (1995) Risk factors for colon neoplasia—epidemiology and biology. *European Journal of Cancer* 31(7), 1033-1038.

Ragnhammar P., Hafstrom L., Nygren P. and Glimelius B. (2001) A systematic overview of chemotherapy effects in colorectal cancer. *Acta Oncol* 40(2-3), 282-308.

Ramsey S.D., Andersen M.R., Etzioni R., Moinpour C., Peacock S., Potosky A. and Urban N. (2000) Quality of life in survivors of colorectal carcinoma. *Cancer* 88(6), 1294-1303.

Raskin L., Dakubo J.C., Palaski N., Greenson J. and Gruber S. (2012) Abstract B92: Molecular characterization of colorectal cancer in Ghana. *Cancer Prevention Research* 5(11 Supplement), B92-B92.

Richards C.H. (2014) An investigation of the determinants of the local and systemic inflammatory responses in patients with colorectal cancer, University of Glasgow.

Ries L., Melbert D. and Krapcho M. (2008) et al. SEER Cancer Statistics Review, 19752005 [based on November 2007 SEER data submission]. Bethesda, MD: National Cancer Institute; 2008.

Roberts A. (2008) Validator: Professor Robin CN Williamson, The Royal Society of Medicine, London.

Rosenberg R., Friederichs J., Schuster T., Gertler R., Maak M., Becker K., Grebner A., Ulm K., Höfler H. and Nekarda H. (2008) Prognosis of patients with colorectal cancer is associated with lymph node ratio: a single-center analysis of 3026 patients over a 25-year time period. *Annals of surgery* 248(6), 968-978.

Rosman A.S. and Korsten M.A. (2007) Meta-analysis comparing CT colonography, air contrast barium enema, and colonoscopy. *The American journal of medicine* 120(3), 203-210. e204.

Roychowdhury D., Hayden A. and Liepa A. (2003) Health-related quality-of-life parameters as independent prognostic factors in advanced or metastatic bladder cancer. *Journal of clinical oncology* 21(4), 673-678.

Sack J. and Rothman J.M. (2000) Colorectal cancer: natural history and management. *Hospital Physician* 3664-73.

Safaee A., Moghimi_dehkordi B., Fatemi S., Ghiasi S. and Zali M. (2012) Pathology and prognosis of colorectal cancer. *Iranian Journal of cancer prevention* 2(3), 137141.

Saha A., Smith K., Sue_Ling H., Sagar P., Burke D. and Finan P. (2011) Prognostic factors for survival after curative resection of Dukes' B colonic cancer. *Colorectal Disease* 13(12), 1390-1394.

Samad A., Taylor R., Marshall T. and Chapman M.A. (2005) A meta_analysis of the association of physical activity with reduced risk of colorectal cancer. *Colorectal Disease* 7(3), 204-213.

Sankaranarayanan R., Swaminathan R., Jayant K. and Brenner H. (2011) An overview of cancer survival in Africa, Asia, the Caribbean and Central America: the case for investment in cancer health services. *IARC Sci Publ* 162257-291.

Santarelli R.L., Pierre F. and Corpet D.E. (2008) Processed meat and colorectal cancer: a review of epidemiologic and experimental evidence. *Nutrition and cancer* 60(2), 131-144.

Scanlon V.C. and Sanders T. (2014) *Essentials of anatomy and physiology*: FA Davis.

Scott R.J. (2003) Familial adenomatous polyposis (FAP) and other polyposis syndromes. *Hereditary Cancer in Clinical Practice* 1(1), 19-30.

Segelman J. (2012) Colorectal cancer: aspects of multidisciplinary treatment, metastatic disease and sexual function.

Seleye-Fubara D. and Gbobo I. (2004) Pathological study of colorectal carcinoma in adult Nigerians: a study of 45 cases. *Nigerian journal of medicine: journal of the National Association of Resident Doctors of Nigeria* 14(2), 167-172.

Seymour M., Stenning S. and Cassidy J. (1997) Attitudes and practice in the management of metastatic colorectal cancer in Britain. *Clinical Oncology* 9(4), 248-251.

Siegel R., Ward E., Brawley O. and Jemal A. (2010) Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA: a cancer journal for clinicians* 61(4), 212-236.

Sighoko D., Curado M.P., Bourgeois D., Mendy M., Hainaut P. and Bah E. (2011) Increase in female liver cancer in the Gambia, West Africa: evidence from 19 years of population-based cancer registration (1988–2006). *PloS one* 6(4), e18415.

Singh H., Nugent Z., Mahmud S.M., Demers A.A. and Bernstein C.N. (2010) Predictors of colorectal cancer after negative colonoscopy: a population-based study. *The American journal of gastroenterology* 105(3), 663-673.

Singh S., Marquet R., de Bruin R., Westbroek D. and Jeekel J. (1987) Promotion of tumor growth by blood transfusions. *Transplantation proceedings* **19**, 1473-1474.

Sinha R. (2002) An epidemiologic approach to studying heterocyclic amines. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis* 506197-204.

Sjo O., Larsen S., Lunde O. and Nesbakken A. (2009) Short term outcome after emergency and elective surgery for colon cancer. *Colorectal Disease* 11(7), 733739.

Sjo O.H. (2012) Prognostic factors in colon cancer.

Society A.C. (2005) Colorectal Cancer Facts & Figures Special Edition 2005. *American Cancer Society*.

Society A.C. (2008) *Cancer facts & figures*: The Society.

Soliman A., Bondy M., El-Badawy S., Mokhtar N., Eissa S., Bayoumy S., Seifeldin I., Houlihan P., Lukish J. and Watanabe T. (2001) Contrasting molecular pathology of colorectal carcinoma in Egyptian and Western patients. *British journal of cancer* 85(7), 1037.

Soliman A.S., Bondy M.L., Levin B., Hamza M.R., Ismail K., Ismail S., Hammam H.M., El-Hattab O.H., Kamal S.M. and Soliman A.-G.A. (1997) Colorectal cancer in Egyptian patients under 40 years of age. *International Journal of Cancer* 71(1), 26-30.

Sprangers M., Taal B., Aaronson N. and Te Velde A. (1995) Quality of life in colorectal cancer. *Diseases of the colon & rectum* 38(4), 361-369.

Spratt J.S. and Spjut H.J. (1967) Prevalence and prognosis of individual clinical and pathologic variables associated with colorectal carcinoma. *Cancer* 20(11), 19761985.

Stubbs R. and Long M. (1986) Symptom duration and pathologic staging of colorectal cancer. *European journal of surgical oncology: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology* 12(2), 127-130.

Sule A. and Mandong B. (1999) Malignant colorectal tumours in patients 30 years and below: a review of 35 cases. *The Central African journal of medicine* 45(8), 209212.

Taha M.O.A., Abdalla A.A.E. and Mohamed R.S. (2015) Pattern & presentation of colorectal cancer in central Sudan, a retrospective descriptive study, 2010–2012. *Afr Health Sci* 15(2), 576-580.

Takada H., Ohsawa T., Iwamoto S., Yoshida R., Nakano M., Imada S., Yoshioka K., Okuno M., Masuya Y. and Hasegawa K. (2002) Changing site distribution of colorectal cancer in Japan. *Diseases of the colon & rectum* 45(9), 1249-1254.

Tan E., Gouvas N., Nicholls R.J., Ziprin P., Xynos E. and Tekkis P.P. (2009) Diagnostic precision of carcinoembryonic antigen in the detection of recurrence of colorectal cancer. *Surgical oncology* 18(1), 15-24.

Terry P., Giovannucci E., Michels K.B., Bergkvist L., Hansen H., Holmberg L. and Wolk A. (2001) Fruit, vegetables, dietary fiber, and risk of colorectal cancer. *Journal of the National Cancer Institute* 93(7), 525-533.

Thomas G., Dixon M., Smeeton N. and Williams N. (1983) Observer variation in the histological grading of rectal carcinoma. *Journal of clinical pathology* 36(4), 385391.

Thompson M., Flashman K., Wooldrage K., Rogers P., Senapati A., O'Leary D. and Atkin W. (2008) Flexible sigmoidoscopy and whole colonic imaging in the diagnosis of cancer in patients with colorectal symptoms. *British journal of surgery* 95(9), 1140-1146.

Thompson M., Perera R., Senapati A. and Dodds S. (2007) Predictive value of common symptom combinations in diagnosing colorectal cancer. *British journal of surgery* 94(10), 1260-1265.

Tisdale M.J. (2009) Mechanisms of cancer cachexia. *Physiological reviews* 89(2), 381410.

Toriola A.T., Kurl S., Laukanen J.A., Mazengo C. and Kauhanen J. (2008) Alcohol consumption and risk of colorectal cancer: the Findrink study. *European journal of epidemiology* 23(6), 395-401.

Tsang N.M., Pai P.C., Chuang C.C., Chuang W.C., Tseng C.K., Chang K.P., Yen T.C., Lin J.D. and Chang J.T.C. (2016) Overweight and obesity predict better overall survival rates in cancer patients with distant metastases. *Cancer medicine*.

Tsong W., Koh W., Yuan J., Wang R., Sun C. and Yu M. (2007) Cigarettes and alcohol in relation to colorectal cancer: the Singapore Chinese Health Study. *British journal of cancer* 96(5), 821-827.

Turkiewicz D., Miller B., Schache D., Cohen J. and Theile D. (2001) Young patients with colorectal cancer: how do they fare? *ANZ journal of surgery* 71(12), 707710.

Umpleby H., Williamson R. and Chir M. (1984) Survival in acute obstructing colorectal carcinoma. *Diseases of the colon & rectum* 27(5), 299-304.

Van Leersum N., Janssen_Heijnen M., Wouters M., Rutten H., Coebergh J.W., Tollenaar R. and Lemmens V. (2013) Increasing prevalence of comorbidity in patients with colorectal cancer in the South of the Netherlands 1995–2010. *International Journal of Cancer* 132(9), 2157-2163.

Vanek V., Whitt C., Abdu R. and Kennedy W. (1986) Comparison of right colon, left colon, and rectal carcinoma. *The American surgeon* 52(9), 504-509.

Vargas A.J. and Thompson P.A. (2012) Diet and nutrient factors in colorectal cancer risk. *Nutrition in Clinical Practice* 27(5), 613-623.

Vogelstein B., Fearon E.R., Hamilton S.R., Kern S.E., Preisinger A.C., Leppert M., Smits A.M. and Bos J.L. (1988) Genetic alterations during colorectal-tumor development. *New England Journal of Medicine* 319(9), 525-532.

Vrieling A. and Kampman E. (2010) The role of body mass index, physical activity, and diet in colorectal cancer recurrence and survival: a review of the literature. *The American journal of clinical nutrition*ajcn. 29005.

Wactawski-Wende J., Kotchen J.M., Anderson G.L., Assaf A.R., Brunner R.L., O'Sullivan M.J., Margolis K.L., Ockene J.K., Phillips L. and Pottern L. (2006) Calcium plus vitamin D supplementation and the risk of colorectal cancer. *New England Journal of Medicine* 354(7), 684-696.

Wallin U. (2011) Cancer of the Colon and Rectum: Prognostic Factors and Early Detection.

Wanebo H.J., Rao B., Pinsky C.M., Hoffman R.G., Stearns M., Schwartz M.K. and Oettgen H.F. (1978) Preoperative carcinoembryonic antigen level as a prognostic indicator in colorectal cancer. *New England Journal of Medicine* 299(9), 448-451.

Ward W.L., Hahn E.A., Mo F., Hernandez L., Tulsky D.S. and Cella D. (1999) Reliability and validity of the Functional Assessment of Cancer TherapyColorectal (FACT-C) quality of life instrument. *Quality of Life Research* 8(3), 181-195.

Whistance R.N., Conroy T., Chie W., Costantini A., Sezer O., Koller M., Johnson C.D., Pilkington S.A., Arraras J., Ben-Josef E., Pullyblank A.M., Fayers P. and Blazeby J.M. (2009) Clinical and psychometric validation of the EORTC QLQ-CR29

questionnaire module to assess health-related quality of life in patients with colorectal cancer. *Eur J Cancer* 45(17), 3017-3026.

Wiggers T., Arends J.W., Schutte B., Volovics L. and Bosman F. (1988a) A multivariate analysis of pathologic prognostic indicators in large bowel cancer. *Cancer* 61(2), 386-395.

Wiggers T., Arends J.W. and Volovics A. (1988b) Regression analysis of prognostic factors in colorectal cancer after curative resections. *Diseases of the colon & rectum* 31(1), 33-41.

Willett W.C., Stampfer M.J., Colditz G.A., Rosner B.A. and Speizer F.E. (1990) Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *New England Journal of Medicine* 323(24), 1664-1672.

Wiredu E.K. and Armah H.B. (2006) Cancer mortality patterns in Ghana: a 10-year review of autopsies and hospital mortality. *BMC public health* 6(1), 1.

Wolin K.Y., Lee I.M., Colditz G.A., Glynn R.J., Fuchs C. and Giovannucci E. (2007) Leisure_time physical activity patterns and risk of colon cancer in women. *International Journal of Cancer* 121(12), 2776-2781.

Yakabe T., Nakafusa Y., Sumi K., Miyoshi A., Kitajima Y., Sato S., Noshiro H. and Miyazaki K. (2010) Clinical significance of CEA and CA19-9 in postoperative follow-up of colorectal cancer. *Annals of surgical oncology* 17(9), 2349-2356.

Yawe K., Bakari A., Pindiga U. and Mayun A. (2007) Clinicopathological pattern and challenges in the management of colorectal cancer in sub-Saharan Africa. *J Chinese Clin Med* 2688-695.

Yeatman T.J. (2001) Colon cancer. *eLS*.

Zell J.A., Honda J., Ziogas A. and Anton-Culver H. (2008) Survival after colorectal cancer diagnosis is associated with colorectal cancer family history. *Cancer Epidemiology Biomarkers & Prevention* 17(11), 3134-3140.

Zhang S., Gao F., Luo J. and Yang J. (2010) Prognostic factors in survival of colorectal cancer patients with synchronous liver metastasis. *Colorectal Disease* 12(8), 754761.

Zisman A.L., Nickolov A., Brand R.E., Gorchow A. and Roy H.K. (2006) Associations between the age at diagnosis and location of colorectal cancer and the use of alcohol and tobacco: implications for screening. *Archives of internal medicine* 166(6), 629-634.

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APPENDIX

THE QLQ-C30 VERSION 1.0 WITH FUNCTIONAL / SYMPTOM SCALES INDICATED

	SCALE		NO	YES	
Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	Physical		1	2	
Do you have any trouble taking a **long** walk?	Physical		1	2	
Do you have any trouble take a **short** walk outside of the house?	Physical		1	2	
Do have to stay in bed or a chair for most of the day?	Physical		1	2	
Do you need help with eating, dressing, washing yourself or using the toilet?	Physical		1	2	
Are you limited in any way in doing either your work or doing household jobs?	Role		1	2	
Are you completely unable to work at a job or to do household jobs?	Role		1	2	
ring the past week:	**SCALE**	**Not at all**	**A little**	**Quite a bit**	**Very much**
Were you short of breath?	Dyspnoea	1	2	3	4
Have you had pain?	Pain	1	2	3	4
10. Did you need rest?	Fatigue	1	2	3	4
Have you had trouble sleeping?	Insomnia	1	2	3	4
Have you felt weak?	Fatigue	1	2	3	4
Have you lacked appetite?	Appetite Loss	1	2	3	4
Have you felt nauseated?	Nausea and Vomiting	1	2	3	4
Have you vomited?	Nausea and Vomiting	1	2	3	4

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ring the past week:	SCALE	Not at a l	A little	Quite a bit	Very much
Have you been constipated?	Constipation	1	2	3	4
Have you had diarrhoea?	Diarrhoea	1	2	3	4
Were you tired?	Fatigue	1	2	3	4
Did pain interfere with you daily activities?	Pain	1	2	3	4
Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	Cognitive	1	2	3	4
Did you feel tense?	Emotional	1	2	3	4
Did you worry?	Emotional	1	2	3	4
Did you feel irritable?	Emotional	1	2	3	4
Did you feel depressed?	Emotional	1	2	3	4
Have you had difficulty remembering things?	Cognitive	1	2	3	4
Has your physical condition or medical treatment interfered with your **family** life?	Social	1	2	3	4
Has your physical condition or medical treatment interfered with your **social** activities?	Social	1	2	3	4
Has your physical condition or medical treatment caused you financial difficulties?	Financial Difficulties	1	2	3	4

GLOBAL HEALTH STATUS

How would you rate your overall **physical condition** during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

How would you rate your overall **quality of life** during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

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EORTC QLQ – CR29

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
31. Did you urinate frequently during the day?	1	2	3	4
32. Did you urinate frequently during the night?	1	2	3	4
33. Have you had any unintentional release (leakage) of urine?	1	2	3	4
34. Did you have pain when you urinated?	1	2	3	4
35. Did you have abdominal pain?	1	2	3	4
36. Did you have pain in your buttocks/anal area/rectum?	1	2	3	4
37. Did you have a bloated feeling in your abdomen?	1	2	3	4
38. Have you had blood in your stools?	1	2	3	4
39. Have you had mucus in your stools?	1	2	3	4
40. Did you have a dry mouth?	1	2	3	4
41. Have you lost hair as a result of your treatment?	1	2	3	4
42. Have you had problems with your sense of taste?	1	2	3	4

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
43. Were you worried about your health in the future?	1	2	3	4
44. Have you worried about your weight?	1	2	3	4
45. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
46. Have you been feeling less feminine/masculine as a result of your disease or treatment?	1	2	3	4
47. Have you been dissatisfied with your body?	1	2	3	4
48. Do you have a stoma bag (colostomy/ileostomy)? (please circle the correct answer)	Yes		No	

Please go on to the next page

During the past week:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
Answer these questions ONLY IF YOU HAVE A STOMA BAG, if not please continue below:				
49. Have you had unintentional release of gas/flatulence from your stoma bag?	1	2	3	4
50. Have you had leakage of stools from your stoma bag?	1	2	3	4
51. Have you had sore skin around your stoma?	1	2	3	4
52. Did frequent bag changes occur during the day?	1	2	3	4
53. Did frequent bag changes occur during the night?	1	2	3	4
54. Did you feel embarrassed because of your stoma?	1	2	3	4
55. Did you have problems caring for your stoma?	1	2	3	4

Answer these questions ONLY IF YOU DO NOT HAVE A STOMA BAG:				
49. Have you had unintentional release of gas/flatulence from your back passage?	1	2	3	4
50. Have you had leakage of stools from your back passage?	1	2	3	4
51. Have you had sore skin around your anal area?	1	2	3	4
52. Did frequent bowel movements occur during the day?	1	2	3	4
53. Did frequent bowel movements occur during the night?	1	2	3	4
54. Did you feel embarrassed because of your bowel movement?	1	2	3	4

During the past 4 weeks:	**Not at All**	**A Little**	**Quite a Bit**	**Very Much**
For men only:				
56. To what extent were you interested in sex?	1	2	3	4
57. Did you have difficulty getting or maintaining an erection?	1	2	3	4

For women only:				
58. To what extent were you interested in sex?	1	2	3	4
59. Did you have pain or discomfort during intercourse?	1	2	3	4