DRUG THERAPY PROBLEMS AND HEALTH RELATED QUALITY OF LIFE AMONG PATIENTS WITH COLORECTAL CANCER AT KENYATTA NATIONAL HOSPITAL

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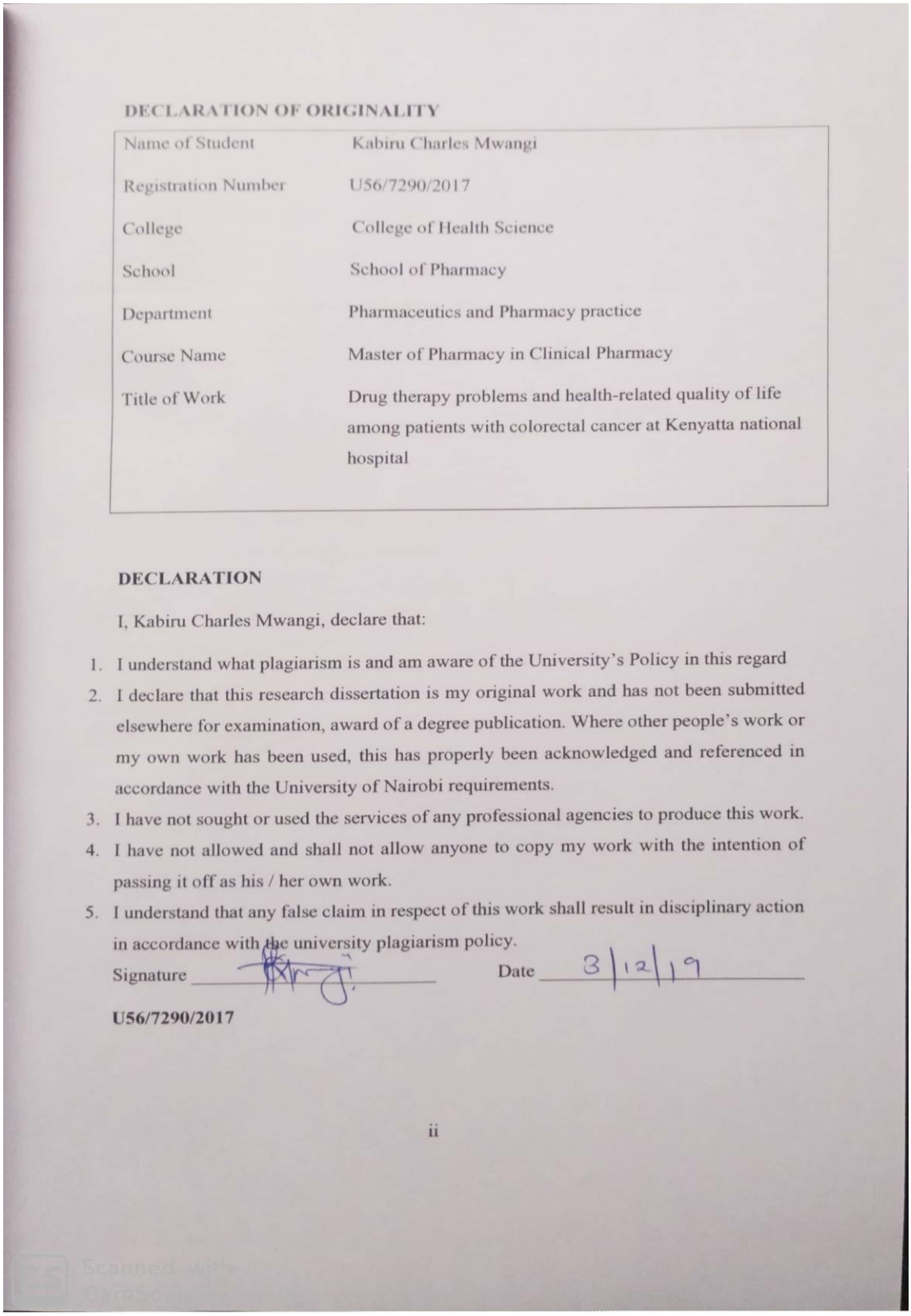
U56/7290/2017

A Research dissertation submitted in partial fulfilment of the requirement for the award of the Degree of Master of Pharmacy in Clinical Pharmacy in the School of Pharmacy of the University of Nairobi

November, 2019

DECLARATION OF ORIGINALITY



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I wish to dedicate this work to my friends and family for their unwavering support and encouragement

ACKNOWLEDGEMENTS

To my Heavenly Father for His Grace is sufficient

Special Thanks to Dr. Karimi P N, Dr. Nyamu DG, and Dr. Weru I. for continuous counsel, advice, guidance, and suggestions throughout the research and dissertation writing.

To the Kenyatta National Hospital staff in the records department, Oncology wards and the patients, for the support and cooperation during the data collection.

To the school of Pharmacy, Departments of Pharmaceutics and Pharmacy practice for providing adequate training and conducive environment for the actualization of the study

To my employer, County Government of Kiambu for accepting to offer study leave and the Ministry of Health, for sponsoring my studies.

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ABBREVIATIONS AND ACRONYMS

5FU	5 Fluorouracil
BMI	Body Mass Index
CRC	Colorectal cancer
CTC	Cancer Treatment Centre
CVD	Cardiovascular disease
DM	Diabetes Mellitus
DTP	Drug Therapy problem
EH	Environmental Health
FOLFIRI	Folinic acid – Fluorouracil - Irinotecan
FOLFIRINOX	Folinic acid – Fluorouracil – Irinotecan - Oxaliplatin
FOLFOX	Folinic acid – Fluorouracil - Oxaliplatin
HRQoL	Health-related quality of life
HTN	Hypertension
IRB	Irritable Bowel disease
KNH	Kenyatta National Hospital
KNH/UON ERC	Kenyatta National Hospital/ University of Nairobi – Ethics and Research Committee
KPCC	Kenyatta Prime Care center
PH	Physical Health
PROMIS	Patient-Reported Outcomes Measurement Information System
Psyc H	Psychological Health
QoL	Quality of Life
SR	Social Relations
WHO	World Health Organisation
WHOQoL	World Health Organisation Quality of life
XELOX	Capecitabine and Oxaliplatin

DEFINITION OF TERMS

Advanced Stage Cancer - "is cancer that is far along in its growth, and has spread to the lymph nodes or other places in the body"

Chemotherapy - "is the treatment of disease by the use of chemical substances, especially the treatment of cancer by cytotoxic and other drugs"

Colorectal Cancer - "is cancer that develops in the colon (the longest part of the large intestine) and/or the rectum, the last several inches of the large intestine before the anus"

Drug Therapy Problem "Any undesirable event experienced by a patient with drug-related needs and prevents him or her from achieving drug-related goals of therapy"

Health-Related Quality of life – "is the state of complete physical, mental and social well-being and not merely the absence of disease and include both objective and subjective perspectives in each of the above domain considering the individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"

Well-Being- "is a state of being comfortable, healthy or happy"

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ABSTRACT

Background: Colorectal cancer is the third most common form of cancer in males and the second in females. The ill-health due to cancer and use of multiple therapies may result in drug therapy problems as well as psychophysical, functional and social impairment which in turn affect the health-related quality of life of the patient.

Objective: To evaluate drug therapy problems and health-related quality of life among patients with colorectal cancer at Kenyatta National Hospital.

Methodology: A descriptive cross-sectional study was conducted to determine the drug therapy problem and health-related quality of life among 71 patients with colorectal cancer at cancer management units of Kenyatta National Hospital. Simple random sampling was used to select the participants. Health-related quality of life was measured using the generic tool World Health Organisation Quality Of Life-BREF, and a structured questionnaire was used to identify drug therapy problems. The data were analysed using descriptive and inferential statistics at 95% confidence limit. STATA version 15.0 was used to analyse the data.

Results: Most patients were females (52.1%), had a mean age of 55.9 (± 4.4) years. Drug therapy problems caused by adverse drug reaction (45.1%) were the most common. Approximately two thirds (67.6%) of participants complained of gastrointestinal problems followed by general systems (36.6%) and cardiovascular (29.6%). Quality of life assessment indicated that psychological health had the highest score at 60.5%. In multivariate regression analysis, the presence of comorbidities (p = 0.021), having insurance cover (p = 0.038), dietary intake without fruits and vegetables (p = 0.02), and drug therapy problems (p = 0.012) were significantly associated with poor health-related quality of life.

Conclusion: The main drug therapy problems were an adverse drug events. Health-related quality of life among was low across all the domains

Recommendation: Strategies to contain drug therapy problems and improve health-related quality of life should be employed among colorectal cancer patients.

CHAPTER ONE: INTRODUCTION

1.1 Background to the study

Colorectal cancer (CRC) is the third commonest form of malignant neoplasm and the fourth main cause of cancer mortality in the world (1). CRC is the third most typical form of cancer in males and the second in females globally. In Kenya, it is the third and fourth most typical form of cancer in males and females respectively (2). The prevalence of CRC is increasing progressively in countries undergoing industrialization. The pathological state caused by cancer and the effects associated with drug therapy problems may cause psychological, physical, functional and social impairment which in turn affects Health related quality of life (HRQoL) (3).

CRC is a significant public health problem in Kenya. Cancer of the colon is placed fourth among cancers reported in both genders, accounting for 3.9% and 2.7% in males and females respectively (2). Cancer of the rectum is placed third and fourth among cancers reported in males and females accounting for 1.9% and 3.1% respectively (4). When combined together, CRCs would account for 7.4 % of male cancers hence becoming the third commonest cancer among men and 5.9% of female cancers thus the third most common form of cancer among women (2,5).

Currently, there is an increase in colorectal cancer cases in Africa where it presents in the late stages and in relatively younger patients. Worse treatment outcomes are tied to treatment access, drug therapy problem, screening practice and presence and nature of comorbidities. In an earlier study in Kenya, CRC mortality was worse in men (6). The follow-up challenges were a major and true clinical outcome in terms of HRQoL remains largely unknown. Abegaz *et al.* observed that HRQoL of cancer patients in Ethiopia was low (7). Patients with a limited rate of disease metastasis had improved HRQoL. However, the unmet needs of cancer patients and the level of satisfaction with the overall care were found to influence the extent of HRQoL. Therefore, early detection of cancer to arrest metastasis was warranted in order to achieve better quality of life (QoL). In addition, addressing the unmet needs of these patients and ensuring a higher satisfaction rate were recommended to maintain adequate HRQoL (7). This study seeks to define CRC and relate it to patients' HRQoL.

There have been several studies done at Kenyatta National Hospital (KNH) on CRC but none had explained the drug therapy problems and health effects of quality of life among patients undergoing treatment.

This study looked at the effect of the disease and the drugs on all the domains of health-related quality of life for patients who attended treatment at KNH.

1.2 Problem statement

Cancer has become a public health concern in Kenya contributing a significant burden to morbidity and mortality within Kenyan Health Systems. The incidence of colon cancer is reported to be increasing and being the 3rd most common cause of mortality after lung and liver cancer. There is a need to focus on the various forms of interventions, the associated drug therapy problem, the procedures used and the HRQoL. CRC has effects on the body based on the size and location of the disease. These include changes in bowel habits, consistency, and blood in the stool, abdominal discomfort, and anemia. When left untreated, it causes death. During treatment, anticancer drugs have adverse effects like hair loss, bleeding, mouth sores, difficulty in swallowing among others that greatly affect the HRQoL (8). Both physical and physiological health is impaired. This is due to the bodily harm associated with drug therapy. These impair patients' self- esteem. However, there seems to be a gap in the studies on drug therapy problems and the quality of life of patients undergoing treatment for colon cancer since it's considered rare in Kenya.

The drug therapy problems have major effects on HRQoL. A study conducted in Tikur Anbessa Ethiopia by Sisay EA *et al*. showed that Drug therapy problems were common among cancer patients in their set up indicating the need for interventions for better treatment outcomes (9). Amsalu *et al*. observed that the common drug therapy problems among cervical cancer patients who attend treatment in KNH are ADRs, drug interactions and the need for additional drug therapy. Using the multivariable binary logistic regression analysis, the advanced stage of cervical cancer and treatment with more than five drugs were significant predictors of ADRs. Moreover, coexisting retroviral disease and treatment with more than five medications were also predictors of drug interactions and dosing problems (10). Despite researches on colorectal cancer, there were no studies that had been done in relation to drug therapy problems and HRQoL among patients on treatment at KNH. This created a need to carry out this study.

1.3 Research Questions

1. What medicines were used to manage patients with colorectal cancer at KNH?
2. What were the drug therapy problems among patients with colorectal cancer at KNH?
3. What were the HRQoL scores of patients with colorectal cancer at KNH?

1.4 Objectives

1.4.1 Main Objective

To evaluate the drug therapy problems and health-related quality of life among patients with colorectal cancer at KNH.

1.4.2 Specific Objectives

1. To describe the patterns of management of colorectal cancer at KNH.
2. To find out the drug therapy problems among patients 18 years and above with colorectal cancer at KNH.
3. To find out the HRQoL of patients with colorectal cancer at KNH.

1.5 Significance of the study

The study identifies the commonly experienced drug therapy problems by colorectal cancer patients that prevents them from achieving their best health-related quality of life. The ability to manage the drug therapy problem will impact positively on patients' HRQoL. The health care workers will get information on drug therapy problems associated with the various regimens and their effects on HRQoL. The results showed a causal relationship between drug therapy being used and its impact on HRQoL.

1.6 Delimitations

This study was carried out in the Cancer Treatment Centre, hemato – oncology ward and clinic and Kenyatta Prime Care Centre at KNH with all the patients who meet the set criteria or are eligible were selected using simple random sampling. The data will be collected using questionnaires, interviews and medical records.

1.7 Limitations

Being a cross-sectional study design, there were constraints to generalizability and application to practice due to the smaller sample size.

Moreover, the study was conducted in cancer treatment centre which had a wide scope of treatment, accessibility, consultants and resources that favor the outcome and the study population presenting with colorectal cases, hence such results obtained could affect generalizability.

Patients may not be willing to give out accurate information, rather give information that they think the investigator wants to hear hence response bias.

Being a cross-sectional design, the causal effect relationship could not be defined explicitly between the dependent and independent variables due to over-representation or under-representation in the sample. Lack of reliable data was also a limitation since KNH has not fully embraced electronic data. There were challenges in retrieving information from the patient files hence compromising the scope of analysis.

Though there had been several studies on CRC at KNH, none had focused on drug therapy problems and health related quality of life.

1.8 Conceptual framework

Drug therapy problems and other intervening variables usually have great impact on the HRQoL. For instance, the DTP associated with unnecessary drug therapy may have a negative effect on both the physical health and physiological health of the patient. The use of neoadjuvant chemotherapy that could not assist in tumor reduction greatly affects the HRQoL.

Need for additional therapy either for synergism or to relieve the side effect of one drug is always important just like its omission could create opportunities for comorbidities to thrive hence affecting the HRQoL.

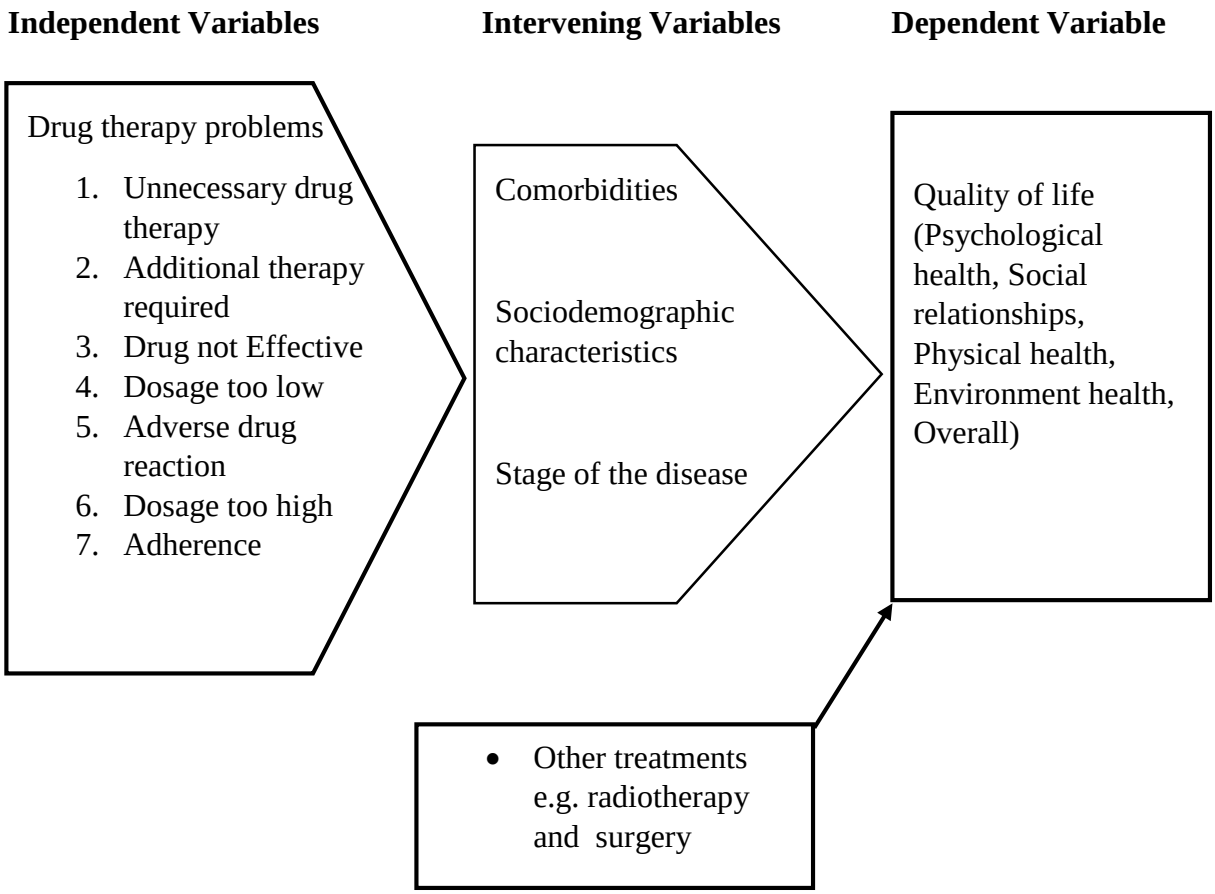

Figure 1. 1 Conceptual framework **(Author: *kabiru, 2019*)**

Ineffective therapy could cause disease progression which imparts negatively on both physical and social health. The QoL of the patient associated with poor prognosis will cause deterioration of patients' health.

Inadequate dosing could cause rapid disease progression due to the inability to minimize the cancer cell growth rate. Ultimately, the physical and physiological health would be impaired thus the disease advancing to late stages if no medication therapy monitoring intervention done.

The adverse drug events have an effect on HRQoL from the patients' perspective since they are symptomatic. Adherence also has an effect on HRQoL. The social relationship would be affected when the patient knows the inevitable occurrence of death hence not be adherent to treatment. This would also be due to challenges in social-economic status (11).

The desire is have an optimal drug use with minimal drug therapy problems thus improve the HRQoL.

Surgery and radiotherapy forms of management were considered as intervening factors that could affect the HRQoL in either way hence considered as confounders. The other factors considered were comorbidities, Social demographic characteristics and the stage of the disease. The late stages of colorectal cancer had an impact on HRQoL due to palliative form of management and the expectation of poor prognosis.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter summarizes studies and findings on factors that affect HRQoL of patients with colorectal cancer. The problems associated with different chemotherapy regimens used are also described.

2.2 Overview of CRC

CRC is one of the leading causes of cancer fatality. In CRC, cancer of the colon represents 72% while the cancer of the rectum represents 28%, although their occurrence are reported together as CRC (12). The classification of CRC depends on the pathological stage, which is observed after surgery. The clinical and the pathological stages are different, just as the imaging tests are different from the observed stage after surgery (13).

In the last decade of cancer studies, it has been observed that during oncogenesis the cells tend to acquire various biological capabilities during the multi-hit development of tumours (14). Hence the tumours are persistent masses of proliferating cells similar characteristic to embryonic cells. The tumours appear as complex tissues of various cell types interacting with one another (15).

For CRC, cells possess an ordered sequence of events called “adenoma-carcinoma sequence,” which oversees the transformation of normal colonic epithelium to an adenomatous intermediate and then into an adenocarcinoma. This evolution to the neoplastic state is facilitated by genomic instability (13).

Cancer occurs due to several DNA damages that affect proto-oncogenes, tumour suppressor genes, and DNA repair genes. In CRC, the molecular changes occurring are chromosome instability (CIN), microsatellite instability (MSI), and CpG island methylator phenotype (CIMP) (16)

About 95% of CRC cases are sporadical. In these cases, the mutation of genes occurs by chance. 5% of CRC are familial cases and are less common. These occur when gene mutations are passed within a family from generation to another. In these cases, the mutated genes or germline mutation are inherited. The inherited forms include the hereditary non-polyposis colorectal cancer (HNPCC), familial adenomatous polyposis (FAP), MYH-associated polyposis (MAP), Peutz-Jeghers syndrome (PJS) and juvenile polyposis syndrome (JPS) (12).

Development of CRC is associated with the following factors; older age, being male, smoking, alcohol, race/ethnicity, consuming red or processed meat, inherited predisposition syndromes, family history of CRC or polyps, physical inactivity and conditions like obesity, diabetes and IRB (17,18). It has been noted that increases in mortality may be as a result of increases in incidence. However. the number of death associated with CRC are set to double by 2035 for most countries hence should be an alarm for the increased future burden of CRC. This will need strong preventive measures and healthier lifestyles (1). The presence of CRC has effects on the HRQoL of the patient.

2.3 Health-Related Quality of Life

HRQoL is a concept involving several dimensions that include domains linked to physical, mental, emotional, and social functioning (3). It exceeds the direct measures of population health, life expectancy, causes of death, and emphasize on the impact the health status has on QoL. HRQoL uses the concept of well-being, that examines the positive aspects of a person's life, like satisfaction and positive emotions in life (3).

Health care professionals have used HRQoL to determine the effects of treatments, chronic illness, and short/long-term disabilities. Having already existing determinants of HRQoL, methodological development in this area is still ongoing. There are various ways and tools that have been used to evaluate and monitor HRQoL (19):

PROMIS is a Global Health Measure that examines global physical, mental, and social HRQoL. The questions are based on self-rated health, physical, mental HRQoL, pain, emotional distress, fatigue, social activities, and roles (20).

Well-Being Measure. It is a tool that analyses the positive evaluations of people's daily lives. It focuses on when one feels very healthy and satisfied with life, the quality of their relationships, positive emotions, resilience and realization of their potential (20).

Participation Measure. It reflects individuals' assessments of the impact of their health on their social participation within their current environment. Participation includes education, civic, employment, social, and leisure activities. It uses the principle that a person with a functional limitation like mobility difficulty, vision loss or intellectual disability can live a long productive life and enjoy a good QoL (21).

The WHOQOL-BREF instrument is the most commonly used tool that comprises 26 items. The domains measured are: physical health, social relationships, psychological health, and environment (22).

2.3.1 Psychological Health

This is a subjective domain of the HRQoL that determines the status of mental health as reported by the patient. It assesses the patient's bodily image and figure, self-esteem, positive and negative emotional feelings, individual belief system as well as the thought process, learning, memory and mental focus (23).

The usual concerns about QoL reported by colorectal cancer patients include: bowel problems, emotional problems, sexual dysfunction, lack of energy, and having undesired body image. The risk features associated with psychological health problems and poorer QoL in colorectal cancer patients are poor social support, lack of optimism, negative threat evaluation, presence of colorectal cancer and its stage, and a persistent stoma (24).

Psychological distress is recurrent among colorectal patients even five years post-diagnosis. Distress is experienced by the patient in the form of anxiety, depression, and traumatic stress symptoms. Furthermore, anxiety and traumatic stress symptoms are associated with pain and gastrointestinal distress (25).

Depression is a common symptom in cancer and is a comorbid disabling syndrome that affects about 15-25% of these patients. Depression leads to complications in treatment majorly through poor compliance to treatment hence worsening the situation. It is noted that patients having colon cancer always report emotional and psychological morbidities due to long treatment duration, adverse effects of treatment, interference of normal life and diminished HRQoL (11,26).

Nordin et al., observes that the measure of depression and anxiety at the time of diagnosis predicts a similar results six months after and that the patients' satisfaction with life was linked to depression (27). In Turkey, a study shows a similar report in which 23.6% of patients had depression which was strongly linked to poor HRQoL. Furthermore, depression has shown a compelling impact on the combined global HRQoL of patients (27).

2.3.2 Physical Health

The physical health or well-being refers to the extent to which colorectal cancer and its treatment induce physical changes that cause hindrance in the capacity to perform daily physical tasks. It is a patient's self-opinion about their perceived HRQoL and how it is affected by the illness or treatment (28).

The decreased physical activity caused by exercise intolerance due to debilitating symptoms and adverse effects of treatment for CRC impairs greatly the QoL of the patient. This affects the individual capacity to perform normal daily routines effectively hence affecting their independence and Quality of life (24).

Caroleen et al observe that the physical health of colorectal patients declined within the 6 months post-diagnosis majorly those in the third and fourth stages. Upon follow-up, CRC patients have significant overall impairment of daily activities such as eating, dressing and walking. CRC patients, particularly stage four, have greater odds of being at risk for major depressive disorder relative to those without (29).

2.3.3 Social Health

The social aspect of a person's life is where they put in most of their time. The dynamics and demands of each one contribute to one's state of health or disease. The balance between the different social aspects of one's life is often a challenge and struggle. These aspects impart a person's mental and emotional health, their motivation and need to recover as well as lifestyle modification and sense of belongingness (23). The HRQoL concept reviews the patient's point of view as a pillar of the health care relationship (4). HRQoL is incorporated into a set of existing tools focused on quantifying the patient's perspective, mostly the results of ill-health condition on the patient's day to day life. The reports on their health are diverse and social factors like gender, age, professional status is likely to impart differently on self-perception and reporting on health. The social aspects of HRQoL seem under-researched (30)

There are four major determinants of social indicators in HRQoL namely: education level, marital status, occupational and net income per household, and they should be independent of age and gender. The social determinants of HRQoL are explored by acquiring a multidisciplinary and multilevel research approach of HRQoL. Moreover, check the individual's ability to participate in the social aspect of their health conditions (30).

Patients encounter with healthcare professionals and the social insurance officials have shown improvement on the HRQoL. This is due to reassurance on the improvement of their condition by the healthcare personnel and payment of medical bills by insurance (31).

In a study by Marventano et al reports that the prevalence of depression, distress, and anxiety among CRC patients is significantly higher when compared to the general population (3)

Therefore, lack of social support may lead to poor compliance to treatment for colorectal cancer thus causing poor treatment outcomes hence poor HRQoL.

2.3.4 Environmental Health

Environmental health has various domains like physical safety, financial resources, and security. It also encompasses the calibre and availability of health and social care enjoyed by patient, the status of the home environment. Furthermore, it covers the physical environment and recreational activities among others (23,32).

A survey done by Magaji *et al.* reported that patients having colorectal cancer undergo financial hardships associated with job loss and increased cost of treatment and the period. Alternatively, patients may fail to honor oncologist's appointments/ visits as well as compliance to the long treatments period due to financial burden and fear to loose job (32).

2.4 Drug Therapy Problems

DTP is any unpleasant occurrence experienced by a patient with drug-related needs and prevents him or her from achieving drug-related goals of therapy (33). This event involves drug treatment that potentially interferes and prevents the patient from encountering an optimum outcome of the medical care. It is estimated that 20% of patients experience a DTP after drug administration (34).

In treatment of diseases, drug therapy usually strengthens the HRQoL. However, the irrational use of drugs may be detrimental and cause DTPs. In order to achieve a quality health care service any DTP should be identified and corrected (34,35). Common DTP include, unnecessary drug therapy, the need for additional therapy, drug not being effective, Dosage being too low, dosage being too high, adverse drug reactions and Adherence (33).

Unneeded drug therapy may be as a result of duplication of drug. Use of multiple drug products to target similar area during treatment of colorectal cancer may be unnecessary if both administered at the same time. Moreover, no medication may be indicated at that time if

the illness has progressed to palliative stage or where only palliative care is advocated. In cases where non-drug therapy is recommended, for example dietary restriction and exercise, administration of therapy may greatly affect the HRQoL for colorectal patients.

Need for additional therapy usually aim for synergism and preventive therapy as well as treatment of untreated condition. Preventive therapy in colorectal cancer patients is essential to protect from comorbidities. Additional drug therapy also plays part in synergistic effect in order to clear the cancer cells. Failure to note the therapy problem may impart challenges in the HRQoL.

Ineffective drug is commonly caused when the condition becomes refractory to the medication and when more effective drug is available but cannot be used due to its cost. Sometimes colorectal cancer may be refractory to the medication therapy hence different drug regimen is essential. In cases where the drug is contraindicated to the patient it may pose a challenge to treatment. This greatly affect the HRQoL of the patient.

Dosage too low is another form of drug therapy problem. In cases where the dose is ineffective, then it may not produce the desired response. Even frequency of administration may be inappropriate hence preventing desired response. Duration of therapy may also be so short to produce the required response. All the above may hinder the patient from achieving the desired outcome hence impacting negative on HRQoL.

Adverse drug reaction is a common effect with anti-cancer drugs. The undesirable effect is not dose related. Some drugs may be unsafe for the patient hence a safer drug is required in order to avoid further risk and impairment of HRQoL. Sometimes drug interaction may cause the adverse effects that are not dose related. In some cases the patient maybe allergic to the drug molecule hence affecting the HRQoL.

Dosage too high is a common DTP. In some cases, the dose of the anticancer drugs may be too high for the patient resulting in toxicity. This may be due to drug interaction or in some cases the duration of the cycle and dosing frequency may be short hence resulting in toxicity in colorectal patients. When there is no monitoring of the dose, this in turn affect the quality of life.

Adherence to treatment is a drug therapy problem that tend to be multi-faceted. It occurs from situations where the patient cannot meet the expense of purchasing the drug, drug not available, the patient prefer not to take either due to social or physical problems associated

with the medication. These in turn affect the quality of life of the colorectal patients leading to poor outcome.

A study done by Ayalew et al. reported that regimen deviation from local procedure accounted for 42.2% of the 155 cases. DTP was identified in 118 of these patients accounting for 76.1% DTP were frequent among patients who had cancer in their system stipulating need for intervention like participation of a pharmacist for better therapeutic outcome (36).

A study done in Norway indicated that the incidence of DTP per patient increased approximately linearly with the increase in the number of medications being used. Moreover, the length of hospital stay is a risk factor for DTPs in collaboration with the presence of co-morbidity and number of medications (37).

Identification and intervention on the potential DTPs, together with recognition of drugs carrying a high-risk for DTPs, are important elements in drug therapy and will contribute to reduction of drug-related morbidity and mortality.

2.5 Chemotherapy regimen used to treat Colorectal cancer

Chemotherapy involve the use of anticancer drugs formulated to slow or stop the growth of fast dividing cancer cells in the body.

Chemotherapy can be administered through parenteral method: - where drugs are injected directly into blood through a vein or administered via oral route. The drug in systemic circulation reduces risk of CRC spread to other body parts (38). Chemotherapy course is administered in several cycles, each with 2 – 4 days protocols separated with rest period for drug wash out(39). This allows the body to recover before the next cycle (40).

Chemotherapy can be used at different times and for different purposes: - Neo-adjuvant chemotherapy is given and sometimes with radiation, before surgery for tumour reduction and easy surgical excision. This is a common practice with rectal cancer treatment. Adjuvant chemotherapy is given after surgery with the aim of destroying any microscopic cancer cells that are undetectable and those that have metastasized to other body parts. This helps lower the chance of the cancer recurring. For CRC that have metastasized to other organs like the liver, chemotherapy tend to reduce the tumour and burden of illness. While it's not likely to cure the cancer, this often helps improve the patients well-being and reduce mortality by improving the HRQoL (13,41).

Based on the American cancer Society guideline, combination of two or three of the following anti-cancer drugs are used in treatment of CRC, 5-Fluorouracil (5-FU),.Irinotecan, Oxaliplatin, leucovorin (folinic acid) and Capecitabine(41). The chemotherapy first-line treatment of metastatic disease is usually a combination of 5-fluorouracil, leucovorin and either oxaliplatin (FOLFOX protocol) or irinotecan (FOLFIRI protocol). 5-FU in the FOLFOX regimen can be replaced by capecitabine, but combining capecitabine with irinotecan is more toxic than combining 5FU and irinotecan(38). It is recommended to use the above anticancer regimen together with targeted therapy like Bevacizumab, Cetuximab, Panitumumab, Regorafenib (Stivarga), Trifluridine and tipiracil (Lonsurf) for metastatic colorectal cancer(41). They are less likely to harm normal cells compared to chemotherapy(40,42). In KNH the following treatment regimen are mostly used, FOLFOX 6 (FOLFOX 4 Sometimes), XELOX and in case of advanced disease FOLFIRI and FOLFIRINOX are used.

2.6 Patient characteristics

There is little evidence that can be obtained from literature explaining the effect of demographic aspects like age and sex in relation to the HRQoL among CRC patients. Peleg-oren *et al.* (39) reported stronger psychosocial adjustment among male having colon cancer than in female. Dibble *et al.* (43) observed that there were no remarkable difference in overall HRQoL on cancer patients from both gender; however, female patients have better interpersonal well-being compared to the males with colorectal cancer. Lundy et al reported that education level is not a determinant for HRQoL (44), because its role is inferior to income. In reference to income, there is proof that low income is associated with poor physical, social and emotional well-being dimensions of HRQoL (3). A wide social network has significant positive impact on patients HRQoL (45). Patients living in solitary reported a lower perception of well-being compared to those who lived with family, but there is no association of marital status with a higher HRQoL (3)

Patients with CRC regularly present at an advanced age with multiple comorbid conditions and complex care needs at the time of diagnosis. Comorbidities in CRC patients can be divided into 5 main groups namely: cardiovascular problems (CVD), diabetes (DM), both cardiovascular problems and diabetes (CVD+DM), other comorbidities (OC), and no comorbidities (46,47). The most recurrent illness is CVD, previous cancers, hypertension and diabetes. The prevalence of comorbidity, particularly the CVD, previous cancer and DM, is

elevated in the ascending colon. Markedly raised in patients having Dukes' stage A, as a result of early detection due to systematic monitoring for the comorbid conditions. Comorbidities have no association with resection rate, although has a negative association with short-term survival. Comorbidities are common in elderly male and influences the prognosis (48). In a study done in China, it was reported that there is a significant relationship among comorbidities and HRQOL among CRC patient. Those with comorbidities generally report lower HRQOL scores. These findings recommended a comprehensive care for CRC patients (49). Sarfati et al reported that patients having comorbidities have dismal survival rate, poorer QoL, and higher health care costs (50).

The advancement of the CRC at the time of diagnosis determines the prognosis. It is estimated that 90% of patients without metastatic disease, and 7% for those diagnosed with metastatic disease may attain five-year survival. Symptoms mostly occur later during evolution of the disease hence consequently diagnosed at an advanced stage (51,52). In patients having advanced-stage disease, cancer treatment therapy will compromise HRQoL instead of improving patient's well-being. HRQoL assessment can also enlighten patients' on their unmet emotional, social and spiritual concerns, which should be addressed in a palliative care setting (52).

Surgery and radiotherapy are best used on localized tumour with favourable histological grade. Moreover, for curative purpose at early stage and when the tumour is small after preoperative biopsies with no unfavourable pathological characteristics, surgery or radiotherapy can be used alone. If the cancer has metastasized, or is inoperable or recurrent, chemotherapy can be combined with surgery or radiotherapy. For most localized colorectal cancer the treatment may lead to cure, although for metastatic state of the disease the purpose is to delay disease progression or alleviate the symptoms (38,53)

Surgery tend to be the preferred treatment for colon and rectal cancers. However, the surgical skill tend to affect the outcome in terms of patient survival and recurrence of tumour. In colonic tumour the surgical procedure involves segmental resection with anastomosis. For rectal tumour it involves trans-anal extirpation, anterior resection with anastomosis or abdominoperineal extirpation with formation of an ostomy. However, Total meso-rectal excision (TME) is preferred and considered a reliable skill in rectal cancer surgery (54). The site of the tumour determines the type and extent of tumour removal. Surgical treatment of CRC may need the formation of an ostomy as part of treatment because unwell patient due to

bowel obstruction by the tumour or perforation will at least give chance to a reasonable QoL or administer radiotherapy in high dose targeting the tumour as a treatment modality (55). The liver is a common metastatic site for the spread of CRC. Surgical extirpation of the liver remains the main treatment modality for the cure of cancer in patients with hepatic - colorectal metastases. Untreated metastasis usually leads to poor prognosis in such patients (18).

2.7 Summary

DTP is any unpleasant occurrence experienced by a patient with drug linked needs and prevents him or her from achieving drug-related goals of therapy and it is estimated to occur in 20% of patients on medication. It tends to increase linearly with increase in number of drugs taken. For colorectal cancer patients it is markedly increased due to treatment of comorbidities associated, hence increasing the pill burden. This greatly contributes to direct or indirect effect on the HRQoL of CRC patients.

Since the number of colorectal cancer survivors is markedly improving, assessment of their HRQoL becomes supreme in order to find out the impact of the disease and the management plan on the survivors. Despite researches on colorectal cancer, there are no studies that have been done in relation to drug therapy problem and HRQoL among patients on treatment at KNH. The information and knowledge obtained from this study can be used to advice care givers on interventions to meet CRC patient support needs and care. The findings would also guide the development of appropriate policies, plans, and intervention programs for the prevention and management of DTPs. This in turn, would improve the quality of care for colorectal cancer patients on treatment in hospitals within the country.

2.8 Study Justification

The goal of therapy for colorectal cancer treatment is life expectancy maximization, improved HRQoL and prevention of the disease progression and hospital admissions. These are achievable with optimal treatment in accordance with the clinical practice guidelines, patient adherence and minimized drug therapy problems.

Having the HRQoL tool is an indicator enough to predict the morbidity and mortality among the colorectal patients on treatment. Determining the HRQoL allowed for the objective evaluation of how and to what extent the drug therapy problem and other intervening factors influenced the patients' HRQoL and how effectively the issues could be dealt with. These assessments were used as a basis for measurements of outcome that provided a framework to

determine the impact of any intervention in the patient's QoL. Moreover, CRC is considered cancer of the bowel which is preventable and together with lung cancer, melanoma skin cancer, and breast cancer they account for almost two-thirds of all preventable cancer cases. Therefore, the knowledge obtained from the factors affecting the HRQol among the colorectal cancer patients on treatment would help in the provision of effective intervention that reduces the debilitating impact associated with the drug therapy problem. Since there are challenges in screening and diagnosis of colorectal cancer, most patients on treatment prefer improved HRQoL more than the survival and hence the importance of maximizing the HRQoL (56)

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter highlights the methodological approach used for this study. It further describes the study design, study site, target population, sampling method, data collection, data analysis and ethical consideration.

3.2 Study design

The study design was cross sectional. The research measured the prevalence of the outcome and the exposures in the study participants at the same time. This study tried to explain the prevalence of outcome of interest in the sub - group and the causal relationship with the variable. However, the study did not answer the cause of the disease or the results of the various interventions.

The design was to give a chance to assess different variables at the same time which may generate hypothesis for future studies. The variables included the independent variables like common drug therapy problems (DTP) which included, unnecessary drug therapy, need for additional therapy, drug not effective, dosage too low, adverse drug reaction, dosage too high and adherence. The intervening variables that were assessed included the comorbidities, social demographic characteristics and the stage of the disease. The dependent variable that could score the outcome was HRQoL which had the following domains; psychological health, social relationships, physical health and environment health.

3.3 Study area and site

The study was carried out at CTC, hemato-oncology ward, ward 8C, and KPCC in Kenyatta National Hospital which catered for patients with cancer. Kenyatta National Hospital is located in the area immediate west of Upper Hill in Nairobi. It is among the oldest and largest hospital in Kenya. It is a public referral hospital for the Ministry of Health. In addition, it is a teaching and referral hospital that serves patients from all regions in the country and neighbouring Eastern African countries. It hosts the University of Nairobi College of health sciences and Kenya Medical training college Nairobi campus. The hospital has well equipped oncology clinic that holds outpatient and inpatient services. It has sizeable number of patients presenting with CRC on monthly basis.

3.4 Target Population

The target population were all patients aged 18 years and above who had been diagnosed with CRC and were undergoing treatment.

3.5 Study population

The study population were patients with the age of 18 years and above with medical diagnosis of CRC attending CTC, hemato-oncology ward and clinic and KPCC at KNH, who met the inclusion criteria. The participants were selected based on the eligibility from inclusion and exclusion criteria set for the study. Once the participants had been selected, the investigator assessed the participant as well as the medical records to determine the exposure and the outcomes.

3.5.1 Inclusion criteria

1. Patients who were 18 years and above
2. Patient who had diagnosis of CRC at least 2 months prior to commencement of the study hence availability of treatment plan
3. Patients who were currently on chemotherapy treatment and who had received at least the first cycle
4. Patient who consented to take part in the study

3.5.2Exclusion criteria

1. Patients with cognitive impairment
2. Patients who did not consent to participate in the study
3. Patient with other conditions, acute or chronic illness that would limit the ability of the patient to participate in the study

3.6 Sampling

3.6.1 Sampling size determination

The sample size was determined using the Cochran formula.

$$N_0 = \frac{z^2 P(1-P)}{d^2}$$

Where:

N_0 = The sample size required for the study

z^2 = The standard normal deviate set at 95% CI (z = 1.96)

d = Margin of error set at 5% = 0.05

p = the estimated prevalence of CRC in patients attending CTC, hemato-oncology ward and clinic and KPCC at KNH. Since the focus was on Medication therapy problem and the prevalence was unknown, p = 0.5 was used.

Therefore substituting for the values,

$$n_0 = \frac{1.96^2 * 0.5(1-0.5)}{0.05^2}$$

n_0 = 384.16 ~ 385 patients

However, since study population was less than 10,000, based on the prevalence of colorectal cancer 4,116 (5.9%) in Kenya(5), the estimated sample size was obtained using the following correction formula for finite population. Given that the duration of the study was also limited and the number of patients available from the medical records at KNH for the year 2018 with CRC was small, hence minimum sample size that would be a representative of the study population was obtained as follows.

$$n = \frac{n0}{1 + n0/N}$$

where;

n = Minimum sample size required

n_0 = calculated sample size (385 Patients)

N = Total number of CRC patient that had attended CTC, hemato-oncology ward and clinic and KPCC during the period of nine months in the year 2018 Jan – Sept. (Actual number of patients was 76) where the records were complete.

$$n = \frac{385}{1+ 385/76} = 63.5 \sim 64 \text{ Patients}$$

To cater for non-response and in accuracy an additional 15% was added to the final sample size.

64 + (15/100*64) = 74 Participants

Data from 71 participants were collected.

3.6.2 Sampling technique

Simple random sampling was used. All patients who met the set criteria had an equal opportunity to be included in the study. The patient list was obtained from KNH dispensing record in oncology pharmacy then combined with information from KNH health records information office. The investigator evaluated the patients who complied with inclusion criteria, took them through the consent document and assessed those who were willing to take part in the study. They were assigned consecutive numbers from 1 to N. From the list, participants were selected until the required sample was achieved.

3.6.3 Participant recruitment

During the oncology clinic days and other days for admitted CRC patients, the eligible CRC patients were comprehensively informed about the study. Thereafter, those selected and willing to volunteer in the study were taken through the consenting process and signed the consent form. Thereafter they were issued with questionnaire and assisted to fill in by the investigator. The process was repeated on all clinic days until the required sample size was achieved. To ensure no duplication, a list of patients who had been interviewed were kept and their files tagged using stickers for the period of study. This occurred between May, 2019 and September, 2019.

3.7 Research Instrument

3.7.1 Questionnaire

A well-structured questionnaire was developed to capture details pertaining to the patient. It contained bio data, socio demographics, clinical information and drug therapy problems experienced by the participant that aided in the analysis of the data (Appendix 3). This was filled by the Principal Investigator and was attached to the WHOQoL tool to assess the HRQoL of the CRC patients. The WHOQoL BREF tool (Appendix 4) was filled by the

participant and took an estimated period of 15 minutes. Participants who could not read and write were assisted by the investigator. Those who were admitted for inpatient treatment were interviewed in the wards the day after admission. The others attending outpatient clinic were interviewed on the day of chemotherapy administration as they awaited their chemotherapy or on their clinic days as they awaited their turn for consultation as there were long waiting times owing to the number of patients in the clinics.

WHOQoL – BREF Tool was used to assess overall HRQoL as well as scores in the four domains namely; physical health, psychological health, social relationships and environmental health (Appendix 4). These sections comprehensively brought out the effects of DTP and HRQoL for CRC patients.

3.7.2 Eligibility screening form

This tool had the study information, participant information, inclusion criteria and exclusion criteria. It was used to determine eligibility of the participants for the study (Appendix 1).

3.7.3 Informed consent form

This form was used to obtain a voluntary consent from the patients who met the inclusion criteria. It was prepared in both English and Kiswahili (Appendix 2A and B). Consent was also given through proxy based on participants' wish.

3.8 Pre – Testing and Pilot study

3.8.1 Pre testing of the questionnaire

A few copies of the questionnaires were issued to 10% of the target participants at the oncology clinic. This enabled identification of any ambiguities, poor question framing and other difficulties. The questionnaires was revised based on the weaknesses observed during pre-testing stage. Redrafting of the questionnaire based on the feedback from the pre-testing phase was done.

3.9 Validity of the study

This was maintained by ensuring that the questionnaires were well formatted and relevant with respect to the objective of the study. The questions were arranged in a sequence using simple clear language. The research assistant was well trained and maintained constant communication with the oncology department. The study site chosen gave a good representation of the general population since Oncology unit in KNH attends to patients from all over the country. The internal validity was strengthened since the study used sample

randomization and the confounding factors were taken to account. The causal relationship between the independent variables and dependent variable were clearly stated.

3.10 Reliability of the data

The data collection tools were tested before the study as described in the pilot study above. This enabled test for reproducibility and ensured that there were no ambiguities in responses. Amendments were done on the questionnaire in order to improve on efficiency and effectiveness.

3.11 Data collection techniques

Data was collected using questionnaires after the consent forms had been signed by the participants. The data obtained were then organized for data cleaning and management. In addition, treatment schedules, prescriptions and medical records belonging to the patient were reviewed and data collected. The scoring, coding and analysing the data was done. A report on the findings and results was then shared and recommendations delivered.

3.12 Data Management

3.12.1 Data Processing

The data obtained from the questionnaires was verified, organized and entered into a microsoft excel document format for subsequent use. The raw data was checked for any errors in order to eliminate incomplete and redundant data. The cleaned data was then exported into data analysis software Stata version 15.5 and translated into usable information that was readable. The methods were then documented to ensure the utility and integrity of the data was maintained.

3.12.2 Data Quality control

Rigorous data collection methods using appropriate questionnaires were adopted, accompanied by clearly defined procedures and precise application of data quality norms and control practices. The practices included data quality assessment, measurement, and incorporating data quality into the functions and processes. Removal of duplicate records and checking completeness and accuracy of data recorded were done. In cases where there were data faults, remedial actions like effective data tracking were used.

3.12.3 Data analysis

All the items in the questionnaire were assessed and all the scores recorded. Calculation of the respective domains were determined by considering the relevant questions according to the

tool. This followed the exploratory data analysis approach which was used to analyse the data sets and summarize their main characteristics, often with descriptive statistics, inferential and linear regression models. These helped in obtaining additional insight regarding the messages within the data and the relationship between the particular variables. (Appendix 5)

3.13 Logistical and Ethical considerations

Before starting data collection, clearance to execute the study was obtained from Ethical research committee of KNH/UON, protocol number P181/03/2019 ref: KNH-ERC/A/173 approved on 09 May 2019. Once cleared by the KNH/UON – ERC to carry out the study, the institutional approval from KNH was obtained dated 3 June, 2019. An approval to use WHOQoL–BREF questionnaire for the study was also be obtained from WHO permission 279313 dated 22 February, 2019. Informed consent from the patients was obtained before their participation in the study (A*ppendix 2*). The participant had a right to refuse or pull out of the study and the information obtained from the respondents were kept confidential.

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter describes the results obtained from the study after the descriptive and inferential analysis of the data. It includes the socio-demographics, clinical profiles, drug therapy problems of the participants and the linear regression analysis of the predictors of health-related quality of life.

4.2 Socio-demographic characteristics

A total of 71 study participants were interviewed using a structured questionnaire where 52.1% were females as shown in **Table 4.1**

Table 4. 1 Socio-demographic characteristics of the study participants

Variables	n (n%)	Variables	n (n%)
Age Years		**Gender**	
≤30	5(7.0)	Male	34 (47.9)
31-59	36(**50.7**)	Female	37 (**52.1**)
≥60	30(42.3)	**BMI**	
Age (mean ±SD) Years	55.9(± 4.42)	0-18.5	5 (7.0)
Range Age	20-80	18.6-24.9	47 (**66.2**)
Alcohol status		25-29.9	14 (19.7)
Yes	27 (**38**)	≥30	5 (7.0)
No	44 (62)	**Smoking status**	
Alcohol consumption duration		Yes	17 (**23.9**)
≤10 years	9 (33.3)	No	54 (76.1)
11-19 years	13 (**48.2**)	**Smoking duration**	
≥20 years	5 (18.5)	≤10 years	6 (**35.3**)
Education level		11-19 years	6 (**35.3**)
Informal	7 (9.9)	≥20 years	5 (29.4)
Primary	21 (**29.6**)	**Type of insurance**	
Secondary	28 (**39.4**)	Public	58 (**95.1**)
Tertiary	15 (21.1)	Private & Public	3 (4.9)
Marital status		**Nutrition**	
Single	17 (23.9)	Balanced diet	56 (**78.1**)
Married	54 (**76.1**)	Unbalanced diet	15 (21.1)
Insurance cover status		Meals per day<3	24 (33.8)
Yes	61 (**85.9**)	≥3	47 (**66.2**)
No	10 (14.1)	Fruits and vegetables <3	37 (**52.1**)
		≥3	34 (47.9)

Key: *BMI- Body Mass Index; SD-Standard Deviation*

The mean age was 55.9 (± 4.42) years and ranged from 20 to 80 years old. Female participants were 52.1%. Most of participants (66.2%) had normal BMI. Twenty-seven (38%) participants had a history of taking alcohol with 13 (48.2%) having done so for 11 to 19 years. Seventeen (23.9%) had a history of smoking with the most (6, 35.3%) having between 0 and ten pack years similar to those who had 11- 20 pack years. Only 15(21.1%) respondents had attained a tertiary level of education while 21(29.6%) and 28(39.4%) of them had attained primary and secondary education respectively. Regarding their marital status, 54(76.1%) were married. Sixty-one participants (85.9%) had insurance of which 58(95.1%) had public insurance. Most participants preferred eating a healthy diet (78.1%) with 47(66.2%) having over three meals a day.

4.3 Clinical Profiles

Twenty-nine (40.9%) participants had their first diagnosis for colorectal cancer within the year, followed by seventeen (23.9%) within the last two years **(Figure 4.1).**

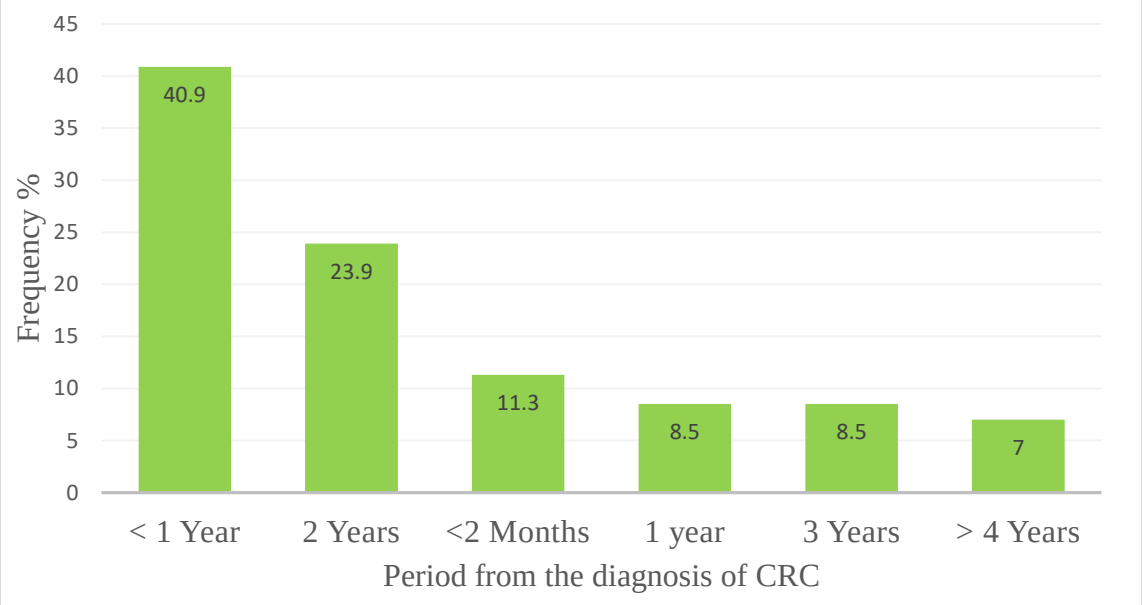

Figure 4. 1: Period from diagnosis for colorectal cancer

Most participants (94.4%) had previous hospital admissions while 53.5% had other illnesses as shown in **figure 4.2**.

Some participants had more than one comorbidity with hypertension being the major associated concurrent illness (26, 36.6%) followed by diabetes mellitus (9, 12.7%).

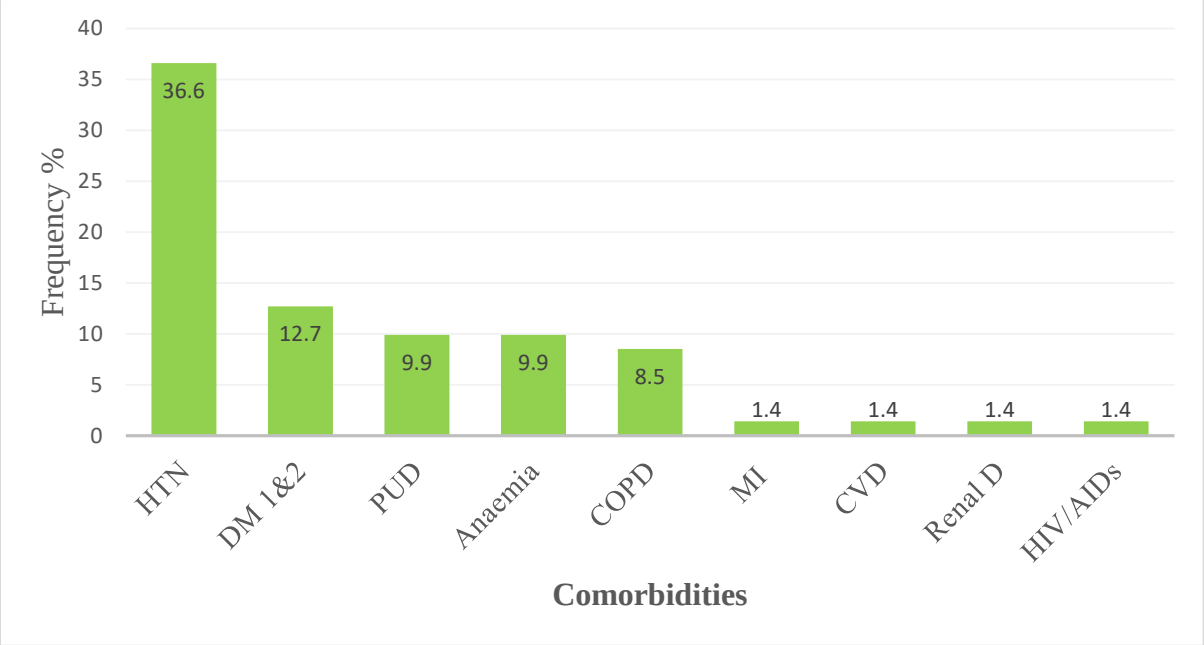

Figure 4. 2: Major comorbidities identified with colorectal cancer

Key: *CVD-Cardiovascular disease; COPD- Chronic Pulmonary Obstructive Disease; DM-Diabetes Mellitus; HTN- Hypertension; MI-Myocardial Infarction; PUD- Peptic Ulcer disease; HIV/AIDS-Human immunodeficiency Virus/Acquired immunodeficiency syndrome*

4.4 Drug Therapy Problems

The major DTPs identified are shown in **Figure 4.3**

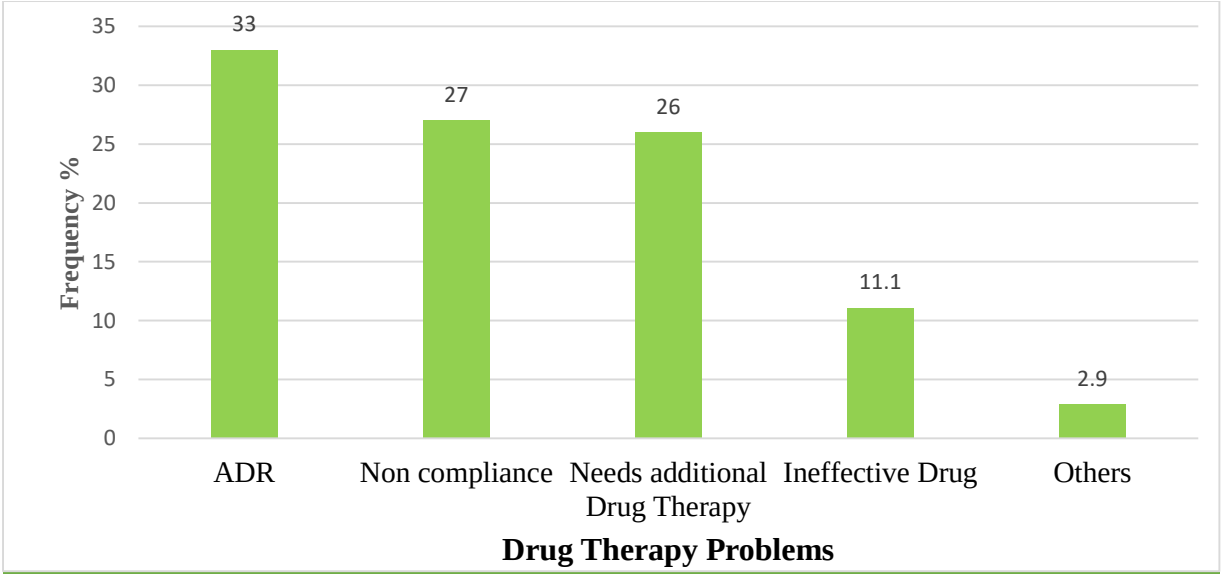

Figure 4. 3: Drug Therapy Problems

Key: *ADR-Adverse drug reaction*

Adverse drug reactions/events manifested in 32 (45.1%) participants and were followed by noncompliance where 18 (25.4%) patients were not able to afford the drugs like capecitabine since they were expensive and the insurance could not fund for drugs not available at treatment centre. The other important DTP included need for additional therapy where 17 (23.9%) participants required preventive therapy as shown in **Table 4.3.**

Table 4. 2: Prevalence of Drug Therapy Problems

DTP and CAUSE	n (%)	DTP And CAUSE	n (%)
Unnecessary drug therapy		**Dosage too low**	
Duplicate therapy	2 (2.8)	Ineffective dose	1 (1.4)
Needs additional Drug Therapy		**ADR**	
Untreated condition	11 (15.5)	Undesirable effect	32 (**45.1**)
prophylactic therapy to reduce risk of developing new condition	17 (**23.9**)	Drug interaction	2 (2.8)
Synergistic/potentiating therapy	6 (8.5)	Allergic reaction	10 (14.1)
Ineffective Drug		**Non compliance**	
More effective drug available	2 (2.8)	Patient can't afford drug product	18 (**25.4**)
Condition refractory to drug	7 (9.9)	Cannot swallow drug	1 (1.4)
Drug not effective for condition	6 (8.5)	Drug product not available	17 (**23.9**)

Key: *ADR-Adverse drug Reaction; DTP-Drug Therapy Problems*

4.5 Systemic enquiry

The participants gave their responses involving a brief screen for symptoms in body systems and the results were summarized in **Table 4.3** Among the participants, 48 (67.6%) presented with gastrointestinal problems manifesting as constipation and abdominal pain. This was followed by constitutional symptoms including poor appetite (16, 22.5%), weight change (16,

22.5%), and pain (12, 16.9%). Moreover, cardiovascular problems (21, 29.6%) were also notable as shown in **Figure 4.4.**

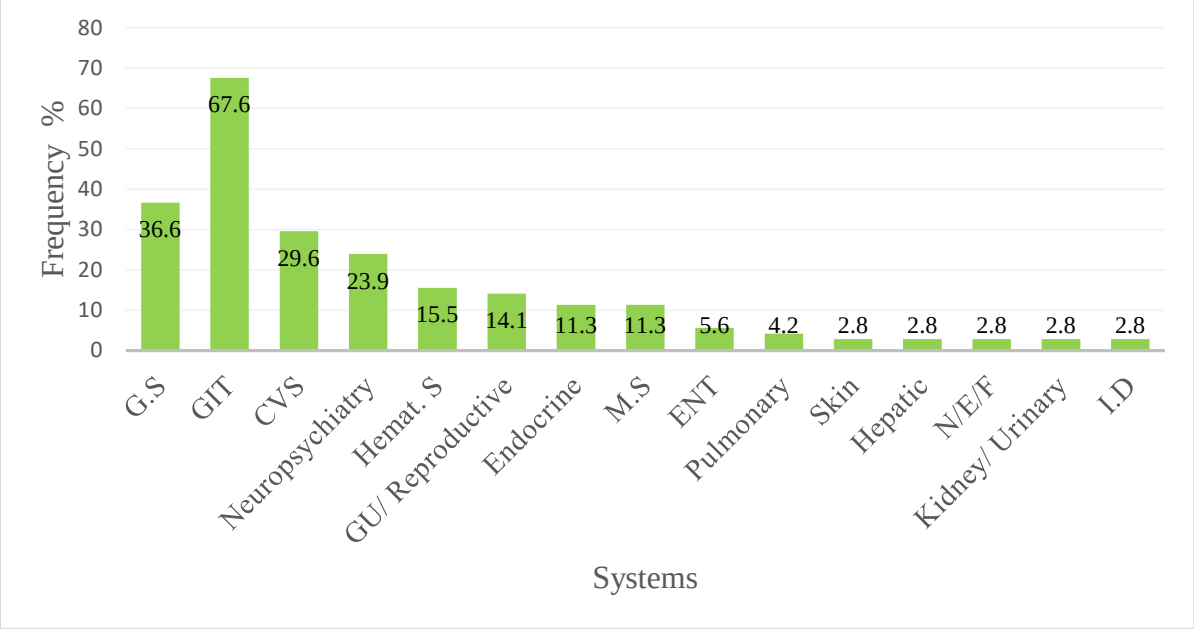

Figure 4. 4: Summary of systemic complaints

Key: *CVS- Cardiovascular disease; ENT-Ear nose and throat; GIT-Gastrointestinal tract; GS-General systems; GU-Genital urinary; Heamat. S-Hematopioetic systems; ID-Infectious disease; MS-Musculoskeletal System; N/E/F- Nutrition/Fluid/Electrolytes*

Table 4. 3: Signs and symptoms during systemic enquiry

System, Sign or symptoms	n (%)	System, sign and symptom	n (%)
General signs and symptoms		**Gastro intestinal**	
Poor appetite	16 (**22.5**)	Heartburn	2 (2.8)
Weight change	16 (**22.5**)	Abdominal pain	24 (**33.8**)
Pain	12 (**16.9**)	Nausea	11 (15.5)
Headache	3 (4.2)	Vomiting	15 (21.1)
Dizziness (vertigo)	5 (7.0)	Diarrhoea	6 (8.5)
Endocrine		Constipation	33 (46.5)
Diabetes	8 (11.3)	**Hematopoietic symptoms**	
GU/ reproductive system		Bleeding	8 (11.3)
Decreased sexual drive	5 (7.0)	Anaemia	3 (4.2)
Vaginal discharge or itching	7 (9.9)	**Neuropsychiatric**	
Cardiovascular		Paraesthesia	4 (5.6)
Chest Pain	2 (2.8)	Loss of Balance	1 (1.4)
Hyperlipidemia	2 (2.8)	Depression	2 (2.8)
Hypertension	21 (**29.6**)	Anxiety, nervousness	11 (15.5)
Orthostatic hypotension	3 (4.2)	Inability to concentrate	2 (2.8)
Pulmonary system		**Infectious diseases**	
Asthma	2 (2.8)	HIV/AIDS	2 (2.8)
Shortness of breath	2 (2.8)	Tuberculosis	1 (1.4)

Key:- *HIV/AIDS-Human immunodeficiency Virus/Acquired immunodeficiency syndrome*

4.6 Chemotherapy

Most participants (64, 90.1%) were on chemotherapy treatment. FOLFOX was the predominant regimen at 39 (54.9%) followed by XELOX and FOLFIRI at 12(16.9%) and 9(12.7%) respectively as shown in **Figure 4.5.**

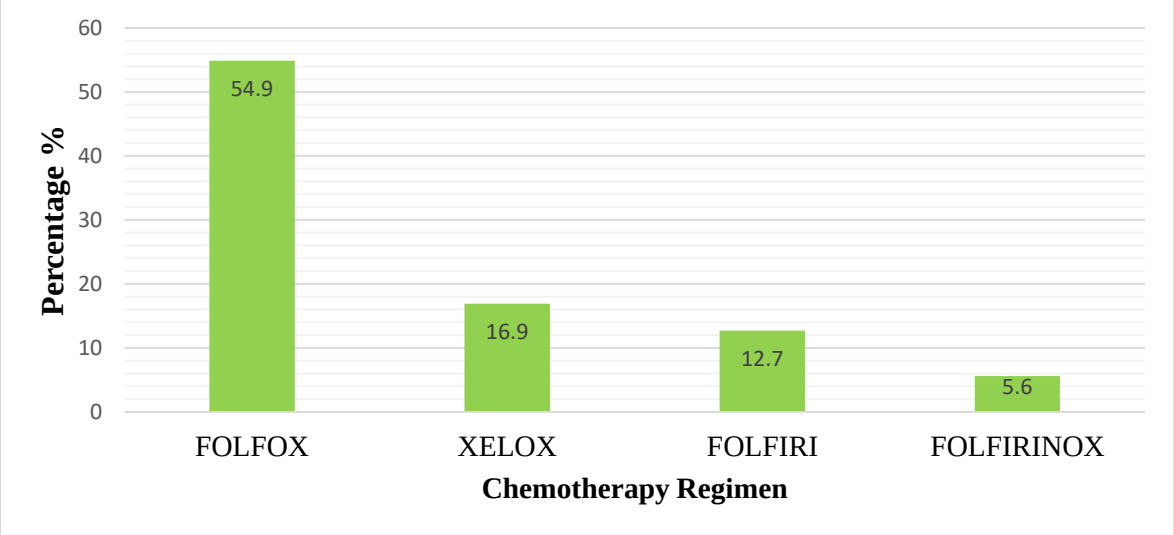

Figure 4. 5: Chemotherapy regimens

Key:-*FOLFOX- Leucovorin, 5-Fluorouracil (5-FU), Oxaliplatin, FOLFIRI- Leucovorin 5-Fluorouracil (5-FU),.Irinotecan, FOLFIRINOX- Leucovorin 5-Fluorouracil (5-FU),.Irinotecan, Oxaliplatin, XELOX- Capecitabine and Oxaliplatin*

The most frequently used drugs were 5FU (52, 73.2%), Leucovorin (52, 73.2%), and Oxaliplatin (51, 71.8%). No patient was put on targeted therapy during the period of study **(Figure 4.6)**

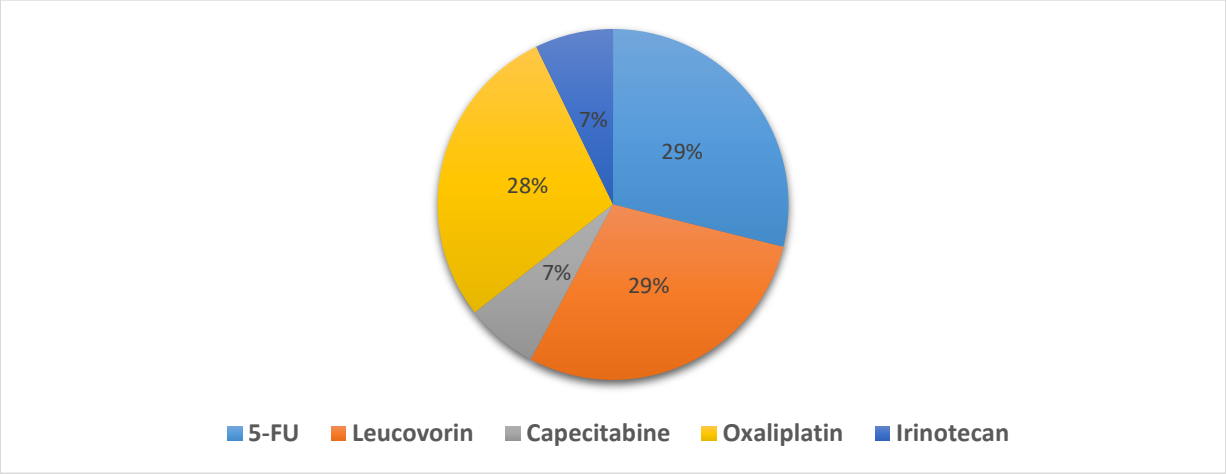

Figure 4. 6: Chemotherapy drugs

Key:-*5FU- 5-Fluorouracil*

4.7 Health Related Quality of life measurements

The HRQoL domain scores are summarized in **Figure 4.7.** The psychological domains had the highest overall mean score (60.5) while the physical domain the lowest score (44.7). The overall QoL among the participants was 50.5.

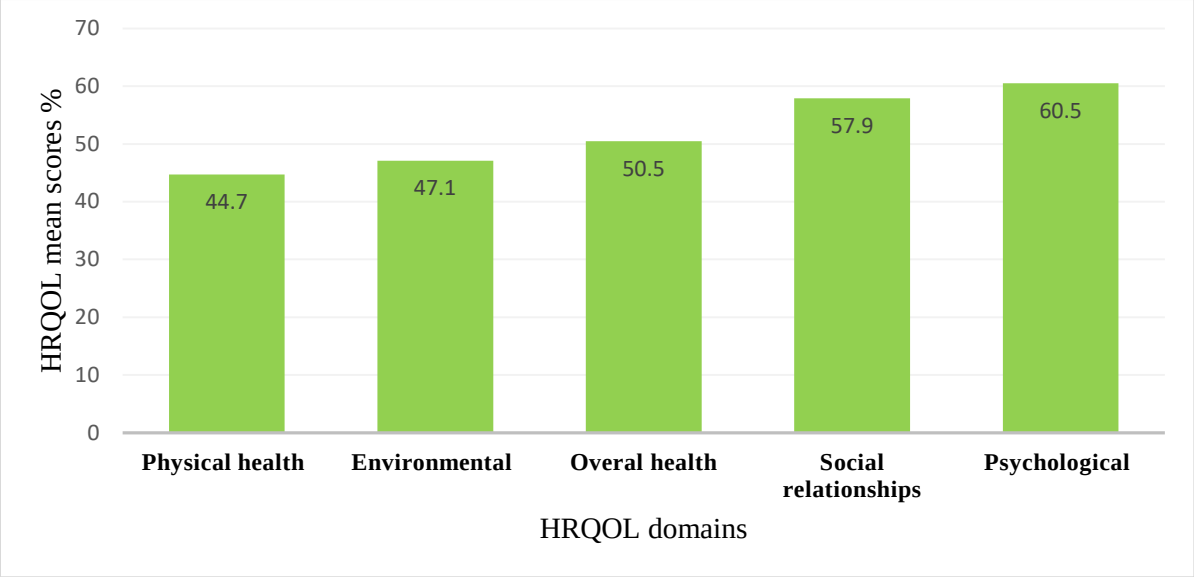

Figure 4. 7: Mean scores of Health-related quality of life domain

Key:-*HRQoL- Health-related quality of life*

4.8 Association between Socio-demographic characteristics and the Quality of life

Associations were done using the Wilcoxon rank-sum and Kruskal Wallis test because the data assumed continuous data pattern with more than two variables **(Table 4.4)**. The data was not normally distributed but was skewed. The level of significance was $p = 0.05$. In WHO HRQoL only the physical health ($p = 0.0023$), psychological health ($p = 0.01$), environment ($p = 0.037$) and overall HRQoL($p = 0.0028$) domains were associated with age.

Table 4. 4: Association between socio-demographic characteristics and Health Related Quality of Life

Variables	Physical health	Psychological health	Social relationships	Environment	Overall HRQoL
Age	**0.0023***	**0.01***	0.13	**0.037***	**0.0028***
BMI	0.209	0.081	0.057	0.187	0.135
Alcohol status	0.896	0.886	0.325	0.962	0.967
Alcohol duration	0.739	0.726	0.863	0.64	0.702
Smoking status	0.745	0.765	0.984	0.886	0.973
Smoking duration	0.644	0.826	0.906	0.682	0.982
Education	0.519	0.63	0.531	0.85	0.684
Marital status	0.120	**0.028***	**0.023***	0.475	**0.043***
Insurance cover status	**0.031***	0.105	0.189	**0.0325***	**0.032***
Insurance type	0.507	0.557	0.216	0.491	0.596
Diet (balanced)	0.209	0.086	0.228	0.305	0.131
Number of snacks eaten in a day	0.126	0.062	0.316	0.108	0.072
Vegetables and fruits eaten in a days meal	0.065	**0.0265***	0.13	**0.035***	**0.0398***

Key: * Statistically significant result

BMI – Body mass index

Marital status was associated with psychological health (p = 0.028), social relationship (p = 0.023) and overall HRQoL (p = 0.043). There was association between physical health (p = 0.031), Environment (p = 0.0325) and overall HRQoL (p = 0.032) domains with participant having insurance cover. Psychological health (p = 0.0265), environment (p = 0.035), and overall HRQoL (p = 0.0398) domains were found to have an association with the intake of daily vegetable and fruits.

4.9 Association between clinical profiles and Health Related Quality of Life

The association with the QoL domains, physical health (p=0.0371) and social relations (p = 0.0299) with the presence of comorbidities were found to be statistically significant. Diabetes had an association with Environmental (p=0.0294) and overall QoL (p=0.0299) domains while anaemia had an association with psychological health (p = 0.008), social relations (p = 0.007), and overall QoL (p = 0.015) domains as shown in **Table 4.5**

Table 4. 5: Association between clinical profile and Health Related Quality of Life

Comorbidity	**p-value**				
	Physical health	**Psychological health**	**Social relationships**	**Environment**	**Overall HRQoL**
Myocardial infarction	0.446	0.248	0.57	0.388	0.474
Cerebral vascular disease	0.446	0.248	0.246	0.227	0.236
Chronic pulmonary disease	0.747	**0.0239***	0.363	0.517	0.167
Peptic Ulcer Disease	0.727	0.467	0.718	0.271	0.612
Hypertension	**0.005***	0.343	0.102	0.74	0.0778
Diabetes mellitus	0.0616	0.194	0.0669	**0.0294***	**0.0299***
Moderate to severe renal disease	0.731	0.122	0.167	0.3	0.152
Anaemia	0.145	**0.008***	**0.007***	0.158	**0.015***
Metastatic solid tumors	0.875	0.847	0.765	0.325	0.972
AIDs	0.731	0.122	0.167	0.3	0.152

Key: * Statistically significant result

AIDs – Acquired immunodeficiency syndrome

4.10 Association between Drug therapy problems and Health Related Quality of Life

Unnecessary drug therapy caused by duplication of therapy was associated with physical health (p = 0.045) and overall HRQoL (p = 0.0397) domains. The ineffective drug therapy problem caused by the condition being refractory to the medication was associated with social relationship (p = 0.0366) while ADR caused by drug interaction was associated with psychological health (p = 0.0158) and overall HRQoL (p=0.028) as shown in **Table 4.6.**

Table 4. 6: Clinical profile association with the Health Related Quality of Life in CRC patients

DTP	CAUSE	P-value				
		Physical health	Psychological	Social relations	Environmental	Overall health
Unnecessary drug therapy	Duplicate therapy	**0.045***	0.133	0.051	0.127	**0.0397***
Needs additional Drug Therapy	Untreated condition	0.37	0.626	0.315	0.368	0.254
	prophylactic therapy to reduce risk of developing new condition	0.823	0.533	0.482	0.119	0.562
	Synergistic/potentiating therapy	0.685	0.349	0.579	0.458	0.572
Ineffective Drug	More effective drug available	0.875	0.847	0.051	0.325	0.574
	Condition refractory to drug	0.382	0.162	**0.0366***	0.149	0.157
	Drug not effective for condition	0.252	0.739	0.503	0.646	0.623
Dosage too low	Ineffective dose	0.0853	0.326	0.57	0.73	0.152
ADR	Undesirable effect	0.82	0.907	0.287	0.793	0.766
	Drug interaction	0.363	**0.0158***	0.175	0.0678	**0.028***
	Allergic reaction	0.338	0.178	0.431	0.153	0.178
Dosage too High	Drug interaction	0.35	0.589	0.12	0.921	0.361
Non compliance	Patient cannot afford drug product	0.456	0.51	0.925	0.679	0.561
	Cannot swallow	0.731	0.09	0.729	0.3	0.152
	Drug product not available	0.635	0.546	0.386	0.586	0.5

Key: ***** *Statistically significant result*, *ADR-Adverse drug Reaction; DTP-Drug Therapy Problems*

4.11 Systemic enquiry associations with Health Related Quality of Life

Association between the HRQoL and presentation of symptoms associated with GIT, endocrine system, and urinary system were found. The abdominal pain was associated with

Table 4. 7: Association between condition, signs and symptoms and Health Related Quality of Life

Sign and Symptom	Physical health	Psychological health	Social relationships	Environment	Overall
Poor appetite	0.100	**0.0377***	0.554	0.536	0.0975
Weight change	0.623	0.967	0.358	0.621	0.631
Pain	0.304	0.883	0.489	0.932	0.774
Chest Pain	0.563	0.074	0.218	0.188	0.176
Hypertension	**0.015***	0.187	0.307	0.707	0.0693
Asthma	0.779	0.930	0.482	0.635	0.783
Shortness of breath	0.624	**0.029***	0.342	0.325	0.948
Abdominal pain	**0.016***	**0.031***	**0.0012***	**0.006***	**0.005***
Nausea	0.625	0.233	0.097	0.231	0.285
Vomiting	0.491	0.419	0.132	0.584	0.454
Diarrhoea	0.399	0.454	0.272	0.77	0.5
Constipation	0.201	0.41	0.161	0.178	0.18
Diabetes	0.062	0.192	0.067	**0.029***	**0.03***
Decreased sexual drive	0.096	0.205	0.125	0.128	0.104
Vaginal discharge or itching	0.431	0.756	0.476	0.697	0.861
Renal dysfunction	0.624	0.214	**0.036***	0.504	0.232
Bleeding	0.087	**0.0238***	0.254	**0.0461***	0.053
Anaemia	0.931	0.463	0.885	0.795	0.654

Key: * *Statistically significant result*

Physical health (p = 0.016), psychological health (p = 0.031) social relations (p = 0.012), environment (p = 0.006), and overall HRQoL (p = 0.005) while diabetes was associated with environment (p = 0.029) and overall HRQoL (p = 0.03) domains respectively. Other associations were found between GUT bleeding with Psychological health (p=0.0238) and environment health (p=0.0461) domains, renal dysfunction with social relationship (p = 0.036). Other associations were between, poor appetite (p = 0.0377), and shortness of breath (p = 0.029) with psychological health domain respectively as well as hypertension with physical health (p = 0.015) domain as shown in **Table 4.7**

4.12 Chemotherapy regimen association with Health Related Quality of Life

There was no statistically significant association among the regimen and HRQoL domains as shown in **Table 4.8**

Table 4. 8: Chemotherapy regimen association with the Health related Quality of life in colorectal cancer patients

Regimen	Physical health	Psychological health	Social relations	Environmental health	Overall
FOLFOX	0.793	0.843	0.337	0.893	0.865
FOLFIRI	0.153	0.069	0.248	0.283	0.159
XELOX	0.957	0.865	0.298	0.852	0.768
FOLFIRINOX	0.9	0.96	0.495	0.48	0.99

Key:-*FOLFOX- Leucovorin, 5-Fluorouracil (5-FU), Oxaliplatin, FOLFIRI- Leucovorin 5-Fluorouracil (5-FU),.Irinotecan, FOLFIRINOX- Leucovorin 5-Fluorouracil (5-FU),.Irinotecan, Oxaliplatin, XELOX- Capecitabine and Oxaliplatin,*

4.13 Predictors of Health-related quality of life

Linear regression was carried out to determine the most parsimonious model by monitoring the changes in adjusted R^2 **(Table 4.9)**. Even though the HRQoL scores are ordered categorical data it is assumed as continuous data since there were more than seven categories(57). The linear regression model carried out with HRQoL variables as the

dependent variable against the various independent variables Social Health, EH – Environmental Health, QoL- Quality of Life.

Table 4. 9: Predictors and determinants of Health-Related Quality of Life

Domains	Variables	Bivariate Analysis		Multivariate Analysis	
		***β* (95% CI)**	***ρ* - value**	***β*(95% CI)**	***ρ*-value**
PH	Stage of Hypertension	-12.7(-20.97- -4.45)	0.003	-7.6(-16.04- -0.81)	0.08
	Age	-8.2(-14.96- -1.58)	0.016	-9.1 (-16.0 - -2.27)	**0.01***
	Duplicate therapy	28.0(3.31 - 52.77)	0.027	30.6 (8.05 - 53.22)	**0.009***
	Insurance status	-12.6(-24.44 - -0.82)	0.036	-12.3(-23.5 -1.08)	**0.032***
PSYC H	ADR	-42.7(-68.24 - -17.18)	0.001	-32.4(-57.6 - -7.27)	**0.012***
	Anemia	-21.6(-36.00 - -7.28)	0.004	-15.9(-29.82 - -2.0)	**0.026***
	Fruits and vegetables intake >3 times a day	10.4(1.66 - 19.19)	0.02	7.5(-0.73 - 15.65)	0.074
SR	Anemia	-21.6(-36.09 - -7.18)	0.004	-15.4(-30.7 - -0.14)	**0.048***
	5-Fluorouracil	10.7(0.66 - 20.7)	0.037	7.9(-1.88 - 17.71)	0.112
	Comorbidities	-10.1(-18.95 - -1.24)	0.026	-6.9(-15.79 - 2.02)	0.127
EH	Diabetes	-14.2(-27.40 - -1.03)	0.035	-14.0(-26.89 - -1.1)	**0.034***
	Insurance status	-12.3(-24.35 - -0.3)	0.045	-12.1(-23.84 - -0.4)	**0.043***
Overall QoL	Anemia	-14.3(-26.15 - -2.46)	0.019	-13.4(-24.7 - -2.07)	**0.021***
	Insurance status	-11.3(-21.54 - -1.12)	0.030	-10.4(-20.1 - -0.57)	**0.038***
	Cardiovascular conditions	-8.3(-16.11 - -0.5)	0.037	-8.1(-15.48 - -0.62)	**0.034***
	Fruits and vegetables intake >3 times a day	7.3(0.20 - 14.49)	0.044	6.4(0.55-13.28)	0.071

Key: * *Statistically significant result. EH- Environmental health, Overall QoL- Quality of Life, PH – Physical Health, PYSC H – Psychological Health, SH- Social relations.*

4.13.1 Predictors of physical health

For every unit increase in the blood pressure, including both systolic and diastolic pressure increase, there was a -12.7(-20.97 - -4.45) (p = 0.003) times increase in PH in bivariable analysis, however, in multivariable analysis it was -7.6(-16.04- -0.81) (p = 0.08) times though no statistically significant changes after controlling for age, duplicate therapy and insurance.

As the age advanced, there was -8.2(-14.96, -1.58) (p = 0.016) chance of increase PH. However, it was found out in multivariable analysis that PH increased by -9.1 (-16.00094, -2.27) (p = 0.01) after controlling for duplicate therapy, insurance, and HTN. The presence of duplicate therapy will lead to a 28.0(3.31 - 52.77) (p = 0.027) times increase in PH compared to those who did not have in bivariate analysis. In multivariable analysis having controlled for HTN, age, and insurance, duplicate therapy led to a 30.6 (8.05 - 53.22) (p = 0.009) times increase in PH. Having insurance increased the PH by -12.6(-24.44, -0.82) (p = 0.036) times in bivariable analysis compared to those who did not have. In multivariable analysis, PH increased by -12.3 (-23.52, -1.08) (p = 0.032) times after controlling for duplicate therapy, age, and HTN.

4.13.2 Predictors of psychological health

The presence of ADR is likely to lead to a 42.7 (p = 0.001) times decrease in physiological health compared to those who did not have ADR in bivariable analysis. In multivariable analysis having controlled for anaemia, fruits, and vegetables, ADR was likely to lead to a 32.4 (p = 0.012) decrease in psychological health. The presence of anemia was likely to lead to 21.6 (p = 0.04) times decrease in Psychological health in bivariate analysis. In multivariable analysis presence of anemia caused 15.9 (p = 0.026) decrease in psychological heath after being controlled for ADR, fruits, and vegetables. Intake of fruits and vegetables more than three times a day increased the psychological health by 10.4 (p = 0.02) in bivariable analysis. However, in multivariable analysis there were no statistically significant changes after controlling for ADR and anemia.

4.13.3 Predictors of social health

The association between social health score, anaemia, FU and comorbidities were investigated whereby the social health score was the dependent variable and comorbidities, and FU were the independent variables. The presence of anaemia was likely to cause a 21.6 (p = 0.04) time decrease in SH compared to those who did not have anaemia in bivariable analysis. In

multivariable analysis having controlled for 5FU and comorbidities it was likely to lead to 15.4 (p = 0.048) times decrease in SH. However, the use of 5FU and comorbidities did not have any statistical significance in multivariable analysis after controlling for confounders.

4.13.4 Predictors of Environment

The presence of diabetes was likely to lead to a 14.2 (p = 0.035) times decrease in EH compared to those who did not have diabetes in BA. In multivariable analysis having controlled for insurance, Diabetes was likely to lead to a 14.0 (p = 0.034) time decrease in EH. Having insurance is 12.3(-24.35, -0.3) (p = 0.045) times likely to have a lower EH quality of life in bivariable analysis. In multivariable analysis having insurance is 12.1(-23.84, -0.4) (p = 0.043) likely to have a lower EH quality of life after controlling for diabetes.

4.13.5 Predictors of the Overall Health-Related Quality of Life

The presence of anemia was likely to cause a 14.3 (p = 0.019) time decrease in overall QoL compared to those who did not have anemia in bivariable analysis. In multivariable analysis having controlled for insurance, cardiovascular and fruits and vegetables intake it was likely to lead to 13.4 (p = 0.021) times decrease in overall HRQoL. Having insurance decreased the overall HRQoL by 11.3 (p = 0.030) times in BA compared to those who did not have. In multivariable analysis overall QoL decreased by 10.4 (p = 0.038) after controlling for anemia, cardiovascular, fruits and vegetables intake. The presence of cardiovascular conditions was likely to cause an 8.3 (p = 0.037) times decrease in overall HRQoL in bivariable analysis compared to those who did not have. In multivariable analysis having controlled for anaemia, insurance, fruits, and vegetable intake, cardiovascular conditions lead to an 8.1 (p = 0.034) times decrease in overall HRQoL. Intake of fruits and vegetables more than three times a day increased the overall HRQoL by 7.3 (p = 0.044) in bivariable analysis. However, in multivariable analysis there was no statistically significant data after controlling for insurance, cardiovascular and anemia.

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

1.1 Introduction

This chapter contains a discussion of the research findings. The conclusions and recommendations are also included.

1.2 Discussion

The prevalence of CRC among the genders were approximately 1:1 which corroborates with Globocan 2018 summary statistics (2). Nearly all the participants had primary and secondary level of education suggesting that they could have lacked awareness of risk factors causing CRC. Perhaps, they accessed only casual labour and other blue color jobs leaving them with no time and facilitation to access screening services that are currently available in selected primary care health facilities. These findings concur with a survey done by Lundy *et al,* that demonstrated a significant association between income and QoL for CRC patients (44)

Most cases are usually diagnosed at an advanced stage which is a common observation in developing countries as has been revealed by Arnold *et al.* (58). A study done in Iran by Akhondi *et al.* also posted similar results (51). Chemotherapy treatment was initiated within the first year of diagnosis. Moreover, most patients who present with CRC at early stage and were not put on chemotherapy had surgical resections and radiotherapy done (40). Most participants had been readmitted and were put on chemotherapy while the others were on radiotherapy and surgery. Most participants were put on FOLFOX 6 regimen and which was the commonly used first-line treatment in KNH. The other regimens included XELOX, FOLFIRI and FOLFIRINOX. Similar protocols are recommended by the American Cancer Society and NCCN (42,59) No patient was put on targeted therapy during the period of study. However, personalized therapy should be performed for CRC patients according to their clinical and biological factors (60). There was no statistically significant association between chemotherapy regimen and HRQoL domains.

Since the participants were being treated for cancer and the cytotoxic drugs do not discern between the normal and neoplastic cells, DTPs seemed to be inevitable. DTPs associated with ADR causing the undesirable effect was most common among the participants. This can be compared to a study done by Ayalew *et al.* that had similar results (36). Noncompliance was caused by drugs being unavailable and at times its cost being higher. This has made accessibility to the drugs difficult and unaffordable. The need for additional therapy caused by medication required to prevent the occurrence of new conditions or for prophylaxis was

also a major DTP. Cancer being a hypercoagulable state medication to prevent the occurrence of conditions like DVT is essential. This was also echoed in a study by Degu et *al.* where adverse drug reactions, drug interactions, and the need for additional drug therapy were the most common DTPs pointed out among cancer patients (10).

In addition, DTPs were also associated with the presence of other illnesses. Hypertension was the most common comorbidity. This suggested the readily available screening and treatment for HTN at primary health care centres made the participants' aware of their state. However, Sarfati *et al.* found out that comorbidity may result in increased contact with health services resulting in more opportunities for screening and early diagnosis; or, conversely, comorbidity may distract either or both the patient and the health professional, resulting in delayed diagnosis of cancer (50).

The study found a significant association between DTP and HRQoL. Unnecessary drug therapy caused by duplication of therapy was associated with physical health and overall QoL. This showed that the presence of multiple drugs used to treat the same condition caused an improved outcome. This may be attributed to synergistic effects. However, this disagrees with a study done by MacDonald *et al.* that identifies poor outcomes when multiple drugs are used to treat a condition(33). The ineffective drug therapy problem caused by the condition being refractory to the medication was associated with social relations domains while ADR caused by drug interaction was associated with psychological and overall HRQoL domains respectively. This portrayed that the personal relationships deteriorated due to the stress of treatment not attaining the desired result. It was also noted that ADR interfered with bodily image and greatly affected self-esteem. This can be compared with a study done by Dunn *et al.* which had similar results (25).

Most participants had gastrointestinal problems with constipation and abdominal pains being the most common. This is suggestive of the manifestation of the colon, rectal or caecum cancers that start from the gastrointestinal tract (7). Other general systems problems were caused by poor appetite, weight change, and pain. These are interlinked. Weight change may be due to cachexia associated with cancer and poor appetite. Pain is a common symptom associated with cancer (40).

Additionally, the association between the HRQoL and presentation of symptoms from GIT, endocrine, and urinary system were found. The abdominal pain was associated with physical

health, psychological health, social relations, environment health, and overall HRQoL domains. This symptom reduced the HRQoL of participants. Diabetes was associated with environmental health and overall HRQoL domains. This meant that financial resources, home environment, participation in recreational activities and physical environment were affected together all together. Other associations were found in GUT bleeding with psychological health, and environmental health domains, renal dysfunction with social relations, poor appetite and shortness of breath with psychological health domain respectively. This seemed to cause negative feelings, low self-esteem, change in bodily appearance and personal relations. Cardiovascular diseases associated with the physical health domain mainly caused dependence on medicinal substances, compromised energy, and fatigue (56,61).

For HRQoL the psychological health had the highest score while physical health had the lowest. These findings, therefore, depict acceptance of one's bodily image, self-esteem, spiritual beliefs, positive feelings, thinking, learning and being able to concentrate. However, daily living activities, dependence on medicinal substances, energy, pain and discomfort, sleep and capacity to work were imminently affected. This can be compared to a study done in Gondar, Ethiopia by Abegaz *et al.* that observed that the highest functional status was emotional functioning and positive feelings among the participants examined (7).

Statistically significant association was found between age and physical health, psychological health, environmental health, and overall HRQoL domains. This showed that every unit increase in age caused a decrease in the above domains. Marital status was associated with psychological, social relations and overall HRQoL. This portrayed that the support among the participants was good. A significant association was found between physical health, psychological, environmental and overall HRQoL domains with insurance status. However, the majority of participants with poor physical health were likely to have insurance compared to those who had good physical health. Nevertheless, this disagrees with Caroleen *et al.* a study that identified insurance cover as a boost to good physical health (29). Those with high Psychological, environmental and overall HRQoL domains had insurance hence their financial resources were not constrained and had the opportunity to participate in recreational activities.

Based on the regression analysis the following was observed. When the stage of hypertension increased, there was a decrease in PH in bivariable analysis, however, in the multivariate analysis showed no statistically significant changes after controlling for age, duplicate therapy and insurance. This hinted at the presence of HTN causing a decrease in physical health but the changes are not statistically significant. When age increased, there was decreased PH. Furthermore, the patients became dependent on medication and their daily activities and competence at work impaired (29). The presence of duplicate therapy led to an increase in PH compared to those who did not have. This implied that duplication of therapy may have alleviated the pain and discomfort hence improving on mobility, energy and work capacity. Having insurance decreased PH. It denoted that those participants with the tendency of having poor physical health were conscious to have insurance cover.

The presence of ADR was likely to lead to a decrease in physiological health compared to those who did not have ADR. This was due to the external manifestation and internal effects of the drug. Bodily image and appearance are the most affected leading negative feelings. The same occurred in the presence of anaemia that led to a 15.9 times decrease in psychological heath after being controlled for ADR, fruits, and vegetables. The presence of anaemia also caused a decrease in SR compared to those who did not have anaemia having controlled for 5FU and comorbidities. This implied that it caused difficulty in social support, personal relations and sexual activity due to the prolonged period of disease burden (62).

The presence of diabetes was likely to lead to a decrease in EH compared to those who did not have diabetes. This showed that freedom, physical safety, health, and social care decreased in the presence of diabetes effects on the patient (32). Having insurance was likely to cause a lower EH. This may suggest that some insurance that do not offer comprehensive services that may be of great help to the patient. Moreover, some insurance may not cater for drugs mostly supplements and block pre-authorisation of service. This causes financial resources depletion since the patient has to spend out of pocket.

The presence of anaemia presumably caused a decrease in overall HRQoL despite the score among the participants being average. Having insurance decreased overall HRQoL decreased, after controlling for anaemia, cardiovascular, fruits, and vegetable intake. The presence of cardiovascular conditions led to a decrease in overall HRQoL having controlled for anaemia, insurance, fruits and vegetable intake, cardiovascular conditions. However, the studies done by Sarfati *et al.* tend to have contrary opinion on some of the variables (50).

1.3 Conclusions

1. Chemotherapy and radiation were the most commonly used modes of management of CRC patients in KNH. FOLFOX 6, XELOX were regularly used as first-line while FOLFIRI and FOLFIRINOX used as the second line.
2. Adverse drug reaction, non-compliance, the need for additional therapy were the most common DTPs identified among the CRC patients.
3. HRQoL among the CRC patients was sub-optimal. There was a significant number of determinants that are potentially modifiable variables like BMI, comorbidities, treatment plans and environment.

1.4 Recommendations for policy and practice

1. The most causes of drug therapy problems were ADR, adherence, and the need for additional therapy. Therefore, the strategies to contain these DTPs should be considered.
2. HRQoL was poor and therefore, sensitization for early diagnosis and treatment of CRC should be considered in order to improve on HRQoL.

1.5 Recommendation for further research

Future intervention studies are needed to improve quality of care to determine if the changes made an increased quality of life. Moreover, the studies should correlate drug therapy problems and health related quality of life with treatment outcomes in colorectal cancer patients.

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APPENDICES

APPENDIX 1: ELIGIBILITY SCREENING FORM

All participants will be screened to meet the eligibility criteria based on inclusion and exclusion criteria detailed as follows.

1. Study information

Title	Drug therapy problems and health-related quality of life o patients with colorectal cancer at Kenyatta National Hospital
KNH/UoN/ERC PNo.	
Investigator	Dr. Kabiru Charles Mwangi

2. Participant information

Study N	
Gender Male ☐ Female ☐	

3. Inclusion Criteria

Inclusion Criteria	Yes	No
Patients aged 18 years and above		
Diagnosis of CRC at least for 2 months		
Patients current on chemotherapy treatment at least completed first cycle		
Patient who will consent to participate in the study		

4. Exclusion criteria

Exclusion criteria	Yes	No
Patients with cognitive impairment		
Patients who will refuse to consent		
Any acute or chronic condition that would limit the ability of the patient to participate in the study		

5. Eligibility statement

The participant is Eligibl ☐ / ☐ Not eligible for the study.

Reason:_____

Name:	
Signature:	Date:

APPENDIX 2: CONSENT FORM

Introduction

I am Dr. Kabiru Charles Mwangi from the University of Nairobi. I am doing my postgraduate study in Clinical Pharmacy. As part of my postgraduate study am doing a study on Drug therapy problem and health related quality of life in colorectal patients on treatment at Kenyatta National Hospital.

My concern majorly focuses on the factors affecting the health-related quality of life leading to you not getting optimum therapy outcomes. Any comorbidities you are suffering from and problems experienced during treatment. This study will enable a comprehensive assessment of your well-being and the impact of colorectal cancer on your quality of life that cannot be adequately assessed by medical outcomes alone.

Procedure involved

If you agree to participate, I will assess your medical file and get more information about colorectal cancer condition affecting you. I will also administer a well-structured questionnaire that will enable gather information about your perception of well-being. This will take approximately 30 minutes and the information obtained will be treated with confidentiality.

Your rights as a Participant

Your participation in the study will be voluntary.

Your choice to participate or not will not affect the quality of medical care that you get.

You have freedom to terminate the interview and withdraw from the study at any given time.

You are free to ask questions before signing the consent form and during the study.

No information obtained from you will be traced back to you or shared to any other party. The information obtained will be used for the purpose of this study only.

Risk and Cost of Participation

There are no risk and cost incurred during participation in the study.

Benefits of participation

There will be no direct benefit to you, but all useful information obtained that will improve the quality of care will be shared with your doctor

Confidentiality

Kindly note that all information that will be obtained will be treated as confidential. Only the researcher will have access to your personal information. The information obtained will be analysed anonymously.

In case of you have any questions during the period of this study, you can contact the following;

1. Dr, Kabiru Charles Mwangi,
   Department of Pharmaceutics and Pharmacy Practice,
   School of Pharmacy, University of Nairobi.
   Mobile; 0723146965

2. Dr, P.N Karimi PhD,
   Department of Pharmaceutics and Pharmacy Practice,
   School of Pharmacy, University of Nairobi.
   P.O. Box 19676 – 00200 Nairobi
   Kindly sign the following consent;

CONSENT TO PARTICIPATE IN THE STUDY

Study Number	Date	Time

I hereby give my written and informed consent to participate in the study on the drug therapy problems and the health related quality of life on colorectal cancer patients on treatment at Kenyatta National Hospital. I have been adequately explained about this study by Dr. Kabiru Charles Mwangi and / his assistant. I do this with full knowledge of the purpose of the study and procedures involved including review of my medical records and answering questionnaire. I understand that my rights will be respected and confidentiality maintained during the study period. I also understand that the consent is voluntary and I am at liberty to withdraw at any time without my quality of care being affected.

Name	Signature

Investigator's statement

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands the purpose of the study and procedures involved.

I confirm that the participant has been given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

Sign	Date

APPENDIX 3 QUESTIONNAIRE

A. BIODATA

	Study Number	
	Physical address/ Contact	
	Date of study	

B. SOCIAL DEMOGRAPHICS

1. Age [ ] yrs
2. Weight [ ] Kgs
3. Height [ ] m
4. BMI

BMI	<18.5	18.5 – 24.9	25 – 29.9	≥ 30
Code	1	2	3	4

5. Did you take alcohol? Yes [ ] No [ ]

	Yes	No
Code	1	0

6. If yes, for how long did you take alcohol ……..……Years

Years	< 10	11 -19	>20
Code	0	1	2

7. Did you smoke cigarette? Yes [ ] No [ ]

	Yes	No
Code	1	0

8. If yes, for how long did you smoke cigarette ……Years

Years	< 10	11 -19	>20
Code	0	1	2

9. What is the highest **education** you received?

Informal [ ] Primary school [ ] Secondary School [ ] Tertiary [ ]

	Informal	Primary	Secondary School	Tertiary
Code	0	1	2	3

10. What is your **marital status**?

Single [ ] Married [ ] Separated [ ] Divorced [ ] Widowed [ ]

	Single	Married	Separated	Divorced	Widowed
Code	0	1	2	3	4

11. Are you on any insurance cover? Yes [ ] No [ ]

	Yes	No
Code	1	0

12. If yes, which one? .....

	Public	Private	Both
Code	0	1	2

13. How would you describe your diet? ……

	Balanced diet/Healthy d	Junk
Code	0	1

14. How many meals and snacks did you eat each day? Meals [ ] Snacks [ ]

Meals	<3	>3
Snacks	<3	>3
Code	0	1

15. How many servings of fruits and vegetables did you take per day?

	<3	>3
Code	0	1

C. CLINICAL PROFILES

16. When were you first diagnosed with the condition? *(please tick one)*

Duration	≤2 months [ ]	< 1 [ ]	1 [ ]	2 [ ]	3 [ ]	4 [ ]	5 [ ]
Code	0	1	2	3	4	5	6

17. Have you been admitted for this condition? *(please tick one)*

	Yes [ ]	No[ ]
Code	1	0

18. Do you have other illnesses (comorbidities) *(please tick one)*

	Yes [ ]	No [ ]
Code	1	0

19. If yes, which illness in this list and for how long have you suffered?

No	Comorbidity	Present	Absent	Duration (Years)
20	Myocardial infarction	1	0	
21	Congestive heart failure	1	0	
22	Peripheral vascular disease	1	0	
23	Cerebral vascular disease	1	0	
24	Dementia	1	0	
25	Chronic pulmonary disease	1	0	
26	Ulcer Disease	1	0	
27	Hypertension	1	0	
28	Diabetes 1&2	1	0	
29	Moderate to severe renal disease	1	0	
30	Diabetes with end organ damage (&2)	1	0	
31	Any tumor (except colorectal cancer)	1	0	
32	Leukemia	1	0	
33	Anaemia	1	0	
34	Moderate to severe liver disease	1	0	
35	Metastatic solid tumors	1	0	
36	AIDs	1	0	
37	Other(Specify)…….			

D. DRUG THERAPY PROBLEMS

Please tick appropriately

DTP	Q No.	CAUSE	Present	Absent
Unnecessary drug therapy	38	No medical indication at this time	1	0
	39	Duplicate therapy	1	0
	40	Nondrug therapy more appropriate	1	0
	41	Treating avoidable ADR	1	0

	42	Addictive/recreational drug use causing the problem	1	0
Needs additional Drug Therapy	43	Untreated condition	1	0
	44	Preventive/prophylactic therapy required to reduce risk of developing new condition	1	0
	45	Synergistic/potentiating therapy	1	0
Ineffective Drug	46	More effective drug available	1	0
	47	Condition refractory to drug	1	0
	48	Dosage form inappropriate	1	0
	49	Drug not effective for condition	1	0
Dosage too low	50	Ineffective dose	1	0
	51	Frequency inappropriate	1	0
	52	Drug interaction	1	0
	53	Duration inappropriate	1	0
ADR	54	Undesirable effect	1	0
	55	Unsafe drug for patient	1	0
	56	Drug interaction	1	0
	57	Dosage administered or changed too rapidly	1	0
	58	Allergic reaction	1	0
	59	Contraindications present	1	0
Dosage too High	60	Dose too high	1	0
	61	Frequency too short	1	0
	62	Duration inappropriate	1	0
	63	Drug interaction	1	0
	64	Incorrect administration	1	0
Non compliance	65	Instructions not understood	1	0
	66	Patient prefers not to take	1	0
	67	Patient forgets to take	1	0
	68	Patient cannot afford drug product	1	0
	69	Cannot swallow /administer the drug	1	0
	70	Drug product not available	1	0

E. SYSTEMIC INQUIRY

System	Q No.	Sign and Symptom	Present	Absent
General Systems	71	Poor appetite	1	0
	72	Weight change	1	0
	73	Pain	1	0
	74	Headache	1	0
	75	Dizziness (vertigo)	1	0
ENT	76	Change in vision	1	0
	77	Loss of hearing	1	0
	78	Ringing in the ears (tinnitus)	1	0
	79	Bloody nose (epistaxis)	1	0
	80	Allergic	1	0
	81	Glaucoma	1	0
	82	Bloody sputum (hemoptysis)	1	0
Cardiovascular	83	Chest Pain	1	0
	84	Hyperlipidemia	1	0
	85	Hypertension	1	0
	86	Myocardial Infraction	1	0
	87	Orthostatic hypotension	1	0
Pulmonary	88	Asthma	1	0
	89	Shortness of breath	1	0

	90	Wheezing	1	0
Gastrointestinal	91	Heartburn	1	0
	92	Abdominal pain	1	0
	93	Nausea	1	0
	94	Vomiting	1	0
	95	Diarrhea	1	0
	96	Constipation	1	0
Skin	97	Eczema/Psoriasis	1	0
	98	Itching (pruritis)	1	0
	99	Rash	1	0
Endocrine Systems	100	Diabetes	1	0
	101	Hypothyroidism	1	0
	102	Menopausal symptoms	1	0
Hepatic	103	Cirrhosis	1	0
	104	Hepatitis	1	0
Nutrition/Fluid/ Electrolytes	105	Dehydration	1	0
	106	Edema	1	0
	107	Potassium deficiency	1	0
GU/ Reproductive	108	Dysmenorrhea/menstrual bleeding	1	0
	109	Incontinence	1	0
	110	Impotence	1	0
	111	Decreased sexual drive	1	0

	112	Vaginal discharge or itching	1	0
	113	Hot flashes	1	0
Kidney/Urinary	114	Urinary Frequency	1	0
	115	Blood urine (hematuria)	1	0
	116	Renal dysfunction	1	0
Hematopoietic Symptoms	117	Excessive bruising	1	0
	118	Bleeding	1	0
	119	Anemia	1	0
Musculoskeletal	120	Back pain	1	0
	121	Arthritis pain (osteo/rheumatoid)	1	0
	122	Tendonitis	1	0
	123	Painful muscles	1	0
Neuropsychiatric	124	Numb, tingling sensation	1	0
	125	Tremor	1	0
	126	Loss of Balance	1	0
	127	Depression	1	0
	128	Suicidal	1	0
	129	Anxiety, nervousness	1	0
	130	Inability to concentrate	1	0
	131	Seizure	1	0
	132	Stroke/TIA	1	0
	133	Memory loss	1	0

Infectious Disease	134	HIV/AIDS	1	0
	135	Malaria	1	0
	136	Syphilis	1	0
	137	Gonorrhea	1	0
	138	Herpes	1	0
	139	Chlamydia	1	0
	140	Tuberculosis	1	0

Q no.	System	Present	Absent
141	General Systems	1	0
142	ENT	1	0
143	Cardiovascular	1	0
144	Pulmonary	1	0
145	Gastro intestinal	1	0
146	Skin	1	0
147	Endocrine	1	0
148	Hepatic	1	0
149	Nutrition/Electrolytes/ Fluids	1	0
150	GU/ Reproductive	1	0
151	Kidney/ Urinary	1	0
152	Hematopoietic Symptoms	1	0
153	Musculoskeletal	1	0
154	Neuropsychiatry	1	0
155	Infectious disease	1	0

CHEMOTHERAPY THERAPY

	Drug Used	YES	NO
156	5-Fluorouracil (5-FU)	1	0
157	Leucovorin	1	0
158	Capecitabine	1	0
159	Oxaliplatin	1	0
160	Irinotecan	1	0
161	Cetuximab	1	0
162	Panitumumab	1	0
163	Regorafenib	1	0
164	Trifluridine	1	0
165	Tipiracil	1	0

	Regimen	Yes	No
166	FOLFOX	1	0
167	FOLFIRI	1	0
168	XELOX	1	0
169	FOLFIRINOX	1	0

170 OTHER DRUGS ……..?

171. Domain 1: physical health score

172. Domain 2: psychological health score

173. Domain 3: social health score

174. Domain 4: environmental score

175. Overall HRQoL score

APPENDIX 4 WHOHRQOL-BREF

QUESTIONNAIRE

Before you begin we would like to ask you to answer a few general questions about yourself: by circling the correct answer or by filling in the space provided.

Instructions

This assessment asks how you feel about your quality of life, health, or other areas of your life. Please answer all the questions. If you are unsure about which response to give to a question, please choose the one that appears most appropriate. This can often be your first response.

Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life in the last two weeks. For example, thinking about the last two weeks, a question might ask:

	Do you get the kind of support from others that you need?	Not at all	Not much	moderately	A great deal	Completely
		1	2	3	4	5

You should circle the number that best fits how much support you got from others over the last two weeks. So you would circle the number 4 if you got a great deal of support from others as follows.

	Do you get the kind of support from others that you need?	Not at all	Not much	moderately	A great deal	Completely
		1	2	3	4	5

You would circle number 1 if you did not get any of the support that you needed from others in the last two weeks.

Please read each question, assess your feelings, and circle the number on the scale for each question that gives the best answer for you.

		Very poor	**Poor**	**Neither poor or Good**	**Good**	**Very good**
1(G1)	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	**Dissatisfied**	**Neither satisfied nor dissatisfied**	**Satisfied**	**Very satisfied**
2(G4)	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about how much you have experienced certain things in the last two weeks.

		Not at all	**A little**	**A moderate amount**	**Very much**	**An extreme amount**
3 (F1.4)	To what extent do you feel that physical pain prevents you from doing what you need to do?	1	2	3	4	5
4(F11.3)	How much do you need any medical treatment to function in your daily life?	1	2	3	4	5
5(F4.1)	How much do you enjoy life?	1	2	3	4	5

6(F24.2)	To what extent do you feel your life to be meaningful?	1	2	3	4	5

		Not at all	**A little**	**A moderate amount**	**Very much**	**Extremely**
7(F5.3)	How well are you able to concentrate?	1	2	3	4	5
8 (F16.1)	How safe do you feel in your daily life?	1	2	3	4	5
9 (F22.1)	How healthy is your physical Environment?	1	2	3	4	5

The following questions ask about how completely you experience or were able to do certain things in the last two weeks.

		Not at all	**A little**	**Moderately**	**Mostly**	**Completely**
10 (F2.1)	Do you have enough energy for life?	1	2	3	4	5
11 (F7.1)	Are you able to accept your bodily appearance?	1	2	3	4	5
12 (F18.1)	Have you enough money to meet your needs?	1	2	3	4	5
13 (F20.1)	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14 (F21.1)	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	**Poor**	**Neither poor or Good**	**Good**	**Very good**
15 (F9.1)	How well are you able to get around?	1	2	3	4	5

The following questions ask you to say how good or satisfied you have felt about various aspects of your life over the last two weeks.

		Very dissatisfied	**Dissatisfied**	**Neither satisfied nor dissatisfied**	**Satisfied**	**Very satisfied**
16 (F3.3)	How satisfied are you with your sleep?	1	2	3	4	5
17 (F10. 3)	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18(F1 2.4)	How satisfied are you with your capacity for work?	1	2	3	4	5
19 (F6.3)	How satisfied are you with yourself?	1	2	3	4	5
20(F1 3.3)	How satisfied are you with your personal relationships?	1	2	3	4	5
21(F1 5.3)	How satisfied are you with your sex life?	1	2	3	4	5
22(F1 4.4)	How satisfied are you with the support you get from your friends?	1	2	3	4	5

23(F17.3)	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24(F19.3)	How satisfied are you with your access to health services?	1	2	3	4	5
25(F23.3)	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last two weeks.

		Never	**Seldom**	**Quite often**	**Very often**	**Always**
26 (F8.1)	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	1	2	3	4	5

Did someone help you to fill out this form?

……..

How long did it take to fill this form out?

…….

Do you have any comments about the assessment?

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THANK YOU FOR YOUR HELP