QUALITY OF LIFE OF COLORECTAL CANCER PATIENTS AT MOI TEACHING AND REFERRAL HOSPITAL AND VALIDATION OF FACT - C QUESTIONNAIRE IN THE KENYAN CONTEXT.

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A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE, MOI UNIVERSITY

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DECLARATION

Declaration by Candidate

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DEDICATION

I dedicate this thesis book to the memory of my most beloved dad, Dr. Isaya Akunga Onyango, PhD, MBS whose outstanding academic and professional legacy I constantly aspire to honor and live up to, through my work and studies; and to my darling mom Mrs. Hephzibah K. Akunga, HSC who without doubt has been the constant wind beneath my wings.

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LIST OF ABBREVIATIONS

AMPATH	Academic Model Providing Access to Healthcare
CRC	Colorectal Cancer
ECOG	Eastern Cooperative Oncology Group
EWB	Emotional Well-being
FACIT	Functional Assessment of Chronic Illness Therapy
FACT – C	Functional Assessment of Cancer Therapy – Colorectal cancer
FACT – G	Functional Assessment of Cancer Therapy – General
FWB	Functional Well-being
HIV	Human Immunodeficiency Virus
PSR	Performance Status Ratings
PWB	Physical Well-being
QLQ	Quality of Life Questionnaire
QoL	Quality of Life
SWB	Social Well-being

DEFINITION OF TERMS

Colorectal cancer: This is a cancer within the colon or rectum (named depending on where it starts) that are often grouped together because they have many similar features.

Content validity: This refers to a statistical estimate of whether a test or tool covers all relevant parts of the subject it aims to measure in order to produce accurate and valid results.

External validity: This refers to whether a test or tool can produce results that are generalizable and/or comparable to results of similar tools that are widely acceptable for use within the same context.

FACT-C questionnaire: This is a patient-reported outcome measure used to assess health-related quality of life in patients who have specifically been diagnosed with colorectal cancer (*Overview*, n.d.).

FACT-G questionnaire: This is a patient-reported outcome measure used to assess health-related quality of life in patients undergoing cancer therapy, for any form of cancer. It assesses the impacts of cancer therapy in four domains: physical, social/family, emotional, and functional (*Overview*, n.d.).

Quality of life: This is the perceived quality of an individual's day to day life based on an assessment of their overall well-being. In specific, health-related quality of life is based on how they may have been affected over time by a health condition (*WHO Quality of Life-BREF (WHOQOL-BREF)*, n.d.).

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ABSTRACT

Introduction: Globally colorectal cancer (CRC) is the third commonest cancer and it accounts for approximately 7.6% of all cancers in Kenya. Advancements in CRC management have increased survival rates with Quality of Life (QoL) becoming critical in survivorship care strategies. QoL is affected by loss of health due to both CRC symptomatology and consequences of treatment; resulting in psychophysical and social impairment which influences treatment outcomes. Studies amongst long-term CRC survivors suggest that those who survive for ≥5 years, experience good QoL with moderately lower physical functioning. Locally, there is paucity of data on QoL of CRC patients and a Kiswahili translation of FACT-C questionnaire which is designed to specifically estimate QoL in CRC, had not yet been validated in Kenya as at the time of this study.

Objectives: To assess the QoL of colorectal cancer patients at Moi Teaching and Referral Hospital (MTRH) and to validate a Kiswahili working translation of the FACT-C questionnaire.

Methods: This was a cross-sectional study conducted at MTRH between April 2019 and January 2020. The study population included 90 patients aged ≥18 years with histologically confirmed CRC, enrolled by census sampling. Structured interviewer administered questionnaires were utilized to collect sociodemographic and clinical data. QoL was assessed using the validated Kiswahili Functional Assessment of Cancer Therapy-General questionnaire (FACT-G), which estimates QoL in any cancer patient regardless of the cancer type. Functional Assessment of Cancer Therapy–Colorectal cancer questionnaire (FACT-C) was used to assess CRC specific QoL, using a Kiswahili working translation developed by the study team. QoL scores were then correlated with ECOG clinical performance status for external validity. Good QoL was based on a total score of ≥81 by FACT-G, ≥21 by FACT-C and 0 or 1 by ECOG. Pearson chi square test of homogeneity was used to test the association between QoL scores as determined by FACT-C compared to the already validated FACT-G to determine the content validity of FACT-C.

Results: A total of 90 participants were enrolled, 55.6% (N=50) were female and 30% (N=27) aged ≥61 years. The predominant histological type was adenocarcinoma, with 48.9% (N=44) having advanced disease. Good clinical performance status by ECOG was observed in 63.3% (N=57), who also had good QoL scores on both FACT-G and FACT-C. Characteristics associated with good QoL included early disease stage and higher level of education; surgery and advanced disease were associated with poor QoL. QoL scores by FACT-G deteriorated significantly (p=0.000) when subjected to FACT-C, suggesting content validity of FACT-C that specifically addresses CRC symptomatology, which may not be highlighted by FACT-G.

Conclusion: Characteristics associated with good QoL were early disease stage and higher education level. Surgery and advanced disease were associated with poor QoL. Kiswahili working translation of FACT-C demonstrated external validity and content validity.

Recommendations: QoL assessment should be done in CRC patients using the disease specific FACT-C questionnaire. Pre-and post-surgical counselling should be done to address potential complications. A multi-center study is recommended for comparability in order to inform evidence based local guidelines on QoL determination in CRC.

CHAPTER ONE: INTRODUCTION

1.1 Study Background

Colorectal cancer (CRC) accounts for 7.6% of all cancer cases in Kenya and ranks sixth highest in the list of the top ten cancers (Korir et al., 2015). According to the 2020 Global Cancer Statistics, CRC was the third most commonly diagnosed cancer with over 2 million new CRC cases being reported worldwide that year; and it was also ranked as the third leading cause of cancer death in both men and women (*GLOBOCAN 2020: New Global Cancer Data | UICC*, n.d.). In the past decade, several advancements in CRC management have contributed to the increased survival rate of the patients and currently, many of the patients survive five years or longer post diagnosis. For those diagnosed with localized disease, 5-year survival exceeds 85% (Siegel et al., 2014).

In diseases with long-term survivorship such as CRC, QoL is an important outcome in the evaluation of the full impact of the disease on the patients, community and health infrastructure. Additionally, in advanced CRC, QoL has been found to be an independent predictor of survival. Consequently, an in-depth understanding of quality of life (QoL) among CRC survivors has become an essential component of providing comprehensive and tailored care, in particular, identification of survivors at risk of low QoL in order to develop effective long term CRC survivorship care (Adams et al., 2016). This will facilitate quality in addition to the quantity added to the lives of CRC survivors by current treatment modalities.

Several studies of QoL in long-term CRC survivors suggest that, on average, CRC survivors who survive for more than 5 years, experience good QoL with only moderately lower physical functioning associated with older age, obesity, co-

morbidities, smoking, and lower socioeconomic status (Buffart et al., 2012; Thraen-Borowski et al., 2013; Weaver et al., 2012). Psychological QoL has been observed to be similar to that of the general population despite possibly higher depression scores (Buffart et al., 2012).

There is limited data on the QoL of CRC patients in Low and Lower-Middle Income Countries, including Kenya. This study objectively evaluated QoL amongst CRC patients on follow up at MTRH in Eldoret, Kenya; and determined the relationship between socio-demographic factors, clinical characteristics and QoL. FACT-G & FACT–C questionnaires were used to assess QoL. FACT-G (Appendix 4 & 5) is a general cancer questionnaire that is used to estimate the quality of life of a patient who has been diagnosed with any form of cancer. It has been validated for use in Kenya in both English and Kiswahili versions; and includes components of physical, social, emotional and functional wellbeing. FACT – C questionnaire (Appendix 3) contains colorectal cancer specific items, that quiz the patient on symptomatology that is unique to colorectal cancer patients. As at the time of this study, a Kiswahili version of the FACT-C questionnaire had not been validated for use in Kenya. A Kiswahili working translation of the FACT-C questionnaire was developed and validated by the study team. All the items on the FACT-G and FACT-C questionnaires are scored based on a five-point Likert scale (0 – 4), with "0" being strong disagreement and "4" being strong agreement with the symptomatology or quality of life aspect in question.

1.2 Problem Statement

In Kenya, there is minimal data on the QoL of CRC patients despite the improved survival rates due to improved modalities of treatment. Additionally, clinicians do not routinely use standardized questionnaires and tools to determine the QoL of CRC patients at diagnosis or thereafter, despite this being an important element in the holistic management of these patients. Patients with CRC experience unique adverse effects due to the primary disease as well as consequences of the disease spreading to other organs in the body. The effects of CRC include frequent gastrointestinal symptomatology, changes in social functioning, decrease in productivity of the patients and strain in their relationships. Subsequently, the interventions that they undergo in the management of the disease, for instance, surgical fashioning of a stoma which may be a new experience for the patient, may further lead to physical complications such as surgical site infections and electrolyte imbalance; as well as affect them psychologically due to how the apparatus is perceived in their social environment. This does not just affect the patients but it also has an impact on their caregivers. All these events affect their quality of life, which directly impacts their treatment compliance and outcomes.

1.3 Study Justification

Data generated from this study is useful because it provides insight on CRC-specific QoL in Kenya that directly impacts patients' management with regards to: understanding how patient characteristics are related to their QoL, how CRC influences the patients' lives physically, emotionally, socially and functionally; as well as how treatment strategies, comorbidities and disease stage relate to QoL. The findings of this study also promote the rationale for incorporation of standardized routine QoL assessment of CRC patients in Kenya, as it highlights the affected QoL domains that may not otherwise be captured in a regular clinic visit, by utilizing standardized questionnaires in the objective determination of the QoL. QoL as determined by FACT-G questionnaire which has been previously validated in Kenya for use in general cancer patients; was compared to the QoL as determined by the colorectal cancer-specific FACT-C questionnaire; and through this study, a Kiswahili working translation of the FACT-C questionnaire was validated, which could be used in future for routine QoL assessments of CRC patients in Kenya.

1.4 Research Questions

1. What is the Quality of Life (QoL) of patients on management for CRC at MTRH?

2. What are the associations between patient sociodemographic and clinical characteristics; and the QoL of patients on management for CRC at MTRH?

3. How does the Kiswahili version of the FACT – C questionnaire compare with the already validated Kiswahili translation of the FACT – G Questionnaire in the Kenyan context?

1.5 Objectives of the Study

1.5.1 Broad objective

To assess the Quality of Life (QoL) of patients on management for colorectal cancer at Moi Teaching and Referral Hospital.

1.5.2 Specific Objectives

i. To assess the Quality of Life (QoL) of patients on management for CRC at MTRH using the FACT – G questionnaire.

ii. To determine the association between patient sociodemographic and clinical characteristics; and the Quality of Life (QoL) of patients on management for CRC at MTRH.

iii. To translate and assess the validity of the FACT - C colorectal cancer QoL module in the Kenyan context.

CHAPTER TWO: LITERATURE REVIEW

2.1 Colorectal Cancer

The worldwide prevalence of CRC in 2008 was more than 3 million persons within 5 years of diagnosis (Ferlay et al., 2015). In Kenya, colorectal cancer accounts for approximately 7.6% of all cancer cases with an Age Specific Incidence Rate (ASIR) of 12.1 per 100,000 (Korir et al., 2015). In the past two decades incidence rates for CRC have been mostly stable but mortality rates have been on a downward trend due to improvements in early diagnosis and CRC treatment (Biondi et al., 2013). In 2018, International Agency for Research on Cancer (IARC) ranked colorectal cancer among the top three cancer types in terms of incidence (together with cancer of the lung and breast), and second in terms of mortality, with cancer of the lung and breast ranking first, fifth respectively (*PRESS RELEASE N° 263*, 2018). In 2020, colorectal cancer was ranked as the third leading cause of cancer death in both men and women (*GLOBOCAN 2020: New Global Cancer Data | UICC*, n.d.). Colorectal cancer together with cancer of the lung and cancer of the breast, are responsible for one third of the cancer incidence and mortality burden worldwide.

Colorectal cancer could present as sporadic (70%), familial clustering (20%) and inherited syndromes (10%) (C & H, 2019). On average, the age at diagnosis of sporadic CRC is older than 50 years and mostly linked to environmental factors. The patients with a true inherited pattern usually carry a higher risk with younger age (< 50 years) at diagnosis. The most common inherited CRC syndromes are familial adenomatous polyposis (FAP) and Lynch syndrome also known as Hereditary Non-Polyposis Colorectal Cancer [HNPCC]), which account for approximately 5% of all CRC (C & H, 2019). However, it has also been observed that as many as 10% to 15% of unselected CRC patients will carry high-risk mutation not related to FAP or

HNPCC. Inflammatory bowel disease (IBD), mainly ulcerative colitis, has a well-known association with CRC with an estimated incidence 0.5% per year between 10 and 20 years after the time of IBD diagnosis and 1% per year after that reaching a 30% risk probability by the fourth decade of patients with pancolitis. Crohn's disease may also increase CRC risk, particularly if present in the ileocolic region (C & H, 2019). Childhood cancer survivors who received abdominal radiation for therapeutic reasons any also be at risk of CRC, and screening is recommended 10 years after exposure or at age 35. Other conditions that may increase the risk of CRC are diabetes mellitus or insulin resistance, uncontrolled acromegaly disease, and long-term immunosuppression following organ transplant (C & H, 2019).

Further epidemiologic study results indicate strong environmental and lifestyle associations for CRC. According to two reports: World Cancer Report 2008 from the International Agency for Research on Cancer (IARC) and the Colorectal Cancer 2011 report from the Continuous Update Project (CUP) of the World Cancer Research Fund International (WCRF), are dietary risk factors including high red and processed meats intake, and low vegetable and fruit intake; cigarette smoking; alcohol drinking; obesity; diabetes; androgen deprivation therapy, cholecystectomy, family history of CRC and physical inactivity (Gu et al., 2018). On the other hand, large population studies with variable strength evidence have found CRC protective factors which include: physical activity, diet (fruits and vegetables, fiber, resistant starch, fish), vitamin supplements (folate, folic acid, pyridoxine, calcium, vitamin D, magnesium), garlic, coffee; and drugs such as aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), hormonal replacement therapy in postmenopausal women, statins, bisphosphonate and angiotensin inhibitors (C & H, 2019). Studies done in High Income Countries (HICs) indicate that increasing age is the greatest risk factor for

sporadic colorectal cancer, with 99% of cases occurring in people aged more than 40 years and 85% in those aged more than 60 (Ballinger & Anggiansah, 2007). However, the scarce research on CRC available from countries in sub-Saharan Africa does demonstrate some similarities, that is, younger ages at CRC diagnosis than are typically seen in HICs, with the proportion of cases aged <40 years reported to be between 19% and 38%, compared to HICs where the proportion of cases aged <40 years has been reported to be between 3% to 7% (Parker et al., 2019). Amongst CRC patients on follow up within various oncology centers in Nairobi in 2011, the peak age affected was 41-50 years, with an all-group mean age of 53 years; the proportion of patients 40 years of age or younger was 17.6% (Saidi et al., 2011).

Colorectal tumorigenesis begins in the normal mucosa with abnormal cell replication and appearance of clusters of enlarged crypts (aberrant crypts) showing proliferative, biochemical and biomolecular abnormalities. Most colorectal malignancies develop from adenomatous polyps, which are well-demarcated masses of epithelial dysplasia with uncontrolled crypt cell division. An adenoma can be considered malignant when neoplastic cells pass through the muscularis mucosae and infiltrate the submucosa (Ponz de Leon & Di Gregorio, 2001). The macroscopic appearance of CRC lesions may be that of a polypoid vegetating mass or of a flat infiltrating lesion. Most of these tumors are adenocarcinomas (96%) that in some cases, show a mucinous component. More rare malignancies of the large bowel include signet-ring cell carcinoma, squamous carcinoma, undifferentiated neoplasms and medullary type adenocarcinoma (Ponz de Leon & Di Gregorio, 2001). Colorectal carcinoma can be graded into well, moderately and poorly differentiated lesions; but it is not clear whether grading has an impact on evaluating prognosis of affected patients.

Typically, CRC does not cause any symptoms at first and may often go undetected until it reaches a later stage. Certain symptoms may be signs of CRC but they are usually caused by another non-cancerous condition. Possible signs include: blood in stool or frank anal bleeding, anemia, anal mucus secretion, change in bowel movements over several weeks (for example constipation or diarrhea, sometimes alternating), the feeling of not being able to empty your bowels completely, abdominal or perianal cramps, unintentional weight loss, tiredness and generalized physical weakness. All of these symptoms are nonspecific because they could also be caused by other diseases such as irritable bowel syndrome (IBS), inflammation of the lining of the stomach (gastritis), a peptic ulcer, food intolerance or an inflammatory bowel disease. Bowel cancer is only rarely the cause, especially in people under the age of 40 (*Signs of Colorectal Cancer - InformedHealth.Org - NCBI Bookshelf*, n.d.). However, it has been demonstrated that a change in bowel habit is suggestive of left sided cancers caused by a progressive narrowing of the bowel lumen, with diarrhea, a change in stool form, and eventually intestinal obstruction (Ballinger & Anggiansah, 2007); while up to 10% of patients with iron deficiency anemia have right sided colorectal cancer (Ballinger & Anggiansah, 2007).

Colorectal cancer is diagnosed through assessment and tissue sampling at colonoscopy. This is achieved during routine screening or scheduled biopsies in cases where there is high clinical suspicion. The goal of cancer screening is usually mortality reduction through early detection and consequently, a reduction in incidence of advanced disease. Modern CRC screening has pushed towards this goal through the detection of early-stage adenocarcinomas and the detection and removal of adenomatous polyps, the latter, generally accepted as nonobligate precursor lesions (L. B et al., 2008). Adenomatous polyps are common in adults aged ≥ 50 years,

although majority of these polyps will not develop into adenocarcinoma. In principle, histology and size determine their clinical importance, with the most common and clinically important polyps being the adenomatous polyps. These represent approximately 50 – 70% of all colorectal polyps and are associated with an increased risk of CRC. As such, most CRC screening studies will focus on the detection of invasive CRC, as well as advanced adenomas. Advanced adenomas typically are defined as polyps greater than or equal to 10 mm or histologically having high-grade dysplasia or significant villous components (L. B et al., 2008). People at increased risk have either 3 or more adenomas, with the aforementioned features on histology. It is recommended that these high risk patients have a 3-year follow-up colonoscopy, while people at lower risk who have 1 or 2 small (<1 cm) tubular adenomas with no high-grade dysplasia can have a follow-up evaluation in 5-10 years; whereas people with hyperplastic polyps only should have a 10-year follow-up evaluation (Winawer et al., 2006). Current screening guidelines by the American College of Gastroenterology (ACG) 2021 recommend CRC screening in average-risk individuals aged 50 to 75 years, and suggest screening in average-risk individuals aged 45 to 49 years (A et al., 2021). The primary modalities for colorectal cancer screening recommended are colonoscopy and Fecal Immunochemical Test (FIT). Further, ACG suggestions regarding colorectal cancer screening include: initiation of CRC screening with a colonoscopy at age 40 or 10 years before the youngest affected relative (whichever is earlier) in individuals in whom a first-degree relative has had CRC or an advanced polyp before age 60 years or in whom two or more first-degree relatives have had CRC or an advanced polyp at any age; with interval follow-up colonoscopy every 5 years. The guidelines (A et al., 2021) also recommend genetic evaluation in individuals with a high familial CRC burden (high number and/or

younger age of affected relatives). Amongst individuals in whom a first-degree relative has had CRC or an advanced polyp at age 60 years or older, CRC screening should be initiated at age 40 or 10 years before the youngest affected relative, then resume screening according to average-risk screening recommendations. For individuals with a second-degree relative with CRC or an advanced polyp, follow average-risk colorectal cancer screening recommendations should be applied. Screening amongst individuals who are beyond age 75 years should be decided on an individualized basis. In individuals unable or unwilling to undergo colonoscopy or FIT, consider screening with flexible sigmoidoscopy, multitarget stool DNA test, Computed Tomography (CT) colonography, or colon capsule (A et al., 2021).

Stage of disease is the strongest predictor of survival for patients with colorectal cancer. Accurate staging also is critical for appropriate patient management and meaningful clinical research. Uniform staging criteria are an essential component of accurate evaluation of therapies as well as outcomes of CRC. Staging is done to determine the amount of penetration of the cancer; done using imaging studies, in order to guide the best treatment option. There are various systems which have been developed over time for staging colorectal cancers, but they all depend on the extent of local invasion, the degree of lymph node involvement and whether there is distant metastasis. In clinical practice, the current system in use is the tumor, node, metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC). This is the standard for CRC staging recommended by the College of American Pathologists, the Royal College of Pathologists, the Commission on Cancer of the American College of Surgeons, and the National Cancer Institute (Common Data Elements). TNM staging system is abbreviated based on the three categories it uses for stage classification; "T"

denotes the Tumor degree of invasion of the intestinal wall, "N" the degree of Lymphatic Node involvement, and "M" the degree of Metastasis (Akkoca et al., 2014); and is widely used by national, regional, and local tumor registries in the United States and internationally, thus making it the international language of colorectal cancer staging in all disciplines. The TNM staging system has three additional advantages over other staging systems. First, it is data-driven and has a process in place for continuous improvement based on ongoing expert review of existing data; it has a comprehensive set of definitions and rules of application that ensure uniform use; and it is multidisciplinary in design and is pertinent to all modern techniques of stage evaluation (Compton & Greene, 2004). The TNM system has replaced older staging systems like the Modified Dukes Criteria. However, for research purposes, the TNM staging may be converted into the corresponding modified Dukes criteria staging for ease of classification and interpretation of data (Appendix 2b).

Treatment options for CRC are dependent on the stage of the disease, the performance status of the patient, and increasingly, the molecular makeup of the tumor. Improvements in have been realized in surgical technique, radiation therapy, systemic therapies as well as targeted therapies directed at the vascular endothelial growth factor pathway and the epidermal growth factor; resulting in more than 75% of patients with localized disease becoming recurrence free at 3 years, and up to 50% of patients with advanced unresectable disease being alive at 2 years (Gill et al., 2007). Surgery is the mainstay curative treatment for patients with non-metastasized colorectal cancer. However, outcome is strongly related to the quality of surgery, the quality of pre-operative staging and treatment selection. The dissection should ideally follow the embryological anatomical planes to ensure that the tumor and its principle

zone of lymphatic spread are excised. In more-advanced cases of rectal cancer, neoadjuvant treatment (for example, pre-operative chemotherapy for T4 colon cancer, and chemo- or radiotherapy for locally advanced cancer) can reduce tumor load and even tumor stage; and might be recommended in order to optimize the chances of a successful resection (Kuipers et al., 2015). A multidisciplinary approach before beginning treatment, which should be based on adequate staging information, is therefore of utmost importance. Part of the pre-operative assessment should include: the patient's age, fitness level, the peri-operative management plan, tumor staging, type of surgery (including resection planes and reconstruction). Another evolving aspect of peri-operative management is quality assurance, which has been defined for several aspects of the care continuum including: performing clinical trials, involvement of multidisciplinary teams, integrated care pathways, shared decision-making, auditing cancer care, centralization of complex procedures and international comparison of cancer outcomes across various oncology centers. Notably, there is increasing attention to quality assurance in CRC care, hence unravelling the effects of treatment on outcome has become of utmost importance and, for this, population-based registries and audits are used to critically assess practice (Kuipers et al., 2015).

With regards to the patient's age, elderly patients with CRC have lower overall survival rates than their younger patients; with post-operative mortality rates increasing in elderly in the immediate postoperative period (first 30 days) and this can double in the first 6–12 postoperative months (Kuipers et al., 2015). However, since 'elderly patients' as a group are heterogeneous, with varying comorbidities, degrees of fitness for surgery and risks for post-operative complications, age alone should not be a reason to exempt a patient from surgery and the approach should be on case-by-case basis. Peri-operative protocols such as fast track and Enhanced Recovery After

Surgery (ERAS) have been designed to minimize surgical complications (K et al., 2009). The protocol describes the peri-operative care pathway and lists elements of care for patients at various steps in the peri-operative process. Considering these elements are supported by evidence to improve recovery time after surgery, ERAS was first implemented for patients undergoing colectomy and includes elements such as pre-operative counselling, bowel preparation, peri-operative fluid management, prevention of ileus (obstipation and intolerance to oral intake), post-operative glucose control and early mobilization (K et al., 2009). Amongst all patients who are at high risk of post-operative ileus, enteral nutrition should be anticipated and prepared for, pre-operatively. Local recurrences after rectal surgery can be minimized using short-course radiotherapy, although long-term data (12-year follow-up) showed no effect on overall survival for this approach (W et al., 2011). The timing of surgery after short-course radiotherapy is important, since surgery after a longer waiting period has been associated with fewer complications than immediate surgery after radiotherapy (D et al., 2010). Importantly, neoadjuvant radiotherapy prior to surgery is associated with an increased risk for low anterior syndrome: a complex of symptoms that include frequent and urgent stools, numerous bowel movements over a few hours, stool incontinence and sexual dysfunction (K et al., 2009).

The resected tumor specimen can be used to judge the quality of surgery; if the margin around the specimen is free of cancer cells in both colon and rectal cancer, the surgery is considered high quality. The removal and assessment of the lymph nodes is also used to determine whether the mesocolic or mesorectal resection is adequate. Internationally, removal of 12 lymph nodes is viewed as the cut-off value needed to provide adequate histopathological staging; the lymph nodes can also be used to prognosticate patients (Kuipers et al., 2015).

The systemic treatment of patients with colorectal cancer has substantially evolved over the past two decades. Major improvements have been achieved in the neoadjuvant setting for rectal cancer, as well as in the adjuvant settings for cancer of the colon. For neoadjuvant treatment, there is no set standard neoadjuvant treatment for colon cancer; however, for rectal cancer, neoadjuvant radiotherapy or chemoradiotherapy are recommended for intermediate-stage and advanced-stage cancer, aimed at reducing the rate of local recurrence. The neoadjuvant treatment can either be given as short-course radiotherapy followed by surgery; or as chemoradiotherapy. Although preoperative chemo-radiotherapy is generally more effective than postoperative treatment in reducing local recurrence, some studies have demonstrated that it does not improve overall survival (W et al., 2011). Strategies that aimed to improve neoadjuvant treatment by intensifying the chemoradiotherapy regimen did not exhibit clear survival benefit, but rather were observed to increase toxicity to the patient (G. B et al., 2013). For adjuvant treatment, the cure rate by surgery alone for colon cancers classified as T3, T4a, T4b and N0M0 colon cancers (see appendix 2B) is high and only approximately 5% of patients benefit from adjuvant chemotherapy (Kuipers et al., 2015). However, guidelines endorsed by European and Japanese societies recommend considering adjuvant therapy in high-risk cases, that is: poorly differentiated tumors; when <12 lymph nodes were resected; in cases with vascular, lymphatic or perineural tumor invasion and in cases with obstructive or perforated tumors (Recio-Boiles & Cagir, 2021). By contrast, adjuvant treatment is standard for any T, N1–2 with ≥3 positive nodes, M0 (see appendix 2B); and currently, there is not enough data to support that the addition of targeted therapies such as epidermal growth factor receptor (EGFR)-specific or vascular

endothelial growth factor (VEGF)-specific monoclonal antibodies improves the outcome for patients in the adjuvant setting (Recio-Boiles & Cagir, 2021).

The survival of patients with metastatic disease has substantially improved over the past two decades and a median overall survival of 30 months has been achieved in clinical trials. This improvement in survival can be attributed to use of advanced chemotherapeutics, the introduction of targeted therapies that address specific properties of the tumor or its microenvironment, and the incorporation of multidisciplinary approaches including surgical resection of liver metastases (Kuipers et al., 2015). Age and comorbidity have been found to be significant predictors of overall survival in CRC (Eeghen et al., 2015). As such, it is important to approach the management of CRC patients beyond their cancer treatment and consider the reduced survival benefit of treatment with increasing age (Eeghen et al., 2015). A longitudinal study done locally amongst CRC patients on follow up at various hospitals within Nairobi, Kenya, in 2011 showed an overall mortality rate of 29.4% (Saidi et al., 2011). The factors that were significantly associated with mortality included the male sex, presence of co-morbidity, tumor recurrence, disease stage and receipt of chemotherapy (Saidi et al., 2011). More recent clinical records show general increase in survival post diagnosis over the past decade, which has led to a rising prevalence of patients living with CRC in Kenya. Survival at 5 years is 56% in Europe and 66% in the United States of America (Marventano et al., 2013). This increase of CRC survivors has also led to greater interest in the impact of CRC on health-related QoL amongst the patients.

2.2 Health Related Quality of Life

Assessment and determination of the state of health and health care is undergoing a paradigm shift, largely informed by the acknowledgement of the importance of the social consequences of disease and the acceptance that one of the main aims of medical interventions is to increase not just the length but also the quality of survival. Consequently, the quality, effectiveness, and efficiency of health care are evaluated based on their impact on the patient's quality of life.

Quality of Life is a multidimensional, dynamic, subjective and patient centered construct, comprising physical, functional, emotional, and social well-being (D. F. Cella & Tulsky, 1993). It is an important outcome in the evaluation of the full impact of the disease on the patients, their family and community. The WHO defines QoL as an individual's perception of their position in life in the context of their culture, value systems, standards and concerns (Badenhorst et al., 2018). Consideration of QoL allows the impact of a health related state, its effect on daily living and the experience from the personal perspective of the patient and care givers to be appreciated more comprehensively (Ravenek et al., 2013). Perceptions of health and its meaning vary between individuals and may also vary within the same individual at different time points of the disease process. In general, people base the assessment of their health related quality of life by comparing their expectations of the illness and health intervention, with their actual experience (Carr et al., 2001). This in effect means that different people affected by the same illness will have different quality of life driven by individual factors including but not limited to their social, emotional, mental and economic status. Comorbidities of the individual and their family members also have an impact on the overall quality of life (Weaver et al., 2012). In clinical practice, it is observed that past experiences, for example, having observed a close family member

or social contact who suffered from similar illness may also influence patients' perception and expectation of the disease and the disease process and this impacts their quality of life, independent of the actual experience of the patient.

Patient-reported questionnaires have become a standard practice in the assessment of QoL. Commonly used tools of quantitative QoL assessment include the WHOQOL-BREF (Jansen van Rensburg et al., 2017), a 26-item version of the WHOQOL-100 assessment which is a cross-culturally valid assessment of QOL comprising of four domains: physical, psychological, social and environment. The Medical Outcomes Study Short Form (SF-36) is also used to operationalize Health Related Quality of Life (HRQL) for a traditional clinical setting (Jansen van Rensburg et al., 2017). These and other QoL questionnaires provide an objective quantitative assessment of patients' quality of life and are usually comparable to the clinical and functional status of the patient.

2.3 Quality of Life in Cancer

Perceived health status independently influences an individual's need for, and uptake of oncological health services and this realization has led to attempts to produce health indicators which assess subjective rather than objective health problems in cancer, such as assessment of quality of life of individual patients. Cancer patients in Africa face unique challenges including poverty, access to health care and under-resourced health-care systems (Jansen van Rensburg et al., 2017). The perspectives of cancer patients living in Kenya who are largely reliant on public healthcare have not been widely studied.

In a South African study assessing the quality of life amongst cancer patients (Jansen van Rensburg et al., 2017), as in many developing countries, poverty was a major

issue and influenced the physical aspects of QoL, as it impacted the participants ability to work and earn a living to support their medical costs and still provide for their dependents. QoL was enhanced by support from family, friends, religion and religious practices. In a Kenyan study done in 2004 by Mwanda et al at Kenyatta National Hospital (KNH), the issues affecting the quality of life of male cancer patients stated were pain, inability to work, poor coping with cancer and psychological reactions of work retardation, insomnia, weight loss, fatigability and depression. Commonly used general cancer-specific questionnaires are the FACT-G (D. F. Cella & Tulsky, 1993) and the European Organization for the Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30) (Sprangers et al., 1993). The questionnaires are quantitative tools of assessing the QoL of cancer patients, thus reproducible. Higher scores on the questionnaires signify a better QoL. Some of the advantages of FACIT questionnaires (including FACT-G & FACT-C) compared to the other QoL questionnaires include: the shorter duration of time required to administer the questionnaire, the items used to assess QoL are phrased as simple statements requiring a recall period of only seven days and they are available in multiple languages thus can even be used in simultaneous research across varied countries (Luckett et al., 2011). Additionally, the FACT-G (details in section 2.5.1), has been translated in Kiswahili and validated for use in Kenya.

2.4 Quality of Life in Colorectal Cancer

Quality of Life is affected by various elements including the loss of health due to CRC, the side effects of the treatment which may result in functional impairment as well as disruption of social and family interactions due to ill health (Marventano et al., 2013). Colorectal cancer survivors often have gastrointestinal disturbances which vary

from mild to severe with generalized ill health as a consequence of the primary illness or treatment complications. They may also suffer from sexually related problems including erectile dysfunction, ejaculation problems, dyspareunia, vaginal dryness, and decreased enjoyment and should be provided with relevant treatments for the same and/or referred to an appropriate specialist. Colorectal cancer patients may also suffer from body image issues, particularly those with a permanent ostomy.

Like many cancers, CRC also has an economic impact on the individual and their family as a result of costs involved to access care coupled with the individual's loss of productivity, which directly influence the day-to-day living of patients and their families. In a recent study carried out in the USA, healthcare cost associated with common cancers including CRC was $20,000 to $100,000 in the initial phase, $1000 to $30,000 annually in the continuing phase, and ≥$60,000 in the end-of-life phase with the annual out-of-pocket costs to recently diagnosed survivors being >$1000 for medical care and time costs, approximately $2000 for productivity losses, and from $2500 to >$4000 for employment disability, depending on age; with the costs related to longer term survival at approximately $1500 for older survivors and $747 for younger survivors, time costs were $831 to $955 for older survivors and $459 to $630 for younger survivors, and productivity losses were approximately $800 (Pisu et al., 2018)

Previously validated HRQL instruments, used to assess QoL amongst CRC patients include: the Instrumental Activities of Daily Living scale (IADL), the 12-Item Short-Form Health Survey (SF-12), the Short-Form-36 (SF-36) Vitality Scale, the European Organization for Research and Treatment of Cancer-Colorectal survey (EORTC-CR38), the Brief Pain Inventory (BPI), the Fatigue Symptom Inventory (FSI), the Life

Orientation Test (LOT), the Impact of Cancer Instrument version 1 (IOC) and the Functional Assessment of Cancer Therapy CRC Questionnaire (FACT – C).

The FACT-C (D. F. Cella & Tulsky, 1993) is among the most commonly used CRC specific questionnaire. The FACT – C, is comprised of the FACT – G as well as an additional component that is CRC specific. The FACT - C has however not been validated in Kenya and Eastern Africa. The FACT-C includes an additional dimension focused on CRC. All the items are based on a five-point Likert scale with a time frame of seven days, except for the one investigating the presence of stoma (yes/no). This questionnaire was principally designed for self-administration, but can also be interviewer administered. Both total and single dimensions scores will be calculated to determine QoL in CRC patients.

In the United States long-term CRC survivors, overall physical and mental health was excellent compared with general population. Other disease-related symptoms did not detract from good overall health (Mooney, 2006). Good access to health care and timely diagnosis has contributed to a decline in mortality rates; and with the advancement in modalities, CRC screening has become a major agenda item for national gastroenterology societies although disparities in access to government-funded screening, between race and gender, continue to exist (Montminy et al., 2019). A Moroccan study of colorectal cancer patients showed that some symptoms could be improved by more supportive care. Neither chemotherapy, nor radiotherapy worsened the long term quality of life of early colorectal cancer patients in that study (Mrabti et al., 2016). At the time of this study, there was limited data on the quality of life of colorectal cancer patients in Eastern Africa, however, there has been a very

recent study at Kenyatta National Hospital on how drug related problems affect the health-related quality of life of CRC patients (Kabiru et al., 2021).

2.5 Functional Assessment of Chronic Illness Therapy (FACIT) questionnaires

The FACIT measurement system is a collection of health-related quality of life (HRQOL) questionnaires used in the management of patients with chronic illness. The measurement system, which has been under development since 1987, started with the creation of a generic CORE questionnaire called the Functional Assessment of Cancer Therapy-General (FACT-G), which is now in Version 4 (section 2.5.1) is appropriate for use with patients with any form of cancer, and extensions of it have been used and validated in other chronic illness condition (e.g., HIV/AIDS; multiple sclerosis; Parkinson's disease; rheumatoid arthritis), as well as in the general population (Webster et al., 2003). The FACIT measurement System currently includes over 400 questions, some of which have been translated into more than 45 languages. Questionnaire administration time for any one assessment is usually less than 15 minutes, which is achieved by the use of specific subscales for relevant domains of Health-Related Quality of Life (HRQOL), or computerized adaptive testing (CAT) of selected symptoms and functional areas. FACIT questionnaires can be administered by self-report (paper or computer) or interview (face-to-face or telephone); and the scales are constructed to complement the FACT-G, addressing relevant disease-, treatment-, or condition-related issues not already covered in the general questionnaire (Webster et al., 2003). Each scale is intended to be as specific as necessary to capture the clinically-relevant problems associated with a given cancer type, condition or symptom, yet the questions are general enough to allow for comparison across diseases, and extension (as appropriate) to other chronic medical

conditions (D. Cella et al., 2002). Currently scoring cut-offs to denote good quality of life are determined in the context of a growing literature base (Webster et al., 2003).

The FACIT measurement system has several documented advantages to an investigator seeking to measure HRQOL in people with cancer. For instance, the item content was determined by combined expert and patient input, ensuring that clinically important issues relevant to patients are included in the scales (Webster et al., 2003). There are several publications detailing the performance of the FACIT measurement system, most of which are based on data obtained from formal validation studies hence offers adequate reference literature to which one can compare and contrast results. FACIT also offers the availability of normative and cross-illness comparative scores to which one can relate results, in addition to a growing body of research that has illustrated clinically significant differences and changes in scores in FACIT scales, aiding in study sample size determination and interpretation of study results (*The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: Properties, Applications, and Interpretation*, n.d.).

There are many questionnaires available to measure HRQOL of people with chronic illnesses. The FACIT questionnaires are some of the more commonly used questionnaires in national and international research settings. Selecting an appropriate outcome measure is often driven by many considerations including the purpose of the study, the patient-reported endpoint required to address the study purpose, the content of the items in the questionnaire with regard to the study purpose, and the validity of the questionnaire. Although no single questionnaire is right for all CRC quality of life studies, the FACIT measurement system stands out as it provides an array of generic and targeted measures with multiple benefits (Webster et al., 2003b) including: ease

of administration (most in 5–10 minutes); demonstrated reliability, validity and sensitivity to change; special consideration for spiritual well-being, palliative care, and treatment satisfaction; more social well-being coverage than most other commonly-used instruments; the questionnaires are written at the 4th Grade reading level (9–10 years old) or below; the questionnaires demonstrated equivalence in mode of administration (interview vs. self-administration); validated for use with special populations such as with the elderly and those living in rural areas; multiple scoring options: subscale scores, total score, and a Trial Outcome Index (TOI); and used by major cooperative clinical trial groups, international-industry sponsored research, other government/military funded research, and health practice self-studies (Webster et al., 2003).

2.5.1 FACT-G questionnaire

The FACT-G questionnaire (Appendix 4 & 5) is used to assess the health-related quality of life in patients with any form of cancer. It is currently available in version 4.0 in both English and Kiswahili versions (both validated for use in Kenya), as a 27-item compilation of general questions divided into four primary QOL domains: Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being. Each of the 27 items is scored based on five-point Likert scale (0-4), with a highest possible total score of 108 (*The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: Properties, Applications, and Interpretation*, n.d.). A total score of ≥ 81 usually denotes good quality of life while a score of <81 denotes poor quality of life.

2.5.2 FACT-C questionnaire

The FACT-C questionnaire (Appendix 3) is used to assess the health-related quality of life in patients with confirmed colorectal cancer. It is currently available in an English but no official Kiswahili translation is available. It contains a colorectal cancer-specific subscale with a highest possible total score of 28 for the compulsory questions (*The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: Properties, Applications, and Interpretation*, n.d.). The non-compulsory questions are only relevant to patients who have a stoma, hence are not considered in the total scoring of the questionnaire. A total FACT-C subscale score of ≥ 21 usually denotes good quality of life while a score of < 21 denotes poor quality of life in a colorectal cancer patient.

CHAPTER THREE: METHODOLOGY

3.1 Study site

This study was conducted at Moi Teaching and Referral Hospital (MTRH) adult oncology outpatient & inpatient units. MTRH, the second largest national referral and teaching hospital in Kenya after Kenyatta National Hospital (KNH), is located along Nandi Road in Eldoret town, approximately 310 kilometers Northwest of Nairobi the capital city of Kenya. It is hosted by Uasin Gishu County, in the North Rift region of Western Kenya and serves a population of approximately 24 million people (*Moi Teaching and Referral Hospital - History*, n.d.) largely drawn from the Western part of Kenya, Northern Uganda, Southern Sudan & Northern Tanzania.

Apart from receiving patients on referral from other hospitals within or outside Kenya for specialized health care, MTRH provides facilities for medical education for Moi University, Kenya Medical Training Centre (KMTC) and for research either directly or through other co-operating health institutions. It has both inpatient and outpatient units with a wide coverage of general as well as specialist medical and surgical services.

The Oncology unit at MTRH is supported by AMPATH and was formed in 2008 to facilitate cancer treatment and prevention. In 2016, MTRH incorporated the Chandaria Cancer and Chronic Disease Centre (CCCDC) which further boosted its capacity as a learning institute; in addition to providing a home for robust research and care. Every month, more than 1,000 cancer patients are seen and treated by specially trained caregivers including oncology doctors, nurses and clinical officers in more than 13 clinical sites established within and around Western Kenya (*Cancer — AMPATH*, n.d.).

3.2 Study design:

This was a descriptive cross-sectional study conducted between April 2019 and January 2020.

3.3 Study population:

All adult patients aged $\geq$ 18 years with histologically confirmed colorectal cancer regardless of treatment status.

3.4 Eligibility criteria

3.4.1 Inclusion criteria

- Age >18 years

- Histological (primary) diagnosis of CRC

3.4.2 Exclusion criteria

- Patients with known neurocognitive disorder, specifically, reduction in mental function affecting memory, understanding and behaviour.

3.5 Sample size calculation

FACIT organization guidelines were used to determine the sample size for the validation of the Kiswahili working translation of the FACT-C questionnaire. For a validation technique to gain reliable estimates, the number of subjects' observations should be 10 times the number of variables in the tool (Ali, 2014), as such the appropriate sample size for the validation of the study was calculated based on this guideline. The CRC specific items are a total of 10 items (8 compulsory and 2 optional). The Kiswahili working translation of the FACT-C questionnaire was initially tested on 10 CRC patients. Additionally, 10 patients were recruited for each of the 8 compulsory components of the CRC subscale of the FACT-C

questionnaire. Thus, the overall required sample size was 90 CRC patients in order to fulfill all the objectives of the study.

3.6 Sampling method

At the time of this study, the patient records at MTRH determined the CRC population to be a relatively small population of approximately 120 patients. As such, the study team applied Census Sampling on all CRC patients who came in for clinic visits and/or hospitalization at MTRH during the study period until the desired sample size of 90 patients was achieved.

3.7 Kiswahili translation of FACT-C questionnaire

The translation process (Appendix 3) of the FACT-C Kiswahili working tool involved two translators who have been trained in medical translation and whose native language is Kiswahili, working independently from one another. They each provided a forward translation from English into the target Kiswahili language. These were then sent to a third translator, who reviewed the English and the two forward Kiswahili translations and chose one of the forward translations or chose a new translation, depending on what the third translator considered as most appropriate (Appendix 3). The reconciled Kiswahili translation by the third translator was then sent to a fourth translator, who provided a back translation of each item from Kiswahili back into English. Once all of those steps were completed, the study PI reviewed the steps, as well as the back translations, and finalized the translations for testing. The Kiswahili working translation of the FACT-C was pilot-tested on 10 study participants before being applied to the rest of the study population.

3.8 Study procedures

3.8.1 Participant recruitment

A total of 90 participants were recruited using the eligibility criteria (section 3.4) and each eligible participant underwent study procedures as detailed on Figure 1:

```
┌─────────────────────────────────────────────────────────────┐
│ Informed consent procedure done by PI / Research assistant  │
└─────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────┐
│ Administration of study questionnaire and ECOG status       │
│ determination by PI / Research assistant                    │
└─────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────┐
│ Administration of FACT-G & FACT-C by PI / Research          │
│ assistant                                                   │
└─────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────┐
│ Participants received routine care in the clinic before exiting. │
└─────────────────────────────────────────────────────────────┘
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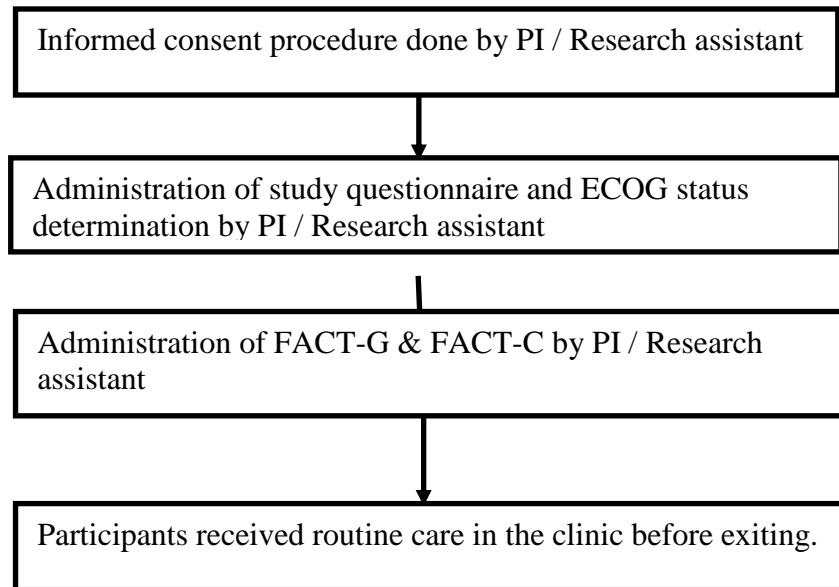
Figure 1: Study procedures

3.8.2 Informed Consent Procedure

Prior to being involved in this study, potential participants who were identified via clinic and inpatient records were approached and taken through detailed information regarding the purpose of the study by the study Principal Investigator (PI) / Research assistant. The benefits and risks of participation in the study were explained in order to guide their informed decision as to whether to voluntarily participate or not. The study information (Appendix 1) was explained in English (the national official language) and/ or Kiswahili (the national local language). The informed consent procedure was clearly documented and the voluntary consent given in writing through signing (or thumb printing) and dating of the informed consent form in duplicate. One copy of the informed consent form was retained in the subject's study file and the

second copy was given to the subject for their reference and records. Each recruited participant who consented to be in the study was assigned a unique study ID.

3.8.3 Questionnaire procedures

The study questionnaires were administered by the PI / Research assistant. Standardized training of the Research assistant was done by the PI and a questionnaire guide used as a working tool was developed during training. A comprehension test was applied at the end of the training including a dry run for training assessment. The first questionnaire to be administered was a structured study questionnaire that collected data on socio-demographic and clinical characteristics of the study participants including: age, sex, residence, ethnicity, marital status, religion, histological type, comorbidities, presence of stoma, treatment status and modalities, disease stage and ECOG performance status.

The ECOG performance status is a standard criteria which is used to measure how the disease impacts a patient's daily living abilities by describing a patient's level of functioning in terms of their ability to care for themselves, daily activity and physical ability (*ECOG Performance Status - ECOG-ACRIN*, n.d.). The scale ranges from 0 – 5: where 0 is fully active and 5 is dead (Appendix 6).

Thereafter, the validated Kiswahili FACT – G QoL assessment tool was used to assess the QoL. The tool includes for main components (Appendix 4 & 5) on a five-point Likert scale ranging from a score of 0 to 4, with minimum to maximum scores as follows: Physical well-being (PWB): 0 – 28; Family / social well-being (SWB): 0 – 28; Emotional well-being (EWB): 0 – 24; Functional well-being (FWB): 0 – 28; Total Score: 0 – 108.

The Kiswahili working translation of the FACT − C colorectal cancer -specific subscale was then administered to determine QoL. In this questionnaire, the first question was on CRC symptomatology with scores ranging from 0 − 28. The second question which is only relevant to patients who have a stoma has scores ranging from 0 − 8 and was not considered in the overall total score as per the FACIT scoring guidelines.

3.9 Study Variables

The participant data that was collected included the descriptive variables of age, sex, residence, ethnicity, marital status, religion, histological type, comorbidities, presence of stoma, treatment modalities (including chemotherapy, radiotherapy & surgery), disease stage, ECOG clinical performance status, QoL score as determined by FACT-G and QoL score as determined by FACT-C.

3.10 Data Management

3.10.1 Data collection tools

Structured interviewer-administered questionnaires were used to collect sociodemographic, clinical and QoL data detailed in section 3.8.3. Each study participant was identified by a unique numeric study ID which was indicated on each questionnaire that the participant as subjected to. Data collected on the questionnaires was subjected to a completeness-check before the participant exited from the study, to ensure no missing data. The paper data was then double-imputed onto Microsoft Excel spreadsheet software and reconciled before being exported to the analysis software.

3.10.2 Data Cleaning

Data cleaning was done at three different stages: at the end of paper data collection, during initial data entry onto the spreadsheet and during data analysis. At each stage, completeness of data was ensured. These tight stepwise checks resulted in no missing data at the point of final analysis.

3.10.3 Data protection and security

The paper-based questionnaires were in the strict custody of the study PI, secured in a fireproof lockable cabinet. The computers used for data entry and analysis were password and antivirus protected, with internet firewalls activated for additional data security. An external hard disk that was used for data backup was only accessible to the study PI.

3.10.4 Data analysis

Study data was analyzed using Stata software version 15.1. Socio-demographic and clinical characteristics were summarized using percentages for categorical variables; and mean and standard deviation (SD) for continuous variables. Chi square test of difference was used to determine the heterogeneity in the distribution of demographic and clinical characteristics.

The FACIT organization guidelines were used to obtain sub-scale as well as total scores for both FACT-G and FACT-C questionnaires. The FACT scale is an acceptable indicator of the patient's quality of life when the overall item response rate is greater than 80%. Any missing data due to incomplete answering of the questions on the FACT – G and FACT – C was substituted using a prorated sub-scale score as per the guidelines (Appendix 8). The prorated sub-scale score is acceptable as long as more than 50% of the items were answered and is calculated by multiplying the sum

of the subscale by the number of items in the subscale, then dividing by the number of items answered (Prorated subscale score = [Sum of item scores] x [Number of items in subscale] ÷ [Number of items answered]).

The FACT-G total score and the specific FACT-C subscale score were analyzed separately. Negatively stated items on the questionnaires were reversed by subtracting the response from "4". After reversing proper items, all subscale items were summed to a total, which made up the subscale score. Overall, the higher the score the better the QOL. Good quality of life was based on a total score of more or equal to 81 on the FACT-G questionnaire and a score of more or equal to 21 on the FACT-C subsection.

To test for Content validity of the FACT-C questionnaire, Pearson chi square test of homogeneity was used to determine whether there was a statistically significant difference in QoL as determined by FACT-G and FACT-C questionnaires, since the FACT-C is designed to be more specific than FACT-G in QoL determination amongst CRC patients. The null hypothesis ($H_{0)}$) was that there was no difference between QoL as determined by FACT-G and QoL as determined by FACT-C. The alternative hypothesis ($H_{a)}$) was that there was a difference between QoL as determined by FACT-G and QoL as determined by FACT-C. The significance level was set at 0.05 for the P-value. In this case, the QoL scores were summarized into two categories, Good QoL or Poor QoL (Table 7). The FACT-G QoL was used as the comparator or "gold standard" since both its English and Kiswahili versions are already validated for use in Kenya.

To test for External Validity, the QoL as determined by FACT-C and FACT-G were compared with the patients' performance status as determined by the ECOG scale. Typically the ECOG scale (Appendix 10) describes a patient's level of functioning in

terms of their ability to care for themselves, daily activity, and physical ability and ranges from a score of zero (fully active) to five (dead) (Oken et al., 1982) and is a tool that widely used in both clinical and research settings.

3.11 Ethical consideration:

Prior to the onset of this study, the study protocol received approval from Moi University Institutional Research Ethics Committees (IREC) and permission from MTRH management (Appendix 9 & 10). FACIT licenses were also obtained for the use of FACT-G and FACT-C questionnaires (Appendix 7).

Informed consent was voluntarily obtained from all study participants by either the study PI or Research assistant in accordance with Good Clinical Practice (GCP) guidelines. Participants were free to withdraw consent at any point during the study. There was no coercion whatsoever; and patients who declined to be in the study were not discriminated upon, nor were they denied routine clinical service and/or treatment. One copy of the informed consent form was retained in the subject's study file and the second copy was given to the subject for their records.

Subject confidentiality was upheld and information regarding a participant was treated strictly, stored in lockable cabinets and password protected computers. No individual participant information was discussed with other participants as per both ethical and medical codes of conduct. Any urgent findings were communicated to the primary clinician for follow up purposes and / or further intervention.

No one from the study team had any conflict of interest to declare in the conduct of this study.

CHAPTER FOUR: RESULTS

4.1 Recruitment

During the study period, the recruitment was conducted on every weekday in the MTRH outpatient and inpatient units. A total of 90 participants met the eligibility criteria, consented to be in the study and successfully completed the study procedures as per the recruitment schema below (Figure 2).
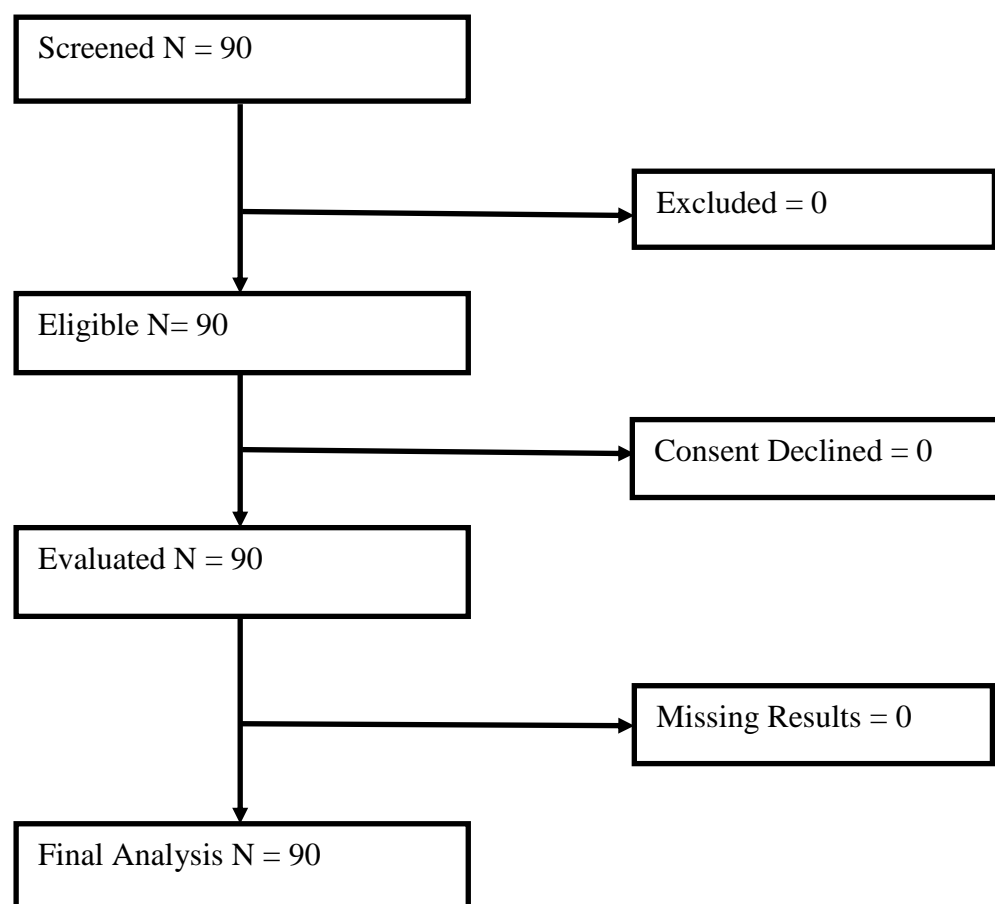
Figure 2: Recruitment schema

As indicated in figure two above, there were no participants who declined consent, likely due to the non-invasive nature of this study with minimal potential risk exposure to the participants. The QoL questionnaires are also not routinely used to assess the well-being of the CRC patients during routine follow up and there is a likelihood that this also contributed to generating the interest to participate in the study. A quality check performed on the study questionnaires for completeness ensured that there was no missing data, prior to exiting the participants from the study. However, should there have been missing data, as explained in section 3.10.4, the FACIT guidelines have a detailed provision for handling the missing data due to incomplete answering of the questions on the FACT – G and FACT – C, through substitution using a prorated sub-scale score (Appendix 8).

4.2 Sociodemographic characteristics of the study participants

Out of the 90 participants, 50 (55.6%) were female. 27 (30%) were aged $\geq$ 60 years, while 26 (33.8%) were aged below 40 years. Majority 62 (80%) of the participants resided in the rural areas. 39 (43.4%) had attained secondary school education or higher; 42 (54.5%) were unemployed. Majority (77.9%) were married; and 19 (11.1%) were widowed.

Chi square test of difference was applied to determine the distribution of the participants in each sociodemographic stratum. The difference in number of patients in each substratum was not statistically significant (p>0.05) and this demonstrated a statistically even and well-balanced distribution across all sociodemographic strata (Table 1).

Table 1: Sociodemographic characteristics of the study participants.

	Adenocarcinoma (N = 77)		SCC (N = 13)		Total (N = 90)		P value
	No.	%	No.	%	No.	%	
Gender							
Female	42	54.5	8	61.5	50	55.6	0.639
Male	35	45.5	5	38.5	40	44.4	
Age category							
18 - 30 Years	10	13	0	0	10	11.1	0.076
31 - 40 Years	16	20.8	0	0	16	17.8	
41 - 50 Years	14	18.2	3	23.1	17	18.9	
51 - 60 Years	14	18.2	6	46.2	20	22.2	
> 61 years	23	29.9	4	30.8	27	30	
Ethnicity							
Kalenjin	35	45.4	8	61.5	43	46.7	0.263
Luhya	20	26	2	15.4	22	24.4	
Luo	9	11.7	1	7.7	10	11.1	
Kisii	5	6.5	1	7.7	6	6.7	
Kikuyu	7	9.1	0	0	7	7.8	
Kamba	1	1.3	0	0	1	1.1	
Not specified	0	0	1	7.7	1	1.1	
Marital Status							
Single	7	9.1	0	0	7	7.8	0.608
Married	60	77.9	11	84.6	71	78.9	
Separated	2	2.6	0	0	2	2.2	
Widowed	8	10.4	2	15.4	10	11.1	
Education level							
Tertiary	13	16.9	1	7.7	14	15.6	0.103
Secondary	24	31.2	1	7.7	25	27.8	
Primary	28	36.4	6	46.2	34	37.8	
< Primary	12	15.6	5	38.5	17	18.9	
Employment status							
Formally Employed	11	14.3	2	15.4	13	14.4	0.696
Self Employed	23	29.9	2	15.4	25	27.8	
Unemployed	42	54.5	9	69.2	51	56.7	
Student	1	1.3	0	0	1	1.1	
Residence							
Rural	62	80.5	10	76.9	72	80	0.931
Semi-urban	6	7.8	1	7.7	7	7.8	
Urban	9	11.7	2	15.4	11	12.2	
Total	77		13		90		

4.3 Clinical characteristics of the study participants

The two main histological subtypes were adenocarcinoma (86%) and squamous cell carcinoma (14%). Disease staging by Dukes criteria (Appendix 2) at the point of recruitment showed that overall, majority of the patients were at Dukes Stage B or higher of the disease, with 25 (27.8%) at Dukes stage D (Table 2). In the adenocarcinoma subtype, 49% of the participants had advanced disease at Dukes stage C & D (Figure 3).
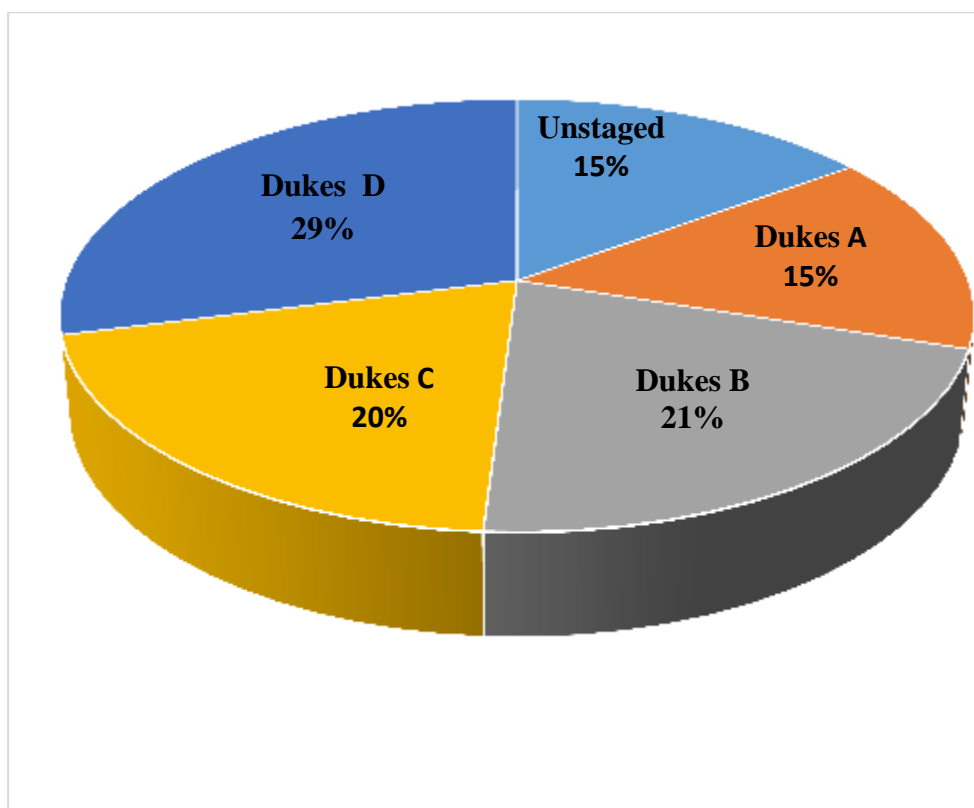
Figure 3: Adenocarcinoma histological subtype disease staging

In the squamous cell carcinoma (SCC) subtype, 49% of the participants also had advanced disease at Dukes stage C & D (Figure 4).
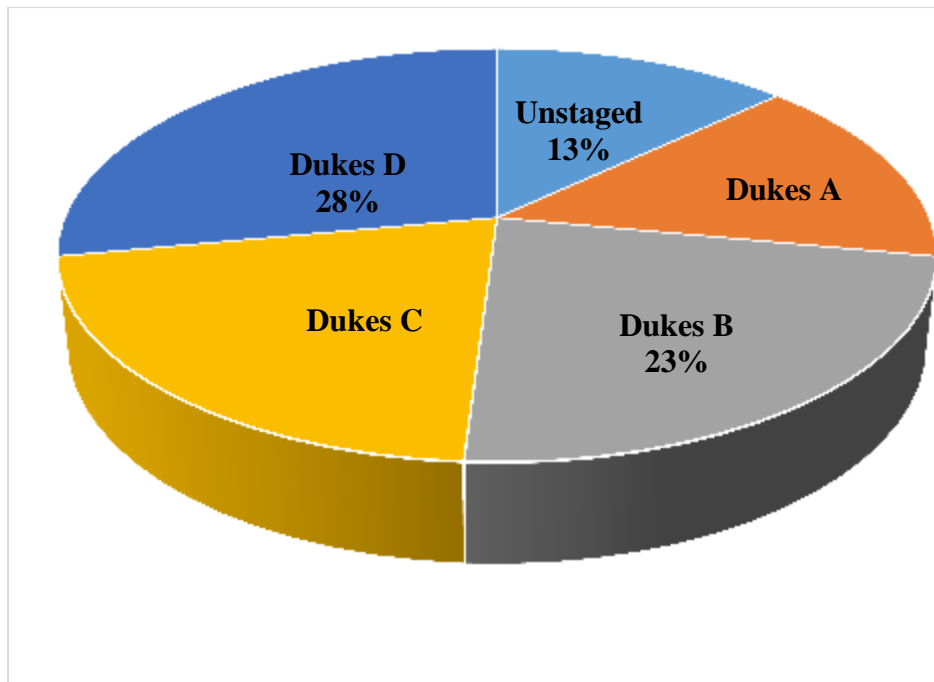
Figure 4: Squamous cell carcinoma (SCC) histological subtype disease staging

At the time of this study, 95% of the patients had undergone some intervention for the CRC, with the commonest modality being a combination of chemotherapy and surgery (47.8%). Only 34 (37.8%) of the CRC patients in the study had surgical fashioning of a stoma.

There were no reported comorbidities in 77% of the study participants. It was noted that 4.4% of the participants had HIV disease and of those, the majority (75 %) had squamous cell carcinoma (Table 2). Notably, all the patients with squamous cell carcinoma histological subtype of CRC were aged above 40 years

Chi square test of difference was applied to determine the distribution of the participants in each clinical stratum; the difference in distribution of participants stratified by comorbidities ($p = 0.002$) and intervention modalities ($p = 0.034$) was statistically significant, demonstrating an uneven distribution in the two strata. All the other clinical strata however demonstrated a statistically even distribution ($p > 0.05$).

Table 2: Clinical characteristics of the study participants.

	Adenocarcinoma (N = 77)		SCC (N = 13)		Total (N = 90)		P value
	No.	**%**	**No.**	**%**	**No.**	**%**	
CRC Staging							
Unstaged	12	15.6	0	0	12	13.3	0.31
DUKE A	12	15.6	1	7.7	13	14.4	
DUKE B	16	20.8	5	38.5	21	23.3	
DUKE C	15	19.5	4	30.8	19	21.1	
DUKE D	22	28.6	3	23.1	25	27.8	
Treatment / Intervention							
None	5	6.5	0	0	5	5.6	**0.034**
Chemotherapy (C)	15	19.5	6	46.2	21	23.3	
Radiotherapy (R)	1	1.3	0	0	1	1.1	
Surgery (S)	13	16.9	4	30.8	17	18.9	
C & R	1	1.3	0	0	1	1.1	
C & R & S	0	0	1	7.7	1	1.1	
C & S	41	53.2	2	15.4	43	47.8	
Other	1	1.3	0	0	1	1.1	
Colostomy							
Yes	31	40.3	3	23.1	34	37.8	0.237
No	46	59.7	10	76.9	56	62.2	
ECOG status							
0 = Fully active	21	27.3	5	38.5	26	28.9	0.053
1 = Ambulatory, light work	30	39	1	7.7	31	34.4	
2 = Ambulatory, no work	16	20.8	2	15.4	18	20	
3 = Limited selfcare	8	10.4	3	23.1	11	12.2	
4 = Disabled	2	2.6	2	15.4	4	4.4	
5 = Dead	0	0	0	0	0	0	
Comorbidity							
None	63	81.8	7	53.8	70	77.8	**0.002**
Diabetes (DM)	3	3.9	0	0	3	3.3	
Hypertension (HTN)	5	6.5	1	7.7	6	6.7	
HIV	1	1.3	3	23.1	4	4.4	
Anemia	1	1.3	0	0	1	1.1	
TB	1	1.3	0	0	1	1.1	
Pneumonia	0	0	1	7.7	1	1.1	
Unspecified	2	2.6	0	0	2	2.2	
DM & HTN	0	0	1	7.7	1	1.1	
HTN, Asthma & COPD	1	1.3	0	0	1	1.1	
Total	77		13		90		

4.4 Quality of life scores stratified by sociodemographic characteristics

A total score of $\geq$81 on FACT-G and $\geq$21 on FACT-C was considered as good QoL in this study (Table 3 & 4). Scores below this were considered as poor QoL.

Good QoL as determined by FACT-G was observed in participants aged $\geq$61 years (mean 85.7, SD 18.81), although the same age group did not meet good QoL cut-off by FACT-C (mean 20.9 SD 5.29). The commonest ethnicity was Kalenjin, accounting for 46.7% of the study population. Participants of Kalenjin and Kisii ethnicity were observed to have good QoL on both FACT-G and FACT-C. Higher level of education was associated with good QoL on FACT-G: tertiary (mean 81.4, SD 14.94) and secondary (mean 82.2, SD 17.17) and the same observation was upheld by FACT-C questionnaire: tertiary (mean 21.7, SD 5.78) and secondary (mean 21.3, SD 4.40). There was a single participant, a student, who was found to have good QoL by both FACT-G (mean 93.0 SD) and FACT C (mean 27.0 SD). Study participants whose marital status was "widowed", were observed to have good QoL by FACT-G questionnaire although this observation did not uphold by FACT-C questionnaire. When stratified by gender and residence, the QoL as determined by both FACT-G and FACT-C was observed to be poor across both strata.

Table 3: FACT-G and FACT C scores stratified by sociodemographic characteristics.

Variables	Total FACT-G Score Good QoL Mean ≥81		Total FACT-C Score Good QoL Mean ≥21	
	Mean	**SD**	**Mean**	**SD**
Gender				
Female	80.2	18.06	20.8	4.95
Male	77.9	19.39	19.2	5.97
Age Category				
18 - 30 Years	74.3	21.16	17.7	9.26
31 - 40 Years	80.8	15.64	20.9	4.49
41 - 50 Years	79.1	19.40	19.8	5.32
51 - 60 Years	71.7	16.71	19.9	4.09
> 61 years	**85.7**	18.81	20.9	5.29
Ethnicity				
Kalenjin	**84.5**	16.44	**21.1**	4.46
Luhya	75.0	20.95	20.3	6.51
Luo	73.1	20.74	16.4	5.82
Kisii	**81.2**	20.04	**22.0**	4.65
Kikuyu	71.7	15.87	19.0	6.00
Kamba	**86.0**	-	19.0	-
Not specified	55.0	-	10.0	-
Marital Status				
Single	76.7	13.88	17.1	6.77
Married	79.9	18.29	20.6	4.98
Separated	48.0	31.11	9.0	12.73
Widowed	**82.1**	18.65	20.8	4.08
Education level				
Tertiary	**81.4**	14.94	**21.7**	5.78
Secondary	**82.2**	17.17	**21.3**	4.40
Primary	75.3	19.57	18.0	5.77
< Primary	80.7	21.39	**21.2**	5.09
Employment Status				
Formally Employed	80.8	19.25	**22.6**	4.29
Self Employed	77.0	16.87	19.1	5.02
Unemployed	79.6	19.56	19.8	5.78
Student	**93.0**	-	**27.0**	-
Residence				
Rural	79.8	18.98	20.5	5.38
Semi-urban	75.1	15.82	17.9	5.49
Urban	77.8	18.80	19.0	5.98

Note: SD denoted as "-" indicates absence of SD as only one participant was in that category. Good QoL scores appear in bold on the table.

4.5 Quality of life scores stratified by clinical characteristics

Participants with Dukes A CRC stage (FACT-G mean 93.9, SD 17.61) and those with Unstaged disease (FACT-G mean 87.5, SD 10.08) were observed to have good QoL by FACT-G and the good QoL status was also upheld by FACT-C scoring. Good QoL was observed in the treatment category of radiotherapy, both as monotherapy, and in combination with chemotherapy, on both FACT-G and FACT-C; although notably there was only one participant in each of the two categories, hence, this finding may not be generalizable. Participants with Hypertension (HTN) had good QoL as determined by both FACT-G (mean 82.2, SD 27.02) and FACT-C (mean 23 SD 5.93). Good QoL was also observed in participants who had Diabetes Mellitus (DM) coexisting with HTN and in the Tuberculosis (TB) stratum, although, these findings may also not be generalizable since there was a single participant in each of the two categories.

The participants who underwent surgery alone or in combination with chemotherapy and radiotherapy were observed to have poor QoL on both FACT-G and FACT-C scoring. Anemia, HIV and Pneumonia were also associated with poor QoL. Interestingly, the participants who had no comorbidities also had poor QoL on both FACT-G and FACT-C. When stratified by, presence or absence of a stoma, all patients were observed to have poor QoL. Those with SCC histological subtype were also noted to have poor QoL on both FACT-G and FACT-C (Table 4).

Table 4: FACT-G and FACT-C scores stratified by clinical characteristics.

Variables	Total FACT-G Score Good QoL Mean ≥81		Total FACT-C Score Good QoL Mean ≥21	
	Mean	**SD**	**Mean**	**SD**
CRC Staging				
Unstaged	**87.5**	10.08	**21.1**	4.85
DUKE A	**93.9**	17.61	**24.3**	2.81
DUKE B	80.0	16.82	20.5	5.03
DUKE C	71.1	18.37	19.8	5.59
DUKE D	73.0	18.65	17.3	5.73
Treatment / Intervention				
None	**93.4**	20.31	20.8	7.60
Chemo C	75.4	19.24	18.9	4.97
Radio R	**82.0**	-	**21.0**	-
Surgery S	77.7	19.99	19.2	5.58
C & R	**88.0**	-	**26.0**	-
C & R & S	44.0	-	20.0	-
C & S	80.1	17.13	20.7	5.59
Other	**96.0**	-	**24.0**	-
Colostomy				
Yes	76.8	18.02	19.3	5.90
No	80.7	18.94	20.6	5.17
Comorbidity				
None	80.5	16.82	20.2	5.48
Diabetes (DM)	73.7	20.31	**21.3**	1.53
Hypertension (HTN)	**82.2**	27.02	**23.0**	5.93
HIV	53.0	9.09	14.5	4.04
Anemia	60.0	-	19.0	-
TB	**102.0**	-	**24.0**	-
Pneumonia	44.0	-	20.0	-
Unspecified	77.5	12.02	18.0	1.41
DM & HTN	**108.0**	-	**28.0**	-
HTN, Asthma & COPD	**100.0**	-	11.0	-
Histology				
Adenocarcinoma	**82.3**	17.19	20.7	5.42
SCC	60.9	16.44	16.6	4.46

Note: Good QoL scores appear in bold on the table.

4.6 Validation of the Kiswahili working translation of the FACT-C questionnaire

4.6.1 External Validity

External validity refers to whether a tool can produce results that are generalizable and/or comparable to results of similar tools that are widely acceptable for use within the same context. As such, the external validity of the Kiswahili working translation of the FACT-C questionnaire was assessed by comparing the QoL scores with the clinical performance status based on ECOG scale where "0" denotes a patient who is fully active, "1" denotes a patient who is ambulatory and can engage in light work, "2" is a patient who is ambulatory but cannot perform any work outside selfcare, "3" is a patient who can only manage limited selfcare, "4" is a disabled patient who's fully dependent on assistance even for selfcare, 5 denotes a dead patient, hence not applicable in this study. ECOG status 0 and 1 generally indicate good QoL while 2 to 5 indicate poorer QoL.

ECOG scores 0 & 1 were observed in 63.3% of the participants. ECOG scores of 0 & 1 that denote good clinical status were associated with good QoL as determined by FACT-G and this observation was upheld by FACT-C. ECOG scores of 2, 3, and 4 were associated with poor QoL as determined by both FACT-G and FACT-C (Table 5).

Table 5: FACT-G and FACT-C QoL scores stratified by ECOG status

ECOG Status	Total FACT-G Score Good QoL ≥81		Total FACT-C Score Good QoL ≥21)	
	Mean	**SD**	**Mean**	**SD**
0 = Fully active	**86.6**	16.52	**21.7**	4.71
1 = Ambulatory, light work	**85.1**	14.93	**21.6**	4.40
2 = Ambulatory, no work	73.8	16.97	19.2	4.79
3 = Limited selfcare	64.5	18.53	15.1	7.61
4 = Disabled	50.0	6.38	16.0	4.24
5 = Dead	N/A		N/A	

Note: Good QoL scores appear in bold on the table.

Overall, there was individual domain score decline observed, with deterioration of ECOG status (Table 6). The most affected QoL domain in the study population was Physical well-being (PWB), while the best scores were observed in the Social well-being (SWB) domain where all the participants had good social well-being regardless of ECOG performance status. Those with ECOG status 0 & 1 had good domain scores for Emotional well-being (EWB) and Functional well-being (FWB).

Table 6: Specific FACT-G QoL domain scores stratified by ECOG status.

ECOG Status	PWB Good QoL ≥21		SWB Good QoL ≥21		EWB Good QoL ≥18		FWB Good QoL ≥21	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0	**21.2**	6.50	**24.1**	5.30	**18.5**	5.03	**22.8**	6.69
1	17.1	6.39	**26.1**	3.14	**20.7**	5.12	**21.1**	6.23
2	14.6	6.92	**22.7**	6.98	**18.0**	5.79	18.6	5.73
3	11.2	6.66	**21.6**	6.74	17.2	5.15	14.5	7.74
4	4.0	2.71	**22.8**	1.26	10.8	4.57	12.5	5.07
5	N/A		N/A		N/A		N/A	

Note: Good QoL scores appear in bold on the table.

4.6.2 Content Validity

Content validity refers to a statistical estimate of whether a test or tool covers all relevant parts of the subject it aims to measure in order to produce accurate and valid results. The content of health-related QoL questionnaires directly determine the scores and so it is paramount that the questions are as specific to the patient's disease as possible, in order to give an accurate estimate of their QoL status. In this study, content validation of the Kiswahili working translation of the FACT-C questionnaire was done using the Kiswahili FACT-G questionnaire as the "gold standard" since it is already validated for use in Kenya (see section 3.10.4). FACT-C was designed to specifically address CRC symptomatology therefore it is expected to give a more precise QoL estimate in a CRC patient. FACT-G which is used to estimate QoL in any form of cancer does not include content which is specific to CRC symptomatology. Pearson chi square test of homogeneity was used to determine whether there was a statistically significant difference in QoL as determined by FACT-G and FACT-C. The null hypothesis (H_0) was that there was no difference between QoL as determined by FACT-G and QoL as determined by FACT-C. The

alternative hypothesis (H_a) was that there was a difference between QoL as determined by FACT-G and QoL as determined by FACT-C. The significance level was set at 0.05 for the P-value. As shown on Table 7, the QoL was classified as Good or Poor for comparison, based on the study cut-offs of $\geq$81 for good QoL by FACT-G and $\geq$21 for good QoL by FACT-C. Since the observed P-value (0.000) was less than the significance level (0.05), the null hypothesis was rejected. This observation indicates that the content of FACT-C produced a significant difference in the QoL as compared to the QoL as determined by FACT-G. The general trend was a deterioration in QoL scores, with the QoL as determined by FACT-C being lower than the QoL as determined by FACT-G.

Table 7: Validation of the Kiswahili working translation of the FACT-C questionnaire, using the already validated Kiswahili FACT-G questionnaire as the "gold standard".

Quality of life as determined by FACT-C	Quality of life as determined by FACT-G		
	Poor QoL	Good QoL	Total
Poor QoL	34	9	43
Good QoL	9	38	47
Total	43	47	90

Pearson chi2 (1) = 32.3146 Pr = 0.000

CHAPTER FIVE: DISCUSSION

5.1 General characteristics of the study participants

Majority of the study participants were female (55.6%). In most studies however, CRC incidence rates tend to be generally 30% higher in men than in women, with a larger disparity for rectal cancer which is 60% higher in men; than for colon cancer which is 20% higher in men (G et al., 2011). However, among individuals 50 and older, women are more likely than men to develop adenomas in the proximal colon, which are less efficiently detected through screening. These gender disparities most likely reflect differences in exposures to risk factors (for example, cigarette smoking) and sex hormones, as well as complex interactions between these influences (G et al., 2011).

In High Income Countries (HICs), the median age at CRC diagnosis is 66 years in men and 69 years in women (*SEER Cancer Statistics Review 1975-2002 - Previous Version - SEER Cancer Statistics*, n.d.). In this study, 30% were aged $\geq$60 years, while 33.8% were aged below 40 years. It has been observed over the past decade that CRC patients overall are getting increasingly younger, shifting from a median age of 72 years in HICs for diagnoses in the early 2000s to 66 years today. This is because incidence is increasing in younger adults and declining in older age groups. A study done in Nairobi, Kenya in 2011, showed that the peak age affected was 41-50 years, with an all-group mean age of 53 years; the proportion of patients 40 years of age or younger was 17.6% (Saidi et al., 2011).

Amongst the study participants 80% resided in the rural area; the difference in distribution of study participants across the areas of residence (rural, semi-urban & urban) was however not statistically significant (p = 0.931). In the past, CRC risk

factors have been associated with urban lifestyle and it was thought that the high fiber diet and active lifestyle enjoyed by those who live in the rural area was protective. More recent surveillance in Kenya has indicated an upsurge of CRC in the rural areas, in part, due to a shift to western diet (Parker et al., 2019). More studies should be done to re-establish the risk factors locally to inform prevention strategies.

The predominant histological subtype in this study was adenocarcinoma (86%). In general, adenocarcinomas account for approximately 96% of all colorectal cancers. (Ponz de Leon & Di Gregorio, 2001).

5.2 Relationship between Quality of life and sociodemographic characteristics

In this study, female gender was associated with slightly higher QoL scores compared to male gender. This is different from a study done in Morocco, North Africa (Mrabti et al., 2016) where the mean QoL score was lower in the females. This observation is attributable to the better coping mechanisms demonstrated by women in our set up, including seeking religious and social support whenever they are faced with a life-threatening circumstance, which may psychosocially impact QoL. However, it should be noted that in this study, both male & female gender were overall seen to have poor QoL when scores were stratified by gender. This observation is similar to other studies where gender has been reported to not have a significant influence on QoL (Marventano et al., 2013).

In the Moroccan study, patients aged >70 years had lower QoL scores, similar to a study done in Seattle, USA (Adams et al., n.d.) while in this study, age >60 years was associated with good QoL by FACT-G questionnaire. This difference is postulated to be due to the socioeconomic demands associated with rural versus urban living. The Moroccan study population was mainly urban while this study population resided

mainly in the rural area. It can also be further postulated that there are specific limitations that predominantly affect younger patients as a result of the health and socioeconomic implications of the disease; and as such, these patients might potentially benefit from psychosocial support measures, health financing counselling and subsidized acquisition of medical supplies such as colostomy bags. However, in this study, the good QoL mean score as determined by FACT-G in this age group did not uphold when subjected to FACT-C questionnaire.

It was interesting to note that higher education level was associated with good QoL. This was comparable to the results of a study done in Seattle, USA (Adams et al., n.d.); and suggests that those with higher education may be in a position to understand and navigate the diagnosis and treatment course better. Higher education which is generally associated with a higher socioeconomic status, may have an influence on QoL through ways such as ability to sustain basic medical insurance cover, routine access to health care and provision of basic needs during the course of illness.

Participants from Kalenjin (which was the predominant ethnicity in the study population) and Kisii ethnic communities were seen to have good QoL overall. Good sociocultural support for chronically ill patients within these communities is likely to have contributed to this observation; however, further studies are recommended to assess how ethnicity and culture may influence treatment support, so that any superior habits demonstrated by one community over the other may be adopted to improve QoL of patients regardless of ethnic background.

5.3 Relationship between Quality of life and clinical characteristics

In the assessment of clinical characteristics, advanced stage of disease was associated with poorer QoL, similar to an American study done in long term CRC survivors (Adams et al., n.d.). Advanced CRC is often associated with increased clinical symptomatology including anorexia and gastrointestinal disturbance in addition to decreased overall functioning due to excessive fatigue.

The study participants who had undergone surgery (67.8%), had been managed via open surgery, which was associated with poor QoL. Surgery is the only curative modality for localized colon cancer and potentially provides the only curative option for patients with limited metastasis to the liver and/or lung. The general principle for all operations includes removal of the primary tumor with adequate margins including areas of lymphatic drainage. Postoperative complications occur in up to one-third of patients undergoing colorectal procedures, with the most common complications being wound and organ space infections; and gastrointestinal motility complications including ileus and bowel obstruction (Tevis & Kennedy, 2016) which may further impact QoL in CRC patients. Laparoscopic- assisted surgery has been shown to be a favorable surgical option with better QoL outcomes and similar long-term oncological control compared with open resection (Biondi et al., 2013), a modality that can be considered in our local set up in the management of CRC patients where possible.

Study participants who had a stoma had lower QoL scores, similar to findings of a 4-year prospective study of CRC patients' QoL conducted in Munich (Engel et al., 2003). Patients who have a stoma usually have issues related to poor stoma irrigation techniques and low self-esteem due to physical changes associated with the stoma. Fewer symptoms and less anxiety is observed when they feel better informed, as such

doctors should spend as much time as possible helping patients understand the disease, the prognosis and the implications of the stoma (Engel et al., 2003).

Participants with some comorbid conditions (Hypertension & Tuberculosis) did not have a lower QoL than those with no comorbidities. HIV was however shown to be associated with poor QoL by both FACT-G and FACT-C. The social stigma associated with HIV has a direct impact on QoL and makes an additional diagnosis of CRC more difficult to cope with, hence lower QoL (Magaji et al., 2012). Anemia which is usually associated with advanced disease and Pneumonia which is a life-threatening condition were both associated with poor QoL. In a study done in North Africa (Mrabti et al., 2016) comorbidity was found to be significantly associated with lower QoL, similar to a study done in America (Adams et al., 2016) amongst the CRC patients.

The most affected QoL domain was physical well-being, while the best scores were observed in the social well-being domain. The effects on physical well-being can be attributed to the symptomatology that is associated with CRC as a consequence of both the disease and its treatment (Magaji et al., 2012). In this case, the FACT-G questionnaire included questions on energy levels, presence of nausea, pain, side effects of treatment and body malaise, which most of the study participants reported to experience; which contributed to their poor physical status.

5.4 Validity of the FACT-C Kiswahili working translation

5.4.1 External validity of the FACT-C Kiswahili working translation

External validity usually compares the "test tool" with a tool that is already in wide use with acceptable and reliable results. As such the ECOG scale of performance status (Appendix 6) was used for external validation of the FACT-C Kiswahili translation. This is because it is a standard criteria which is reproducible and is commonly used by physicians and researchers to measure how the disease impacts a patient's daily living abilities (performance status), by describing a patient's level of functioning in terms of their ability to care for themselves, daily activity and physical ability (*ECOG Performance Status - ECOG-ACRIN*, n.d.). The QoL of the study participants as determined by FACT-C corresponded with the widely used ECOG performance status assessment, where good QoL scores were observed in participants who were classified as 0 & 1 on the ECOG scale; while poor QoL was observed in participants with worse ECOG performance status (Table 5). These findings demonstrated external validity of the Kiswahili working translation of the FACT-C questionnaire.

5.4.2 Content validity of the FACT-C Kiswahili working translation

While the FACT-G questionnaire estimates the QoL in any cancer patient, the content of FACT-C seeks to specifically address symptomatology and QoL aspects in a patient with colorectal cancer, which are not included in the FACT-G (*The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: Properties, Applications, and Interpretation*, n.d.). In assessment of the content validity, the determination of whether there was a significant difference in the QoL content as covered by FACT-C Kiswahili working translation as compared to the Kiswahili FACT-G questionnaire was done via hypothesis testing (section 4.6.2).

A statistically significant difference (p=0.000) was observed in the QoL of patients, when the QoL as determined by the FACT-C questionnaire was compared to the QoL as determined by FACT-G questionnaire (section 4.6.2). This suggests that the content of the two questionnaires is different, which in effect produces different QoL scores with the general trend being deterioration in QoL scores, with the QoL as determined by FACT-C being lower than the QoL as determined by FACT-G. This is an important observation because accuracy in QoL estimation has implications on the choice of interventions that directly influence treatment compliance and outcomes.

The conclusion therefore, was that there is an added value of using FACT-C questionnaire which has been specifically designed to assess unique QoL components which affect patients with colorectal cancer and thus, content validity of the FACT-C Kiswahili working translation.

5.5 Study strengths and limitations:

Particular strengths of this study included the high overall response rate, the recruitment of patients from a wide range of counties across the Western part of Kenya since MTRH serves as a referral hospital in the region; and the application of well-established instruments (FACT-G questionnaire, FACT-C questionnaire and ECOG scale) to assess health-related QOL.

One of the limitations is that it was a one time-point collection of data, thus, there is a limitation in the capacity to draw definitive conclusions on how the QoL evolves with disease progression from the time of diagnosis and throughout the survival period. Also acknowledging that this was a single center study, it would be desirable if other oncology centers across Kenya would conduct similar studies for comparability of findings.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

Good QoL was associated with early disease and higher education level, while poor QoL was associated with surgery and advanced disease. The most affected QoL domain as determined by FACT-G questionnaire was physical well-being, while the best scores were observed in the social well-being domain. The Kiswahili working translation of the FACT-C questionnaire demonstrated both external and content validity.

6.2 Recommendations

FACT-G and FACT-C questionnaires should be considered for adoption in Kenyan oncology units for objective assessment of the QoL in CRC patients during the course of their management, as they highlight specific QoL domains that have been affected, which is important in facilitation of tailor-made treatment strategies for each patient.

CRC patients should undergo pre- & post-surgical counselling to ensure that potential concerns are adequately addressed and to foster better preparedness in the event of post-surgical complications.

The FACIT organization could consider the adoption of the Kiswahili working translation of the FACT-C questionnaire used in this study in the development of a formal Kiswahili translation of the same, for use in Kenya and other Kiswahili speaking countries.

A longitudinal study to assess the evolution of QoL with disease progression and CRC-survivorship is recommended; as well as a similar multicenter study in Kenya for comparability, in order to inform local evidence-based guidelines on QoL determination in colorectal cancer.

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APPENDICES

Appendix 1: Study Consent Form

Study Title

Quality of life of colorectal carcinoma patients on follow up at Moi Teaching and Referral Hospital and validation of the FACT-C questionnaire in the Kenyan context.

Investigator

Dr. Olive Akunga (Postgraduate Student, Department of Medicine, Moi University).

Supervisors

Dr. F. Some (Senior Lecturer, Department of Medicine, School of Medicine, Moi University)

Dr. E. Njiru (Lecturer, Department of Medicine, School of Medicine, Moi University)

ENGLISH: CERTIFICATE OF CONSENT

RESEARCH TOPIC: Quality of life of colorectal carcinoma patients on follow up at Moi Teaching and Referral Hospital and validation of the FACT-C questionnaire in the Kenyan context.

INVESTIGATOR: Dr. Olive Akunga

MOBILE NO: 0723924615

I………………………………………… of P.O Box……………………

Tel…………………………. hereby give informed consent to participate in this study at Moi Teaching and Referral Hospital. The study has been explained to me clearly by Dr. Olive Akunga (or her appointed assistant). I have understood that by participating in this study, I shall volunteer information regarding my illness and other co-morbidities. I am aware that I can withdraw from this study at any time. I have also been assured that all information shall be treated and managed in confidence. I have not been induced or coerced by the investigator (or her appointed assistant) to cause my signature to be appended in this form and by extension participate in this study.

Initials of participant: ……………………………

Signature or thumbprint: …………………………………

Date………………………………

KISWAHILI: FOMU YA KIBALI

MADA YA UTAFITI: Quality of life of colorectal carcinoma patients on follow up at Moi Teaching and Referral Hospital and validation of the FACT-C questionnaire in the Kenyan context.

MTAFITI: Dr. Olive Akunga

RUNUNU: 0723924615

Mimi _____ wa Sanduku la Posta _____, Nambari ya Simu_____ najitolea kwa hiari yangu mwenyewe kutoa kibali cha kujihusisha katika utafiti uliotajwa hapo juu unaendelezwa katika hospitali ya Rufaa ya Moi. Nimepokea maelezo ya tafsili kuhusu utafiti huu kutoka kwa Dr Olive Akunga (au mtafiti msaidizi wake) katika lugha, kanuni na masharti ninayoelewa vyema. Nimehakikishiwa kuwa, sitaadhirika kamwe kutokana na kujihusisha kwangu katika utafiti huu. Ilibainishwa kuwa kujihusisha katika utafiti huu ni kwa hiari na nina uhuru wa kujiondoa wakati wowote ule bila ya kuhujumiwa. Zaidi ya hayo, nilihakikishiwa kuwa, kanununi zote za maadili ya utabibu,uhuru, haki, na manufaa zitazingatiwa katika utafiti huu.

Jina la Mhojiwa: _____

Sahihi au alama ya kidole: _____

Tarehe: _____

STATEMENT BY THE RESEARCHER/PERSON TAKING CONSENT

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the person understands that the following will be done:

1. He or she will be included in the study as a study participant.

2. Results of the study will be communicated to all the involved stakeholders.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked have been answered as correctly as possible. I confirm that the participant has given consent freely and voluntarily, and has not been coerced.

 A copy of this ICF has been provided to the participant.

Name of Researcher / person taking the consent: _____

Signature of Researcher / person taking the consent: _____

Date: _____

Appendix 2: Study Questionnaire

Study ID: _____

Please fill in the blanks or place an X or check mark next to the word or phrase that best matches the study participant's response.

Sociodemographic Information

1. What is the study participant's gender?

Female	
Male	

2. What is the study participant's age in years?

18 – 30	
31 – 40	
41 – 50	
51 – 60	
61 and above	

3. What is the study participant's ethnicity?

Kalenjin	
Luhya	
Luo	
Kisii	
Kikuyu	
Other (Specify)	

4. What is the study participant's marital status?

Single	
Married	
Separated	
Divorced	
Widowed	

5. What is the study participant's highest level of completed education?

Tertiary level	
Secondary level	
Primary level	
Below primary level	

6. What is the study participant's current employment status?

Formally employed	
Self employed	
Unemployed	
Student	

7. In which of the following areas does the study participant live?

Rural	
Suburban	
Urban	

Clinical Information:

8. What is the study participant's CRC histological type? _____

9. What is the study participant's CRC staging by Dukes criteria (use Appendix 2B)?

10. What form of treatment has been administered to the study participant?

Chemotherapy only	
Radiotherapy only	
Surgery only	
Chemotherapy and Radiotherapy	
Chemotherapy + Radiotherapy + Surgery	
Chemotherapy + Surgery	
Radiotherapy + Surgery	
Other (specify)	

11. Does the study participant have a stoma?

Yes	
No	

12. Is the study participant on management for any other medical comorbidities?

None	
Diabetes	
Hypertension	
Chronic　　　Kidney　Disease	
Asthma / COPD	
HIV	
Other (specify)	

Form Completed By:

Name: --

Date: ---

Appendix 2B: Dukes / TNM classification of Colorectal Cancer

	Dukes	Astler-Coller	TNM
Tumor invasion confined to the mucosa	A	A	Tis, N0
Tumor invasion limited to the submucosa, no lymph node involvement	A	B1	T1, N0
Tumor invasion limited to the submucosa, lymph node involvement	C	C1	T1, N1-2
Limited tumor invasion into the muscle layer, no lymph node involvement	A	B2	T2, N0
Limited tumor invasion into the muscle layer, lymph node involvement	C	C1	T2, N1-2
During the whole muscle layer tumor involvement, no lymph node involvement	B	B2	T3, N0
During the whole muscle layer tumor involvement, lymph node involvement	C	C2	T3, N1-2
Tumors have kept the neighboring organs, no lymph node involvement	B	B2	T4, N0
Tumors have kept the neighboring organs, lymph node involvement	C	C2	T4, N1-2
Other factors not withstanding distant metastases	D	D	T1-4, N0-2, M1

(Akkoca et al., 2014)

Appendix 3: FACT-C English Version 4.0 with Kiswahili working translation

Translators: 1. Nicholas Murabu (NM) 2. Priscah Matoi (PM) 3. Boniface Mumbo (BM)

Compilation and Edits: Olive Akunga (OA)

Note:

NM, PM, BM and OA are the abbreviations of the names of the four translators.

In the questionnaire below:

The original English statement of FACT-C questionnaire is highlighted in yellow

The preferred study Kiswahili working translation is highlighted in blue

C1 I have swelling or cramps in my stomach area 0 1 2 3 4

Translation 1: Nina uvimbe au maumivu kwenye eneo la tumbo langu

Translation 2: Sehemu yangu ya tumbo imefura au imekuwa ngumu

Translation 3: Nina uvimbe/gango tumboni

C2 I am losing weight... 0 1 2 3 4

Translation 1: Ninapoteza uzani wa mwili

Translation 2: Ninapunguza uzito

Translation 3: Nimepunguza uzito

C3 I have control of my bowels... 0 1 2 3 4

Translation 1: Utumbo wangu unaweza kudhibiti chakula kilicho lainishwa

Translation 2: Niko na uwezo wa kuzuia matumbo yangu

Translation 3: Naweza kudhibiti uinjilishaji wangu

C4 I can digest my food well 0 1 2 3 4

Translation 1: Ninaweza kulainisha chakula changu vizuri

Translation 2: Naweza lainisha chakula vizuri nakuweza pita kwenye njia za damu

Translation 3: Naweza kusaga chakula vizuri

C5 I have diarrhea (diarrhoea) 0 1 2 3 4

Translation 1: Ninaendesha.

Translation 2: Ninaendesha/harisha

Translation 3: Ninaharisha

C6 I have a good appetite 0 1 2 3 4

Translation 1: Ninahamu nzuri ya kula.

Translation 2: Niko na hamu ya kula vizuri

Translation 3: Ninahamu nzuri ya chakula

C7 I like the appearance of my body 0 1 2 3 4

Translation 1: Ninapendezwa na muonekano wa mwili wangu

Translation 2: Ninapenda vile mwili wangu uko

Translation 3: Naupenda muonekano wa mwili wangu

Q2 Do you have an ostomy appliance? Mark one box ⬛ No ⬛ Yes

Translation 1: Je uko na kifaa kinacho kusaidia kupitisha hajakubwa? (chagua jibu moja) La au Ndio.

Translation 2: Je uko na kile kifaa chakukusaidia kutoa uchafu kutoka kwenye mwili wako umebeba kwa tumbo badala ya kutoa uchafu kwa ile njia ya kawaida? (weka alama kwa boksi moja) La ama Ndio

Translation 3: Je, uliekwa kifaa kilichounganishwa kwa tumbo cha kupitishia choo?

If yes, please answer the next two items:

Translation 1: Kama ndio, Tafadhali jibu maswali mawili yafuatayo

Translation 2: Kama ndio, tafadhali jibu haya mengine mawili

Translation 3: Kama ndio, tafadhali jibu maswali yafuatayo

C8 I am embarrassed by my ostomy appliance 0 1 2 3 4

Translation 1: Ninagadhabishwa na kifaa kinacho nisaidia kupitisha hajakubwa

Translation 2: Naaibika kwa hiki kifaa changu

Translation 3: Nahisi aibu na kifaa cha kupitishia choo nilichoekwa

C9 Caring for my ostomy appliance is difficult 0 1 2 3 4

Translation 1: Ni vigumu kutunza kifaa kinacho nisaidia kupitisha hajakubwa

Translation 2: Ni ngumu kukibeba

Translation 3: Kuna ugumu wa kukitunza kifaa chenyewe

Appendix 4: FACT-G English Version 4.0

FACT-G ENGLISH VERSION 4.0

Below is a list of statements that other people with your illness have said are important. Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

SOCIAL/FAMILY WELL-BEING

		Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

EMOTIONAL WELL-BEING

		Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

FUNCTIONAL WELL-BEING

		Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

Appendix 5: FACT-G Kiswahili Version 4.0

FACT-G VERSION 4.0
KISWAHILI TRANSLATION

Yafuatayo ni mambo ambayo wagonjwa walio na Ugonjwa kama wako huona ni muhimu.

Tafadhali chagua jawabu mwafaka linalokuhusu kwa siku saba zilizopita.

	AFYA YA MWILI	Hapana kabisa	Kidogo tu	Pengine	Ndio kiasi	Ndio kabisa
GP1	Sina nguvu	0	1	2	3	4
GP2	Nahisi/Nasika kutapika	0	1	2	3	4
GP3	Kwa sababu ya kukosa nguvu mwilini, siwezi kutosheleza mahitaji ya familia yangu	0	1	2	3	4
GP4	Nina maumivu mwilini	0	1	2	3	4
GP5	Ninashurutishwa au ninasumbuliwa na madhara ya matibabu ya ugonjwa wangu	0	1	2	3	4
GP6	Najisikia mgonjwa	0	1	2	3	4
GP7	Ninalazimika kuwa kitandani au kumpumzika wakati mwingi	0	1	2	3	4

	AFYA YA KIJAMII	Hapana kabisa	Kidogo tu	Pengine	Ndio kiasi	Ndio kabisa
GS1	Nina uhusiano bora/mzuri na marafiki	0	1	2	3	4
GS2	Ninapata usaidizi wa kihisia au mawazo kutoka kwa familia yangu	0	1	2	3	4
GS3	Ninapata usaidizi kutoka kwa marafiki wangu	0	1	2	3	4
GS4	Familia yangu imeukubali ugonjwa wangu	0	1	2	3	4
GS5	Nimeridhika/Nimetosheleka na mawasiliano na familia yangu kuhusu ugonjwa wangu	0	1	2	3	4
GS6	Ninajihisi upendo na mpenzi//mchumba/ Rafiki/mume/mke/msaidizi wangu mkubwa)	0	1	2	3	4
Q1	*Hata kama haufanyi mapenzi na mtu yeyote, tafadhali jibu swali lifuatalo. Kama hutaki kulijibu, waweza kuweka alama kwenye kisanduku hiki*					
GS7	Ninaridhishwa na hali yangu kimapenzi	0	1	2	3	4

Tafadhali chagua jawabu mwafaka linalokuhusu kwa siku saba zilizopita.

	AFYA YA HISIA/MAWAZO	Hapana kabisa	Kidogo tu	Pengine	Ndio kiasi	Ndio kabisa
GE1	Nina huzuni kuhusu ugonjwa wangu	0	1	2	3	4
GE2	Nimeridhika/Nimetosheleka na jinsi na jinsi ninapambana na ugonjwa wangu	0	1	2	3	4
GE3	Nimeanza kukata tamaa kupambana na ugonjwa wangu	0	1	2	3	4
GE4	Ninawasiwasi kuhusu ugonjwa wangu	0	1	2	3	4
GE5	Ninahofu/Ninaogopa/Ninahuzuni kuhusu kifo	0	1	2	3	4
GE6	Nina wasiwasi kwamba hali yangu itazidi/ itaendelea kuwa mbaya	0	1	2	3	4

	AFYA UTENDAJI	Hapana kabisa	Kidogo tu	Pengine	Ndio kiasi	Ndio kabisa
GF1	Ninaweza kufanya kazi (pia kazi ya nyumbani)	0	1	2	3	4
GF2	Kazi yangu(hata ya nyumbani) inatosheleza	0	1	2	3	4
GF3	Ninaweza kufurahia maisha	0	1	2	3	4
GF4	Nimekubali ugonjwa wangu	0	1	2	3	4
GF5	Ninalala vyema	0	1	2	3	4
GF6	Ninafurahia kujihusisha na mambo/vitu vyangu vinavyoleta raha/vifurahishavyo "fun"	0	1	2	3	4
GF7	Nimeridhika/Nimetosheleka na hali ya maisha hivi	0	1	2	3	4

Appendix 6: ECOG Performance Status Scale

ECOG Performance Status

These scales and criteria are used by doctors and researchers to assess how a patient's disease is progressing, assess how the disease affects the daily living abilities of the patient, and determine appropriate treatment and prognosis. They are included here for health care professionals to access.

ECOG PERFORMANCE STATUS*	
Grade	**ECOG**
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

* As published in Am. J. Clin. Oncol.:
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.:
Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol
5:649-655, 1982.

Appendix 7: Functional Assessment of Chronic Illness Therapy (FACIT) Licensing Agreement

FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY (FACIT) LICENSING AGREEMENT

March 5, 2018

The Functional Assessment of Chronic Illness Therapy system of Quality of Life questionnaires and all related subscales, translations, and adaptations ("FACIT System") are owned and copyrighted by David Cella, Ph.D. The ownership and copyright of the FACIT System - resides strictly with Dr. Cella. Dr. Cella has granted FACIT.org (Licensor) the right to license usage of the FACIT System to other parties. Licensor represents and warrants that it has the right to grant the License contemplated by this agreement. Licensor provides to **Olive Akunga** *the licensing agreement outlined below.*

This letter serves notice that **Olive Akunga** ("INDIVIDUAL") is granted license to use the Swahili and Kiswahili versions of the **FACT-G** in one study.

This current license extends to (INDIVIDUAL) subject to the following terms:

1) (INDIVIDUAL) agrees to provide Licensor with copies of any publications which come about as the result of collecting data with any FACIT questionnaire.

2) Due to the ongoing nature of cross-cultural linguistic research, Licensor reserves the right to make adaptations or revisions to wording in the FACIT, and/or related translations as necessary. If such changes occur, (INDIVIDUAL) will have the option of using either previous or updated versions according to its own research objectives.

3) (INDIVIDUAL) and associated vendors may not change the wording or phrasing of any FACIT document without previous permission from Licensor, including unauthorized translations. If any changes are made to the wording or phrasing of any FACIT item without permission, the document cannot be considered the FACIT, and subsequent analyses and/or comparisons to other FACIT data will not be considered appropriate. Permission to use the name "FACIT" will not be granted for any unauthorized translations of the FACIT items. Any analyses or publications of unauthorized changes or translated versions may not use the FACIT name. Any unauthorized translation will be considered a violation of copyright protection.

4) In all publications and on every page of the FACIT used in data collection, Licensor requires the copyright information be listed precisely as it is listed on the questionnaire itself.

5) Licensor reserves the right to withdraw this license if (INDIVIDUAL) engages in scientific or copyright misuse of the FACIT system of questionnaires.

6) There are no fees associated with this license.

Appendix 8: FACIT Administration and Scoring Guidelines

Administration: The FACIT scales are designed for patient self-administration, but can also be administered by interview format. For self-administration, patients should be instructed to read the brief directions at the top of the page. After the patient's correct understanding has been confirmed, he/she should be encouraged to complete every item in order without skipping any. Some patients may feel that a given question is not applicable to them and will therefore skip the item altogether. **Patients should be encouraged to circle the response that is most applicable.** If, for example, a patient is not currently receiving any treatment, the patient should circle "not at all" to the question "I am bothered by side effects of treatment."

During interview administration, it is helpful to have the patient hold a card on which the response options have been printed. Interview administration is considered appropriate given adequate training of interviewers so as to elicit non-biased patient responses. One of the aims of a large multi-center study of cancer and HIV patients (N=1227) was to test the psychometric properties and statistical equivalence of the English and Spanish language versions of the FACT subscales across literacy level (low vs. high) and **mode of administration** (self vs. interview). Technical equivalence across mode of administration was demonstrated in the high literacy patients; there were no differences in data quality or in mean QOL scores, after adjustment for performance status rating, socioeconomic status, gender and age. Technical equivalence between modes of administration with the FACT permits unbiased assessment of the impact of chronic illnesses and their treatments on patients from diverse backgrounds.

Scoring the FACT-G:

The FACT-G scoring guide identifies those items that must be reversed before being added to obtain subscale totals. Negatively stated items are reversed by subtracting the response from "4". After reversing proper items, all subscale items are summed to a total, which is the subscale score. **For all FACIT scales and symptom indices, the higher the score the better the QOL.**

Handling missing items. If there are missing items, subscale scores can be prorated. This is done by multiplying the sum of the subscale by the number of items in the subscale, then dividing by the number of items actually answered. This can be done on the scoring guide or by using the formula below:

  Prorated subscale score = [Sum of item scores] **x** [N of items in subscale] ÷ [N of items answered]

When there are missing data, prorating by subscale in this way is acceptable as long as **more than** 50% of the items were answered (e.g., a minimum of 4 of 7 items, 4 of 6 items, etc.). The total score is then calculated as the sum of the un-weighted subscale scores. The FACT scale is considered to be an acceptable indicator of patient quality of life as long as **overall item response rate** is greater than 80% (e.g., at least 22 of 27 FACT-G items completed). This is not to be confused with individual subscale item response rate, which allows a subscale score to be prorated for missing items if greater than 50% of items are answered. In addition, a total score should only be calculated if ALL of the component subscales have valid scores.

NOTE: Computer programs written in SPSS and SAS for the FACIT scales and symptom indices are provided on diskette in Section 4 of the manual or can be

downloaded from the website at www.facit.org for a nominal fee. Standard raw score scoring templates for all FACIT scales and symptom indices are also provided in Section 4 of the manual or under the "Validity and Interpretation" section of the website.

Scoring the Specific Scales & Symptom Indices:

For the "Additional Concerns" subscale (e.g., cancer-specific questions) and the symptom indices, the procedure for scoring is the same as described above for the FACT-G. Again, **over** 50% of the items (e.g., 5 of 9 items, 7 of 12 items) must be completed in order to consider each subscale score valid.

NOTE: scoring algorithms for the FACIT-TS-G and FACIT-TS-PS are different from other FACIT scales. Please refer to the specific scoring templates for more detail.

Deriving a Total Score:

The total score for the specific FACIT scales is the sum of the FACT-G (the first 4 subscales common to almost all scales) plus the "Additional Concerns" subscale. The symptom indices do not include the FACT-G in the total score. By following this scoring guide and transcribing the FACT-G score, the two totals can be summed to derive the **TOTAL FACT/FACIT SCORE**.

Notes:

1. Multilingual versions can be scored on the English language scoring guides.
2. Several scales have more items listed in the "Additional Concerns" subscale than are currently recommended for scoring. This is usually because additional work on a given subscale has suggested a need for additional items. However, it may take a

while for the new items to be validated so we don't formally recommend they be included in the scoring until we know more about how the item(s) function. We include the items on the scale to encourage investigators who have the time or resources to evaluate their data according to the existing scoring recommendations and to test out the value of the new item(s). As always, we welcome collaborators to share any relevant data of this nature to help further reliability and validity testing of the FACIT questionnaires

Selecting Scores for Analyses:

These scoring templates allow one to obtain two different total scores in addition to each individual subscale score. The FACT-G total score provides a useful summary of overall quality of life across a diverse group of patients. The disease-specific questionnaire total scores (i.e., FACT-G plus disease-specific subscale score) may further refine the FACT-G summary score. Two alternative approaches are noteworthy, however. One is to separately analyze the FACT-G total score and the specific subscale score. Another is to select subscales of the FACT which are most likely to be changed by an intervention being tested. For example, the Physical, Functional, and Cancer-specific subscales would be most likely to change in a chemotherapy clinical trial. One could also consider creating a separate a priori index which sums two or three subscales. This has been done with the FACT-L and many other FACIT scales, combining the Physical, Functional and 7-item Lung Cancer Subscales into a 21-item **Trial Outcome Index** (Cella, Bonomi, Lloyd et al, 1994; Brady, Cella, Mo, 1997; Cella, 1997). On the other hand, the Emotional or Social Well-being subscale would be expected to change most when evaluating a psychosocial intervention.

Comparing Version 4 scores to Previously Published (Version 2 & 3) Scores:

Most of the questions from Version 3 remain intact in Version 4 (see item history table in section 3 of the manual for details), although some items have been reworded and a few have changed from being negatively stated to positively stated items. Comparison between scale scores in these two versions is fairly straightforward. Adjustments must be made, however, when comparing the total FACT/FACIT score and when comparing the Emotional Well-Being (EWB) subscale score between the two versions. To compare Version 3 and 4 EWB scales, item GE6 (#25 in Version 3) must be omitted from the scoring of version 4. This can be done by scoring the first 5 items of the EWB subscale, multiplying by 5 (not 6), and dividing by the number of questions answered (not including the sixth question). The Version 4 total FACT-G score has been affected by the dropping of the Relationship with Doctor subscale and the addition in the scoring of item GE6 (#25 in Version 3). One way to compare total scores is to drop item GE6 from the Version 4 scoring and add **6.85** (mean score of the RWD subscale as reported in Cella et al., 1993) to the sum of the four subscales (Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being). This will give you the best estimate for comparison of published FACT/FACIT data.

Appendix 9: IREC Approval Letter

MU/MTRH-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3
Reference: IREC/2019/37
Approval Number: 0003270

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET
14th March, 2019

Dr. Olive Akunga,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

Dear Dr. Akunga,

RE: FORMAL APPROVAL

The MU/MTRH- Institutional Research and Ethics Committee has reviewed your research proposal titled: -

"Quality of Life of Colorectal Carcinoma Patients at Moi Teaching and Referral Hospital and Validation of the FACT-C Questionnaire in the Kenyan Context".

Your proposal has been granted a Formal Approval Number: *FAN: IREC 3270* on 14th March, 2019. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; hence will expire on 13th March, 2020. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date. You will be required to submit progress report(s) on application for continuation, at the end of the study and any other times as may be recommended by the Committee.

Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. You will also be required to seek further clearance from any other regulatory body/authority that may be appropriate and applicable to the conduct of this study.

Sincerely,

DR. S. NYABERA
DEPUTY-CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

INSTITUTIONAL RESEARCH &
ETHICS COMMITTEE
1 4 MAR 2019
APPROVED
P. O. Box 4606-30100 ELDORET

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

Appendix 10: MTRH Approval Letter

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

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

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

19th March, 2019

Dr. Olive Akunga,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Quality of Life of Colorectal Carcinoma Patients at Moi Teaching and Referral Hospital and Validation of the FACT-C Questionnaire in the Kenyan Context".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

19/03/2019

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

MOI TEACHING AND REFERRAL HOSPITAL
C E O
APPPROVED
1 9 MAR 2019
P. O. Box 3 - 30100, ELDORET

cc - Senior Director, (CS)

- Director of Nursing Services (DNS)

- HOD, HRISM

All correspondence should be addressed to the Chief Executive Officer
Visit our Website: www.mtrh.go.ke
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