# PREVALENCE OF NON-ANEMIC IRON DEFICIENCY IN CANCER PATIENTS BEFORE INITIATION OF THERAPY AND IT'S CORRELATION TO HEALTH-RELATED QUALITY OF LIFE

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## DECLARATION

This dissertation is my original work and has not been presented for award of degree in any other university. The references to thework done by other persons have been clearly cited.

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## DEDICATION

I dedicate this work to my sister Bisieri Mageto, a friend and mentor who stood as a bulwark supporting my childhood.

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## LIST OF ABBREVIATIONS

ANCOVA: Analysis of Covariance

CBC: Complete Blood Count

CHF: Congestive Cardiac Failure

CHr: Reticulocyte Hemoglobin Content

CITI: Collaborative Institutional Training Initiative

CLAS: Cancer Linear Analog Scale

CTC: Cancer Treatment Centre

DNA/RNA: deoxyribonucleic acid/ribonucleic acid

EDTA: Ethylenediaminetetraacetic Acid

ERC: Ethics Review Committee

FACIT-AN Functional Assessment of Chronic Illnesses Test- Anemia

HDF: Hemodiafiltration

ID: Iron Deficiency

ISO: International Organization for Standardization

KNH: Kenyatta National Hospital

LINAC Centre: Linear Accelerator Centre

NHL: Non-Hodgkin Lymphoma

OSHA: Occupational Safety Health Administration

SF: Serum Ferritin

sTfR: Serum Transferrin Receptor

TIBC: Total Iron Binding Capacity

TSAT: Transferrin saturation

WHO-PS: WHO Performance Indicator

## OPERATIONAL DEFINITION OF TERMS

**Cancer Patient:** A person diagnosed after a biopsy and a histopathology report documented. It excludes those with a provisional diagnosis for cancer awaiting biopsy reports.

**Health-Related Quality of Life** (**HRQL**): The methodology adopted in defining HRQL is on an individual, subjective view of well-being reflecting the lived experience and personal expectations; and objective, the discernible judgment of another person's position in life (Karimi & Brazier, 2016).

**Iron Deficiency (ID)**: The decline of body iron content below 27.2 pg. for pediatric and 28.7 pg. for adults may cause diminished erythropoiesis and, consequently, anemia. It manifests as absolute iron deficiency (AID) when total body iron stores are low or exhausted. It may also result in functional iron deficiency (FID), a disease in which whole-body iron stores are of typical values or increased. Still, the iron in circulation and the supply to the bone marrow is inadequate for optimal erythropoiesis.

**Non-Anemic Iron Deficiency (NAID)**: The disease state that leads to depletion of iron reserves, making the victim prone to iron-deficient erythropoiesis but in normal hemoglobin (Hb) milieu (Elawamy Hayam Abdalla et al., 2020).

**Patient Navigation Program:** It's a process by which a trained health worker guides patients diagnosed with cancer through and around barriers in the complex cancer care continuum to help ensure optimal access to care.

**Quality of Life (QOL)**: It has an inherent meaning to everyone, and it's a person's perception of robust health, meaningful relationships, work and leisure, and general safety within different cultural settings and contexture that brings overall gratification and happiness (Bergner, 1989)

**Reticulocyte Hemoglobin Content (CHr)**: The emerging iron status marker for cellular hemoglobin, reflecting the hemoglobin content in the most immature red blood cell (reticulocytes).

**Therapy:** The treatment modalities for cancer provided in Kenyatta National Hospital: chemotherapy, radiotherapy, immunotherapy, and radioiodine therapy.

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## ABSTRACT

***Background**: Non-anemic iron deficiency (NAID) is a subclinical state in the serum iron continuum that leads to depletion of iron reserves, making the victim prone to iron-deficient erythropoiesis. Because of the complexity in cancer care, and the multicriteria approach to the monitoring of iron status, deteriorating health-related quality of life (HRQL) is commonplace among cancer patients.*

***Objective**: To determine the prevalence of NAID in cancer patients before initiation of therapy and its correlation to (HRQL) at (KNH).*

***Methods:** This was a cross-sectional analytical study carried out in KNH among adult cancer patients on an initial clinic visit. 331 participants were selected through consecutive sampling. The FACIT-AN tools were used in interviews and samples of blood obtained in vacutainer, to be run in SYSMEX XN-1000 analyzer to produce reportable reticulocyte hemoglobin content (CHr).*

***Results:** Data analysis was done in R-program. Descriptive, inferential statistics; multivariate regression was applied to determine associations between variables. The prevalence of NAID was (2.4%). All the HRQL domains statistically predicted CHr levels, F (4, 106) = 2.789, p=.030, R2 = .309. There was a significant difference in the observed CHr mean in solid tumors, Welch's F (7, 172.914) = 2.906, p=.008. The esophageal, colorectal, cervical cancer had statistically significantly low mean CHr mean compared to other tumors.*

***Conclusion:** The prevalence of NAID before initiation of therapy was (2.4%). Participants with tumors of gynecological and gastrointestinal descent were more predisposed to NAID than other tumors. This study finding acquiesces to the rejection of the null hypothesis that HRQL has no significant association with Serum Iron in cancer patients before therapy initiation.*

***Recommendation:** Optimal timing for CHr assay should be incorporated in cancer screening protocols for early NAID detection and its management. A public health strategy is instituted to promote awareness of the risk for deterioration of HRQL caused by NAID.*

# CHAPTER 1: INTRODUCTION

## 1.1 Background information

Iron, an essential micronutrient, is highly conserved and strictly regulated to meet daily body requirements. According to WHO, ferritin, storage form of iron, has a cutoff value of above 12 µg/L in children and 15 µg/L in adults, and in inflammation, a value above100 µg/L are considered normal (Daru et al., 2017). Its deficiency is a common complication associated with the global burden of disease (Pasricha et al., 2021). It's the most common nutritional disorder that affects a third of the worldwide population (Elstrott et al., 2020), widespread in both developed and developing nations with a high preponderance towards women of reproductive age (WRA) and preschool children (Lopez et al., 2016). Rapid physiologic growth experienced in preschool children may result in absolute iron deficiency (AID) due to the increased cellular consumption of iron reserves accumulated during gestation. Also, WMA, especially adolescents, drain their iron reserves through menstrual losses.

Iron status is considered as a continuum ranging from deficiency to iron overload. Iron deficiency (ID) is the most common etiological factor for anemia, as is reflected by the high global prevalence of anemia (32.9%) and by the attendant years lived with disability in affected patients (Kassebaum et al., 2014). ID is a widespread micronutrient deficiency in both developed and developing worlds associated with chronic disease (Elstrott et al., 2020). Its seen in congestive heart failure (CHF), inflammatory bowel disease (IBD), and chronic kidney disease (CKD) (Cappellini et al., 2017), among others. It has a wide variability in prevalence (42.6%), in CKD (24–85%), in (IBD) (45%), CHF (43– 100%) (Peyrin-Biroulet et al., 2015).

Studies in Africa indicate the prevalence of ID 29% (95% CI, 24–35). This prevalence is slightly lower than the global prevalence of 32.9% in non-pregnant women, but higher, 38% (95% CI, 34–43) in pregnant women, and 43% (95% CI, 38–47) in children (Stevens et al.,

2013). In the United States (USA), the ID prevalence ranges from 4·5% to 18·0%. Children and women of reproductive age (WRA) are mostly affected. The USA, together with Canada (2.9%), has the lowest burden globally. The highest prevalence is in Asian countries, South Asia (54·8%), Central Asia (64·7%), and Latin America (62·3%) (Lopez et al., 2016). The varied ID ranges may be due to diverse risk factors, including malaria endemicity, chronic inflammatory conditions, and helminth infestation in children from different geographical matrices.

Non-anemic iron deficiency (NAID) is a subclinical state in the serum iron continuum that leads to depletion of iron reserves, making the victim prone to iron-deficient erythropoiesis in a usual hemoglobin milieu (Elawamy Hayam Abdalla et al., 2020). Current evidence has shown that NAID is a disease which further research is needed to develop policies for diagnosis and treatment (Pratt & Khan, 2016).

Because of the complexity in the cancer care continuum and the long intervals that cancer patients must wait for in-between clinics in the hospital, the multicriteria approach in monitoring iron status, development of NAID, and deterioration of HRQL are commonplace. Also, NAID is common among older adults, with an increased mortality rate and high hazard ratios, 1·58 (95% CI 1·29–1·93) (Philip et al., 2020). The functional impairment in cancer patients could improve tremendously with early screening and primary prevention of iron deficiency (Toxqui & Vaquero, 2015). The rationale for the study is to establish the burden of NAID in cancer patients and its correlation to (HRQL).

Laboratory finding consistent with NAID employed was reticulocyte hemoglobin content (CHr), an emerging marker of iron status which indicates cellular hemoglobin content in the youngest erythrocytes (reticulocytes). This assay provided precise information for the diagnosis of NAID, different from the multi-criterion model described below. At the 27.2 pg for pediatric and 28.7 pg for adults, diagnosis has a specificity of 83.2% and sensitivity of

92%. (Brugnara et al., 2006). Therefore, this study explored and utilized the nadir CHr assay because of its superior specificity and sensitivity compared to other tests in iron status determination.

Reticulocyte Hemoglobin Content (CHr): The emerging iron status marker for cellular hemoglobin, reflecting the hemoglobin content in the most immature red blood cell (reticulocytes) (Nissenson & Fine, 2017). The CHr level drops within days of diminished erythropoiesis, making it a suitable marker for the insidious NAID. The assay is not affected by the infection, inflammatory state, or malignancy; however, it may present a false normal in thalassemia.

Serum Ferritin (SF), an acute-phase reactant, is an early marker for iron status with both superior specificity and sensitivity, but its level is affected by infection and inflammation. It requires a C-reactive protein (CRP) test to rule out the presence of a disease. A low level of ferritin, according to WHO, is a value below 12 μg/L in children and 15 μg/L in adults. A group below 100 μg/L forms the new cutoff (Daru et al., 2017).

Transferrin saturation (TSAT) is a valuable indicator of iron status, and it comes in handy when (SF) is of level is high, between 100 to 300 μg/L. It's the ratio of iron to total iron-binding capacity (TIBC). However, this marker exhibits diurnal variation, and it's also affected by inflammatory processes and malignancy, rendering it unreliable for patients with cancer (Cappellini et al., 2017).

Serum iron is a measure of ferric iron bound mainly to transferrin but does not capture the ferrous unbound iron. For this reason, ingestion of meals with beefy products or hemolysis may be the reason for the diurnal variations, which makes it an unreliable indicator for iron status (Cohen-Solal et al., 2014)

Elevated serum transferrin receptor (sTfR) is a good indicator of diminished erythropoiesis consistent with NAID. A reduced sTfR is indicative of marrow hypoplasia. Though an infection does not confound this assay, it lacks internationally set standards for research (Anand & Gupta, 2018)

Stainable bone marrow iron assay is the barometric standard for serum iron monitoring; however, it is too invasive for population studies. The CHr assay that has high sensitivity and specificity in the diagnosis of ID and broad diagnostic efficacy is better than other conventional indicators such as serum ferritin( SF) and serum transferrin receptor(TR) (Cai et al., 2017). Practice guidelines recommendations of iron management include CHr check for baseline and periodic iron monitoring (Steinmetz, 2012).

### 1.2 Statement of the problem

Non-Anemic Iron Deficiency is a subclinical state in the Serum Iron continuum (Baart et al., 2013), common in cancer by dint of local tumor invasion and angiogenesis; and systemic neoplastic effects leading to increased mortality (Ludwig et al., 2015). NAID is a prognosticator of mortality in chronic diseases (Peyrin-Biroulet et al., 2015). In a 2018 hospital survey conducted in KNH, one-third of the patients missed or delayed cancer therapy while seeking blood transfusion services in regional health facilities. Because of preventable NAID, seeking supportive care away from the main center for definitive cancer care contributed to the loss of follow-up for cancer patients. The interruption in the treatment schedule is a barrier to unhindered access to care. However, early screening and primary prevention of NAID could avert the missed opportunities in cancer care.

### 1.3 Research Questions

What is the prevalence of Non-Anemic Iron Deficiency in cancer patients before initiation of therapy and its correlation to Health-Related Quality of Life?

#### 1.3.1 Null hypothesis:

The level of Serum Iron has no significant association with Health-Related Quality of Life among patients with cancer before therapy initiation

#### 1.3.2 Alternative hypothesis:

The level of Serum Iron has a significant association with Health-Related Quality of Life among patients with cancer before therapy initiation

### 1.4 Broad objective

To determine the prevalence of NAID in cancer patients before initiation of therapy and its correlation to HRQL at KNH

#### 1.4.1 Specific objectives

i. To determine the prevalence of NAID in cancer patients before initiation of therapy at KNH
ii. To assess the association between CHr level and the HRQL in cancer patients before initiation of therapy at KNH
iii. To assess the predisposition to NAID among patients with different solid tumors before initiation of therapy at KNH

### 1.5 Study Justification

Many studies on the prevalence of NAID in cancer exhibit a gap between knowledge and practice in clinical settings and have not highlighted its endemicity in cancers (Busti et al., 2018b). Most datasets on the iron status originate in the Western world; however, potential etiological and age profile differences exist within the African population. Also, the latter group is generally poorly food-resourced, prone to malaria and helminth endemicity have conditions that may exacerbate iron deficiency with or without anemia. Finally, with such a high prevalence of NAID reported in studies, it may be underestimated in the tropics, thereby calling for further clinical research (Muriuki et al., 2020). Thus, this study focused on determining the local burden of NAID in cancer patients before initiation of therapy in the national referral hospital.

### 1.6 Significance of the study.

This study will be the first of its kind in Kenyatta National Hospital, and the findings will support strategic policy formulation for iron status monitoring. The study emphasizes using an emerging marker for iron status monitoring that does not require additional tests to moderate for parametric confounders in the traditional multicriteria iron status screening process. The study finding will establish a baseline prevalence rate for the tropics that would be comparable to other research datasets. The results on HRQL would inform the interventions offered by clinical navigators by identifying the most susceptible to NAID among patients with cancer according to primary tumor sites.

# CHAPTER 2: LITERATURE REVIEW

## 2.1 The burden of Iron Deficiency among patients with cancer

Iron deficiency (ID) in cancer has been strongly linked to tumor bleeding, the effect of cancer pathogenesis, and its treatment. In a meta-analysis by (Ludwig et al., 2015), they found out that, high ID prevalence occurs in solid tumors. Absolute iron deficiency (AID) in cancer was analogous with higher mortality, which is similar to that in cardiac conditions at (21.4%) compared to controls (2.4%), $p = 0.02$. (Sonnweber et al., 2018). Hitherto, no data-driven guidelines support the regular screening of NAID, and there is a dearth of published data on the prevalence of iron deficiency among patients with cancer (Aapro et al., 2012a). Select studies indicate that the bulk of ID in women of reproductive age was (57.5%) compared with men (7.6%) (Abuaisha et al., 2020).

## 2.2 Assessment of Health-Related Quality of Life and the associated tools

Quality of Life (QOL) has an inherent meaning to everyone. A person's perception of robust health, meaningful relationships, work, leisure, and general safety within different cultural settings and contexts brings overall gratification and happiness. The methodology adopted in defining HRQL is by individual's subjective view of well-being reflecting the lived experience and personal expectations; and an objective, discernible judgment of another person's position in life (Karimi & Brazier, 2016).

The HRQL assessment in cancer is essential to enable systematic appraisal of the performance of patients before and during therapy and after administration of treatments, thus evaluating the quality of care (Saad et al., 2018). This assessment may indicate when to begin palliative care for a patient with regional or advanced disease (Basch et al., 2014). There are several tools for assessment of HRQL: the WHO Performance Indicator (WHO-PS), which estimate the patient's ability to undertake some activities without support from other persons (Mittelman et al., 1997); cancer linear analog scale (CLAS), a self-rated score for activity and energy levels

after treatment for anemia (Glaspy et al., 1997). These two offer a general performance status that may not be directly related to the patient's condition.

The functional assessment cancer therapy-anemia (FACIT-AN) tool assesses anemia related symptoms and their effect on the quality of life of the patients with cancer (Cella, 1997); and its psychometric properties subjected to evaluation and validation as a measure for outcomes of the anemia disease process (Yellen et al., 1997). The Generic short-form health survey (SF-36) is a multilevel questionnaire with different dimensions for assessing anemic patient's outcomes which is also extensively validated for use (McHorney et al., 1994).

A group of anemic cancer patients diagnosed with lung cancer, breast cancer, ovarian cancer, and multiple myeloma were enrolled to assess the correlation between hemoglobin level and the HRQL. Two sets of tools, the FACIT-AN, and the generic SF-36, were used, and the regression model established a positive relationship between the hemoglobin level and HRQL (Lind et al., 2002). Similarly, this study employed the FACIT-AN assessment tool in interviewing participants. The tool has four major domains: physical, emotional, mental, and functional well-being. It has an additional field, the additional concerns, which were conveniently not evaluated because it was outside the study's objectives.

### 2.4 The correlation of Non-Anemic Iron Deficiency to functional well-being.

The HRQL is a widely researched subject in clinical practice which contributes to effective communication among healthcare providers (Hijmans et al., 2010). In a study conducted in a hospital setting on women aged between 18 and 55 years comprising both public and private primary care centers, fatigue is the major reason for consulting a physician (Ludwig et al., 2015). The study also revealed Paleness, weakness headache, loss of sleep and alopecia among other physical symptoms. On the other hand, Iron repletion through intravenous iron supplementation in CHF patients improved exercise capacity, HRQL, and disease state independently whether patients were anemic or not (Aapro et al., 2012a). A review article on the relationship between ID and infection susceptibility among pediatric patients in

Africa (Jonker et al., 2017) established that serum iron influences the cell-mediated and innate immune systems. Also, in the review, ID has been associated with a decline in immune responses of macrophages, neutrophils. Poor responses of macrophages that serve as iron reservoirs lead to the inadequate production release of iron to circulation for proper erythropoiesis. The vicious cycle is responsible for chronic fatigue in patients with cancer and other chronic diseases. Therefore, the HRQL of patients with cancer can improve tremendously with early screening and primary prevention strategies on ID patients (Toxqui & Vaquero, 2015).

### 2.5 Non-Anemic Iron Deficiency and its correlation to cognitive and affective wellbeing

The NAID affects cognitive and affective wellbeing. In infancy, subjects with chronic ID develop anxiety, depression, and attention problems (Chen et al., 2013), thus affecting their HRQL performance. In a study conducted in Brazil, Aug 2014, on 100 children attending a public school, children with difficulties in early learning skills showed lower serum ferritin levels, a storage form of iron, $p < 0.02$, compared with those without such problems $p < 0.04$. (Arcanjo et al., 2016). Because ID diminishes cognitive performance in school-going children, it may also negatively influence the performance of patients with cancer

In Japan, a study enrolled 124 patients undergoing dialysis thrice a week to evaluate the NAID's influence on the deterioration of symptoms in patients. The study established that NAID influenced cognitive and affective symptoms in patients on hemodiafiltration (HDF). The multivariate odds ratios at a 95% CI; difficulties falling asleep ( OR 1.71, P = 0.22), depressive mood, (OR 0.93, P = 0.87), loss of interest and pleasure (OR 1.42, P= 0.42) irritability, (OR 1.34, P=0.64) dissatisfaction with life (OR 1.55, P=0.40) was established (Motonishi et al., 2018). These results indicate that NAID affects the HRQL in patients with chronic illnesses and may also deteriorate the cognitive and affective symptoms in patients with cancer. This deterioration is because of their increased susceptibility to iron

deficiency caused by chronic blood loss in specific primary tumor sites, such as gastrointestinal tumors. However, there is minimal data published on the prevalence and the impact of NAID among cancer patients.

### 2.5 Non-Anemic Iron Deficiency and its correlation to social well-being

A dearth of published data highlights the temporal relationship between NAID among cancer patients and social well-being. However, in Medellin Colombia, (Velez and Psacharopoulos, 1992) found that a boost by one standard deviation of cognitive achievement has significantly increased wages earned by 9%. A prior study determined the causal relationship between cognitive attainment and the number of earnings for primary and secondary school leavers. This study enrolled participants in Dar es Salaam and Nairobi. An increase by one standard deviation in cognitive attainment had a 17% and 23% increase in hourly wages for primary and secondary school participants, respectively (Hortona & Rossb 2003). A decline in the number of achievable wages caused by ID portends a poor social well-being performance for patients with chronic non-communicable diseases, including cancer.

A cohort study enrolled 172 women aged 18-45 years to evaluate the relationship between ID and sexual function. It employed a female sexual function index scale (FSI) and a Larson sexual satisfaction tool (LSS) to determine the sexual functional dimensions. The serum iron indices had a statistically significant relationship with sexual function (Nikzad et al., 2018). The effect of ID, lower serum ferritin levels, a storage form of iron was associated with diminished cognitive performance (Arcanjo et al., 2016). The performance would improve with early screening and primary prevention strategies (Toxqui & Vaquero, 2015).

## 2.6 Theoretical Framework

This study espouses the Systems Biology Theory, which incorporates several scientific disciplines focusing on the fundamental genetic, physiologic, and biologic processes that drive human function (Hill, 2005). The central tenet of this theory is its holistic focus (Founds, 2009), with four major holistic focal points incorporated into patient care: prediction, prevention, personalization, and participation (Thimmesch, 2011). Holistic focus emphasizes handling patients with dignity. The maintenance will make them feel socially part of the team. The process entails managing patients' physical needs, including pain-related distress, encouraging patients to express their spiritual connection to their deity, and counseling patients to bolster their sense of worth and self-esteem.

**Optimization of cancer care** requires a proper understanding of the disease process. However, because of the nonlinear progression of malignancies, the clinical manifestation of cancer is diverse and is associated with co-morbidities. A plethora of symptoms of iron deficiency occur in spite, and this requires a knowledge of the disease pathophysiology to enable detailed assessment and diagnosis of iron status.

**Predictive domain**: In malignancy, biochemical substances such as tumor markers and laboratory findings can enable one to predict the occurrence of the disease. The tumor markers could also serve as prognosticators of the outcomes with or without treatment. Also, tumor markers indicate a genetic predisposition to the condition that could affect close family members of the patient. Therefore, the role of the health care worker is to ensure that there is adequate genetic counseling for the family members who may be at risk of the disease.

**Prevention domain**: Here, the framework emphasizes the interventions poised to prevent the incidences of cancer development. These interventions would include adequate nutritional uptake, protection from ionizing radiation that may cause cancer, and prevention of oncogenic viral infections. The prevention domain also comprises the interventions breaking the natural

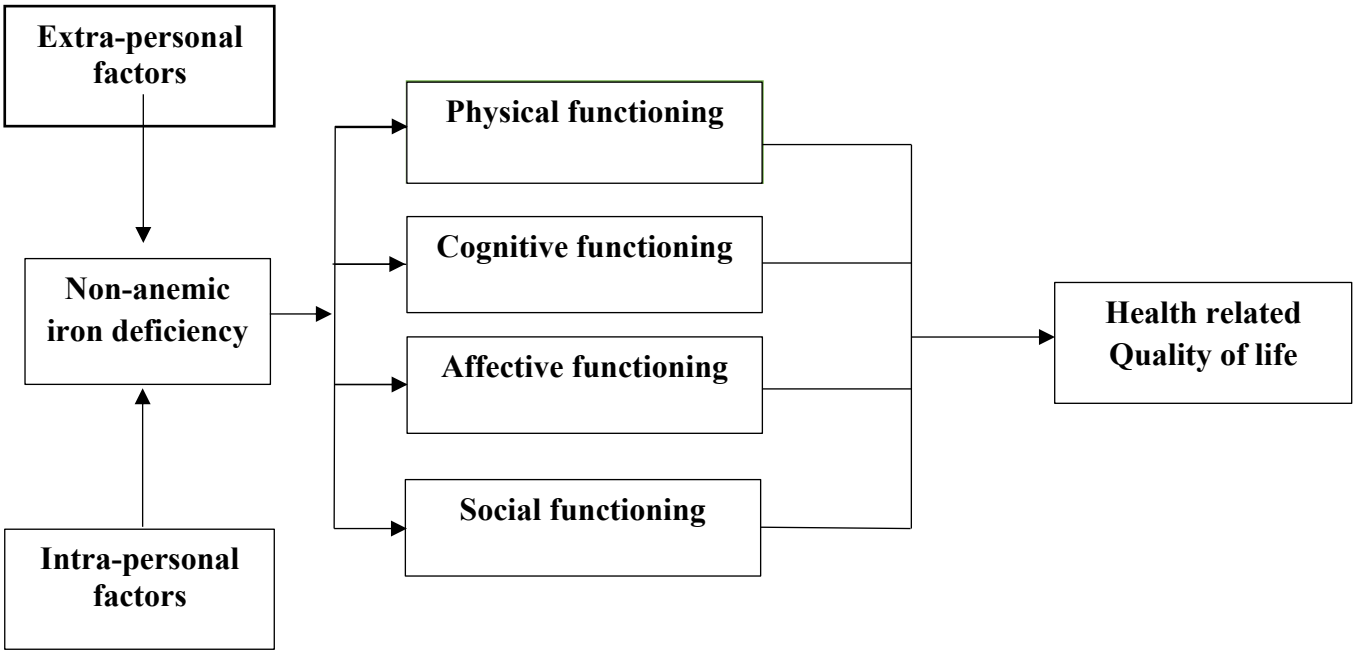
disease process that are causing the worse outcome. These include screening persons at risk of contracting a disease and instituting early interventions to control or halt the disease's progress.

**Personalization domain**: Different persons would respond differently to disease. Persons also experience varied outcomes of the same treatment regimen. In malignancy, all cancer treatment modalities pose a risk for adverse reactions. Herein, healthcare workers care for every cancer patient, as per the severity of adverse reactions, hypersensitivity to drugs, pain levels, and impairment caused by treatment. The psychosocial needs of persons with cancer are unique to individuals and significantly impact the outcome of clinical interventions.

**Participation domain**: Patient education, as conceptualized in this domain, enables cancer patients to continue performing health-promoting activities in the community. Community sensitization to ease the assimilation of patients is vital, and it helps the patient adapt to his new condition in the community. Also, community mobilization would play a significant role in facilitating government interventions, such as cervical cancer screening and vaccination against the human papillomavirus (HPV).

## 2.7 Conceptual framework

***Figure 2.1 Conceptual framework showing the association NAID in cancer to HRQL***




**Key**

***Intra-personal factors****: These are the independent variables that are unique to either the patient or the disease. These are specific to every person. They include chronic bleeding from a tumor, anorexia, presence of a gynecologic or gastrointestinal tumor.* ***Extra-personal factors****: These are independent variables that occur because of the environmental conditions where a person lives. These variables include a diet devoid of nutrients such as ascorbic acid, excessive coffee consumption, and soy products in food. Phyto-nutrients in soy products debar iron absorption. The poor social-economic status may predispose one to inadequate dietary intake, and the prevailing covid 19 pandemic has affected the food supply chain.* ***Health-related Quality of life:*** *The methodology adopted in defining HRQLIt is the individual, subjective view of eudaemonia reflecting the lived experience, and personal expectations and objective, the discernible judgment of another person's position in life (Karimi & Brazier, 2016).*

# CHAPTER 3: METHODOLOGY

## 3.1 Introduction

This chapter highlights the study design and materials employed in the study. It has the targeted population in the study area, the inclusion-exclusion criteria, sample-size determination formulae, and sampling procedures. This study used a data collection tool, with the tool's validity, trial outcome index, and internal consistency included. It provides quality assurance and relevant cutoff points for the laboratory method—ethical considerations for the study, data management, and analysis.

## 3.2 Study Design

The study was a cross-sectional analytical study carried out in a hospital setting to determine the prevalence of NAID in patients seeking cancer. Patients who were above 18 years were enrolled in the initial clinic through enumerative sampling. Using the study tool, the patients that had consented to the study were interviewed, and with further granting, the investigators collected blood samples. Only those with hemoglobin above the cutoff, 12g $dl^{-1}$ females and 13g $dl^{-1}$ males, underwent the CHr test.

## 3.3 Study Area

The study area was KNH, a hospital established in 1901 that provides specialized patient-centered care, training, and research. The hospital has a bed capacity of 1800 beds, and runs 22 outpatient clinics, has 50 wards, and has 24 theatres. The area covers 45.7 hectares, thus accommodating several government institutions, including the college of health sciences and research organizations. This study was carried out in LINAC Cancer Centre, a clinic that runs from Monday to Friday. On average, 80 patients attending the initial clinic are seen on the first two days of the week in this clinic.

### 3.4 Study Population

The target population was all cancer patients in the initial clinic visit who had obtained histopathology reports for cancer diagnosis at Linear Accelerator (LINAC) Cancer Centre, Kenyatta National Hospital.

#### 3.4.1 Inclusion criteria

i. The initial clinic visit patient who had a histopathology report showing a diagnosis for cancer.

ii. The initial clinic visit patient with hemoglobin above 12g $dl^{-1}$ females and 13g $dl^{-1}$ males.

iii. The initial clinic visit patient who had consented to the study.

iv. The initial clinic visit patient who had not started treatment.

v. The initial clinic visit patient above 18 years in any stage of disease

#### 3.4.2 Exclusion criteria

i. The initial clinic visit patient who has a history of blood transfusion in the past month.

ii. The initial clinic visit patient who was on supplemental iron therapy.

iii. The initial clinic visit patient who had inherited blood dyscrasias.

iv. The initial clinic visit patient who had peptic ulcers

### 3.5 Sample size determination

Sample size determination was about a study done in Europe (Busti et al., 2018) that showed the prevalence of ID 42% in congestive heart failure patients. Given the target population for this study was higher than 10000 persons, with Fisher's formula applied, the sample size was **385**.

· $\mathbf{Z^2}$, the statistic for the level of confidence **($1.96^2$)**

· **P**, the hypothesized population proportion **42%** (Busti et al., 2018) a study in Europe.

·**e,** the desired precision level in proportion of **1**: if **5%** then it is e= **0.05**

·, when **N** was previous estimated sample **358** and **e,** was the precision level of **0.05**

· The calculation of sample size for prevalence and proportion $\mathbf{n = Z^2 P(1-P)/ e^2}$ (Kirkwood et al., 2003):

$$\mathbf{n = Z^2 P(1-P)/ e^2}$$

$$\mathbf{n = \frac{1.96^2 * 0.5 * 0.5}{0.05^2}}$$

$$\mathbf{n = \frac{3.8416*0.25}{0.0025}}$$

$$\mathbf{n = 384.16}$$

$$\mathbf{= 385 \text{ participants}}$$

### 3.6 Sampling procedure

Consecutive sampling was applied to patients attending the LINAC Cancer Center due to the prevailing protocol timelines to achieve the sample size. The researchers prescreened participants to determine those who met the inclusion criteria by checking the patient's records for the current hemoglobin level and the details of the diagnosis. Researchers then invited the patients who had consented to the study to the interviewer's room for data collection to commence.

### 3.7 Study tools

The researchers used The FACIT-AN tool in the interview. The tool assesses anemia-related symptoms and their effect on the HRQL in cancer (Cella, 1997). After evaluation and validation, the tool offers psychometric properties useful in measuring outcomes of anemia (Yellen et al., 1997). A randomized open-label trial recruited initial clinic patients with renal cancer from 28 countries; using the FACIT-G tool, it determined respondents with moderate to poor risk to HRQL. There was a statistically significant improvement on FACIT-G domains:

Physical, functional affective well-being domain scores were predictors of overall and progression-free survival (Cella et al., 2018)

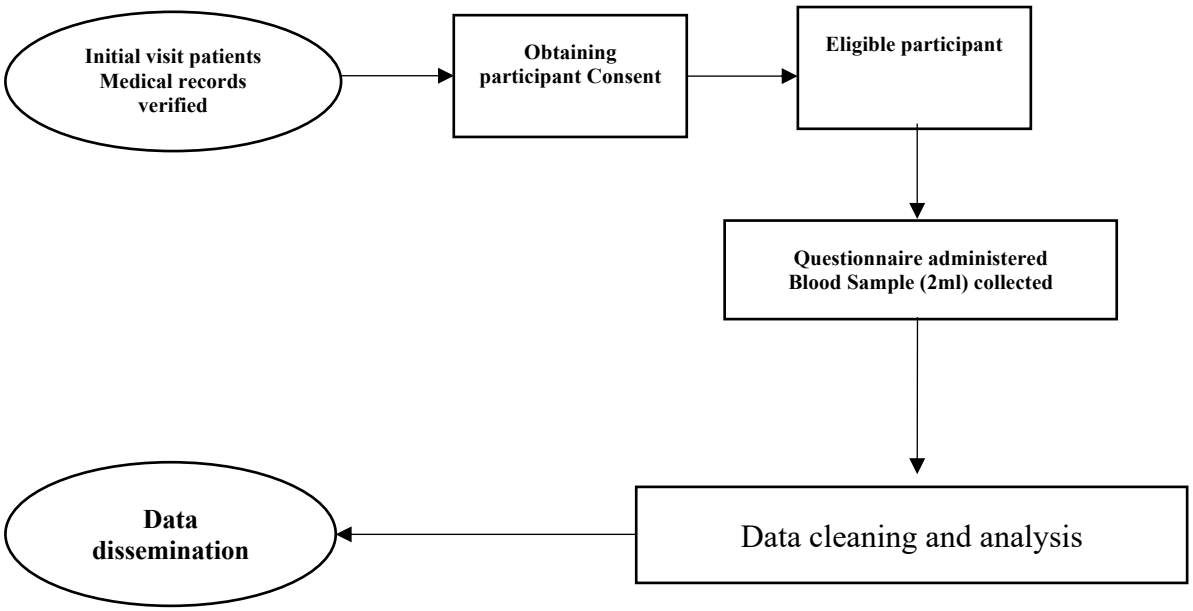
### 3.8 Reliability of the study tool

The FACIT-AN tool was licensed (see appendix 7) to evaluate HRQL for people with chronic illnesses. Retrospective studies validated the use of the tool in Non-Hodgkin Lymphoma (NHL) clinical research (Hlubocky et al., 2013); and could be administered in the Arabic language with a validity of (0.89), and its Trial Outcome Index (0.91) demonstrating good internal consistency (Soudy et al., 2018). The researchers conducted a pretest of the tool on 30 patients in the Cancer Navigation Clinic.

### 3.9 Data collection procedures

The Principal Investigator (PI) trained three research assistants on KNH/UON-ERC Covid 19 guidelines, data collection, and entry process. The investigators identified the participants, explained the aim and procedure of the study, and revealed the tools intended for use. the researchers obtained verbal and written consent from the patient before the interview. The interviews took, on average, 15 minutes using the FACIT-AN tool. The investigators drew blood (2ml) from the antecubital fossa in a single-use syringe, kept it at room temperature in a blood box before transporting it to the hematology lab for testing.

***Figure 3.1. Showing the procedure for data collection and management***



### 3.10 Laboratory methods

The researchers collected and transported blood samples in an EDTA vacutainer to the KNH laboratory for analysis. To minimize sample aging, blood was transported within four hours; kept at room temperature until the analysis time in an SYSMEX XN-1000 analyzer. The analyzer uses laser beam 633nm and hydrodynamic focusing on dedicated channels of blood cells. The CHr lower limits: was set at (27.2pg) for pediatric, and (28.7pg) (Brugnara et al., 2006).

### 3. 11 Quality assurance

The researchers did the CHr test at KNH ISO 9001:2015 certified laboratory. The principal investigator obtained a license to conduct a laboratory study from the KNH Director for Laboratory and Diagnostic Services. The lab technologist dedicated and calibrated a machine to produce one parameter CHr for the research. The researchers labeled all blood samples collected using aseptic techniques in a sterile EDTA vacutainer with the participants' study code, dated, and timed. Also, the researchers transported blood to the laboratory in a cool box which they kept at room temperature.

### 3.12 Ethical consideration

The PI obtained approval from the KNH/UON-ERC on Aug. 26, 2021, and authorization from the Heads of Departments, Cancer Treatment Centre (CTC), and Medical Research, Laboratory, and Diagnostic Services, to conduct the study. The participants who declined to participate in the study were rendered all the services without discrimination. The researchers assisted the participants in reading the consent statement and gave forms for filling.

### 3.13 Data Management

The researchers checked filled-up study tools, for completeness before entering to the excel database and storing them in a secured office. Computer software for coding and cleaning was done on-site in LINAC Cancer Centre, two separate entry points for cross-checks, and the spreadsheet was forwarded to the statistician for analysis.

### 3.14 Data Analysis

The social demographic data was analyzed using descriptive statistics, with R-*statistic program*. Multivariate analysis established the association between serum iron status and he health related quality of life. Chi-squire, Linear regression, and Pearson correlation were applied to establish the variations in serum iron status (CHr) viz a vis primary tumor site. The findings were graphically presented in scatter plots, box and whisker, bar graphs, and tables.

### 3.15 Benefits of the study

This study will support the quest for treatment protocols to include CHr assay for early detection of ID and appropriate intravenous iron supplementation in susceptible patients. Also, it will support the clinical navigators to introduce purposive, individualized psychological counseling for initial clinic visit cancer patients. The study also highlights the utilization of the emerging Reticulocyte Hemoglobin Content (CHr) assay. This marker of iron status reflects the hemoglobin content in the earliest of the erythrocytes, suitable for the insidious NAID. The marker may not be affected by the infective or inflammatory state, and malignancy unlike the conventional serum ferritin (SF), transferrin saturation (TSAT), total iron-binding capacity (TIBC), serum transferrin receptor (sTfR).

### 3.16 Dissemination of the study findings

The study will be published on the UON digital repository and in journals to facilitate public access. The study findings shall be shared with the HOD in Cancer Treatment Centre and the medical laboratory department. Submissions will be made to conferences and opportunities for presentation and peer critiquing of the study will be pursued herein.

# CHAPTER 4: RESULTS

## 4.1: Introduction

Between August 2021 and October 2021, the researchers recruited all participants who consented and met the study's criteria. They enrolled only adult participants above 18 for the study. This chapter highlights the study identifies demographic details of the participants for the study. The frequency distributions of the tumor site according to the counties and the nature of primary tumor sites. The chapter has results for the frequency of stages of the disease and the prevalence of NAID among cancer patients.

Analytical results here reflect the correlation between CHr and the hemoglobin level. The researcher established a linear regression equation, allowing a scatter plot of various CHr values vis their paired hemoglobin values vis a viz. Also, a correlation coefficient was determined to establish how strong the relationship between the CHr and the hemoglobin level. The researcher evaluates the association between CHr level and the HRQL among patients with cancer in multiple regression.

A multivariate regression table shows the prediction of the CHr from the HRQL as presented here. The researcher tested the variance of NAID among different solid tumors to evaluate the predisposition inherent in various primary tumor sites to NAID. He also shows the frequency distribution of CHr among males and females in a box and whisker plot. The correlation analysis to assess whether the CHr value had any association with the disease stage was presented in the Chi-square table. Finally, multivariate regression was conducted to demonstrate homogeneity of variance between primary tumor sites vis a viz the CHr values. Due to the violation of the assumption of homogeneity, the Welsh's analysis of variance was adopted to determine the statistical significance of the differences between primary tumor sites regarding the CHr values.

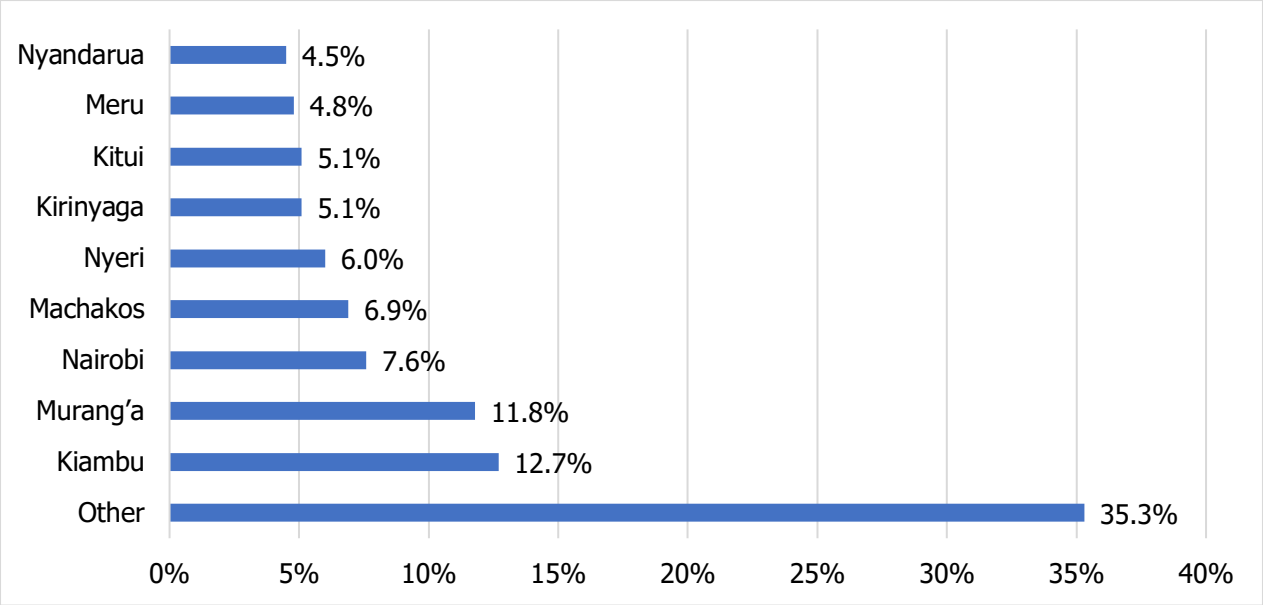
## 4.2 The social demographic findings for initial clinic visit cancer patients

*Table 4.3: Showing social demographic findings of the participants*

| | | Frequency (n) | Percent (%) |
|---|---|---|---|
| **Age (years)** | | | |
| | Below 40 years | 58 | 17.5 |
| | 40 – 50 | 69 | 20.8 |
| | 51 - 60 | 79 | 23.9 |
| | 61 - 70 | 77 | 23.3 |
| | More than 70 | 43 | 13.0 |
| | Not indicated | 5 | 1.5 |
| | **Age (median IQR)** | 56 (IQR 43.8, 66) years | |
| **Gender** | | | |
| | Female | 199 | **60.1** |
| | Male | 132 | 39.9 |
| **Marital Status** | | | |
| | Married | 297 | **89.7** |
| | Single | 35 | 8.2 |
| | Not indicated | 7 | 2.1 |
| **Religion** | | | |
| | Christian | 321 | **97.0** |
| | Muslim | 10 | 3.0 |
| **Hb level** | | | |
| **Male (n=132)** | < 7gd/l | 2 | 1.5 |
| | 7 - 9.9 | 11 | 8.3 |
| | 10 – 12.9 | 35 | 26.5 |
| | > 12.9 | 52 | **39.4** |
| | Not documented | 32 | 24.2 |
| | | | |
| **Female (n=199)** | < 7gd/l | 3 | 1.5 |
| | 7 - 9.9 | 26 | 13.1 |
| | 10 – 11.9 | 51 | 25.6 |
| | > 11.9 | 79 | **39.4** |
| | Not documented | 40 | 20.1 |

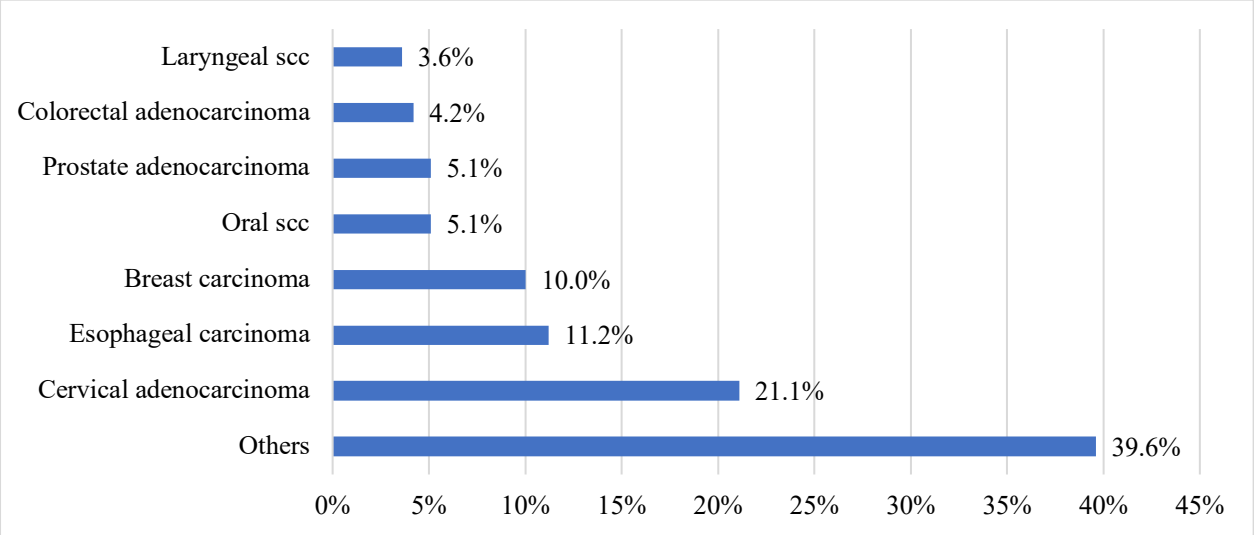
A total of 331 participants were enrolled, almost a quarter of the respondents (23.9%, n=79) were aged between 51 to 60 years, 23.3% (n=77) 61 to 70, 20.8% (n=69). The median age of the study respondents was 56 (IQR 43.8, 66) years within a range of 19 to 89 years.

***Figure 4.1 Showing the percentage distribution of participants per home county***




Forty-two participants in among those selected, (12.7%) were from Kiambu county, 39 (11.8%) Murang'a, 25 (7.6%) Nairobi, 23 (6.9%) Machakos, 20 (6.0%) Nyeri among others.

***Figure 4.2 Showing the percentage distribution graph of primary tumor sites for the participant***




Seventy patients (21.1%) were diagnosed with cervical adenocarcinoma, 37 (11.2%) esophageal carcinoma, 33 (10.0%) breast carcinoma, 17 (5.1%) oral scc, 17 (5.1%) prostate adenocarcinoma, 14 (4.2%) colorectal adenocarcinoma and 12 (3.6%) laryngeal scc among others. Other diagnoses included gastric adenocarcinoma (11), lung carcinoma (11), squamous cell carcinoma (11), Nasopharyngeal carcinoma (10), Thyroid carcinoma (9), Sarcoma soft tissue (8), Tongue scc (8) and Hypopharyngeal scc (6).

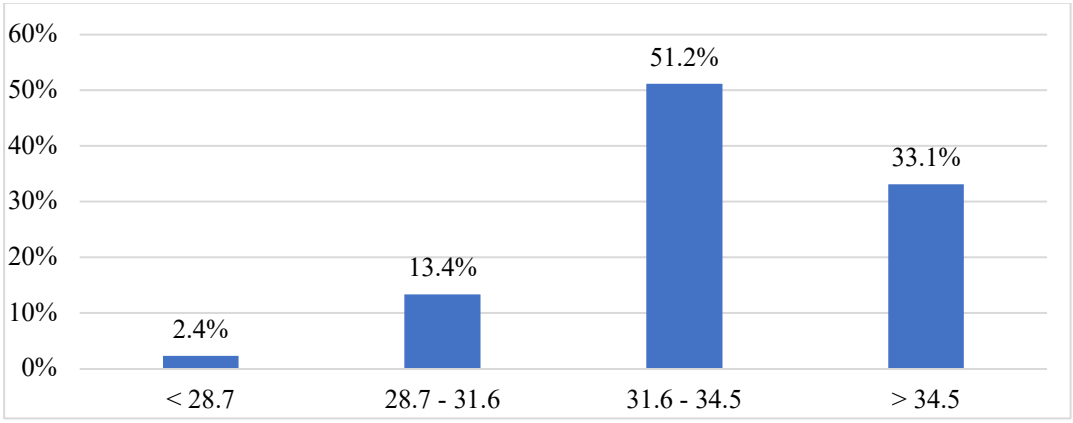
***Table 4.2 showing the frequency distribution of stages of the disease as per the (7) most prevalent primary tumor site among the participants.***

| | Stages | | | | |
|---|---|---|---|---|---|
| **Primary cancer sites** | **I** | **II** | **III** | **IV** | **Un-staged** |
| **Cervical carcinoma** | **1** | **19** | **30** | **13** | **7** |
| **Esophageal carcinoma** | **2** | **6** | **5** | **6** | **16** |
| **Breast carcinoma** | **1** | **6** | **4** | **11** | **11** |
| **Oral scc** | **1** | **2** | **1** | **4** | **9** |
| **Prostate carcinoma** | **0** | **2** | **0** | **6** | **9** |
| **Colorectal carcinoma** | **0** | **4** | **3** | **2** | **5** |
| **Laryngeal scc** | **2** | **1** | **1** | **4** | **4** |
| **Others** | **9** | **12** | **6** | **30** | **74** |
| **Total** | **16** | **52** | **50** | **76** | **135** |

Most of the participants were observed to be in stage 4. Almost one third had not undergone metastatic workups for determining the stage of disease by the time they were having their initial clinic visit at the LINAC Cancer Centre.

### 4.3 Prevalence of NAID in cancer patients before initiation of therapy

***Figure 4.3: Showing the prevalence of NAID among patients with cancer before initiation of therapy at the LINAC Cancer Centre***




The CHR assay was done, (n= 331,). Majority of the respondents had the CHr value above the normal 28.7 pg. cut-off. A total of (2.4%, n=7,) of the participants had CHr level of below the 28.7 pg. cut-off.

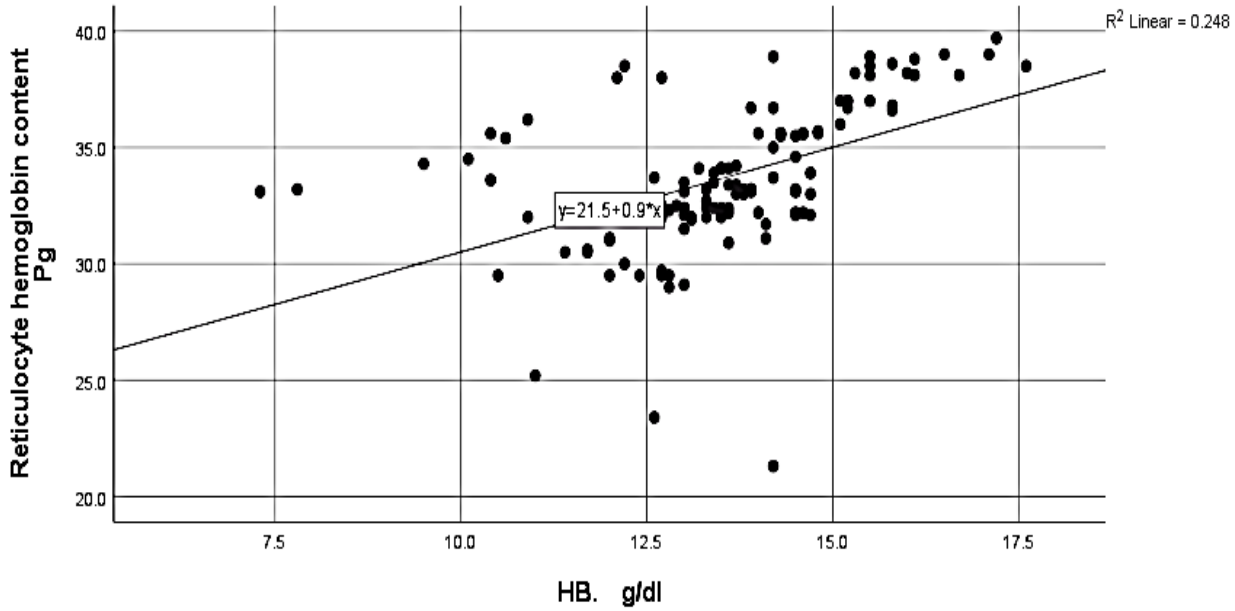
### 4.4 The multivariate regression between CHr level and the scores of HRQL domain

***Table 4.3 Showing a Pearson correlation of CHr and the hemoglobin level of initial clinic visit participants at the LINAC cancer Centre***

| | | Reticulocyte hemoglobin content pg | HB. g/dl |
|---|---|---|---|
| **Reticulocyte hemoglobin content pg** | Pearson Correlation | 1 | **.498**** |
| | Sig. (2-tailed) | | 0.000 |
| | N | 127 | 127 |
| **HB. g/dL** | Pearson Correlation | **.498**** | 1 |
| | Sig. (2-tailed) | 0.000 | |
| | N | 127 | 259 |

A Pearson product-moment correlation was done to determine the relationship between CHr and HB level. There was a moderate, positive correlation between CHr and hemoglobin level, which was statistically significant (r =.498, n= 127, p<.001).

***Figure 4.4 Showing linear relationship of a scatter plot of paired values of CHr and hemoglobin levels for participants at LINAC Cancer Centre***




A significant regression equation was found (F (1, 126) =41.170, p<.001., with an R2 of .248. This scatter plot indicates a moderate, positive correlation between CHr and hemoglobin level, which was statistically significant (r =.498, n= 127, p<.001).

***Table 4.4 Showing the regression analysis between CHr and HB levels for initial clinic visit participants at the LINAC cancer Centre***

| Coefficients[a] | | | | | | |
|---|---|---|---|---|---|---|
| **Model** | | **Unstandardized Coefficients** | | **Standardized Coefficients** | **t** | **Sig.** |
| | | **B** | **Std. Error** | **Beta** | | |
| 1 | **(Constant)** | 21.499 | 1.907 | | 11.271 | .000 |
| | **HB. g/dl** | .901 | .140 | .498 | 6.416 | .000 |

**a.** Dependent Variable: Reticulocyte hemoglobin content Pg

A simple linear regression was calculated to predict CHr based on HB level, b=21.5, t=11.27, p<.001.

***Table 4.5 Showing the multivariate regression between CHr level for the participants at initial clinic visit and their scores of the four HRQL domains***

| ANOVA[a] | | | | | | |
|---|---|---|---|---|---|---|
| **Model** | | **Sum of Squares** | **df** | **Mean Square** | **F** | **Sig.** |
| 1 | **Regression** | 103.670 | 4 | 25.918 | **2.789** | **.030[b]** |
| | **Residual** | 984.926 | 106 | 9.292 | | |
| | **Total** | 1088.596 | 110 | | | |

| Coefficients[a] | | | | | | |
|---|---|---|---|---|---|---|
| **Model** | | **Unstandardized Coefficients** | | **Standardized Coefficients** | **t** | **Sig.** |
| | | **B** | **Std. Error** | **Beta** | | |
| 1 | **(Constant)** | | 2.202 | | 16.256 | .000 |
| | **Physical well-being domain** | .026 | .076 | .035 | .349 | .728 |
| | **Social well-being domain** | .063 | .081 | .083 | .778 | .438 |
| | **Emotional well-being domain** | -.225 | .071 | **-.307** | -3.156 | **.002** |
| | **Functional well-being domain** | -.094 | .059 | -.177 | -1.598 | .113 |

A multiple regression was done to predict CHr from the effective, cognitive, and functional well-being. All the HRQL domains statistically predicted CHr levels, F (4, 106) = 2.789, p=.030, $R^2$ = .309. Only the Emotional well-being domain added statistically significantly to the prediction, p = .002.

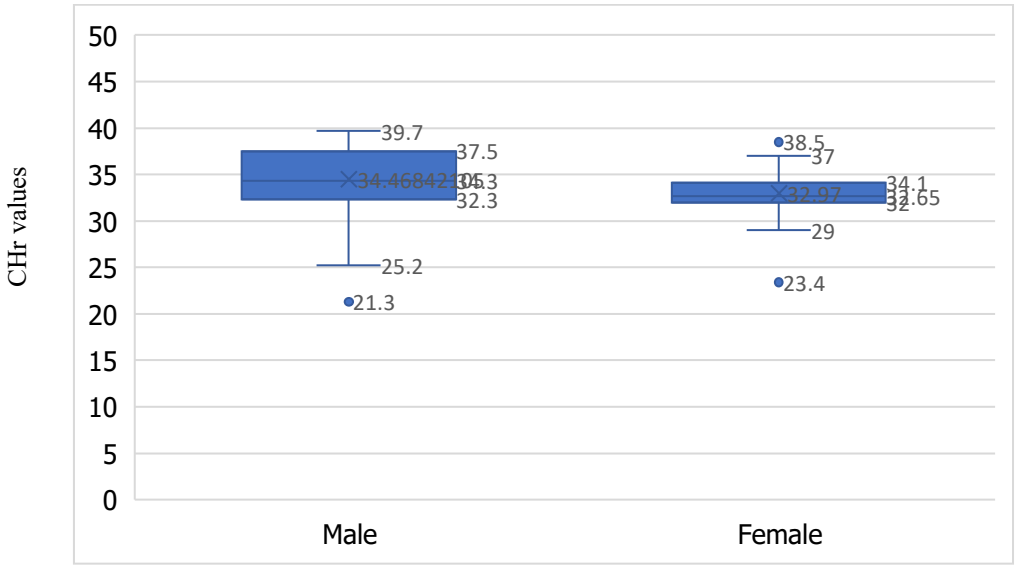
### 4.5 Predisposition within different solid tumors to NAID

***Table 4.6 Showing inherent predisposition within different solid tumors to NAID in participants at initial clinic visit.***

| Clinical factor Mean (SD or n (valid %) | Cervical carcinoma n=70 | Esophageal carcinoma n=37 | Breast carcinoma n=33 | Oral scc n=17 | Prostate carcinoma n=17 | Colorectal carcinoma n=14 | Laryngeal scc n=12 | Others n=131 | ANOVA F, p-value |
|---|---|---|---|---|---|---|---|---|---|
| **Mean (s.d) age in years** | **51.6 (10.7)** | **60.8 (14.6)** | **53.4 (13.6)** | **53.9 (17.2)** | **69.1 (8.4)** | **61.3 (15.8)** | **58.2 (15.0)** | **52.8 (14.3)** | **5.647, p<.001** |
| **Hemoglobin level mean (s.d)** | **11 (2)** | **11.7 (2.2)** | **12.1 (1.7)** | **13.0 (2.4)** | **12.7 (1.5)** | **10.5 (2.6)** | **14.4 (1.7)** | **12.7 (2.5)** | **5.564, p<.001** |
| **CHr level mean (s.d)** | **32.8 (1.4)** | **32.8 (1.7)** | **31.4 (2.8)** | **35.3 (3.4)** | **33.4 (5.8)** | **32.2 (0.3)** | **35.3 (2.8)** | **-** | **2.322, p=.043** |
| **Females n (%)** | 69 (98.6) | 15 (40.5) | 32 (97.0) | 7 (41.2) | 0 | 7 (50.0) | 2 (16.7) | 67 (51.1) | |
| **Males n (%)** | 1 (1.4) | 22 (59.5) | 1 (3.0) | 10 (58.8) | 17 (100) | 7 (50.0) | 10 (83.3) | 64 (48.9) | |
| **Married /living as married n (%)** | 66 (94.3) | 35 (94.6) | 32 (97.0) | 14 (82.4) | 17 (100) | 12 (85.7) | 10 (83.3) | 111 (84.7) | |
| **Christian n (%)** | 67 (95.7) | 34 (91.9) | 31 (93.9) | 16 (94.1) | 17 (100) | 14 (100.0) | 12 (100) | 130 (99.3) | |
| **Muslim n (%)** | 3 (4.3) | 3 (8.1) | 2 (6.1) | 1 (5.9) | 0 | 0 | 0 | 1 (0.8) | |

There was statistically significant difference in the mean age of patients with different types of cancers as determined by one-way ANOVA (F (6, 189) =5.647, p<.001). A Tukey post hoc test revealed group age differences within patients with cervical adenocarcinoma and esophageal carcinoma (p<.05), breast carcinoma and prostate adenocarcinoma (p<.05), oral scc and prostate adenocarcinoma (p<.05). The findings also revealed a statistically significant difference between hemoglobin level and types of cancers (F (6, 152) =5.564, p<.001). The test of variance of Gender, marital status, and religion between and within different primary tumor sites were inane and could not elucidate statistical significance in initial clinic visit participants. Herein, the analysis of variance, F statistic, was not executed on the gender, marital status, and religion.

***Figure 4.5 Showing the frequency distribution of CHr values among male and female initial clinic visit participants at the LINAC Cancer Centre***



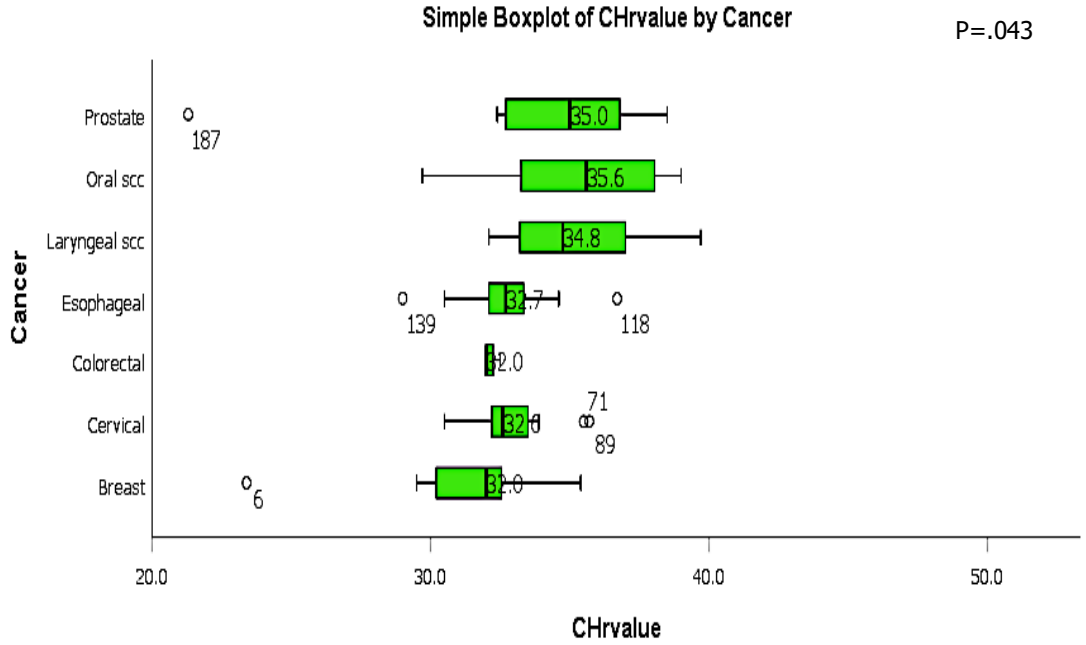

The box plot below shows the distribution of CHr values among males and females. CHr values were more slightly dispersed among male patients' min, max (25.2, 39.7). A test of variance revealed a statistically significant difference between the CHr mean values of male patients (34.5±3.5) pg and female patients ((33.0±2.5) pg) (F (1, 125) =7.916, p=.006. Eta squared was of medium size (η2=.06).

***Table 4.4: Showing Chi-square test of association between CHr in the four stage of disease for initial clinic visit participants***

| | | Stage of disease | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | I | II | III | IV | *df* | $X^2$ Statistic | p-value |
| < 28.7 | 1 | 0 | 1 | 1 | 0 | 12 | 14.664 | .260 |
| 28.7 – 31.6 | 6 | 1 | 4 | 5 | 1 | | | |
| 31.6 – 34.5 | 32 | 4 | 9 | 11 | 9 | | | |
| > 34.5 | 21 | 2 | 7 | 1 | 11 | | | |
| Total | 60 | 7 | 21 | 18 | 21 | | | |

There was no statistically significant association between CHr levels and stage of disease. Almost one third had not undergone metastatic workups for determining the stage of disease by the time they were having their initial clinic visit at the LINAC Cancer Centre.

***Figure 4.6 Showing CHr distribution across primary tumor sites for in initial clinic visit participants at the LINAC Cancer Centre***




The mean CHr value of primary tumor sites: esophageal, colorectal, cervical, and the breast was statistically significantly lower p=.043, compared with that of prostate, oral, and laryngeal primary tumor sites.

***Homogeneity of variance in primary tumor sites***

The assumption of homogeneity was violated, Levene's test of homogeneity of variance, F (7, 126) p=2.906, P=.008. Welch's robust test was then performed to determine whether there was a statistically significant difference of the observed CHr mean between different solid tumors.

***Table 4.8 Showing Multivariate regression between CHr levels and different primary tumor sites in initial clinic visit participants ant the LINAC Cancer Centre***

**ANOVA**

| Reticulocyte hemoglobin content Pg | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| **Between Groups** | 172.914 | 7 | 24.702 | 2.906 | **.008** |
| **Within Groups** | 1011.476 | 119 | 8.500 | | |
| **Total** | 1184.390 | 126 | | | |

**Descriptive(s)**

| Reticulocyte hemoglobin content Pg | N | Mean | Std. Deviation | Std. Error | 95% Confidence Interval for Mean | | Minimum | Maximum |
|---|---|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound | | |
| **Cervical carcinoma** | 17 | 32.847 | 1.3992 | .3393 | 32.128 | 33.566 | 30.5 | 35.7 |
| **Esophageal carcinoma** | 15 | 32.793 | 1.7429 | .4500 | 31.828 | 33.759 | 29.0 | 36.7 |
| **Breast carcinoma** | 15 | 31.407 | 2.7809 | .7180 | 29.867 | 32.947 | 23.4 | 35.4 |
| **Oral scc** | 7 | 35.271 | 3.3841 | 1.2791 | 32.142 | 38.401 | 29.7 | 39.0 |
| **Prostate carcinoma** | 7 | 33.400 | 5.8043 | 2.1938 | 28.032 | 38.768 | 21.3 | 38.5 |
| **Colorectal carcinoma** | 3 | 32.167 | .2887 | .1667 | 31.450 | 32.884 | 32.0 | 32.5 |
| **Laryngeal scc** | 6 | 35.250 | 2.7905 | 1.1392 | 32.322 | 38.178 | 32.1 | 39.7 |
| **Other** | 57 | 34.430 | 3.0455 | .4034 | 33.622 | 35.238 | 25.2 | 39.0 |
| **Total** | 127 | 33.643 | 3.0659 | .2721 | 33.104 | 34.181 | 21.3 | 39.7 |

*Welch's F* statistic at 0.05 level of significance revealed a significant difference of the observed CHr means between the different solid tumors, *Welch's F* (7, 172.914) = 2.906, p=.008. While evaluating whether the difference between means in solid tumors is statistically significant, we compared the p-value to the significance level; the low P-value of (.008) is proved that results are statistically significant. This findings lender evidence to conclude that the CHr means of different solid tumors are not equal in the population.

# CHAPTER 5: DISCUSSION, CONCLUSION, & RECOMMENDATION

## 5.1 Introduction

The chapter discusses the results, including the social and demographic results of participants in the initial clinic visit at the LINAC cancer Centre. The study elucidates the prevalence of NAID among the initial clinic visit cancer patients. It includes the relationship between the HRQL and the CHr among initial visit cancer patients at LINAC cancer Centre and its significance. The inherent predisposition in the cancer patients with various primary tumor sites to NAID is presented. This study explored the prevalence of non-anemic iron deficiency, its spread in different tumors, and its association to health-related quality of life in cancer. Out of the 331 participants who were enrolled in the study, the median age was 56 years.

## 5.2 Demographic findings in the initial clinic visit cancer patients at LINAC Cancer Centre

Almost half of the respondents (47.1%) were above 51 years and above, with a median age of 56 years. The average age at which cancer is diagnosed in Africa is lower than in high-income countries. Because age is a significant risk factor for most cancers, mortality and incidence are bound to be lower in the African population skewed towards younger average ages. However, Africa has the most pandemic infectious diseases like human immunodeficiency virus (HIV) and the emerging non-communicable diseases causing double disease burden (Vento, 2013). The most common primary tumor site at the initial visit was the cervix uteri (21.1%), followed by the esophagus (11.2%), and the third commonest was the breast at (10.1%). These findings are contrary to the estimates by (Globocan 2020), where the incidence rate of breast cancer in Africa was high (16.8%), and the breast was the most prevalent primary tumor site. A large majority of the respondents were Christians, and they reported to be married adults.

More than half (60.1%) were females, and more participants from Kiambu, Murang'a, and Nairobi counties combined (30.6%) due to the counties' proximity to the hospital, KNH.

### 5.3 The prevalence of NAID in cancer patients before initiation of therapy at the LINAC Cancer Centre

In a baseline study on the prevalence of non-anemic iron deficiency, in the United Kingdom (UK) population for participants above 50 years was (8.8%), (CI) (8.0-9.7) (Philip et al., 2020), a figure higher than in our population, (2.5%). The prevalence of NAID was higher among female respondents, making them more susceptible to NAID compared to the males. This is due to the phylogenetic differences between males and females where females have a 12% lower mean hemoglobin level compared to men. Albeit there is no mean difference in circulating erythropoietin levels between males and females (Murphy, 2014). In Africa, infectious diseases with a strong causal linkage to cancer, Human papillomavirus (HPV) and hepatitis B and C virus mostly plague women, and one quarter of all cancers in Africa are caused by infectious diseases (Vento, 2013).

### 5.4 The Pearson correlation between hemoglobin value and the reticulocyte Hemoglobin content in cancer patients before initiation of therapy

About (24%) of the variability in hemoglobin level could account for the variance in CHr level while the remainder could not be observed in the variable. The outliers: participants with normal hemoglobin levels but presenting with very low CHr level, as it was revealed in the scatter plot, presented a phenomenon that could be explained by the pathophysiology in iron metabolism. Inflammation, as it occurs in cancer, stimulates tumor necrotic factor (TNF), interferon delta, and interleukins 1& 6 leading to the release of hepcidin from the liver that causes the internalization of ferroportin, the membrane transport proteins in the macrophages. This is leads to functional deficiency in iron because the iron in storage in macrophages is not available for circulation in plasma. (Rodwell et al., 2018). In functional iron deficiency (FID), the downregulation of ferroportin, the membrane transport protein, debars the release of iron

$Fe^{2+}$ from the macrophage to the circulation. This makes $Fe^{2+}$ unavailable for reticulocyte erythropoiesis and it's the hallmark of iron deficiency in the cancer. FID is the most predominant pathogenesis in cancer that accounts for ID, its occurrence increases with advancement in disease stage, and is associated with poor HRQL. (Naoum, 2016).

### 5.5 The multivariate relationship between CHr values and the HRQL in cancer patients before initiation of therapy

All the HRQL domains statistically predicted CHr levels, at p=.030. About (30%) of the variability in the HRQL domains accounted for the changes in the reticulocyte haemoglobin content at $R^2$ = .309. When potential confounding variables, the other three domains were controlled by elimination, the emotional well-being domain added statistically significantly to the prediction, p = .002. These outcomes are supported (Motonishi et al., 2018), where the HRQL domain scores for hemodiafiltration patients were assessed. It was noted that, iron deficiency in all its forms was an etiological factor of cognitive and affective symptoms in patients on hemodiafiltration (HDF). The multivariate odds ratios at a 95% CI; depressive mood, (OR 0.93 0.41-2.08 P = 0.87), loss of interest and pleasure (OR 1.42 95% CI 0.60- 3.40 P= 0.42). In conclusion, traces of data hinting at the effect NAID on cancer patients hypothesize a correlation between low CHr level and poor HRQL (Aapro et al., 2012). The deterioration in HRQL in cancer patients with NAID is because of increased patient requirements related to anorexia, nausea, diarrhea, vomiting, inadequate supply such as vegetarian diet, increased coffee consumption, and increased blood loss (Soppi, 2018).

### 5.6 The predisposition to NAID inherent in different primary tumor sites in cancer patients before initiation of therapy

The esophageal, colorectal, cervical, and breast cancer participants had statistically significantly low mean CHr levels compared to their counterparts oral, prostate, and laryngeal cancer participants. The increased susceptibility of the esophageal, colorectal, and cervical tumors is a consequence of hemorrhage and inflammatory response in tumors (Ludwig et al.,

2015). Similarly (Aapro et al 2012) in a 6-month survey on cancer patients, colorectal cancer had the highest prevalence of ID, (60%). The increased median age (56) years may be associated with increased comorbid conditions, where some patients could be on antiplatelets, and anticoagulants. This leads to increased susceptibility to ID. However, chronic blood loss in primary tumor sites of gastrointestinal descent is the probable risk for ID among patients with cancer.

The prevalence of NAID in cancer before initiation of therapy, (2.4%) is significant, mirrors the majority in the UK population; herein a reference point is established for subsequent studies**.** Participants with gynecological and gastrointestinal primary tumor sites are more predisposed to NAID compared to participants with other tumors. NAID. This study finding acquiesce to a rejection the null hypothesis that. HRQL has no significant association with serum iron in cancer patients before therapy initiation.

**Conclusion**

The prevalence of NAID in cancer before initiation of therapy (2.4%) is significant, which mirrors the majority in the UK; herein, a reference point is established for subsequent studies**.** Participants with gynecological and gastrointestinal primary tumor sites are more predisposed to NAID than participants with other tumors. NAID in patients with cancer causes poor performance in all domains of the HRQL, with the affective domain deteriorating more significantly. This study finding acquiesces to a rejection of the null hypothesis that, HRQL has no significant association with Serum Iron in cancer patients before therapy initiation.

**Recommendation**

CHr assay should be incorporated in cancer screening protocols with intervals for testing and timing clearly defined, for early NAID detection and management. The clinical navigators (nurses) to increase awareness of inherent predisposition to NAID in patients with cancer of gynecological and gastrointestinal descent. The oncology nurse to bolster the knowledge of iron deficiency in cancer patients and its correlation to poor health-related quality of life in

continuous professional development sessions and conferences. The oncology nurse to conduct community sensitization on the benefits of primary prevention of iron deficiency through adequate balanced nutrition, and abundant use of natural food sources of iron.

**Study limitations**

Due to the cross-sectional study design of the study, one cannot assume causality. The findings may not uncritically represent patients from different resource settings, and the study did not explore the dietary preferences of the participants; a factor that could affect serum iron indices.

**Recommendations for further studies**

I recommend a study on: "*assessment of clinical outcomes of intravenous iron supplementation therapy in cancer patients diagnosed with NAID at Kenyatta National Hospital*."

## REFERENCES


Aapro, M., Österborg, A., Gascón, P., Ludwig, H., & Beguin, Y. (2012a). Prevalence and management of cancer-related anaemia, iron deficiency and the specific role of i.v. Iron. *Annals of Oncology*, *23*(8), 1954–1962. https://doi.org/10.1093/annonc/mds112

Aapro, M., Österborg, A., Gascón, P., Ludwig, H., & Beguin, Y. (2012b). Prevalence and management of cancer-related anaemia, iron deficiency and the specific role of i.v. Iron. *Annals of Oncology*, *23*(8), 1954–1962. https://doi.org/10.1093/annonc/mds112

Anand, I. S., & Gupta, P. (2018). Anemia and Iron Deficiency in Heart Failure: Current Concepts and Emerging Therapies. *Circulation*, *138*(1), 80–98. https://doi.org/10.1161/CIRCULATIONAHA.118.030099

Basch, E., Snyder, C., McNiff, K., Brown, R., Maddux, S., Smith, M. L., Atkinson, T. M., Howell, D., Chiang, A., Wood, W., Levitan, N., Wu, A. W., & Krzyzanowska, M. (2014). Patient-reported outcome performance measures in oncology. *Journal of Oncology Practice*, *10*(3), 209–211. https://doi.org/10.1200/JOP.2014.001423

Bergner, M. (1989). Quality of life, health status, and clinical research. *Medical Care*, *27*(3 Suppl), S148-156. https://doi.org/10.1097/00005650-198903001-00012

Brugnara, C., Schiller, B., & Moran, J. (2006). Reticulocyte hemoglobin equivalent (Ret He) and assessment of iron-deficient states. *Clinical and Laboratory Haematology*, *28*(5), 303–308. https://doi.org/10.1111/j.1365-2257.2006.00812.x

Busti, F., Marchi, G., Ugolini, S., Castagna, A., & Girelli, D. (2018). Anemia and Iron Deficiency in Cancer Patients: Role of Iron Replacement Therapy. *Pharmaceuticals*, *11*(4), 94. https://doi.org/10.3390/ph11040094

Cai, J., Wu, M., Ren, J., Du, Y., Long, Z., Li, G., Han, B., & Yang, L. (2017). Evaluation of the Efficiency of the Reticulocyte Hemoglobin Content on Diagnosis for Iron Deficiency Anemia in Chinese Adults. *Nutrients*, *9*(5), 450. https://doi.org/10.3390/nu9050450

Cappellini, M. D., Comin-Colet, J., de Francisco, A., Dignass, A., Doehner, W., Lam, C. S., Macdougall, I. C., Rogler, G., Camaschella, C., Kadir, R., Kassebaum, N. J., Spahn, D. R., Taher, A. T., Musallam, K. M., & on behalf of the IRON CORE Group. (2017). Iron deficiency across chronic inflammatory conditions: International expert opinion on definition, diagnosis, and management: CAPPELLINI et al. *American Journal of Hematology*, *92*(10), 1068–1078. https://doi.org/10.1002/ajh.24820

Cella, D. (1997). The Functional Assessment of Cancer Therapy-Anemia (FACT-An) Scale: A new tool for the assessment of outcomes in cancer anemia and fatigue. *Seminars in Hematology*, *34*(3 Suppl 2), 13–19.

Cohen-Solal, A., Leclercq, C., Mebazaa, A., De Groote, P., Damy, T., Isnard, R., & Galinier, M. (2014). Diagnosis and treatment of iron deficiency in patients with heart failure: Expert position paper from French cardiologists. *Archives of Cardiovascular Diseases*, *107*(10), 563–571. https://doi.org/10.1016/j.acvd.2014.07.049

Daru, J., Allotey, J., Peña-Rosas, J. P., & Khan, K. S. (2017). Serum ferritin thresholds for the diagnosis of iron deficiency in pregnancy: A systematic review: Serum ferritin for defining iron deficiency in pregnancy. *Transfusion Medicine*, *27*(3), 167–174. https://doi.org/10.1111/tme.12408

Elawamy Hayam Abdalla, Elmhdwi Maraia Farag, Abdulla Sara Ali, Jaber Nesrin Hussin, & Algathafy Khlid Gbril. (2020). Iron deficiency in non-anemic individuals: A retrospective analysis of Libyan population. *GSC Biological and Pharmaceutical Sciences*, *11*(1), 171–179. https://doi.org/10.30574/gscbps.2020.11.1.0088

Elstrott, B., Khan, L., Olson, S., Raghunathan, V., DeLoughery, T., & Shatzel, J. J. (2020). The role of iron repletion in adult iron deficiency anemia and other diseases. *European Journal of Haematology*, *104*(3), 153–161. https://doi.org/10.1111/ejh.13345

Fayers, P. M., & Machin, D. (2000). *Quality of Life: Assessment, Analysis and Interpretation* (1st ed.). Wiley. https://doi.org/10.1002/0470846283

Glaspy, J., Bukowski, R., Steinberg, D., Taylor, C., Tchekmedyian, S., & Vadhan-Raj, S. (1997). Impact of therapy with epoetin alfa on clinical outcomes in patients with nonmyeloid malignancies during cancer chemotherapy in community oncology practice. Procrit Study Group. *Journal of Clinical Oncology*, *15*(3), 1218–1234. https://doi.org/10.1200/JCO.1997.15.3.1218

Hijmans, C. T., Fijnvandraat, K., Oosterlaan, J., Heijboer, H., Peters, M., & Grootenhuis, M. A. (2010). Double disadvantage: A case control study on health-related quality of life in children with sickle cell disease. *Health and Quality of Life Outcomes*, *8*(1), 121. https://doi.org/10.1186/1477-7525-8-121

Hlubocky, F. J., Webster, K., Cashy, J., Beaumont, J., & Cella, D. (2013). The Development and Validation of a Measure of Health-Related Quality of Life for Non-Hodgkin's Lymphoma: The Functional Assessment of Cancer Therapy—Lymphoma (FACT-Lym). *Lymphoma*, *2013*, 1–9. https://doi.org/10.1155/2013/147176

Jonker, F. A. M., te Poel, E., Bates, I., & Boele van Hensbroek, M. (2017). Anaemia, iron deficiency and susceptibility to infection in children in sub-Saharan Africa, guideline dilemmas. *British Journal of Haematology*, *177*(6), 878–883. https://doi.org/10.1111/bjh.14593

Karimi, M., & Brazier, J. (2016). Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *PharmacoEconomics*, *34*(7), 645–649. https://doi.org/10.1007/s40273-016-0389-9

Kassebaum, N. J., Jasrasaria, R., Naghavi, M., Wulf, S. K., Johns, N., Lozano, R., Regan, M., Weatherall, D., Chou, D. P., Eisele, T. P., Flaxman, S. R., Pullan, R. L., Brooker, S. J., & Murray, C. J. L. (2014). A systematic analysis of global anemia burden from 1990 to 2010. *Blood*, *123*(5), 615–624. https://doi.org/10.1182/blood-2013-06-508325

Kirkwood, B. R., Sterne, J. A. C., & Kirkwood, B. R. (2003). *Essential medical statistics* (2nd ed). Blackwell Science.

Lind, M., Vernon, C., Cruickshank, D., Wilkinson, P., Littlewood, T., Stuart, N., Jenkinson, C., Grey-Amante, P., Doll, H., & Wild, D. (2002). The level of haemoglobin in anaemic cancer patients correlates positively with quality of life. *British Journal of Cancer*, *86*(8), 1243–1249. https://doi.org/10.1038/sj.bjc.6600247

Lopez, A., Cacoub, P., Macdougall, I. C., & Peyrin-Biroulet, L. (2016). Iron deficiency anaemia. *The Lancet*, *387*(10021), 907–916. https://doi.org/10.1016/S0140-6736(15)60865-0

Ludwig, H., Evstatiev, R., Kornek, G., Aapro, M., Bauernhofer, T., Buxhofer-Ausch, V., Fridrik, M., Geissler, D., Geissler, K., Gisslinger, H., Koller, E., Kopetzky, G., Lang, A., Rumpold, H., Steurer, M., Kamali, H., & Link, H. (2015). Iron metabolism and iron supplementation in cancer patients. *Wiener Klinische Wochenschrift*, *127*(23–24), 907–919. https://doi.org/10.1007/s00508-015-0842-3

McHorney, C. A., Ware, J. E., Rachel Lu, J. F., & Sherbourne, C. D. (1994). The MOS 36-ltem Short-Form Health Survey (SF-36): III. Tests of Data Quality, Scaling Assumptions, and Reliability Across Diverse Patient Groups: *Medical Care*, *32*(1), 40–66. https://doi.org/10.1097/00005650-199401000-00004

Mittelman, M., Zeidman, A., Fradin, Z., Magazanik, A., Lewinski, U. H., & Cohen, A. (1997). Recombinant Human Erythropoietin in the Treatment of Multiple Myeloma-Associated Anemia. *Acta Haematologica*, *98*(4), 204–210. https://doi.org/10.1159/000203625

Motonishi, S., Tanaka, K., & Ozawa, T. (2018). Iron deficiency associates with deterioration in several symptoms independently from hemoglobin level among chronic hemodialysis patients. *PLOS ONE*, *13*(8), e0201662. https://doi.org/10.1371/journal.pone.0201662

Naoum, F. A. (2016). Iron deficiency in cancer patients. *Revista Brasileira de Hematologia e Hemoterapia*, *38*(4), 325–330. https://doi.org/10.1016/j.bjhh.2016.05.009

Nikzad, Z., Iravani, M., Abedi, P., Shahbazian, N., & Saki, A. (2018). The relationship between iron deficiency anemia and sexual function and satisfaction among reproductive-aged Iranian women. *PLOS ONE*, *13*(12), e0208485. https://doi.org/10.1371/journal.pone.0208485

Nissenson, A. R., & Fine, R. N. (Eds.). (2017). *Handbook of dialysis therapy* (5th edition). Elsevier.

Pasricha, S.-R., Tye-Din, J., Muckenthaler, M. U., & Swinkels, D. W. (2021). Iron deficiency. *The Lancet*, *397*(10270), 233–248. https://doi.org/10.1016/S0140-6736(20)32594-0

Peyrin-Biroulet, L., Williet, N., & Cacoub, P. (2015). Guidelines on the diagnosis and treatment of iron deficiency across indications: A systematic review. *The American Journal of Clinical Nutrition*, *102*(6), 1585–1594. https://doi.org/10.3945/ajcn.114.103366

Philip, K. E. J., Sadaka, A. S., Polkey, M. I., Hopkinson, N. S., Steptoe, A., & Fancourt, D. (2020). The prevalence and associated mortality of non-anaemic iron deficiency in older adults: A 14 years observational cohort study. *British Journal of Haematology*, *189*(3), 566–572. https://doi.org/10.1111/bjh.16409

Rodwell, V. W., Bender, David A, Botham, Kathleen M, Kennelly, Peter J, & Weil, P. Anthony. (2018). *Harper's illustrated biochemistry*. https://accessmedicine.mhmedical.com/book.aspx?bookid=2386

Saad, F., Cella, D., Basch, E., Hadaschik, B. A., Mainwaring, P. N., Oudard, S., Graff, J. N., McQuarrie, K., Li, S., Hudgens, S., Lawson, J., Lopez-Gitlitz, A., Yu, M. K., Smith, M. R., & Small, E. J. (2018). Effect of apalutamide on health-related quality of life in patients with non-metastatic castration-resistant prostate cancer: An analysis of the SPARTAN randomised, placebo-controlled, phase 3 trial. *The Lancet. Oncology*, *19*(10), 1404–1416. https://doi.org/10.1016/S1470-2045(18)30456-X

Sonnweber, T., Nairz, M., Theurl, I., Petzer, V., Tymoszuk, P., Haschka, D., Rieger, E., Kaessmann, B., Deri, M., Watzinger, K., Steringer-Mascherbauer, R., Tancevski, I., Weiss, G., & Löffler-Ragg, J. (2018). The crucial impact of iron deficiency definition for the course of precapillary pulmonary hypertension. *PLOS ONE*, *13*(8), e0203396. https://doi.org/10.1371/journal.pone.0203396

Soudy, H., Maghfoor, I., Elhassan, T. A. M., Abdullah, E., Rauf, S. M., Al Zahrani, A., & Akhtar, S. (2018). Translation and validation of the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) version 4 quality of life instrument into Arabic language. *Health and Quality of Life Outcomes*, *16*(1), 47. https://doi.org/10.1186/s12955-018-0861-7

Steinmetz, H. T. (2012). The role of intravenous iron in the treatment of anemia in cancer patients. *Therapeutic Advances in Hematology*, *3*(3), 177–191. https://doi.org/10.1177/2040620712440071

Stevens, G. A., Finucane, M. M., De-Regil, L. M., Paciorek, C. J., Flaxman, S. R., Branca, F., Peña-Rosas, J. P., Bhutta, Z. A., & Ezzati, M. (2013). Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: A systematic analysis of population-representative data. *The Lancet Global Health*, *1*(1), e16–e25. https://doi.org/10.1016/S2214-109X(13)70001-9

Toxqui, L., & Vaquero, M. (2015). Chronic Iron Deficiency as an Emerging Risk Factor for Osteoporosis: A Hypothesis. *Nutrients*, *7*(4), 2324–2344. https://doi.org/10.3390/nu7042324

Yellen, S. B., Cella, D. F., Webster, K., Blendowski, C., & Kaplan, E. (1997). Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *Journal of Pain and Symptom Management*, *13*(2), 63–74. https://doi.org/10.1016/S0885-3924(96)00274-6

# APPENDIX 1: PARTICIPANT INFORMATION

**Title of Study: Prevalence of Non-Anemic Iron Deficiency in Cancer Patients Before Initiation of Therapy and it's Correlation to Health-Related Quality of Life**

**Principal Investigator:** Aganyo Joseck Mageto, MScN, UoN

**Introduction:**

I would like to tell you about a study being conducted by the above listed researcher. The purpose of this consent form is to give you the information you will need to help you decide whether to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear.

When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. Once you understand and agree to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in medical research:

i) Your decision to participate is entirely voluntary
ii) You may withdraw from the study at any time without necessarily giving a reason for your withdrawal
iii) Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. We will give you a copy of this form for your records.

May I continue? **YES / NO**

This study has approval by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No. **P365/05/2021**

**WHAT IS THIS STUDY ABOUT?**

The researcher listed above is interviewing individuals who are visiting the hospital for the first time to seek cancer treatment. The purpose of the interview is to find out whether one has a form of iron deficiency that may not show in normal hemoglobin test.

A structured questionnaire will be used to obtain information from participants with questions touching on their body-perception for past seven days which will be recorded in a form. Participants will also have the choice to undergo test that requires 2ml (half a teaspoon) amount of blood from the arm. There will be approximately 400 participants in this study randomly selected. We are asking for your consent to consider participating in this study.

## WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

**If you agree to participate in this study, the following things will happen**:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately 20 minutes. The interview will cover topics such as fatigue. After the interview is completed, I will explain in detail how I am going to draw blood.

## ARE THERE ANY RISKS, HARMS DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional, and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be secure.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview, or any questions asked during the interview.

It may be somewhat painful for you to have blood drawn from the vein in the arm. We will do everything we can to ensure that this is done professionally. Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews. Also, some questions about your feelings may be repetitive.

In case of an injury, related to this study, contact the study staff right away at the number provided at the end of this document. The study staff will treat you for minor conditions or refer you when necessary.

## ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may benefit by receiving free counselling, testing, and health information. We will refer you to the clinic for care and support where necessary. Also, the information you provide will help us better understand more about your general state of health. This information is a contribution to science and patient care.

## WILL BEING IN THIS STUDY COST YOU ANYTHING?

Being in this study will not cost you any money.

**WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?**

There will be no money given to any participant for engaging in this study the participant will also not spend any money in the study.

**WHAT IF YOU HAVE QUESTIONS IN FUTURE?**

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

**WHAT ARE YOUR OTHER CHOICES?**

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice.

## APPENDIX 2: CONSENT FORM (STATEMENT OF CONSENT)

**Participant's statement**

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study.

I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

**I agree to participate in this research study: Yes No**

**Participant printed name:**

_____

Participant signature / Thumb stamp _____Date_____

**Researcher's statement**

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

**Researcher's Name**: _____

Date: _____ Signature_____

**Role in the study: _____ (i.e., study staff who explained informed consent form.)**

**For more info contact.** Joseck Aganyo Mageto at UoN June to Sept 2021

**Witness Printed Name (A witness is a person mutually acceptable to both the researcher and participant)**

Name _____ Contact information_____

Signature /Thumb stamp: _____ Date_____

# APPENDIX 3: FOMU YA MAELEZO YA UKUSANYAJI DATA

**Mtafiti mkuu:** Joseck Aganyo Mageto nambari: 0724454538
**Kutoka**: Chuo Kikuu Cha Nairobi.
**Mchakato wa utafiti wa kiwango cha upungufu wa madini iron kwa wagonjwa wenye ugonjwa wa saratani, na athari zake kwa ustawi wa kafya**
**Maelezo kwa Mkusanyaji wa data**
Utafiti huu ni wa kutazama kama mtu ana upungufu wa madini ya iron mwilini na jinsi hayi hiyo inathiri ustawi wake kiafya. Hii utafiti inasajiri watu ambao bado hawajaanza matibabu ya dawa zetu au matibabu ya miale ya radiation. Kila msajiliwa anahitaji angalau awe na majibu ya majaribio ya damu CBC na ripoti ya ugonjwa wa saratani kabla ya kuanza mahojiano.
Wakati wa kusoma maswali, wakusanyaji data wanapaswa kutumia maandishi yote ya mwongozo kwenye fomu hii na kuuliza maswali jinsi yanavyoorodheshwa hapa.
Kwa kurekodi data, wakusanyaji wa data wanaweza kuchagua kuingiza majibu ya mshiriki moja kwa moja kwenye toleo la matandaoni au waweke alama kwenye toleo hili la karatasi na kuhamisha majibu kwenye toleo la matandaoni baadaye. Bila kujali chaguo lako, unapaswa kupea kila mshiriki nakala yake ya fomu ya idhini (hakuna haja ya saini yao, lakini ni muhimu kupitia mchakato mzima wa idhini).
**Maandishi ya kusimulia** yamepeanwa kwa mkusanyaji wa data kutanguliza maswali fulani au kuelezea chaguzi kadhaa za majibu na nilazima mshiriki asomewe. Maandishi haya yanatangulizwa na maneno **Maandishi ya kusimulia** na yameandikwa na *muundo wa kulala.*
***{Maagizo ya mkusanyaji data} yameorodheshwa kila wakati kwa mabano haya* {}.**
Kwa hali yoyote, majina, nambari za simu, anwani au habari nyingine yoyote inayoweza kutambulisha mshiriki haiwezi kurekodiwa kwenye waraka huu (iwe kama majibu ya maswali au maoni mengine yoyote).
Unapowasiliana kupitia simu ama ujumbe mfupi na mtu yeyote mwenye nia ya kushiriki na angetaka usaidizi, tafadhali fuata mwongozo huu: **mfahamishe mshiriki utampigia kwa nambari hiyo yake ili kuokoa pesa zake za rununu. Ikiwa uko na shughuli ingine na huwezi kupiga simu mara moja, panga na yeye wakati utakaompigia.**

**Mchakato wa idhini ya kufanya uchunguzi**

Tafadhali kumbuka kuwa katika sehemu hii, ni muhimu kuelezea mchakato wa uchunguzi kwa washiriki, kuhakikisha wanaelewa juu ya hatari zozote za kushiriki na jinsi data zao zitatumika. Kwa kuweka rekodi ya idhini, hatutamuuliza mshiriki kutia saini kwenye fomu, lakini tutawauliza wajibu "nakubali" au "Sitakubali" mwisho wa mchakato wa idhini. **Unapaswa kuendelea kwa hatua inayofuata ikiwa mshiriki ametoa idhini yake.**

***Maandishi ya kusimulia:*** *Asante kwa kutaka kushiriki kwa uchunguzi wetu! Kusudi la utafiti huu ni kutaka kujua kama wagonjwa wa saratani wanadhihirisha dalili zozote za ukosefu wa madini ya iron mwilini na kama ukosefu huo umeweza kuathiri ustawi wake wa kiafya. Tutazungumza na watu wengi wenye wako katika hali kama yako na tutatayarisha ripoti ya matokeo ya utafiti.Tutashiriki ripoti ya utafiti huu na wale wanaofanya kazi ya udhibiti wa saratani nchini Kenya. Kusudi letu ni kwamba matokeo ya ripoti hii itatumiwa kuboresha hali ya wagonjwa wa saratani kama wewe.*

**kwa ukusanyaji wa data kupitia mahojiano ya moja-kwa-moja: kwa sasa, tafadhali mpe mhusika nakala yake ya fomu ya idhini iliyochapishwa ambayo anaweza kutumia kufuata wakati unaisoma.**

***Maandishi ya kusimulia: (kuendelea):***

Ningependa kukujulisha kuhusu utafiti unaofanywa na mtafiti aliyeorodheshwa hapo juu. Madhumuni ya fomu hii ya idhini ni kukupa habari utakayohitaji kukusaidia kuamua ikiwa utashiriki au hautashiriki katika utafiti huu. Jisikie huru kuuliza maswali yoyote kuhusiana na madhumuni ya utafiti, nini kitatokea ikiwa unashiriki katika utafiti, hatari na faida zinazoweza kutokea kwa kushiriki, haki zako kama mwenye amejitolea kushiriki, na kingine chochote juu ya utafiti au fomu hii ambacho hautaelewa. Tukijibu maswali yako yote na kukuridhisha, unaweza kuamua kushiriki kwenye utafiti au la. Utaratibu huu unaitwa 'idhini yenye habari'. Unapaswa kuelewa kanuni za jumla ambazo zinatumika kwa washiriki wote wa utafiti: i) Uamuzi wako wa kushiriki ni wa hiari kabisa ii) Unaweza kujiondoa kwenye utafiti wakati wowote bila kutoa sababu ya kujitoa kwako iii) Kukataa kushiriki katika utafiti hakutaathiri huduma unazostahiki katika kituo cha afya au vituo vingine.

NAWEZA ENDELEA? **Ndio / la**

**{Mkusanyaji data, endelea tu ikiwa jibu ni ndio}**

***Maandishi ya kusimulia***: Utafiti huu umeidhinishwa na Kamati ya Maadili na Utafiti ya Hospitali ya Kitaifa ya Kenyatta na Chuo Kikuu cha Nairobi itifaki nambari._____

**UTAFITI HUU UNAHUSU NINI?**
Huu ni utafiti wa kuchunguza kama wagonjwa wa saratani wanadhihirisha ukosefu wa madini ya iron kwa mwili na kama hiyo limeathiri ustawi wao wa kiafya. Utafiti huu unapanga kuhoji takriban wagonjwa 200 wa saratani kutoka kote Kenya. Tutashiriki ripoti ya uchunguzi na wale wanaofanya kazi ya udhibiti wa saratani nchini Kenya. Tafadhali endelea ikiwa:

i. Wewe ni mgonjwa wa saratani ama daktari amekwambia ya kwamba unaweza kuwa na saratani
ii. Wewe ni mtu mzima kisheria (miaka 18 au zaidi), na
iii. Wewe in mkazi wa Kenya.

Ikiwa haujatimiza vigezo vyote hapo juu, tafadhali usiendelee.

**NINI KITATOKEA UKIAMUA KUSHIRIKI KWENYE UTAFITI HUU?**
Ukikubali kushiriki, tutakuuliza maswali kadhaa kukuhusu (kama vile umri wako, aina ya saratani ambayo unaweza kuwa nayo n.k.). Tutakuuliza kuhusu jinsi umekuwa ukijijihisi mwilini kwaa mda wa wikim mbili zilizopita.

*Hatutakuuliza* habari yoyote ya kibinafsi, kama vile jina lako, tarehe ya kuzaliwa, au habari yoyote ya kuwasiliana nawe kama vile nambari ya simu.

Utafiti huu unapaswa kukuchukua takriban dakika 20 kukamilisha.
KUNA ATHARI, MADHARA AU HASARA ZOZOTE ZINAZOHUSIANA NA UTAFITI HUU?
Kushiriki katika uchunguzi huu kuna hatari kidogo sana kwako. Hatari kuu ni kwamba mtu anaweza kujua kuwa umeitikia kushiriki katika uchunguzi huu. Ili kupunguza hatari hii, hatutakuuliza habari yoyote ambayo inaweza kukutambulisha.

**Majibu yako yasiyokutambulisha yatahifadhiwa kwenye fomu zetu hapa Hospitali ya Kitaifa ya Kenyatta**

Tutahifadhi majibu kwa angalau miaka mitatu. *Tafadhali kumbuka kuwa, utakapowasilisha majibu yako, hatutaweza kuyafuta kwa sababu hatutakuwa na njia yoyote ya kutambua majibu yako.*

**Tutashiriki matokeo ya utafiti huu kwa upana nchini Kenya na Kimataifa.**
Tutashiriki matokeo ya utafiti huu na serikali na mashirika yanayohusika na kazi ya udhibiti wa saratani. Tunaweza pia kuchapisha matokeo katika majarida au kuwasilisha kwenye mikutano.

***{Ngojea kidogo hapa, uliza mshiriki kama ako na swali lolote na umjibu ikiwa ako nalo. Endelea na uchunguzi ukiwa tayari kuendelea}***

KUNA FAIDA YOYOTE KUSHIRIKI KATIKA UTAFITI HUU?
**Hautapokea fidia au faida yoyote ya kibinafsi ukishiriki utafiti.**

Hatutakupa fidia au faida yoyote ya kibinafsi ukikamilisha utafiti huu. Lakini matokeo ya utafiti yanaweza kufaidi wagonjwa wa saratani kama wewe katika siku zijazo.

**JE, UTARUDISHIWA PESA YOYOTE UTAKAYOTUMIWA KATIKA SEHEMU YOYOTE YA UTAFITI HUU?**
Utafiti huu hauhitaji au kutarajia utumie pesa yoyote kwa sehemu yoyote ya utafiti, na kwa hivyo hakutakuwa na marejesho yoyote ya pesa.

**JE, KUSHIRIKI UTAFITI HUU KUNA GHARAMA YOYOTE?**
Kushiriki katika utafiti huu hakutakugharimu chochote isipokuwa muda wako wa takriban dakika 25.

**NA UKIWA NA MASWALI ZAIDI BAADAYE?**
Ukitaka kujua zaidi kuhusu utafiti huu au una maswali yoyote, tafadhali wasiliana na:

**Joseck Aganyo Mageto**, **Chuo Kikuu cha Nairobi**. **Nambari ya simu: 0724454538**

Katibu wa Kamati ya Maadili na Utafiti ya KNH-UoN – Nambari ya simu: +2542726300 ext. 44102, Barua pepe: uon_knherc@uonbi.ac.ke

**UKO NA CHAGUO GANI ZINGINE?**
**Kushiriki kwa utafiti huu ni kwa hiari na hakuna matokeo mabaya ukiamua kutoshiriki.**
Ushiriki wako katika utafiti huu hautaathiri kwa njia yeyote matibabu yako, msaada, au huduma zingine unazopokea sasa au unazoweza kupokea katika siku zijazo. Mimi ama mtu mwingine yeyote anayewasiliana nawe juu ya uchunguzi huu hapati fidia yoyote kwa idadi ya watu anaowaalika kukamilisha uchunguzi**.**
Ukiamua kutoshiriki uchunguzi - hiyo ni sawa. Funga ukurusa huu kama unajaza kwa mtandao kwa simu ama kompyuta. Kama mtu anakusaidia kukamilisha uchunguzi, mwambie hutaki kuendelea na atasitisha mahojiano.

Asante!
***{Ngojea kidogo hapa, uliza mshiriki kama ako na swali lolote na umjibu ikiwa ako nalo. Endelea na uchunguzi ukiwa tayari kuendelea}***
***{*Ikiwa mko na mshiriki hapo, mpatie fomu hii iliyochapishwa, mwambie kuwa kila kitu ambacho umesoma kiko kwenye fomu hiyo. Mweleze habari ya mawasiliano yenye yako chini ya fomu na umwarifu kuwa ikiwa ana maswali yoyote anaweza wasiliana na waandaaji wa uchunguzi**

## APPENDIX 4: IDHINI YA MSHIRIKI

***Maandishi ya kusimulia:*** Sasa nitakuuliza maswali mawili kuhusu idhini yako ya kushiriki. Tafadhali jibu ndio au hapana
**Je! Unaelewa kuwa uko na haki ya kujibu au kutojibu maswali yote kwenye utafiti huu, na chaguo lako halitaathiri matibabu yako au huduma zingine ambazo unapokea?**
Hapana {muulize mshiriki ikiwa unaweza kufafanua chochote}
Ndio {endelea kwa swali linalofuata}

**Je! Unakubali kushiriki kwenye utafiti huu?**
Hapana {Shukuru mshiriki na utamatize uchunguzi}
Ndio {endelea kwa hatua ya pili}
**Participant printed name: _____**

**Participant signature / Thumb stamp _____Date_____**

**Researcher's statement**
I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

**Researcher's Name: _____Date: _____**

**Signature_____ Role in the study: _____**

**(i.e., study staff who explained informed consent form.)**
**Joseck Aganyo Mageto**, **Chuo Kikuu cha Nairobi**. **Nambari ya simu: 0724454538**

Witness Printed Name (A witness is a person mutually acceptable to both the researcher and participant)
**Name _____ Contact information_____**

**Signature /Thumb stamp: _____Date_____**

*{Tafadhali kumbuka kuwa HATUMUULIZI mshiriki kusaini fomu ya idhini kwa kuwa hatutakusanya ushahidi wowote wa ushiriki wao ili kulinda habari yao ya kibinafsi inayoweza kuwatambulisha. Lakini, ni lazima mkusanyaji wa data aachie mshiriki nakala iliyochapishwa (isiyo kuwa na saini) ya fomu ya idhini. Kwa ukusanyaji wa data kupitia kwa simu, ni lazima mkusanyaji data aeleze mshiriki ni wapi anaweza kuchukua fomu ya idhini.}*

## APPENDIX 5: THE QUESTIONNAIRE

SECTION A: SOCIAL DEMOGRAPHIC DATA

STUDY ID
Interviewer's name _____ Date (DD/MM/YYYY)

Hemoglobin

Diagnosis _____
Grade of disease _____
Stage of disease _____

SECTION 1 Identification Information

| | | |
|---|---|---|
| A1 | **What is your gender?** | □ Male<br>□ Female |
| A2 | **What is your County?** | _____ |
| A3 | **What is your Religion?** | □ Islam/Muslim □ Christianity/Christian<br>□ Hindu □ None |
| A4 | **Are you (informant) married?** | □ Yes<br>□ No |
| A5 | **What is your Occupation?** | □ Employed □ Trade □Unemployed<br>□Student □Others |
| A6 | **What was the highest level of schooling that you completed?** | □Primary □ Secondary □College<br>□University<br>□Madrassa □None |

## SECTION B: FUNCTIONAL ASSESSMENT OF CANCER THERAPY – ANEMIA (FACT-AN)

**PATIENT POPULATION: Cancer patients 18 years and older without anemia**
**RECALL PERIOD: Past 7 days**
**RESPONSE SCALE: 5-point Likert-type scale**
**ADMINISTRATION: Interview**
**SUBSCALE DOMAINS: Physical Well-Being,**
**Social/Family Well-Being,**
**Emotional Well-Being,**
**Functional Well-Being,**
**Anemia Subscale**
**TIME FOR COMPLETION: 10-15 minutes**
**SCORING: Manual scoring template, some items are reverse scored.**

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 past 7 days.**

| | **PHYSICAL WELL-BEING** | **Not at all** | **A little bit** | **Some-what** | **Quitea 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 | Quitea 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 |

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

| | ADDITIONAL CONCERNS | Not at all | A little bit | Some -what | Quite a bit | Very much |
|---|---|---|---|---|---|---|
| HI7 | I feel fatigued | 0 | 1 | 2 | 3 | 4 |
| HI12 | I feel weak all over | 0 | 1 | 2 | 3 | 4 |
| An1 | I feel listless ("washed out") | 0 | 1 | 2 | 3 | 4 |
| An2 | I feel tired | 0 | 1 | 2 | 3 | 4 |
| An3 | I have trouble <u>starting</u> things because I am tired | 0 | 1 | 2 | 3 | 4 |
| An4 | I have trouble <u>finishing</u> things because I am tired | 0 | 1 | 2 | 3 | 4 |
| An5 | I have energy | 0 | 1 | 2 | 3 | 4 |
| An6 | I have trouble walking | 0 | 1 | 2 | 3 | 4 |
| An7 | I am able to do my usual activities | 0 | 1 | 2 | 3 | 4 |
| An8 | I need to sleep during the day | 0 | 1 | 2 | 3 | 4 |
| An9 | I feel lightheaded (dizzy) | 0 | 1 | 2 | 3 | 4 |
| An10 | I get headaches | 0 | 1 | 2 | 3 | 4 |
| B1 | I have been short of breath | 0 | 1 | 2 | 3 | 4 |
| An11 | I have pain in my chest | 0 | 1 | 2 | 3 | 4 |
| An12 | I am too tired to eat | 0 | 1 | 2 | 3 | 4 |
| BL4 | I am interested in sex | 0 | 1 | 2 | 3 | 4 |
| An13 | I am motivated to do my usual activities | 0 | 1 | 2 | 3 | 4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| An14 | **I need help doing my usual activities** | 0 | 1 | 2 | 3 | 4 |
| An15 | **I am frustrated by being too tired to do the things I want to do** | 0 | 1 | 2 | 3 | 4 |
| An16 | **I have to limit my social activity because I am tired** | 0 | 1 | 2 | 3 | 4 |

# APPENDIX 6: QUESTIONNAIRE (SWAHILI VERSION)

**KITENGO A: Takwimu Za Kijamii**

**Nambari ya utafiti**
**Jina la mtafiti** _____ **Tarehe (DD/MM/YYYY)**

**Hemoglobini**

**Utambuzi** _____
**Gredi ya ugonjwa** _____
**Stegi ya ugonjwa** _____

**KITENGO A: Takwimu Za Kijamii**

| | | |
|---|---|---|
| **A1** | **Jinsia?** | □ Mume<br>□ Mke |
| **A2** | **Kaunti** | _____ |
| **A3** | **Dini?** | □ Muislamu □ Mkristo<br>□ Mhindi □ Nyingine |
| **A4** | **Je umeolewa?** | □ Ndio<br>□ La |
| **A5** | **Je unafanya kazi Gani** | □Nimeajiriwa □Biashara □Sina Kazi<br>□ Mwanafunzi □Nyingine |
| **A6** | **Kiwango cha juu cha elimu?** | □ Primari □Shule Ya Upili □ College<br>□ Chuo Kikuu<br>□ Hakuna □ Madrassa |

## KITENGO B: FUNCTIONAL ASSESSMENT OF CANCER THERAPY – NON-ANEMIA (FACT-AN)

**WASHIRIKI: wagonjwa wa saratani waliozidi miaka 18 wasio na upungufu wa damu**
**KIPINDI CHA KUKUMBUKA: siku saba zilizopita**
**WAKATI WA KUKAMILISHA: dakika 10-15**
**KIWANGO CHA MAJIBU: nukta tano**
**MCHAKATO: Mahojiano**

**VIKOA VYA MASWALI: Ustawi wa kimwili**
**Ustawi wa kazi**
**Ustawi wa utambuzi**

Kauli zilizotolewa na watu wengine ambao wanaugua ugonjwa wa saratani zinafuatia hapa chini**.Onyesha majubu yako kwa kuweka alama ya duara kwa nambari inayoambatana na kauli yako kwa siku 7 zilizopita.**

| | **USTAWI WA KIMWILI** | **Hapana kabisa** | **Kidogo tu** | **Kiasi fulani** | **kabisa** | **Sana kabisa** |
|---|---|---|---|---|---|---|
| GP1 | **Sina nguvu** | 0 | 1 | 2 | 3 | 4 |
| GP2 | **Nina kichefuchefu** | 0 | 1 | 2 | 3 | 4 |
| GP3 | **Kwa sababu ya hali yangu ya afya nina ugumu kukidhi mahitaji ya familia** | 0 | 1 | 2 | 3 | 4 |
| GP4 | **Nina maumivu** | 0 | 1 | 2 | 3 | 4 |
| GP5 | **Nasumbuliwa na athari za matibabu** | 0 | 1 | 2 | 3 | 4 |
| GP6 | **Najiskia mgonjwa** | 0 | 1 | 2 | 3 | 4 |
| GP7 | **Ninalazimika kutumia mda kitandani** | 0 | 1 | 2 | 3 | 4 |

| | **USTAWI WA KIKAZI** | **Hapana kabisa** | **Kidogo tu** | **Kiasi fulani** | **kabisa** | **Sana kabisa** |
|---|---|---|---|---|---|---|

| | | | | | | |
|---|---|---|---|---|---|---|
| GF1 | **Nina uwezo wa kufanya kazi** | 0 | 1 | 2 | 3 | 4 |
| GF2 | **Kazi yangu inatimiza** | 0 | 1 | 2 | 3 | 4 |
| GF3 | **Nina uwezo wa kufurahia maisha** | 0 | 1 | 2 | 3 | 4 |
| GF4 | **Nimekubali ugonjwa wangu** | 0 | 1 | 2 | 3 | 4 |
| GF5 | **Ninalala vizuri** | 0 | 1 | 2 | 3 | 4 |
| GF6 | **Ninafurahia vitu ambavyo kawaida hufanya kuwa najufurahia** | 0 | 1 | 2 | 3 | 4 |
| GF7 | **Nimeridhika ana ubora wa Maisha yangu hivi sasa** | 0 | 1 | 2 | 3 | 4 |

| | USTAWI WA UTAMBUZI | Hapana kabisa | Kidogo tu | Kiasi fulani | kabisa | Sana kabisa |
|---|---|---|---|---|---|---|
| HI7 | **Ninahisi nina uchovu** | 0 | 1 | 2 | 3 | 4 |
| HI12 | **Ninajihisi dhaifu** | 0 | 1 | 2 | 3 | 4 |
| An1 | **Najisikia kuwa bila orodha** | 0 | 1 | 2 | 3 | 4 |
| An2 | **Nahisi nimechoka** | 0 | 1 | 2 | 3 | 4 |
| An3 | **Nina shida kuanza vitu kwa sababu nimechika** | 0 | 1 | 2 | 3 | 4 |
| An4 | **Nina shida kumaliza vitu kwa sababu nimechoka** | 0 | 1 | 2 | 3 | 4 |
| An5 | **Nina nguvu** | 0 | 1 | 2 | 3 | 4 |
| An6 | **Nina shida kutembea** | 0 | 1 | 2 | 3 | 4 |
| An7 | **naweza fanya shughuli za kawaida** | 0 | 1 | 2 | 3 | 4 |
| An8 | **Nahitaji kulala mchana** | 0 | 1 | 2 | 3 | 4 |
| An9 | **Nahisi kizunguzungu** | 0 | 1 | 2 | 3 | 4 |
| An10 | **Huwa Napata maumivu ya kichwa** | 0 | 1 | 2 | 3 | 4 |
| B1 | **Huwa nashindwa kupumua** | 0 | 1 | 2 | 3 | 4 |
| An11 | **Nina uchungu kwa kifua** | 0 | 1 | 2 | 3 | 4 |
| An12 | **Nimechoka sana kula** | 0 | 1 | 2 | 3 | 4 |
| BL4 | **I am interested in sex** | 0 | 1 | 2 | 3 | 4 |
| An13 | **Nina motisha kufanya shughuli za kawaida** | 0 | 1 | 2 | 3 | 4 |
| An14 | **Nahitaji msaada kufanya shuguli za kawaida** | 0 | 1 | 2 | 3 | 4 |
| An15 | **Nimefadhaia kuchoka kufanya shughuli zangu** | 0 | 1 | 2 | 3 | 4 |
| An16 | **Nina mipaka kufanya kazi zangu kutona na uchovu** | 0 | 1 | 2 | 3 | 4 |

# APPENDIX 7: FACIT TOOL LICENSE


*PROVIDING A VOICE FOR PATIENTS WORLDWIDE*

## FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY (FACIT) LICENSING AGREEMENT

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Name ("Licensee"): University of Nairobi/ Joseck Aganyo

Measurement: FACT-An Language(s): English

Study Title ("Study"): PREVALENCE OF NON-ANEMIC IRON DEFICIENCY IN CANCER PATIENTS BEFORE INITIATION OF THERAPY AND IT'S CORRELATION TO QUALITY OF LIFE

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**Signature:** Aganyo Joseck (Aug 2, 2021 20:08 GMT+3)

**Email:** aganyomj@students.uonbi.ac.ke

# APPENDIX 8: KNH-UON ERC APPROVAL LETTER

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/293

26th August , 2021

Joseck Aganyo Mageto
Reg. No.H56/34056/2019
School of Nursing Sciences
College of Health Sciences
University of Nairobi

26 AUG 2021

Dear Joseck

**RESEARCH PROPOSAL: PREVALENCE OF NON-ANEMIC IRON DEFICIENCY IN CANCER PATIENTS BEFORE INITIATION OF THERAPY AND ITS CORRELATION TO HEALTH-RELATED QUALITY OF LIFE (P365/05/2021)**

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH-UoN ERC) has reviewed and approved your above research proposal. The approval period is 26th August 2021 – 25th August 2022.

This approval is subject to compliance with the following requirements:

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



2.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

**PROF. M.L CHINDIA**
**SECRETARY, KNH- UoN ERC**

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Director, School of Nursing Sciences, UoN
Supervisors: Dr.Angeline Kirui, School of Nursing Sciences, UoN
Dr.Mary Kamau, School of Nursing Sciences, UoN



3.

# APPENDIX 9: AUTHORIZATION LETTER TO CONDUCT STUDY IN CTC

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

## Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   JOSECK AGANYO MAGETO
2. Email address: gganyomj@students-uonbi.ac.ke Tel No. 0724454538
3. Contact person (if different from PI) N/A
4. Email address: N/A Tel No. .....
5. Study Title
   Prevalence of Non-anemic iron deficiency in cancer patients before initiation of therapy and its correlation to Health-related quality of life.
6. Department where the study will be conducted Cancer Treatment Centre
   *(Please attach copy of Abstract)*
7. Endorsed by KNH Head of Department where study will be conducted.
   Name: Dr Catherine Nyongesa Signature ..... Date 1/9/2021
   KENYATTA NATIONAL HOSPITAL HEAD OF DEPARTMENT CANCER TREATMENT CENTRE MEDICAL RECORDS NAIROBI
8. KNH UoN Ethics Research Committee approved study number P365/05/2021
   *(Please attach copy of ERC approval)*
9. I Joseck Aganyo Mageto commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.
   Signature ..... Date 1st Sept 2021
10. Study Registration number (Dept/Number/Year) CTC 1/20/2021
    (To be completed by Medical Research Department)
11. Research and Program Stamp
    KENYATTA NATIONAL HOSPITAL 13 SEP 2021 P.O. Box 20723 Research & Programs

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Medical Research and investigators **must commit** to share results with the hospital.

# APPENDIX 10: AUTHORIZATION LETTER TO CONDUCT STUDY IN LAB

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

## Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   Joseck Agantyo Mageto
2. Email address: agantomj@students.uonbi.ac.ke Tel No. 0724454588
3. Contact person (if different from PI) N/A
4. Email address: N/A Tel No.
5. Study Title
   Prevalence of non-anemic iron deficiency in Cancer patients before initiation of therapy and its correlation to health related quality of life.
6. Department where the study will be conducted Ofc to Medical Laboratory
   *(Please attach copy of Abstract)*
7. Endorsed by KNH Head of Department where study will be conducted.
   Name: Dr Mungania M Signature [signature] Date 3/9/21
8. KNH UoN Ethics Research Committee approved study number P365/05/2021
   *(Please attach copy of ERC approval)*
9. I Joseck Agantyo Mageto commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.
   Signature [signature] Date 1st Sept 2021
10. Study Registration number (Dept/Number/Year) LAB Medicine 1125/2021
    (To be completed by Medical Research Department)
11. Research and Program Stamp KENYATTA NATIONAL HOSPITAL 13 SEP 2021

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Medical Research and investigators **must commit** to share results with the hospital.

4.

## APPENDIX 11: BUDGET

| Item | Unit | Unit cost | Total cost |
|---|---|---|---|
| **INITIAL COST** | | | |
| Purchase of printing papers | 4 rims | 500 | 2,000 |
| ERC proposal processing fee | | | 2,000 |
| Minor Stationaries | | | 1,500 |
| Total | | | **5,500** |
| **DATA HANDLING** | | | |
| Data collection research assistant | | | 20,000 |
| Development of a data base | | | 1,500 |
| Data entry | | | 3,500 |
| Data analysis/ statistician | | | 20,000 |
| Total | | | **45,000** |
| **LABORATORY** | | | |
| Reticulocyte hemoglobin concentration | 100 | 375 | 37,500 |
| Phlebotomy kits | 200 | | 2,500 |
| Total | | | **32,500** |
| **DISSEMINATION OF THE RESULTS** | | | |
| Binding of final thesis | 4 copies | 1,000 | 4,000 |
| Total | | | **4,000** |
| Contingency (10%) | | | **9450** |
| **GRAND TOTAL** | | | **101,500** |

## APPENDIX 12: STUDY TIMELINES

| Time / Activity | Feb | March | April | May | June | July | Aug | Sept |
|---|---|---|---|---|---|---|---|---|
| Concept development | | | | | | | | |
| Proposal writing and presentation | | | | | | | | |
| Ethical approval | | | | | | | | |
| Pretesting of study tools | | | | | | | | |
| Data collection and Data analysis | | | | | | | | |
| Report presentation | | | | | | | | |
| Results dissemination | | | | | | | | |

## APPENDIX 13: SIMILARITY INDEX REPORT

PREVALENCE OF NON-ANEMIC IRON DEFICIENCY IN CANCER PATIENTS BEFORE INITIATION OF THERAPY AND IT'S CORRELATION TO HEALTH-RELATED QUALITY OF LIFE

ORIGINALITY REPORT

| 9% | 7% | 6% | 2% |
|---|---|---|---|
| SIMILARITY INDEX | INTERNET SOURCES | PUBLICATIONS | STUDENT PAPERS |

PRIMARY SOURCES

| | | |
|---|---|---|
| 1 | worldwidescience.org<br>Internet Source | 1% |
| 2 | link.springer.com<br>Internet Source | <1% |
| 3 | www.mdpi.com<br>Internet Source | <1% |
| 4 | www.ncbi.nlm.nih.gov<br>Internet Source | <1% |
| 5 | Recombinant Human Erythropoietin (rhEPO) in Clinical Oncology, 2008.<br>Publication | <1% |
| 6 | Ludwig, H., E. Muldur, G. Endler, and W. Hubl. "Prevalence of iron deficiency across different tumors and its association with poor performance status, disease status and anemia", Annals of Oncology, 2013.<br>Publication | <1% |
| 7 | Submitted to Universiti Teknologi MARA | |