PHARMA COLLEGE

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HAWASSA CAMPUS

DETERMINANTS OF DELAYED TIME TO TREATMENT INITIATION AMONG PATIENTS WITH COLORECTAL CANCER AT HAWASSA UNIVERSITY COMPREHENSIVE SPECIALIZED HOSPITAL, SIDAMA REGION, SOUTHERN ETHIOPIA: A RETROSPECTIVE COHORT STUDY.

BY

DERESSE DAKA

JULY, 2025

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HAWASSA ETHIOPIA

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Table of contents

List of tables

List of figures

Abbreviations/acronym

AOR: Adjusted odds ratio

ASCO: American Society of Clinical Oncology

CI: Confidence interval

CRC: Colorectal cancer

DM: Diabetes mellites

GLOBOCAN: Global Cancer Observatory

DTTI: Delayed time treatment initiations

FAP: Familial adenomatous polyposis

HTN: Hypertension

HIV: Human immunodeficiency virus

HR: Hazard ratio

HUCSH: Hawassa University comprehensive specialized hospital

LMICs: Low- and middle-income countries

NCCN: National Comprehensive Cancer Network

NHS: National Health Service

SDG: Sustainable development

SSA: Sub-Sharan Africa

TTI: Treatment initiation

TV: Television

WHO: World Health Organization

ABSTRACT

Background: Colorectal cancer (CRC) is a prevalent cancer in Ethiopia, with an estimated 3,347 new cases in 2022. The disease is projected to rise to 2.2 million new cases and 1.1 million deaths by 2030. Delays in treatment can lead to disease progression, complications, and increased healthcare costs. This study aimed to address the gap in availability of local evidence on delayed treatment initiation among CRC patients, by examining how patient-related, health system, and socioeconomic barriers interact in resource-limited settings.

Objective: This study aims to identify the determinants of delayed treatment initiation among patients with CRC at Hawassa University Comprehensive Specialized Hospital, Sidama Regional state, Southern Ethiopia

Methods: A retrospective cohort study was conducted at HUCSH, analyzing the time to dalliance of treatment initiation for colorectal cancer patients diagnosed and treated. The study included 469 participants, covering the period from May 1, 2017 to April 30, 2025. The analysis focused on baseline characteristics and dependent variables, categorizing patients as delayed or not delayed. The study used logistic regression to determine the net effect of each explicatory variable on treatment initiation time.

Result: Of the 469 CRC patients, the overall incidence of delayed treatment initiation was 77.2% (95% CI, 73.37, 81.00) with median time of 130 days. In this study different predictors were identified: married individuals (AOR=3.71), rural residents (AOR=2.11), and lack of health insurance was associated with increased risk (AOR=2.41). Additionally, rectal tumor site (AOR=8.00), TNM stage III disease (AOR=0.91), and elective surgery (AOR=21.16) were independent predictors of treatment initiation delay of ≥60 days.

Conclusion: This study revealed a high rate of delayed treatment initiation among colorectal cancer patients, driven by factors such as marital status, rural residence, lack of health insurance, rectal tumor site, and elective surgery. Interestingly, Stage III patients were less likely to face delays, possibly due to prioritization. The unexpected delay among married individuals

underscores the influence of local context. Overall, the findings remind us expand insurance coverage, health access, and optimize surgical scheduling to reduce delays among CRC patients.
Keywords: Colorectal Cancer, Treatment Delay, Time to Treatment Initiation, Retrospective Cohort Study, Sidama Region

1. Introduction

1.1. Background

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells, known as metastasis. It can originate in virtually any organ or tissue of the body, and the spread of these abnormal cells can lead to the formation of new tumors in other parts of the body. The most common cancers are colon and rectum, breast, lung and prostate cancers(1).

Colorectal cancer (CRC), also known as bowel cancer, is a type of cancer that develops in the colon or rectum, which are parts of the large intestine. It typically starts as benign growths called polyps that can become cancerous over time (2). CRC is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases and is the second leading cause of cancer-related deaths worldwide(3). With aging populations and advances in diagnostics and therapies, the number of cancer patients has increased, putting pressure on the cancer care system and highlighting its growing importance(4).

In 2020, CRC caused approximately 935,000 deaths globally, with 1.93 million new cases diagnosed (5). By 2030, the burden of CRC is projected to rise to 2.2 million new cases and 1.1 million deaths, driven by population growth, aging, and economic development(6). Between 2010 and 2019, Africa experienced a significant increase in CRC incidence and mortality rates, with cases rising by 48% and deaths by 41%(6). The prognosis for CRC is heavily dependent on the stage at diagnosis—early detection significantly improves survival rates, whereas late-stage diagnosis often results in poor outcomes and increased mortality(3).

Despite improvements in screening and treatment, CRC outcomes reveal significant disparities. Countries with high incomes have experienced a decrease in both incidence and mortality rates due to successful screening initiatives. In contrast, many LMIC, along with younger populations, are witnessing an increase in both incidence and mortality rates(3). Projections suggest that the global burden of CRC will continue to rise, with an anticipated 3.2 million new cases and 1.6 million deaths each year by 2040—representing increases of 63% and 73%, respectively(7).

In Ethiopia, CRC is among the top three most common cancers, with an estimated 3,347 new cases in men and 3,204 in women reported in 2022(8). Ethiopia has experienced an increasing burden of CRC, with a mortality rate of 40.5% among affected patients, underscoring gaps in early diagnosis and management(9). In 2020, CRC was a major contributor to cancer-related deaths in the country, with approximately 1,967 new cases and 1,289 fatalities, positioning it as one of the leading causes of cancer mortality (10).

The shift toward Westernized diets and more sedentary lifestyles in LMIC, driven by urbanization, has increased exposure to key CRC risk factors, including processed foods and physical inactivity, contributing to the growing global burden of CRC(11). Detecting CRC at an early stage allows for more effective interventions, often leading to better patient outcomes and reduced healthcare costs. The WHO emphasizes that early cancer diagnosis significantly increases survival rates and reduces treatment costs. Late-stage diagnosis often results in unnecessary suffering and early death, whereas early detection enables more effective and less expensive treatment(12).

The WHO reports that 8.8 million people die from cancer annually, with a significant number in LMICs due to late diagnosis and inadequate treatment options. This late-stage diagnosis, combined with inadequate treatment options, results in unnecessary suffering and premature death for many individuals (13). Delays in CRC treatment in Ethiopia are attributed to limited access to diagnostic facilities, low public awareness, socioeconomic barriers, disease-related factors, shortages of trained specialists, limited multidisciplinary cancer care, and resource constraints. Patients may wait up to 10-12 months for essential treatments, such as radiotherapy, at major referral centers (14). Global strategies to reduce CRC treatment delays align with SDG 3 include developing National Cancer Control Policies, screening and early detection initiatives, multilevel interventions, health system strengthening, and addressing stigma. These policies aim to facilitate timely referral, diagnosis, and treatment for suspected cases, prioritizing clinician education, investments in diagnostic infrastructure, workforce training, and multidisciplinary care teams (15).

1.2. Statement of the problem

CRC remains one of the leading causes of cancer-related morbidity and mortality worldwide(16). Timely initiation of treatment following diagnosis is a critical factor influencing clinical outcomes, patient survival, and quality of life(17). However, a significant proportion of patients with colorectal cancer experience delays in starting treatment, which may contribute to disease progression, reduced treatment efficacy, and increased healthcare costs(18).

Delays in the initiation of treatment for CRC can significantly impact patient outcomes by allowing disease progression, increasing complications, and raising the risk of metastasis, including survival rates(19). As treatment is postponed, the cancer advances to higher stages, where tumor size, lymph node involvement, and metastasis become more severe, making therapeutic interventions more challenging and less effective(20). Research shows that each 4-week delay in treatment initiation raises mortality risk by 12–39%, with survival rates declining further at 8- and 12-week delays. Early intervention is critical to improving prognosis, enhancing treatment efficacy, and ultimately increasing survival rates(21). Understanding the factors that contribute to these delays is crucial for improving healthcare delivery and patient care (22).

Delays in cancer treatment are caused by patient-related, health system, and socioeconomic barriers. Fear of diagnosis and treatment initiation, lack of awareness, and reluctance to seek medical attention can lead to advanced disease, reducing survival rates (23). Inadequate healthcare infrastructure, long waiting times, and restricted access to specialized services exacerbate delays(24). Lower-income patients are disproportionately affected by financial constraints, lack of insurance coverage, and geographic disparities, leading to extended treatment delays and diminished survival prospects(25). In Ethiopia, a study indicates that there are significant delays in colorectal cancer treatment initiation, with patients experiencing an average delay of 5 to 6 months, and some modalities like radiotherapy facing delays of up to 164.4 days(26).

Ethiopia is addressing the growing burden of non-communicable diseases, including CRC, through various strategies. These include the National Cancer Control Plan, which aims to

improve cancer prevention, diagnosis, and treatment services. The country is also expanding oncology centers, integrating cancer screening programs for early detection and enhancing health workforce training for oncologists, pathologists, and specialized healthcare workers to improve diagnostic accuracy and treatment planning. Despite interventions, significant gaps persist in Ethiopia's cancer screening programs, leading to late-stage diagnoses and poor survival rates, limited access to diagnostic methods, shortage of trained specialists, financial constraints, limited insurance coverage, and insufficient data on Ethiopia-specific CRC risk factors.

The study aims to identify factors influencing delayed treatment and outcomes in CRC patients that have been inadequately addressed by previous research. While some studies may have explored CRC incidence, survival rates, and risk factors, few have investigated specific socioeconomic, healthcare access, molecular, or genetic determinants that might explain disparities in diagnosis and treatment delays.

1.3. Significant of the study

Colorectal cancer affects patients' quality of life, causing chronic pain, fatigue, and gastrointestinal dysfunction (27). Limited resources lead to late-stage diagnoses, affecting treatment efficacy and financial burden(28). Low- and middle-income countries face worsening healthcare outcomes due to delayed treatment initiation due to a lack of advanced infrastructure, skilled healthcare professionals, and diagnostic tools (29). Delayed treatment is a significant challenge, with many patients presenting at advanced stages, resulting in poor outcomes (30).

By identifying the factors associated with delayed treatment, this study could inform the development of targeted interventions to improve CRC management. These interventions could include increasing awareness about CRC, improving access to healthcare facilities and diagnostic services, and developing effective screening programs.

Furthermore, this study has the potential to advance the understanding of CRC management in the study area, where healthcare services are delivered to a large population but patient outcomes—including care quality and survival rates—remain markedly lower than those in

high-income countries. The insights gained could inform the development of targeted interventions aimed at improving CRC management in other resource-limited settings facing comparable challenges. This study holds promise for enhancing the quality of life and survival outcomes of CRC patients in Ethiopia while also supporting global initiatives to alleviate the CRC burden in low- and middle-income countries.

2. Literature review

2.1. Global burden of Colorectal Cancer

CRC remains one of the most significant public health challenges worldwide, characterized by high incidence, mortality, and socioeconomic disparities. According to the Global Cancer Observatory (GLOBOCAN) 2022, CRC is the third most commonly diagnosed cancer (1.93 million new cases annually) and the second leading cause of cancer-related deaths (935,000 deaths), accounting for approximately 10% of all cancer cases and 9.4% of cancer mortality globally (5, 31). These figures reflect a steady rise in CRC burden over the past decade, driven by population aging, urbanization, and lifestyle changes such as sedentary behavior, dietary shifts to Westernized diets (e.g., high red/processed meat consumption, low fiber intake)(32, 33) obesity, and alcohol and tobacco use (33).

High-income countries exhibit higher incidence rates of colorectal cancer due to extensive screening and early detection programs. However, they also experience relatively lower mortality rates, attributed to enhanced treatment infrastructure. Globally, CRC incidence rates vary significantly by region. Southern Europe, Northern Europe, and Australia/New Zealand report the highest rates of colon cancer, while Eastern Europe, Eastern Asia, and Australia/New Zealand exhibit elevated rates of CRC overall. North America also experiences a substantial burden, with persistently high CRC incidence (34, 35).

Hungary has the highest incidence of CRC among males at 70.6 per 100,000 population, while Norway leads for females at 29.3 per 100,000. Additionally, CRC is the most diagnosed cancer among men in Japan, South Korea, Saudi Arabia, Oman, Yemen, UAE, Bahrain, Qatar, Kuwait, and Slovakia. Conversely, all regions of Africa and Southern Asia exhibit the lowest incidence rates across genders (35).

CRC in Africa is not yet the most commonly diagnosed cancer, but its incidence is increasing, with over 58,000 new cases in 2020 and over 47,000 deaths, indicating poor survival outcomes (5, 36). Ethiopia's Federal Ministry of Health has identified CRC as one of the top five most prevalent cancers in the country. Evidence from oncology units at major hospitals and regional

facilities shows an increasing number of cases being diagnosed among both younger and older populations, despite limited data on the disease's incidence (37).

2.2. Risk Factors of Colorectal Cancer development

A study conducted in China found that 45.5% of colorectal cancer cases can be attributed to the combined influence of seven primary risk factors. Low vegetable intake emerged as the leading factor (17.9%), followed by physical inactivity (8.9%), high red/processed meat consumption (8.6%), inadequate fruit intake (6.4%), excessive alcohol use (5.4%), overweight/obesity (5.3%), and smoking (4.9%) (38). Also, age, particularly in individuals over 50 years old (39), family history of the disease or genetic conditions like Lynch syndrome and familial adenomatous polyposis (FAP), personal history who have previously had colorectal cancer, lifestyle factors such as a diet high in processed meats and low in fruits and vegetables, sedentary behavior, obesity are significantly contribute to the likelihood of developing CRC (39).

Studies have shown a potential link between increased fruit and vegetable consumption and a lower risk of colorectal cancer, especially colon cancer (40). A meta-analysis of several studies highlighted that consuming fruits such as citrus fruits, apples, watermelon, and kiwi might significantly reduce the likelihood of developing colorectal cancer(41).

Physical inactivity increases the risk of colon cancer, while regular physical activity reduces this risk and supports overall health. Sedentary behaviors, such as prolonged sitting or watching TV, are linked to a higher risk (42). Inactivity can cause metabolic changes, such as insulin resistance and hormone changes, which may contribute to cancer development(43). Physical activity also shapes the gut microbiome, influencing its composition and function (44).

Alcohol consumption has been linked to various types of cancer, including colon cancer, breast, liver, pancreatic, throat, and mouth cancer(45). Studies show that the risk of colon cancer increases with each glass of alcohol consumed, even with a standard drink per day (46, 47). Moderate beer and wine consumption also heightens the risk of bowel cancer compared to occasional or non-drinkers (47). Being overweight or obese is a recognized risk factor for colon cancer, significantly raising both the chances of developing the disease and mortality rates. Excess body fat can result in elevated levels of insulin and related hormones in the bloodstream,

which may stimulate cancer growth. Furthermore, obesity fosters an inflammatory environment within the body, further increasing cancer risk. It is also closely associated with type 2 diabetes, another established risk factor for colon cancer(48).

Consuming large amounts of red and processed meats has been shown to increase the risk of colon cancer. According to a 2024 study, individuals who consumed the highest levels of red meat faced a 30% higher risk of developing colon cancer, while those with the highest intake of processed meat experienced an even greater risk, at 40%. These findings highlight the importance of reducing red and processed meat consumption for better health outcomes(49).

2.3. Treatment and intervention of CRC

According to guidelines from the National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) surgical intervention for early-stage CRC should ideally take place within 4–6 weeks following diagnosis to maximize treatment efficacy (39, 50). Adjuvant chemotherapy should begin within 6–8 weeks after surgery to maximize survival benefits, as delays beyond this period are linked to increased recurrence and mortality risks(51). The United Kingdom's National Health Service (NHS) Cancer Plan recommends treatment initiation within 31 days of diagnosis and within 62 days from initial referral for suspected cancer(52).

However, in many sub-Saharan African (SSA) countries, CRC is frequently diagnosed at advanced stages (Stage III or IV), when curative treatment is either less effective or no longer feasible (53). This challenge arises from several factors, including low public awareness, the absence of routine screening programs, limited diagnostic facilities, and delays in accessing specialized care. For example, studies conducted in Nigeria, Kenya, and Ghana reveal that over 60–80% of CRC cases are diagnosed at an advanced stage. This late presentation contributes significantly to the region's poor survival rates(54).

Timely initiation of CRC treatment is crucial for improving survival rates, quality of life, and reducing health system burdens (55). Delays in therapy can lead to disease progression, higher mortality rates (a 6–8% increase per four-week delay, according to Hanna et al., 2020)(24), and

reduced effectiveness of interventions like surgery, chemotherapy, and radiotherapy. Prompt treatment alleviates physical and psychological symptoms, prevents emergency complications, and improves long-term outcomes, especially in early-stage disease. In low-resource settings like Ethiopia, delays are exacerbated by limited oncology specialists, inadequate surgical capacity, and restricted access to treatment, making early intervention a critical public health priority to reduce preventable deaths and enhance patient care (56).

The definition of treatment delay varies across clinical studies and cancer registries, depending on healthcare system capacity and local conditions. Standard thresholds often include delays of more than 30 or 60 days from diagnosis to the initiation of treatment (55, 57). In low- and middle-income countries (LMICs), where healthcare infrastructure faces significant constraints, delays exceeding 90 days are frequently considered critical (56). The definition of delay should thus be context-specific, acknowledging both clinical urgency and health system capacity. In resource-limited settings such as Southern Ethiopia, even longer timeframes may be common, but they are still considered detrimental if they exceed locally feasible benchmarks.

Delays in cancer care—especially in the period between diagnosis and treatment initiation—are a growing concern worldwide. Numerous global studies have demonstrated that such delays are associated with advanced disease at presentation, reduced survival, and poorer quality of life across multiple cancer types, including CRC. Research from high-income countries (HICs) highlights the severe impact of treatment delays on CRC outcomes. Biagi et al. (2011) found that starting adjuvant chemotherapy beyond 8 weeks post-surgery increased mortality by 20–30%, with the optimal window being 6–8 weeks(58). Neal et al. (2015) reviewed over 80 studies and concluded that delays of 30–60 days significantly worsened survival rates across cancers, including CRC(55). Similarly, Hanna et al. (2020) conducted a large systematic review and found that every four-week delay in surgery, chemotherapy, or radiotherapy raised mortality risk by 6–13%, with CRC being particularly affected by surgical delays(24).

Colorectal cancer treatment delays in low- and middle-income countries are often prolonged due to limited healthcare infrastructure, workforce shortages, financial barriers, and geographical challenges. In Brazil, over 40% of patients face delays exceeding 60 days, while in India, the median time from diagnosis to surgery is over 75 days (59).

2.4. Determinants of delayed time to treatment initiation

Time to Treatment Initiation (TTI) for CRC is defined as the interval between the date of diagnosis, typically confirmed by histopathology or imaging, and the date when the first definitive treatment, such as surgery, chemotherapy, or radiation therapy, is administered (60). Delayed time to treatment initiation is characterized by a prolonged interval between diagnosis and the start of definitive therapy, often considered to exceed 60 days in many LMIC, can lead to worse prognoses, lower survival rates, and reduced quality of life (50).

Delayed time to treatment initiation (TTI) in CRC is influenced by multifaceted factors spanning patient demographics, healthcare systems, and tumor biology. Delays in healthcare delivery in resource-limited environments like Ethiopia are attributed to factors such as insufficient diagnostic facilities, limited access to specialized care, delayed referrals from primary care to specialists, financial barriers, and a lack of patient awareness about health issues and available services. These factors hinder timely and accurate diagnoses, prolong the waiting period for necessary treatments, and hinder patient engagement in healthcare (18).

2.4.1. Patient-Related Factors

Socioeconomic disparities such as lower education levels, lack of health insurance, and rural residency contribute to delays in treatment for certain populations. The 2016 Zarcos-Pedrinaci et al. study revealed that 65.5% of colorectal cancer patients start treatment later than recommended due to socioeconomic disparities, including income, education, and healthcare resources(4). A study on stage III colon cancer patients found that 24.3% initiated chemotherapy more than eight weeks after surgery, influenced by unplanned readmission, prolonged stay, comorbidity, and nonclinical factors like insurance lack, and residence over 100 miles(61).

Sociocultural barriers significantly affect healthcare access and utilization, especially among underprivileged populations, resulting in asymptomatic disease presentations, low health literacy, fear of diagnosis, and stigmatization of certain health conditions (4). Asymptomatic presentation can lead to a lack of awareness about potential health issues, causing individuals to underestimate their risks and delay seeking medical advice. Low health literacy hinders informed decision-making and access to necessary services, leading to poorer health outcomes and increased hospitalizations. Fear of diagnosis can deter individuals from seeking care due to concerns about personal lives, employment status, or family dynamics. Stigma surrounding certain illnesses can further inhibit healthcare services, exacerbate existing health issues, and perpetuate a cycle of neglecting health needs(62).

Delays in colorectal cancer treatment are often linked to older age and male sex, as well as younger patients under 50 from marginalized groups (61). Factors contributing to these delays include health complications, comorbidities, and complex healthcare systems. Males may face systemic biases and differences in treatment compared to females. Younger individuals from marginalized communities face additional barriers like socioeconomic challenges, lack of access to healthcare resources, and potential discrimination, leading to prolonged periods before they receive necessary treatment(63).

2.4.2. Healthcare System Factors

In Ethiopia, cancer treatment delays are primarily due to infrastructure limitations, referral and diagnostic systems, and geographic accessibility. The mean delay for radiotherapy is 164 days, with a lack of multidisciplinary care exacerbated (62). This is particularly concerning for colorectal cancer patients, as only 35% receive timely multidisciplinary team input. Inefficient referral systems and diagnostic capacity gaps also contribute to delays (61, 62). Geographic accessibility is crucial, especially for patients in remote areas, where delays, especially in chemotherapy, are more pronounced. Addressing these challenges is essential for timely and effective cancer care(61).

Colorectal cancer in sub-Saharan Africa faces challenges like lack of trained oncologists, delayed pathology results, and limited access to chemotherapy and radiotherapy (14). Patients in Ethiopia face long travel and systemic delays, leading to disease progression and lower prognosis, with a five-year survival rate often under 30%(33).

Primary care misdiagnoses and referral delays significantly contribute to prolonged CRC treatment initiation, especially in low-resource settings like Ethiopia, where systemic barriers extend delays to 164 days, with only 35% of patients receiving timely multidisciplinary care (64) (65). Chemotherapy stockouts further worsen treatment gaps, increasing the risk of suboptimal therapy, nonstandard regimens, and disease progression (66). In Botswana, patients facing stockouts experience an average delay of 7.8 days per cycle, compared to 3.2 days for those without stockouts (66). These disruptions in stage II–III CRC patients are associated with inferior survival outcomes, compounding metastasis risks (67).

Waiting time critically affects treatment delays, with prolonged intervals between symptom onset, diagnosis, and therapy exacerbating mortality (68). Delays of ≥1 year in colon cancer increase all-cause mortality by 31%, while post-diagnosis delays exceeding 30 days raise mortality risk 1.5–1.6-fold, especially in stage III CRC. In Ethiopia and Sri Lanka, healthcare infrastructure limitations (radiotherapy shortages, colonoscopy wait times) worsen treatment delays to 42–164 days, disproportionately affecting rural and underserved populations (69). Limited specialist availability, fragmented healthcare systems, and long travel distances to tertiary centers further hinder timely diagnosis and therapy, contributing to poorer survival rates (70, 71).

Delays in CRC treatment initiation are influenced by distance to healthcare facilities, occupation, and marital status. Patients living >50–100 miles from specialized centers often face logistical barriers, late-stage diagnoses, and prolonged waits due to limited access(72, 73). Socioeconomic factors also play a role, with unemployed or informal workers experiencing delays due to financial hardship, while employed individuals benefit from workplace support. Married patients initiate treatment faster due to emotional and financial assistance, whereas single, divorced, or widowed individuals encounter challenges linked to social isolation(74). Additionally, symptom

duration significantly affects treatment delays, as prolonged symptoms lead to advanced-stage diagnoses due to late recognition or low health literacy. Although religion's direct impact remains understudied, cultural and spiritual beliefs may contribute to delays through reliance on traditional healing or hesitancy toward medical care. Addressing symptom awareness and improving equitable healthcare access can help mitigate these delays(74).

2.4.3. Tumor-Related Factors

Studies from major referral hospitals in Ethiopia reveal that colorectal cancer management is significantly influenced by tumor-specific characteristics and systemic healthcare challenges. Over 84.5% of CRC cases in Ethiopia present at stages III or IV, with 32% already metastatic at diagnosis(14). This is due to limited screening programs and delayed clinical recognition of symptoms, which persist for a median of 13.9 months before diagnosis(75). Younger age is linked to advanced-stage presentation of tumors, possibly due to aggressive tumor biology or delayed healthcare-seeking behavior(76). Studies show that 67% of patients diagnosed with a disease are 50 years or younger, with a median age of 46, often in an advanced stage(14, 75).

Tumor localization and symptom heterogeneity are additional factors influencing the early initiation of CRC treatment. As reported by Biniyam and his collogues, 69% of CRC cases are rectal compared to 16% being colon cancers(76). Rectal tumors frequently present with rectal bleeding 64.8% and bowel habit changes, whereas right-sided colon tumors are more often associated with weight loss 78.6% and abdominal pain. These differences in clinical presentation influence the early initiation of CRC treatment (75).

2.5. Conceptual framework

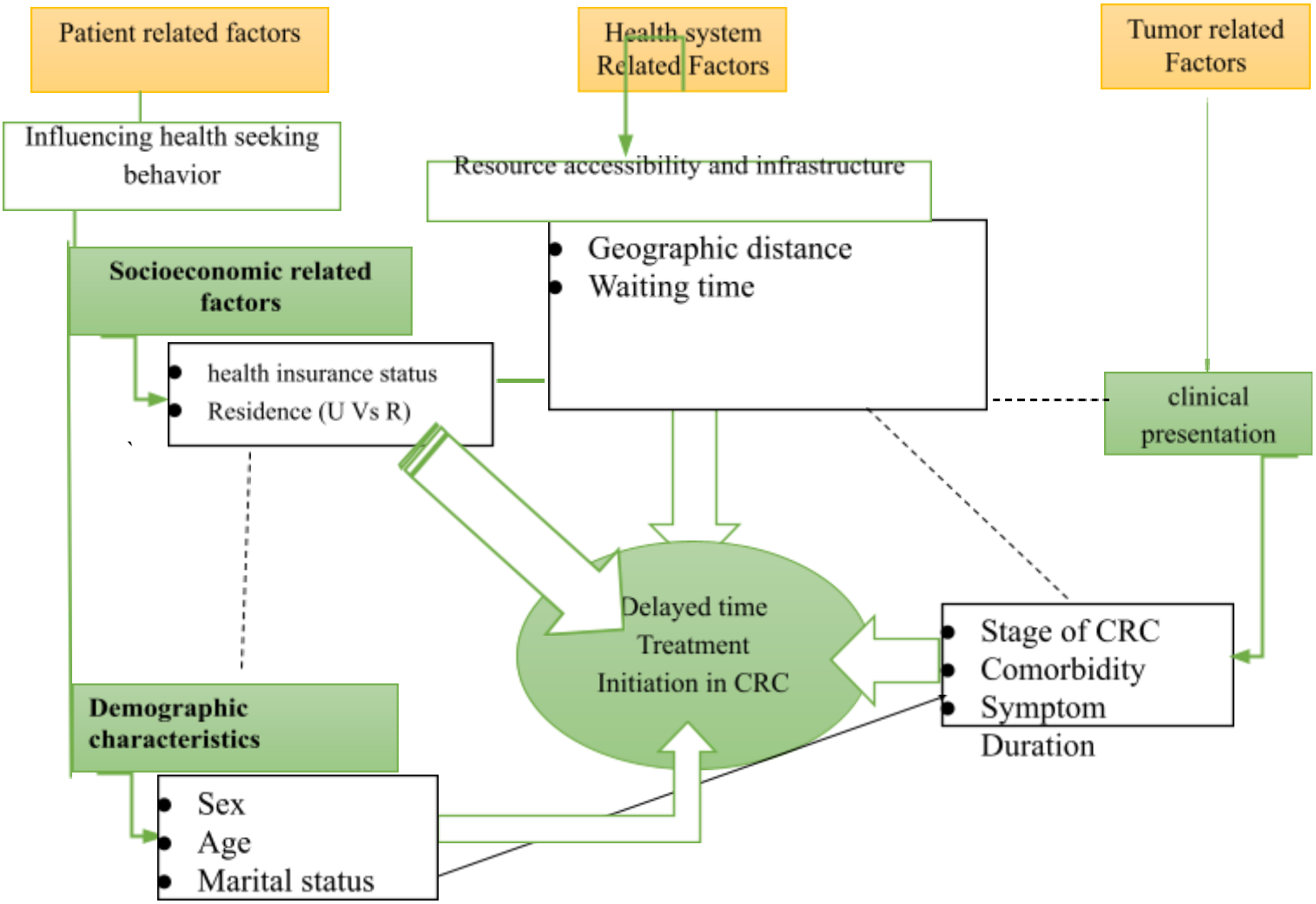

Figure 1: - The conceptual framework to assess Delayed time treatment initiation and associative factors of CRC. **Source**: (14, 18, 33, 61, 62, 66, 75)

3. Objectives

3.1. Main objectives

To identify the determinants of delayed time to treatment initiation among CRC patients at Hawassa University Comprehensive Specialized Hospital, Sidama Regional state, Southern Ethiopia.

3.2. Specific objectives

- To determine the incidence proportion of patients with CRC who experienced a delayed initiation of treatment (>=60 days) at Hawassa University Comprehensive Specialized Hospital, Sidama Regional state, Southern Ethiopia

- To estimate the median time from diagnosis to treatment initiation among colorectal cancer patients at Hawassa University Comprehensive Specialized Hospital, Sidama Regional state, Southern Ethiopia

- To identify the determinants of delayed time to treatment initiation among CRC patients at Hawassa University Comprehensive Specialized Hospital, Sidama Regional state, Southern Ethiopia

Research questions

- What the incidence proportion of colorectal cancer patients experience delayed treatment initiation?
- What is the median time from diagnosis to treatment initiation among CRC patients at Hawassa University Comprehensive Specialized Hospital?
- What are the determents associated with delayed time to treatment initiation among CRC patients at Hawassa University Comprehensive Specialized Hospital, Sidama Region, Southern Ethiopia?

4. Methods

4.1. Study area

The hospital has a diverse team of professionals, including four oncologists specializing in cancer diagnosis and treatment, a medical physicist for radiation safety, and three radiographers performing essential diagnostic procedures. The nursing staff includes two MSc oncology nurses, general nursing staff, and three pharmacists managing medication therapies and ensuring patient safety. The team is supported by other supportive staff members who contribute to the overall functioning of the hospital. The hospital handles around 400 monthly outpatient department visits, offering daily services such as chemotherapy, radiotherapy, and palliative care. The research was done at Hawassa University Comprehensive Specialized Hospital (HUCSH), located in Hawassa City, which ranks as the fifth largest city in Ethiopia (77). HUCSH serves as the sole hospital serving to a population exceeding 25 million people in the southern region of Ethiopia. It is recognized as the largest and most prominent public hospital in this area. The facility faces challenges such as limited human resources, a shortage of chemotherapy supplies, and the unavailability of radiation therapy (77).

4.2. Study Design

An institutional-based single group retrospective cohort study was conducted among all CRC patients diagnosed and treated at Hawassa University Comprehensive Specialized Hospital (HUCSH) oncology center. The study was reviewed by medical records of patients diagnosed with CRC between May 1, 2017, to April 30, 2025. Data collection was carried out from June 1–30, 2025.

4.3. Source population

All patients diagnosed with colorectal cancer who were seen and managed at Hawassa University Comprehensive Specialized Hospital, Sidama Region, Southern Ethiopia, during May 2017 to April 30, 2025 defined historical period.

4.4. Study Population

The study population were included randomly selected and histologically confirmed CRC patients who received treatment at HUCSH during the study period.

4.5. Inclusion criterion

Patients who had a complete medical record including a clinical examination that confirmed the presence of a CRC.

4.6. Exclusion criterion

- Patients with carcinoma in situ, unknown clinical stage or histology, other colon conditions that were not CRC, and patients with multiple cancers.
- Those who were referred to other facilities for alternative treatment initiation
- Comorbidity with other types of cancers
- Diagnosed during emergency hospitalization due to cases other than CRC
- Pediatric patients

4.7. Sample Size Determination and Sampling Technique

This study was included all colorectal cancer (CRC) patients within the study period from May 1, 2017, to April 30, 2025. Medical records of confirmed CRC diagnoses registered at HUCSH during this timeframe were thoroughly reviewed. All eligible participants who meet the inclusion criteria were identified and incorporated into the study.

Sample size for determination of the proportion of patients with CRC who experienced a delayed initiation of treatment (>60 days) at Hawassa University Comprehensive Specialized Hospital, Sidama Regional state, Southern Ethiopia were calculated using a single population proportion formula:

$$n = \frac{\left(z_{\frac{\alpha}{2}}\right)^2 p(1-p)}{d^2}$$

Where sample size is = n

$Z_{\alpha/2}$ = Z value with a 95% confidence interval = 1.96

P = is taken from a study conducted in Addis Ababa, Black Lion Hospital found that 65.0%

of CRC patients experienced delayed treatment initiation (26).

d = margin of error (5%)

n= $(1.96)^2(0.602)\ (1\text{-}0.602)/\ (0.05)^2$

$$n = \frac{(1.96)^2 0.66(1-0.65)}{0.05^2}$$

$$= \underline{350}$$

Adding 10% non-response rate

$$\frac{n}{1-Non\ Response\ rate} = \frac{350}{1-0.1} = \frac{350}{0.9} = 388.88 = 389$$

the final sample size becomes 389. Hence the study encompassed 389 participants. A systematic random sampling technique were applied to select patient records from the hospital's cancer registry.

The sample size were calculated using a two-population proportion formula:

$$n = \left(\frac{Z_{1/2}\sqrt{2P(1-P)} + Z_B\sqrt{Po(1-Po)+P1)}}{(P1-Po)^2}\right)2$$

Table 1: Sample size determination for predictors of delayed treatment initiation

Variables	**CI%**	**Power**	**HOR**	**% of outcome in unexposed group**	**Sample size**	**Reference**
Surgery appointment	95	80%	0.37	39	182	(26)
Education 2^0 and above	95	80%	0.56	66.7	422	(4)
Size of tumor	95	80%	0.51	58.6	304	(4)
Sign and symptom	95	80%	0.31	71.8	112	(4)

Where sample size is = n

$Z_{\alpha/2}$ = Z value with a 95% confidence interval = 1.96

P= average of P1 and P2

Po: prevalence of the delayed

P1: prevalence of not delayed

n: number of cases

Therefore, determinant variables such as surgery, tumor size, signs and symptoms, and education were identified as predictors, with a sample size determined using proportions. Among these, the largest sample size is 422 for the predictors. Following the rule of thumb, the appropriate sample size being large size is 422.

Again, the adjusts sample size using 10% non-response rate were,

$$\frac{n}{1-non\ Response\ rate} = \frac{422}{1-0.1} = \frac{422}{0.9} = 468.88 = 469$$

Hence, the final sample size for this study was 469.

4.8. Measurements

We have collected baseline characteristics about each patient including age, gender, marital status, place of residence, age at diagnosis, tumor location, tumor stage, carcinoembryonic antigen (CEA), histology type, tumor grade, chemotherapy, surgery, and delayed treatment defined as starting treatment >60 days after diagnosis. Our primary outcome variable were time to treatment initiation.

4.9. Data Collection tools and Procedures

Data collection was carried out from July 1–30, 2025. Data was extracted from patients' medical records using a structured checklist that include: Socio-demographic characteristics (age, sex, residence, marital status, education level). Clinical factors (stage at diagnosis, tumor location, comorbidities, symptoms at presentation). Health system-related factors (referral pathways, diagnostic delays, time from diagnosis to treatment). Treatment-related factors (type of treatment initiated, time to treatment initiation).

The data extraction tool was prepared by using different studies (24, 26, 78, 79) and evaluated by oncology experts. Data from the eligible patients' medical records were extracted and imported into the Kobo toolbox. To evaluate the primary outcome of delayed treatment initiation, we have checked the time of diagnosis and initiation of the treatment that recorded on the medical records. In case of absence of the date or other important variables, further observation form HMIS were performed. Then, all charts of colorectal cancer patients, diagnosed between May 1, 2017 to April 30, 2025 at HUCSH was retrieved and reviewed. One BSc nurses and one MSc oncology nurse were involved on the data collection and supervision respectively.

4.10. Data quality assurances

Pre-test on 5% of medical record review was done on a confirmed diagnosis of patients enrolled in 2017 and 2025 two weeks prior to the actual data collection time out of Hawassa University Cancer Treatment Centre. As a result, some unrecorded variables were reduced from the data extraction tool. A training guide was prepared for further quality. The data collectors and supervisors were trained for half day prior to data collection. Review of data extraction tool were checked for completeness by the principal investigator and supervisors on daily basis. Kobo toolbox as well as paper based were used for data collection to assure the quality.

4.11. Variables

Dependent Variable

Delayed Time to treatment initiation (>60 days)

4.12. Independent Variables

Socio-demographic factors: age, sex, residence, income, education, Clinical factors: tumor stage, histologic type, comorbidities, Health system factors: referral status, diagnostic intervals, accessibility, a patient-related factors: symptom duration before seeking care.

4.13. Operational definition or definition of terms

- Delayed time to treatment initiation (TTI): the period between a confirmed diagnosis and the start of actual treatment which is > 60 days from diagnosis to first treatment.
- Colorectal cancer (CRC), also known as bowel cancer, is a type of cancer that develops in the colon or rectum, which are parts of the large intestine.

4.14. Data Analysis

Data was analyzed using SPSS 27 v. Basic descriptive analysis (mean, median, proportions) were summarized a baseline characteristic. The dependent variables were dichotomized into delayed (>60 days) and not delayed (<60 days). Before running the logistic regression model, multi-collinearity diagnosis was checked using VIF, a value below 10 showing that there is no multicollinearity between two or more predictors. The necessary assumption for the model was checked using goodness of fit test by Schoenfeld residual and variables having P- value >0.05 was considered as fulfilling the supposition. Bivariable logistic regression was fitted and those independent variables that fitted on the bivariable regression lower than or equal to 0.25 position of significance were included in the multivariable analysis. Multiple logistic regression was done at 0.05 level of significance to determine the net effect of each explicatory variable on time to delay of treatment initiation. The P value lower than 0.05 in the multivariable analysis was considered statically significant. The results of these models were expressed as odds ratio with a 95-CI and p- values was used to measure the strength of association and to identify statistically significant predictors.

4.15. Ethical clearances

This study was conducted in accordance with Declaration of Helsinki. Ethical approval was obtained from Pharma university college IRERC. Patient confidentiality was maintained by anonymizing records, and data was used solely for research purposes. Permission letter was obtained from Hawassa University comprehensive Specialized Hospital.

4.16. Dissemination of findings

The result of the study was submitted to Pharma college, Hawassa campus School of Public health. It will be presented on different workshop, meetings, conference and also will be published on different journals as much as possible.

5. Result

5.1. Sociodemographic background

From a total of over 7,680 registered cases at the oncology center of Hawassa University Comprehensive Specialized Hospital (HUCSH) between 2017 and 2025, a subset of 469 medical records was selected for analysis. These records, spanning from May 1, 2017 to April 30, 2025, were reviewed to assess delayed treatment initiation among patients diagnosed with colorectal cancer (CRC). The largest number of samples were collected in the year 2022, while the final list was compiled in 2025 figure 1.

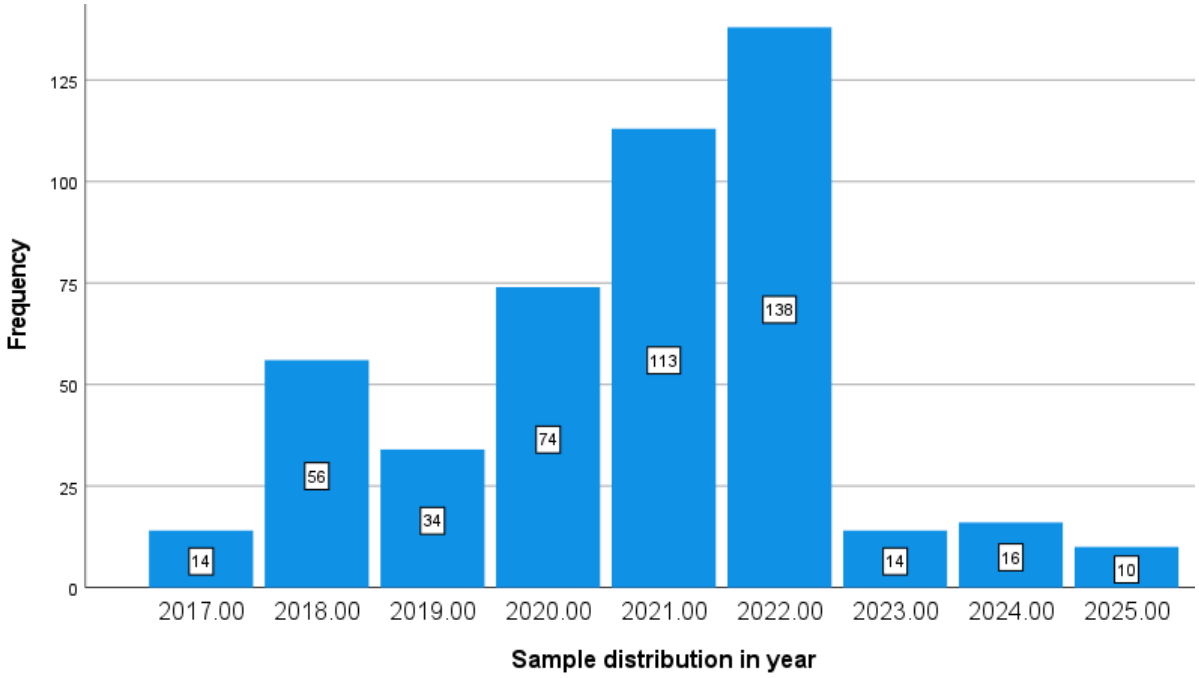

Figure 2: Sample distribution for CRC patients chart reviewed from (2017-2025)

Of the 469 colorectal cancer patients, nearly half 225(48.0%) were middle-aged (45-64 years), while 53(32.6%) were under 45 and 91(19.4%) were 65 or older. The mean age was 50.9(SD± 13.39) years, while the median age of 50 years with interquartile range (IQR) of 50 years (Q1=40, Q3=60) and mode stood at 50 years, indicating a relatively symmetrical distribution centered around this age. The age is ranged from 23 to 79 years, yielding a total range of 56 years. The participants were predominantly male 266(56.7%) and married 419(89.3%). The study participants were nearly evenly distributed across the Sidama 163(34.8%), Oromia 151(32.2%), and SNNPR 155(33.0%) regions, with a majority 273(58.2%) residing in rural

areas. From 332 respondents who provided financial data, a slight majority 171(51.5% of the total sample reported having health insurance coverage, while 161(48.5%) were uninsured (Table 2).

Table 2: Distribution of Sociodemographic variables among colorectal cancer patients in Hawassa comprehensive specialized Hospital Southern Ethiopia (N = 469)

Variables	Categories	Number	Percentage
Age (years)	<45	153	32.6
	45-64	225	48.0
	>=65	91	19.4
Sex	Male	266	56.7
	Female	203	43.3
Region	Sidama	163	34.8
	Oromia	151	32.2
	SNNPR	155	33.0
Marital status	Single	50	10.7
	Married	419	89.3
Place of residence	Urban	196	41.8
	Rural	273	58.2
Health insurance (n=332)	Insured	171	51.5
	Uninsured	161	48.5

5.2. Clinical and pathological Characteristic of colorectal cancer patients

In this study 469 colorectal cancer patients participated, and the majority of them had colon tumors, 302(64.4%) and 412(87.8%) are classified as adenocarcinoma. At diagnosis, half of the patients 238(50.7%) presented with metastatic disease, most commonly to the liver 78(23.3%) or lungs 62(18.5%), and over half 239(51.0%) had a significant comorbidity burden (Charlson score ≥2). The most common treatment was a combination of chemotherapy and surgery 215(45.8%), with FOLFOX and CAPOX being the predominant chemotherapeutic regimens. Most tumors were well-differentiated 270(64.7%), though vascular invasion was present in a third of cases 150(32.0%). Regarding the patient profile, there was a high rate of non-normal BMI 259(55.2%) and a few had history of smoking 38(12.9%) or alcohol consumption 105(22.4%) (Table 3).

Table 3: Clinical, pathological, and behavioral characteristics of colorectal cancer patients in Hawassa comprehensive specialized Hospital Southern Ethiopia (N = 469)

Vriables	Category	Number	Percentage
Site of tumor	Colon	302	64.4
	Rectum	167	35.6
Charles score	0	80	17.1
	1	150	32.0
	>=2	239	51.0
Preoperative chemotherapy	Yes	57	12.2
	No	412	87.8
Baseline CEA (carcinoembryonic antigen) (n=239)	>=5	58	24.3
	<5	181	75.7
Tumor grade (n=417)	Well differentiated	270	64.7
	Moderately differentiated	88	21.1
	Poorly differentiated	59	14.2
Histologic	Adenocarcinoma	412	87.8
	Mucinous carcinoma	57	12.2
Vascular invasion	Yes	150	32.0
	No	319	68.0
TNM (n=268)	Stage I	75	27.9
	Stage II	44	16.4
	Stage III	53	19.8
	Stage IV	96	35.8
Mode of surgery (265)	Elective	119	44.9
	Emergency	146	55.1
Clinical Cancer stage at diagnosis	Localized	120	25.6
	Locally advanced	111	23.7
	Metastasis	238	50.7
Distance metastasis (n=335)	Liver	78	23.3
	Lung	62	18.5
	Brian	32	9.6
	Others	163	48.7
Treatment	none	122	26.0
	Surgical treatment only	50	10.7
	Chemotherapy only	82	17.5
	Both chemo and surgery	215	45.8
Type of Chemotherapy (n=297)	FOLFOX	122	41.1
	CAPOX	120	40.4

	FOLFIRI	55	18.5
Smoking status (n=294)	Yes	38	12.9
	No	256	87.1
Alcohol consumption	Yes	105	22.4
	No	364	77.6
BMI	Not Normal	259	55.2
	Normal	210	44.8
Treatment initiation status	Delayed (>=60 days)	362	77.2
	Not delayed (<60 days)	107	22.8

5.3. Incidence of colorectal cancer

This study showed that the incidence of delayed treatment initiation among CRC patient was 77.2% (95% CI, 73.37, 81.00). The median time for treatment initiation among CRC was 130 days with an interquartile range (IQR) of 149 days (Q1 = 67, Q3 = 216), indicating substantial variability in treatment delays.

An analysis of follow-up time between diagnosis and treatment initiation among 469 colorectal cancer (CRC) patients revealed a cumulative delay of 71,236 days, averaging approximately 152 days or 5.1 months per individual. This extended interval suggests a significant lag in initiating treatment post-diagnosis, which may have critical implications for disease progression, patient outcomes, and overall healthcare efficiency. The prolonged delay could reflect systemic challenges such as limited access to oncology services, referral inefficiencies, or socioeconomic barriers. These findings underscore the need for targeted interventions to streamline diagnostic-to-treatment pathways and reduce delays in care delivery for CRC patients.

The study reveals that delayed treatment initiation among female cancer patients were 82.8%, while Sidama has the highest delay rate 81.6%. Married patients have a higher delay rate 80.2%). Rural dwellers experience more delays 82.8% than urban residents 69.4%. Patients without insurance have higher delays 83.9%) than those with insurance 66.7%. Preoperative chemotherapy patients have significantly fewer delays (8.8%), suggesting that pre-treatment planning may expedite care (Table 4).

Table 4: Factors Associated with Delayed Treatment Initiation Among Colorectal Cancer Patients in Hawassa comprehensive specialized Hospital Southern Ethiopia (N = 469)

Variables	Categories	Delayed treatment initiation for CRC	
		Yes (>=60 days)	No (<60 days)
Age	<45	116(75.8%)	37(24.2%)
	45-64	178(79.1%)	47(20.9%)
	>=65	68(74.7%)	23(25.3%)
Sex	Male	194(72.9%)	72(27.1%)
	Female	168(82.8%)	35(17.2%)
Region	Sidama	133(81.6%)	30(18.4%)
	Oromia	110(72.8%)	41(27.2%)
	SNNPR	119(76.8%)	36(23.2%)
Marital status	Single	26(52.0%)	24(48.0%)
	Married	336(80.2%	83(19.8%)
Place of residence	Urban	136(69.4%	60(30.6%)
	Rural	226(82.8%	47(17.2%)
Health insurance (n=332)	Yes	114(66.7%)	57(33.3%)
	No	135(83.9%	26(16.1%)
Smoking status	Yes	33(86.8%)	5(13.2%)
	No	196(75.1%)	65(24.9%)
Alcohol consumption	Yes	72(68.6%	33(31.4%)
	No	290(79.7%)	74(20.3%)
BMI	Not normal	203(78.4%)	56(21.6%)
	Normal	159(75.7%)	51(24.3%)
Site of tumor	Colon	217(71.9%)	85(28.1%)
	Rectum	145(86.8%)	22(13.2%)
TNM (Tumor nodes metastasis)	Stage I	70(93.3%)	5(6.7%)
	Stage II	30(68.2%)	14(31.8%)

	Stage III	30(56.6%)	23(43.4%)
	Stage IV	75(78.1%)	21(21.9%)
Clinical Cancer stage at diagnosis	Localized	100(83.3%)	20(16.7%
	Locally advanced	98(88.3%)	13(11.7%)
	Metastasis	164(68.9%	74(31.1%)
Charles score	0	44(55.0%)	36(45.0%)
	1	130(86.7%)	20(13.3%)
	>=2	188(78.7%)	51(21.3%)
Preoperative chemotherapy	Yes	52(91.2%)	5(8.8%)
	No	310(75.2%)	102(24.8%)
CEA (carcinoembryonic antigen)	>=5	49(84.5%)	9(15.5%)
	<5	135(74.6%)	46(25.4%)
Tumor grading (n=417)	Well differentiated	211(78.1%)	59(21.9%)
	Moderately differentiated	62(70.5%)	26(29.5%)
	Poorly differentiated	47(79.7%)	12(20.3%)
Histologic type	Adenocarcinoma	313(76.0%)	99(24.0%)
	Mucinous carcinoma	49(86.0%)	8(14.0%)
Vascular invasion	Yes	42(28.0%)	108(72.0%)
	No	65(20.4%)	254(79.6%)
Mode of surgery (265)	Elective	159(94.1)	10(5.9%)
	Emergency	85(59.0%)	59(41.0%)
Treatment	None	100(82.0%)	22(18.0%)
	Surgical only	31(62.0%)	19(38.0%)
	Chemo only	68(82.9%)	14(17.1%)
	Both	163(75.8%)	52(24.2%)

5.4. Predictors of median time for treatment initiation

In this study about six sociodemographic variables were analyzed and three of them showed independent predictors of the outcome after controlling for other variables effect on CRC occurrence such as marital status, place of residence, and health insurance. Married patients had 3.71 times higher adjusted odds of the late initiation of treatment compared to single patients (AOR=3.71, 95% CI: 1.88-7.32, p<0.001). Similarly, rural residents had 2.11 times higher adjusted odds than urban residents (AOR=2.11, 95% CI: 1.24-3.60, p=0.006). Furthermore, not having health insurance was significantly associated with the outcome, with uninsured patients having 2.41 times higher adjusted odds than those with insurance (AOR=2.41, 95% CI: 1.38-4.18, p=0.002). While female sex showed a significant crude association (COR=1.78, 95% CI: 1.13-2.80, p=0.013), it was not statistically significant in the adjusted model (AOR=1.69, 95% CI: 0.98-2.95, p=0.06), indicating its effect may be influenced by other sociodemographic factors (Table 5).

The multivariate logistic regression analysis identified three factors as independent predictors of a treatment initiation delay of ≥60 days: tumor site, TNM stage III disease, and mode of surgery. Patients with rectal tumors had significantly higher odds of delay compared to those with colon tumors (AOR=8.00, 95% CI: 1.19-14.03, p=0.033). On the other hand, a diagnosis of TNM stage III cancer was associated with significantly reduced odds of delay compared to stage IV disease (AOR=0.91, 95% CI: 0.14-5.8, p=0.011). Most patients undergoing elective surgery had dramatically increased probability of a prolonged delay compared to those requiring emergency operations (AOR=21.16, 95% CI: 2.80-59.78, p=0.003). Other variables, including Charles score, preoperative chemotherapy, vascular invasion, and smoking status, were not found to be independently significant predictors after adjustment (Table 6).

Table 5: Multivariable analysis of Sociodemographic variables among colorectal cancer patients in Hawassa comprehensive specialized Hospital Southern Ethiopia.

Variables	**Categories**	**>=60**	**<60**	**COR 95%CI**	**P. value**	**AOR 95% CI**	**P. value**
Age	<45	116	37	1.06(0.58, 1.93)	0.848		
	45-64	178	47	1.28(0.72, 2.27)	0.396		
	>=65	68	23	1			
Sex	Male	194	72	1			
	Female	168	35	1.78(1.13, 2.80)	0.013	1.69(0.98, 2.95)	0.06
Region	Sidama	133	30	1.34(0.78, 2.31)	0.290		
	Oromia	110	41	0.81(0.48, 1.36)	0.429		
	SNNPR	119	36	1			
Marital status	Single	26	24	1			
	Married	336	83	3.74(2.04, 6.84)	<0.001	3.71(1.88, 7.32)	<0.001*
Place of residence	Urban	136	60	1			
	Rural	226	47	2.12(1.37, 3.28)	<0.001	2.11(1.24, 3.60)	0.006*
Health insurance (n=332)	Yes	114	57	1			
	No	135	26	2.6(1.53, 4.40)	<0.001	2.41(1.38, 4.18)	0.002*

Table 6: Multivariable analysis of clinical, pathological, and behavioral characteristics of colorectal cancer patients in Hawassa comprehensive specialized Hospital Southern Ethiopia (N = 469)

Vriables	Category	Delayed >=60 days	Not delayed <60 days	COR 95%CI	P. value	AOR 95% CI	P. value
Site of tumor	Colon	217	85	1			
	Rectum	145	22	2.58(1.54, 4.32)	<0.001	8.00(1.19, 14.03)	0.033*
Charles score	0	44	36	1			
	1	130	20	5.32(2.79, 10.13)	<0.001	9.00(0.69, 11.76)	>0.05
	>=2	188	51	3.02(1.76, 5.17)	<0.001	2.81(0.34, 22.96)	>0.05
Preoperative chemotherapy	Yes	52	5	3.42(1.33, 8.80)	0.011	0.35(0.01, 10.01)	>0.05
	No	310	102	1			
Vascular invasion	Yes	42	108	0.66(0.42, 1.03)	0.068	3.44(0.92, 45.21)	>0.05
	No	65	254	1			
TNM (Tumor nodes metastasis)	Stage I	70	5	3.92(1.40, 10.96)	0.009	3.01(0.31, 9.20)	>0.05
	Stage II	30	14	0.6(0.27, 1.33)	0.21	0.99(0.11, 8.87)	>0.05
	Stage III	30	23	0.367(0.18, 0.76)	0.007	0.91(0.014, 0.98)	0.011*
	Stage IV	75	21	1			
Mode of surgery (265)	Elective	159	10	7.82(3.78, 16.17)	<0.001	21.16(2.80, 59.78)	0.003*
	Emergency	85	59	1			
Clinical Cancer stage at diagnosis	Localized	100	20	2.26(1.30, 3.92)	0.004	0.96(0.03, 8.99)	>0.05
	Locally advanced	98	13	3.40(1.79, 6.45)	<0.001	0.26(0.03, 2.07)	>0.05
	Metastasis	164	74	1			
Smoking status	Yes	33	5	2.25(0.84, 5.99)	0.106	2.1(0.22, 20.42)	>0.05
	No	196	65	1			
Alcohol consumption	Yes	72	33	0.56(0.34, 0.91)	0.019	1.11(0.21, 5.91)	>0.05
	No	290	74	1			
Surgical treatment alone	Yes	31	19	2.31(1.24, 4.28)	0.008	0.76(0.09, 6.36)	>0.05
	No	331	88	1			

6. Discussion

The findings of the study suggest that colorectal cancer (CRC) can affect individuals across a broad age range, with the mean age of onset being 50.9 (±13.39) years and identical median and mode ages of 50 years. These findings, confirm that CRC affects individuals across the adult lifespan and are consistent with existing literature indicating that while incidence rises with age, the disease can occur at any age (80) (81, 82). The increased incidence of CRC in young adults (<50 years) is might be due to lifestyle change which related with BMI, smoking, alcohol consumption and other factors.

This study found that the incidence of delayed treatment initiation among colorectal cancer (CRC) patients was 77.2% (95% CI: 73.37–81.00). This rate is lower than that reported in Brazilian women with breast cancer (89.1%)(83), but higher than findings from several other studies, including Black Lion Hospital in Ethiopia (65%) (62), Spain (65.5%)(84), and Woods' study (46.8%)(85). This discrepancy may be obtained from disparities in how "delayed treatment" is defined across studies, with some using shorter time thresholds or different starting points for measuring time-to-treatment initiation (TTI).

The median time to treatment initiation among colorectal cancer (CRC) patients in this study was 130 days (IQR: 149), which is slightly lower than the 138 days reported by Der Van Hout et al. (2011) (86), but notably higher than the 44 days observed by Korsgaard et al. (2008)(87) and the 62 days reported by Hoffmann et al. (2014) (88). These discrepancies may be attributed to differences in healthcare system efficiency, referral pathways, and diagnostic infrastructure across countries. Additionally, variations in how "treatment initiation" is defined—whether measured from symptom onset, diagnosis, or first specialist consultation—can significantly influence reported timelines. Socioeconomic factors, patient awareness, and institutional capacity also play critical roles in shaping treatment delays.

In this study, marital status emerged as a significant predictor of treatment delay among colorectal cancer (CRC) patients. Married individuals were found to be 3.71 times more likely to experience treatment delay compared to their single counterparts (95% CI: 1.88–7.32, $p < 0.001$) in this study. Even though most evidence supports marriage as a factor for earlier diagnosis and better survival in CRC, the result of this study showed that married people being 3.71 times more

likely to experience treatment delay may reflect unique local or study-specific factors that diverge from the broader trend(89-91). Furthermore, the study's population, setting, and methodology variation might be affected the result (19, 90).

The finding that rural residence is associated with approximately twice the odds of colorectal cancer (CRC) treatment initiation delay compared to urban residence (AOR = 2.11, 95% CI: 1.24-3.60, p = 0.006). This is consistent with previous studies, conducted in Victoria, Australia, found rural CRC patients had significantly longer total intervals from first symptom or screening to treatment compared to urban patients, particularly due to longer diagnostic intervals (92). Also, the Scottish study found the rural patients had less radiotherapy for CRC, likely reflecting travel distance considerations, but overall treatment modalities like surgery or chemotherapy were similarly delivered in rural and urban groups. In other study done in Scottish observed that there was no increased delays treatment for rural patients; in fact, treatment was sometimes quicker for rural patients after adjusting for disease stage and emergency admissions. This may arise due to differences in healthcare systems, geography, access to specialists, reduced access to diagnostic resources or how delays are measured (total interval vs. post-referral treatment interval) across studies(92).

This study also revealed that lack of health insurance was significantly associated with delayed treatment initiation among colorectal cancer (CRC) patients. Individuals without insurance were 2.6 times more likely to experience treatment delays compared to those with insurance (COR = 2.60, 95% CI: 1.53–4.40, p < 0.001). This association remained strong even after adjusting for other variables, with an adjusted odds ratio (AOR) of 2.41 (95% CI: 1.38–4.18, p = 0.002), indicating that insurance status independently influences timely access to care. Similarly, studies from world, Tennessee Cancer Registry(93), Puerto Rico(94) and UK (71) showed that patients who were uninsured were more likely to be diagnosed and initiated treatment with advanced-stage colorectal cancer (CRC). Hence, these individuals experienced poorer overall survival, largely due to reduced access to recommended adjuvant therapies, which contributed to less favorable treatment outcomes (93). This explains the critical need for insurance coverage to reduce colorectal cancer treatment delays and improve survival rates (93). This might be due to financial constraints often compel patients to delay or skip essential treatments (95), while inefficiencies within the healthcare system can result in extended wait times for diagnostics and

specialist appointments (19, 96, 97). Additionally, psychological stress particularly anxiety over treatment costs—may discourage individuals from early treatment initiation (95).

In this study, tumor location was identified as a strong predictor of treatment delay (≥60 days) among colorectal cancer (CRC) patients, with those having rectal tumors being eight times more likely to experience delayed treatment compared to those with colon tumors (AOR = 8.00, 95% CI: 1.19, 14.03, p = 0.033). This is in line with the studies of Asian, Native Hawaiian, and other Pacific Islander Patients which indicted that CRC located at rectal is more prone to delay on time treatment initiation(98). Also, another study done in elsewhere show that the CRC patients with rectal cancer more likely to delay treatment initiation(4, 62, 99). This is rectal tumor location in colorectal cancer (CRC) is strongly linked to delayed treatment initiation due to complex clinical management and patient/tumor-specific factors(62). Rectal cancer often requires more complex surgical planning and neoadjuvant therapy, unlike colon cancer, which typically involves simpler resection(100).

In this study an elective surgery treatment showed a strong association with treatment delays (AOR = 21.16, 95% CI: 2.80, 59.78, p = 0.003), which is likely explained by scheduling constraints and limited resource availability. Unlike emergency surgery procedures that typically receive immediate prioritization due to their urgent nature, elective surgeries must be scheduled within healthcare systems facing limited operating room capacity, personnel shortages, and prioritization challenges that prolongs the waiting times. Several studies support this explanation including a systematic review showed that elective surgery take over a longer time to be dalliance for treatment initiation(101). Also, an international cohort study on colorectal cancer patients found that elective surgery makes long delays on CRC patients treatment initiation and causes poor survivals of CRC patients(102). Furthermore, the 2023 study on the global impact of COVID-19 revealed significant delays in elective colorectal surgeries worldwide, raising concerns about postponed CRC treatment initiation and its potential effect on patient mortality (103). This is might be due to its triaging and prioritization that emergency cases always jump the queue, pushing elective cases back. Moreover, resource limitation, other health conditions before surgery adds time to the process.

The study found that Stage III colorectal cancer patients are less likely to experience treatment delays (AOR = 0.91, 95% CI: 0.014–0.98, p = 0.011), suggesting that patients with advanced but potentially curable disease are prioritized for timely treatment possibly due to clinical urgency or structured treatment protocols. Supporting evidence shows that Stage III CRC, which involves lymph node metastasis but remains potentially curable, attracts greater clinical attention to expedite treatment due to the higher risk of disease progression and poorer prognosis if delayed (104). Conversely, earlier-stage patients may not always receive the same urgency, potentially contributing to longer treatment intervals. Previous studies reported that delays in adjuvant chemotherapy beyond recommended windows (>=60 days) are associated with worse overall and recurrence-free survival in Stage III CRC patients, thereby reinforcing the need for prompt therapy in this group (105). This is might be due to clinical urgency, system protocols, patient behavior that higher levels of fear, motivation, and compliance leading to prioritized personal schedules.

Strength and Limitations

Clinically relevant and actionable findings are insurance status, surgery type, cancer stage that are directly modifiable through policy changes (e.g., expanding insurance coverage) and systemic improvements (e.g., resource allocation for elective surgeries). The findings are theoretically grounded and align well with existing literature, demonstrating strong consistency with prior research and supported by sound logical reasoning.

This study is limited due to data quality and completeness of pre-existing records, which may be incomplete, inconsistent, or inaccurate. Also, missing data can introduce bias or limit the ability to adjust for confounders. Moreover, measurement and definition of variables are varied from different study settings so that this makes difficult to compare directly.

7. Conclusion

This study determined a high prevalence of delayed treatment initiation among colorectal cancer (CRC) patients, with multiple sociodemographic and clinical factors contributing to these delays. Marital status, rural residence, lack of health insurance, rectal tumor location, and elective surgical treatment all of which significantly increase the likelihood of treatment postponement. Conversely, patients with Stage III disease were less likely to experience delays, likely due to clinical prioritization. While the unexpected finding that married patients experienced more delays contradicts some existing literature, it highlights the context-specific nature of these barriers. Therefore, these findings emphasize the need for targeted interventions to address systemic barriers, improve healthcare access, and streamline treatment pathways particularly for CRC patients by expanding insurance coverage, and improving resource allocation for elective surgeries, to mitigate delays and improve oncologic outcomes particularly CRC outcomes.

8. Recommendations

Based on the study findings the following evidence-based recommendations are proposed to mitigate treatment delays for colorectal cancer (CRC) patients:

1. For Policymakers and Healthcare Administrators:
    - Strengthen health insurance coverage: Implement policies to expand health insurance coverage and reduce financial barriers to care. This is a proven, independent factor in reducing delays and improving outcomes.
    - Invest in Rural Healthcare Infrastructure: Address geographic disparities by investing in diagnostic equipment (e.g., CT scanners, MRI) in rural hospitals, establishing mobile health clinics for screening, and providing telemedicine links to specialist centers to reduce travel burdens for initial consultations and follow-up.
    - Implement Standardized Time-Target Protocols: Establish and enforce national or institutional maximum wait-time targets for key steps in the CRC pathway, from diagnosis to multidisciplinary team discussion to treatment initiation.

2. For Healthcare Institutions and Clinicians:
    - Develop and implement a fast-track, standardized protocol for managing colorectal cancer by mandatory rapid staging and scheduled multidisciplinary team (MDT) meetings
    - Optimize surgical scheduling
    - Utilize Patient Navigation Programs: Implement community health worker-led navigation programs to guide patients, especially those from rural areas or without strong social support, through the complex diagnostic and treatment process, helping to overcome logistical and administrative hurdles.
3. Further research particularly using large scale sample size with different study design especially qualitative and other explorative study designs are more important.

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ANNEXES

PHARMA COLLEGE HAWASSA CAMPUS
SCHOOL OF GRADUATE STUDIES
DEPARTMENT OF PUBLIC HEALTH

Annex I: Declaration

Declaration I am Deresse Daka, the under signed Public Health student declared that this is my original work in partial fulfillment of the requirement for the degree of Master of Public Health in Epidemiology. This work has never been presented in this or any other University, and that all the resources and materials used for the thesis, have been fully acknowledged.

Name: Deresse Daka **Signature**: _____

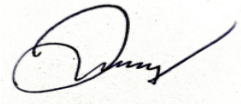
Place of submission: Department of public Health coordinator office, Pharma College.

Date of Submission: _____

This thesis work has been submitted for examination with my approval as Deresse Daka's

Thesis advisor(s).

Name: Dr. Dejene Hailu, Associate professor



Signature _____

ANNEX-II: Assurance of Investigator

The undersigned agrees to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as pre terms and conditions of the research and publications office of the college.

Name of the student: Deresse Daka Date: _____

Signature: _____

Approval of the advisor (s)

This work of thesis over all ethical and scientific consideration can be approved by me

Advisors 

Name:

_____Signature: _____(Associate professor)

ANNEX-III: checklist for CRC data collection to determine the factors

Part I – Socio-demographic and economic characteristics		
S#	**Questions**	**Options for answer**
1.	Patient ID	
2.	Age	----------
3.	Sex	1. Male 2. Female
4.	Region	----------
5.	Religion	1. Orthodox 2. Protestant 3. Muslim 4. Catholic 5. Other specify_____
6.	Marital status	1. Single 2. Married 3. Divorced 4. Widowed
7.	Place of residence	1. Urban 2. Rural
8.	Education	1. No formal education 2. Can read and write 3. Primary 4. Secondary 5. Tertiary (university/ college)
9.	Occupation	1. Farmer 2. Merchant 3. Student

		4. House wife 5. Government Employed 6. Non-government Employed 7. Daily laborer 8. Any Other----------
10.	Health insurance coverage:	1. Yes 2. No
11.	Monthly income if available in ETB	----------
Section 2: Clinical Factors		
12.	Date of first symptom noticed	_____/_____/_____
13.	Date of diagnosis	_____/_____/_____
14.	Date of treatment initiation	_____/_____/_____
15.	Site of tumor	1. Colon 2. Rectum
16.	Charles score	3.
17.	Preoperative chemotherapy	1. Yes 2. No
18.	Baseline CEA	----------
19.	Tumor grade	1. Well differentiated 2. Moderately differentiated 3. Poorly differentiated 4. Unknown
20.	Histologic	1. Adenocarcinoma 2. Mucinous carcinoma 3. Unknown
21.	Vascular invasion	1. Yes 2. No
22.	TNM	1. Stage I 2. Stage II 3. Stage III 4. Stage IV 5. Unknown
23.	Mode of surgery	1. Elective 2. Emergency
24.	Clinical Cancer stage at diagnosis	1. Localized 2. Locally advanced 3. Metastasis
25.	Distance metastasis	----------

26.	Treatment	1. surgical treatment only 2. chemotherapy only 3. both chemo and surgery 4. none
27.	Type of colorectal cancer:	1. Colon cancer 2. Rectal cancer
28.	Type of Chemotherapy	
29.	Presence of comorbidities (e.g., diabetes, hypertension):	1. Yes 2. No
30.	If yes what type of comorbidities	1. DM 2. HTN 3. HIV 4. Other specify _____
31.	Smoking status	1. Yes 2. No
32.	Alcohol consumption	1. Yes 2. No
33.	BMI	----------
Section 3: Healthcare System Factors		
34.	Type of first healthcare facility visited	1. Primary health center 2. Secondary hospital 3. Tertiary hospital 4. Private clinics
35.	Referral process:	1. Directly diagnosed 2. Referred from another facility 3. Self-referred to a specialist
36.	Waiting time for diagnostic tests (e.g., colonoscopy, biopsy)	1. <1 week 2. 1-2 weeks 3. 2-4 weeks
37.	Waiting time for treatment initiation after diagnosis:	1. <2 weeks 2. 2-4 weeks 3. 1-2 months 4. >2 months 5. <2 weeks
38.	Reasons for delay in healthcare system (if any)	1. Lack of specialists 2. Long waiting lists 3. Administrative delays 4. Other (Specify: _____)

39.	Time from diagnosis to treatment	_____days (Calculate: Treatment date – Diagnosis date)
40.	Reason for delay (if >60 days)	1. Lack of oncologist 2. Diagnostic delays 3. Financial barriers 4. Equipment shortage 5. Patient refusal 6. Other (specify_____)
41.	First treatment modality	1. Chemotherapy 2. Surgery 3. Radiation 4. Combined therapy
Section 4: Socioeconomic & Patient-Related Factors		
42.	Distance to the nearest cancer treatment center	1. <10 km 2. 10-50 km 3. >50 km
43.	Transportation availability:	1. Own vehicle 2. Public transport 3. Dependent on others 4. Financial constraints for travel
44.	Did financial constraints delay your treatment?	1. Yes 2. No
45.	Did you experience fear or denial about diagnosis/treatment?	1. Yes 2. No
46.	Did you seek alternative/traditional medicine before conventional treatment?	1. Yes 2. No
47.	Family/social support during treatment process	1. Strong support 2. Moderate support 3. Poor support

ANNEX-IV: Information sheet

Title of the research project: **Determinants of delayed time to treatment initiation among patients with Colorectal Cancer at Hawassa University Comprehensive Specialized Hospital, Sidama Region, Southern Ethiopia: A retrospective cohort study.**

Name of principal investigator: **Deresse Daka**
Name of the organization: **Pharma Health Science College Hawassa**
Name of the sponsor: **principal investigator**

Introduction: This information sheet is prepared for Hawass University comprehensive referral hospital Director Office. The aim of the form is to make the above concerned offices clear about the purpose of the research work, data collection procedure and get permission to undertake the research.

Purpose of the research project: -To assess Determinants of delayed time to treatment initiation among patients with Colorectal Cancer at Hawassa University Comprehensive Specialized Hospital, Sidama Region, Southern Ethiopia: A retrospective cohort study.

Procedures: -In order to achieve the above objective, the record Cancer log books, charts, patient card and contact tracing log book) of CRC enrolled since 2020 will be reviewed by using check list.

Risk and discomfort: -By participating in this research project, there is no risk that comes to the CRC clinic in general and the client whose record will be review. Whereas the review is of great important to the research project which is in turn important for overall planning of program.

Benefit: -The research has no direct benefit to those who have participated in this project. But the indirect benefit of the research for the participant and all other clients in the program is great. As identifying area of improvement and taking appropriate decision helps to improve the service, increase access and overall effectiveness of the program and reduce incidence of mortality attributed to CRC patients.

Confidentiality: -To keep the confidentiality the name of client will not be mentioned rather code number will be used and no unauthorized access to the information is allowed

Right to Refusal or Withdraw: -in behalf of the clients the center has all the right to refuse to participate in this study and shall have stopping the process at any steps of the data collection process.

Person to contact: -This research project will be reviewed and approved by the institutional review department of public health, post graduate program, Pharma College. If at any case you want to know more information about the research and its undertakings, you can contact the committee through the address of advisor and /or principal investigator.

1. Dr. Dejene Hailu, Associate professor) Department of public health, post graduate program, Hawassa University
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2. Deresse Daka, department of public health, post graduate program, Pharma College
   Principal investigator,
   +251911968912 email. drsdzk200@gmail.co

Permission: Finally, we are kindly requested to permit and forward your permission to concerned body in your organization so that the researchers can get cooperation from responsible body in the consecutive units.

Name: _____ signature: _____

Responsibility: _____

ANNEX-V: Consent form

ID #_____ _____ Date of collection

Introduction

Hello! Madam/sir

My name is_____. I am data collector for the research by a team of researchers from Pharma college. The purpose of this checklist is to gather information for "Determinants of delayed time to treatment initiation among patients with Colorectal Cancer at Hawassa University Comprehensive Specialized Hospital, Sidama Region, Southern Ethiopia: A retrospective cohort study". This retrospective data analysis will help identify healthcare system barriers and inform improvements in cancer care delivery.

Thank you for being voluntary to participate in the study!