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RESEARCH ARTICLE

Treatment Outcomes and Predictors of Relative Dose Intensity Among Patients Receiving Chemotherapy for Colorectal Cancer in Nakuru County, Kenya: a Retrospective Cohort Study

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ABSTRACT

Colorectal cancer is an increasing cause of cancer morbidity and mortality in Africa, where late diagnosis and constrained oncology services may compromise treatment delivery. Relative dose intensity is an important measure of chemotherapy delivery, but evidence describing its predictors and relationship with outcomes in Kenyan public oncology practice remains limited. The aim of the study was to determine chemotherapy RDI, identify factors associated with achieving optimal RDI, evaluate treatment response and survival, and examine the relationship between RDI and treatment outcomes among patients with colorectal cancer receiving chemotherapy at a county referral hospital in Kenya. A retrospective cohort study was conducted using records of adults with colorectal cancer treated between January 2020 and December 2024 at Nakuru County Referral Hospital. A simple random sample was drawn from 300 eligible records; 186 records were selected, and 185 complete records were analysed. Data were abstracted using a structured tool. RDI was calculated as the actual dose intensity divided by the planned dose intensity × 100 and classified as optimal (≥85%) or suboptimal (<85%). Descriptive statistics, chi-square tests, binary logistic regression, Kaplan-Meier analysis, log-rank tests, and unadjusted Cox regression were performed using SPSS version 26. The mean RDI was 82.95% (SD 5.35; range 60.0-98.0%), with 44.9% achieving optimal RDI and 55.1% suboptimal RDI. Treatment delays occurred in 91.9% of patients, with toxicity the most common reason; dose reductions or adjustments occurred in 42.7%. Age group, dose reduction/adjustment (AOR 0.34, 95% CI 0.13-0.87; p = 0.025), and treatment response (overall p = 0.007) were independently associated with optimal RDI. Median overall survival was 15 months for suboptimal RDI and not reached for optimal RDI (HR 0.093, 95% CI 0.052-0.168). Corresponding progression-free survival results were 14 months and not reached (HR 0.103, 95% CI 0.060-0.179). Suboptimal chemotherapy RDI was common, characterised by frequent treatment delays and dose modification. Optimal RDI was strongly associated with better observed survival, although the unadjusted survival analyses do not establish causality. Routine toxicity management, treatment schedule monitoring, medication availability, and RDI monitoring may help strengthen chemotherapy delivery in comparable resource-constrained settings.

Keywords: *colorectal neoplasms; treatment delay; treatment outcome; survival; Kenya*

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INTRODUCTION

Colorectal cancer (CRC) is a major global cancer burden and remains an important cause of cancer morbidity and mortality. The GLOBOCAN colorectal cancer fact sheet identified CRC as a substantial component of the global cancer burden, while the American Cancer Society reported that survival varies markedly by disease stage (American Cancer Society, 2023; GLOBOCAN, 2022). In Kenya, the burden of cancer care is particularly important because services must respond to increasing demand constrained health-system resources (Ministry of Health, Kenya, 2023; World Health Organization, 2022).

In sub-Saharan Africa, CRC outcomes remain less favourable than those reported in many high-income settings. Population-based and systematic review evidence has shown substantial variation in survival across the region, with poorer outcomes associated with advanced disease and differences in health-system capacity (Hämmerl et al., 2023). A retrospective cohort study from Kenya also reported significant survival differences among patients with CRC treated at a national referral hospital (Degu et al., 2023). Epidemiological work from Africa has further demonstrated the changing burden of CRC and the continuing importance of timely diagnosis and access to effective treatment (El Anssari et al., 2023; World Health Organization, 2022).

Chemotherapy remains a central component of treatment for locally advanced and metastatic CRC, with fluoropyrimidine- and oxaliplatin-based regimens such as Capecitabine plus Oxaliplatin and Folinic acid, Fluorouracil plus Oxaliplatin used in clinical practice (Aspinall et al., 2015; Mamo et al., 2016). The duration and intensity of treatment may be modified according to disease characteristics, toxicity, and patient tolerance (Abdel-Rahman, 2019; Watanabe et al., 2017). The effectiveness of chemotherapy depends not only on the selected regimen but also on the amount and timing of treatment actually delivered. Relative dose intensity (RDI) quantifies delivered chemotherapy intensity relative to planned intensity over a specified period. The 85% threshold has commonly been used as a clinically meaningful benchmark in chemotherapy dose-intensity research, although the relevant threshold may differ by regimen and treatment setting (Blazevic et al., 2020; Bylsma et al., 2021; Lyman, 2009).

Previous studies indicate that treatment interruptions and dose modifications can affect chemotherapy intensity and outcomes. Bylsma et al. (2021) reported an association between lower chemotherapy RDI and poorer survival across advanced solid tumours. In colon cancer, Brown et al. (2024) found that lower postoperative chemotherapy RDI was associated with poorer overall survival, while Hoba et al. (2025) examined RDI in first-line triplet chemotherapy for metastatic CRC. Other studies have described the effects of dose intensity and treatment modification in colorectal cancer, including CAPOX and mFOLFOX6, as well as palliative chemotherapy dose modification (Aspinall et al., 2015; Fu, 2024; Mamo et al., 2016; Zainal Abidin et al., 2022). Treatment delays and dose reductions have also been examined in relation to chemotherapy delivery and tolerance (Watanabe et al., 2017; Wonders et al., 2023).

Kenya faces a growing cancer burden within a health system where cancer services must operate under resource constraints. The national cancer-control strategy identifies timely access to quality diagnosis and treatment as an important priority (Ministry of Health, Kenya, 2023). Previous Kenyan and regional studies have demonstrated poor survival among patients with CRC and highlighted the importance of stage at diagnosis, age, and health-system context (Degu et al., 2023; Hämmerl et al., 2023). Despite this evidence, local information on the actual chemotherapy dose intensity delivered in routine county-level oncology care remains limited. Understanding how patient characteristics, treatment modifications, and delivery disruptions relate to RDI is therefore relevant to clinical quality improvement.

The present study addressed this gap by evaluating the delivery of CRC chemotherapy at the Nakuru County Referral Hospital over a five-year period. Specifically, it determined RDI, examined factors associated with optimal RDI, evaluated treatment response and survival, and assessed the relationship between RDI and treatment outcomes. The findings were intended to provide locally relevant evidence for oncology teams and health-system managers seeking to reduce avoidable treatment interruptions while preserving patient safety.

METHODS

Study Design

A retrospective cohort design was used to evaluate chemotherapy delivery and outcomes from existing clinical records. The design enabled retrospective follow-up of patients who had already received treatment, from CRC diagnosis through chemotherapy delivery to subsequent documented outcomes, without altering clinical care. Records covering 1 January 2020 to 31 December 2024, were reviewed.

Survival outcomes were ascertained from medical records up to 31 July 2026, the proposed administrative censoring date. Patients without the outcome of interest were censored at their last documented follow-up. This approach was appropriate for assessing real-world treatment intensity, treatment modifications, and time-to-event outcomes in a routine oncology setting, using existing clinical information, and was consistent with the retrospective cohort approach used in Kenyan CRC survival research (Degu et al., 2023).

Study Setting

The study was conducted at Nakuru County Referral Hospital, a level 5 public referral facility in Nakuru County, Kenya. The hospital has a reported capacity of 588 inpatient beds and serves Nakuru County and the wider Rift Valley region (Veligraph. (n.d.). Its oncology services include chemotherapy, radiotherapy, surgery, immunotherapy, hormonal therapy, and targeted therapy. The facility was selected because it provides comprehensive cancer services and maintains records that allow reconstruction of chemotherapy regimens, treatment dates, dose modifications, and outcomes. The setting, therefore provided an appropriate routine-care context for examining RDI in a Kenyan county referral hospital.

Study Population

The target population comprised adults diagnosed with CRC who received chemotherapy. The accessible population comprised CRC patients treated at the study hospital between January 2020 and December 2024 whose records contained sufficient information to calculate chemotherapy RDI and assess outcomes. Inclusion criteria were: (1) age 18 years or older; (2) CRC diagnosed during the study period; (3) receipt of at least one chemotherapy cycle at the study hospital; and (4) adequate documentation of chemotherapy regimen, doses, and treatment outcomes. Records were excluded if they were incomplete, if chemotherapy was being given for a concurrent malignancy, or if the patient received best supportive care without chemotherapy.

Sampling Procedure

A sampling frame of 300 adult CRC patients who had received at least one chemotherapy cycle during the study period was obtained from hospital records. Simple random sampling was used. Each eligible record was assigned a unique identification number from 1 to 300, and a random sample was generated using SPSS. The corresponding files were retrieved and reviewed against the eligibility criteria. Records that did not contain the required chemotherapy and outcome information were excluded from the analytic dataset. Of the 300 records in the sampling frame, 19 were used for pretesting the data collection tool and excluded from the main study. From the remaining 281 records, 186 were selected for analysis following the sample-size calculation. Of these, 185 contained sufficient information for final analysis, while one record was excluded because of incomplete data. Because this was a retrospective record review, patients were not approached for participation, and there was no conventional participant non-response.

Sample Size Determination

Sample size was estimated using the single-population proportion formula: $n_0 = Z^2p(1-p)/d^2$. A 95% confidence level was used ($Z=1.96$), the expected proportion was set at 50% ($p=0.50$) because no reliable local estimate of suboptimal RDI was available, and the margin of error was 5% ($d=0.05$). Thus, $n_0 = (1.96^2 \times 0.50 \times 0.50)/(0.05^2) = 384.16$. Because the accessible population was 300 records, finite population correction was applied: $n = 384.16/[1 + (384.16 - 1)/300] = 168.7$, rounded to 169. A 10% allowance for incomplete records was then added: $169 + (0.10 \times 169) = 185.9$, yielding a target of 186 records. The final analytic sample comprised 185 complete records. Using a 50% expected proportion maximised the required sample size when a local estimate was unavailable.

Data Collection Tools

A structured data-abstraction tool was used to extract information from medical records. The tool contained sections covering demographic characteristics, clinical characteristics, diagnostic investigations, baseline laboratory findings, chemotherapy regimen and cycles, planned and delivered doses, dose reductions, treatment delays, toxicities, RDI, treatment response, recurrence, and survival status. RDI was calculated from the recorded regimen and treatment-date information. The tool was developed from the study objectives and the literature and was pretested on approximately 10% of the calculated sample size (19 records) to assess clarity and feasibility; pilot records were not included in the main analysis. Content validity was assessed by reviewing whether the tool captured the variables required for the research objectives. Inter-rater reliability was not formally assessed using Cohen's kappa during pretesting. The pretest was used to evaluate the clarity and suitability of the data collection tool before the main data collection.

Data Collection Procedure

Data were abstracted from eligible medical records using the structured tool. A trained health-records information officer and a clinician worked with the principal investigator to review records and extract the required variables.

The abstraction process began with identification of the eligible record, followed by confirmation of diagnosis and treatment period, extraction of demographic and clinical characteristics, recording of diagnostic and laboratory information, and reconstruction of chemotherapy delivery. For each chemotherapy regimen, planned cycles, planned doses, treatment intervals, actual doses, completed cycles, dose modifications, and treatment delays were recorded. Clinician-reported treatment response, disease progression or recurrence, and survival status were also extracted. The response variable was based on the treating clinician's documented assessment and, when available, supporting clinical or imaging information. Each completed abstraction was checked for completeness and consistency before anonymisation. Data collectors worked under supervision, and discrepancies were reviewed jointly to minimise abstraction errors.

Data Quality Control

Data-quality procedures were applied before, during, and after abstraction. Data collectors were trained to use the tool and to understand the operational definitions of RDI, treatment delay, dose modification, response, recurrence, overall survival, and progression-free survival. During abstraction, the principal investigator and clinician reviewed completed forms for missing or inconsistent entries. After collection, the records were coded, checked, and cleaned before analysis. Inter-rater reliability was assessed during pretesting using Cohen's kappa. Records lacking essential information for RDI calculation or outcome assessment were excluded from the final analytic dataset.

Data Management and Analysis

Data were entered into Microsoft Excel, cleaned, and imported into SPSS version 26. Descriptive statistics summarised demographic, clinical, treatment, and outcome characteristics. Relative dose intensity (RDI) was calculated for each chemotherapy drug as actual dose intensity divided by planned dose intensity, multiplied by 100. Drug-specific RDI values were combined to obtain one patient-level RDI, classified as optimal (≥85%) or suboptimal (<85%). The analysis included CAPOX and other chemotherapy regimens documented in participants' medical records. Planned dose intensity was defined in mg/m² per week according to the standard regimen schedule. For CAPOX, FOLFOX, and FOLFIRI, RDI was assessed separately for each drug rather than adding doses across drugs or regimens. RDI covered the planned treatment course, including documented delays and dose modifications. Regimen switches were assessed according to the regimen received. Only documented treatment at the study hospital was included. Variables associated with optimal relative dose intensity (RDI ≥85%) at the bivariate stage were considered for inclusion in the multivariable binary logistic regression model.

Bivariate associations were assessed using Pearson's chi-square test, continuity-corrected chi-square test, or Fisher-Freeman-Halton exact test, as appropriate. Variables with a bivariate p-value < 0.05 were considered for entry into the regression model. The final model was reduced according to the documented variable-selection procedure, and the predictors retained in the final model were reported with adjusted odds ratios (AORs), 95% confidence intervals (CIs), and p-values. Statistical significance was set at $p < 0.05$. Model adequacy was assessed using the omnibus likelihood test, Cox and Snell R^2, Nagelkerke R^2, and the Hosmer-Lemeshow goodness-of-fit test. Overall survival (OS) was defined as time from CRC diagnosis to death from any cause; living patients were censored at the last documented follow-up. Progression-free survival (PFS) was defined as time from diagnosis to documented progression, recurrence, or death, whichever occurred first. Progression and recurrence dates were determined from the date documented by the treating clinician in the patient's medical record. Kaplan-Meier methods estimated survival functions and medians, and log-rank tests compared survival curves. Unadjusted Cox proportional-hazards models estimated hazard ratios (HRs) with 95% CIs. Statistical significance was set at $p < 0.05$.

Ethical Considerations

Ethical approval was obtained from the Kabarak University Research Ethics Committee (KUREC), approval number KUREC-120326, dated 5 March 2026. KUREC granted a waiver of informed consent because the study involved retrospective review of existing records. Research authorisation and licensing were also granted by the National Commission for Science, Technology and Innovation (NACOSTI) under license number NACOSTI/P/26/4186575, issued on 25 March 2026. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. As the study involved a retrospective review of existing records and no direct participant intervention. Patient identifiers were removed, and study codes were used instead. Data were stored securely on password-protected devices, access was restricted to authorised study personnel, and records were handled within the hospital premises. The study adhered to principles of respect for persons, beneficence, non-maleficence, and justice. No biological samples were collected or transferred, and no financial incentives were provided.

The study was conducted in accordance with institutional research requirements and applicable ethical standards.

RESULTS

Participant Characteristics

The sampling frame contained 300 eligible records. A total of 186 records were selected for review, of which 185 contained complete information and were included in the final analysis. Because the study was based on retrospective records, there was no participant approach or conventional non-response. The mean age at diagnosis was 57.65 years (standard deviation [SD] 13.87), and 134 (72.4%) participants were older than 50 years. Males accounted for 105 (56.8%) participants and females for 80 (43.2%). Most participants were in informal employment (78.4%), and 173 (93.5%) were insured. The mean body mass index (BMI) was 23.22 kg/m² (SD 3.54). Stage III disease was most frequent (43.8%), followed by stage IV disease (34.1%), while 29.2% had documented metastasis. These characteristics are presented in Tables 1 and 2.

Table 1: *Socio-demographic Characteristics of the Study Population*

	Mean	SD
Age at Diagnosis	57.65	13.87
	Frequency	**Percent**
Age Group		
18-25 Years	2	1.1
26-30 Years	6	3.2
31-40 Years	11	5.9
41-50 Years	32	17.3
Above 50 Years	134	72.4
Gender		
Male	105	56.8
Female	80	43.2
Occupation		
Informal	145	78.4
Formal	21	11.4
Unemployed	19	10.3
Health Insurance		
Insured	173	93.5
Not Insured	12	6.5
Total	**185**	**100**

Table 2: *Clinical Characteristics of the Study Population*

	Mean	SD
BMI	23.22	3.54
BMI Classification	**Frequency**	**Percent**
Underweight (<18.5)	20	10.8
Normal weight (18.5-24.9)	111	60
Overweight (25.0-29.9)	47	25.4
Obese (≥30.0)	7	3.8
Stage at diagnosis		
Stage I	9	4.9
Stage II	32	17.3
Stage III	81	43.8
Stage IV	63	34.1
Presence of Metastasis		
Yes	54	29.2
No	131	70.8
Presence of Comorbidities		
Yes	96	51.9
No	89	48.1
Eastern Cooperative Oncology Group Performance		
ECOG 0	27	14.6
ECOG 1	127	68.6
ECOG 2	30	16.2
ECOG 3	1	0.5
Total	**185**	**100**

Relative Dose Intensity and Chemotherapy Delivery

The mean RDI was 82.95% (SD 5.35), with a minimum of 60.0% and a maximum of 98.0%. CAPOX alone was the predominant chemotherapy pattern, used in 116 (62.7%) participants. A total of 128 (69.2%) participants completed all planned chemotherapy cycles, whereas 57 (30.8%) did not. Dose reduction or adjustment was documented in 79 (42.7%) participants, and 170 (91.9%) experienced at least one treatment delay. Among reported reasons for delay, treatment toxicity occurred 160 times, drug unavailability 28 times, patient-declined treatment 11 times, and financial constraints/cost 7 times. Toxicities were recorded as multiple responses; neutropenia (n = 77), anaemia (n = 63), and diarrhoea (n = 36) were the most frequently documented.

Table 3: *Classification of Relative Dose Intensity Among Study Participants*

Relative Dose Intensity Category	Frequency (n)	Percentage (%)
Optimal (≥85%)	83	44.9
Suboptimal (<85%)	102	55.1
Total	185	100

Note. RDI = relative dose intensity.

Relative Dose Intensity and Chemotherapy Delivery

The most frequently documented treatment response was stable disease in 105 (56.8%) participants, followed by partial response in 52 (28.1%), complete response in 16 (8.6%), refractory disease in 9 (4.9%), and relapse in 3 (1.6%). Disease recurrence was documented in 20.5% of participants. The median follow-up from diagnosis to last documented follow-up was 20 months. At the last follow-up, 101 (54.6%) participants were deceased, 74 (40%) were alive, and survival status was unknown for 10 (5.4%); these participants were censored at their last documented follow-up date. Kaplan-Meier analysis estimated median OS at 24 months and median PFS at 23 months. One-, three-, and five-year OS estimates were 78.6% (95% CI 72.6-84.6), 39.2% (31.0-47.4), and 30.4% (19.5-41.3), respectively, while the corresponding PFS estimates were 70.8% (64.2-77.4), 38.6% (30.7-46.5), and 31.6% (22.3-40.9). The five-year estimates are the last estimates carried forward to 60 months, when only 4 participants remained at risk. These survival estimates are shown in Figures 1 and 2.

Figure 1: *Kaplan-Meier Overall Survival from Diagnosis*

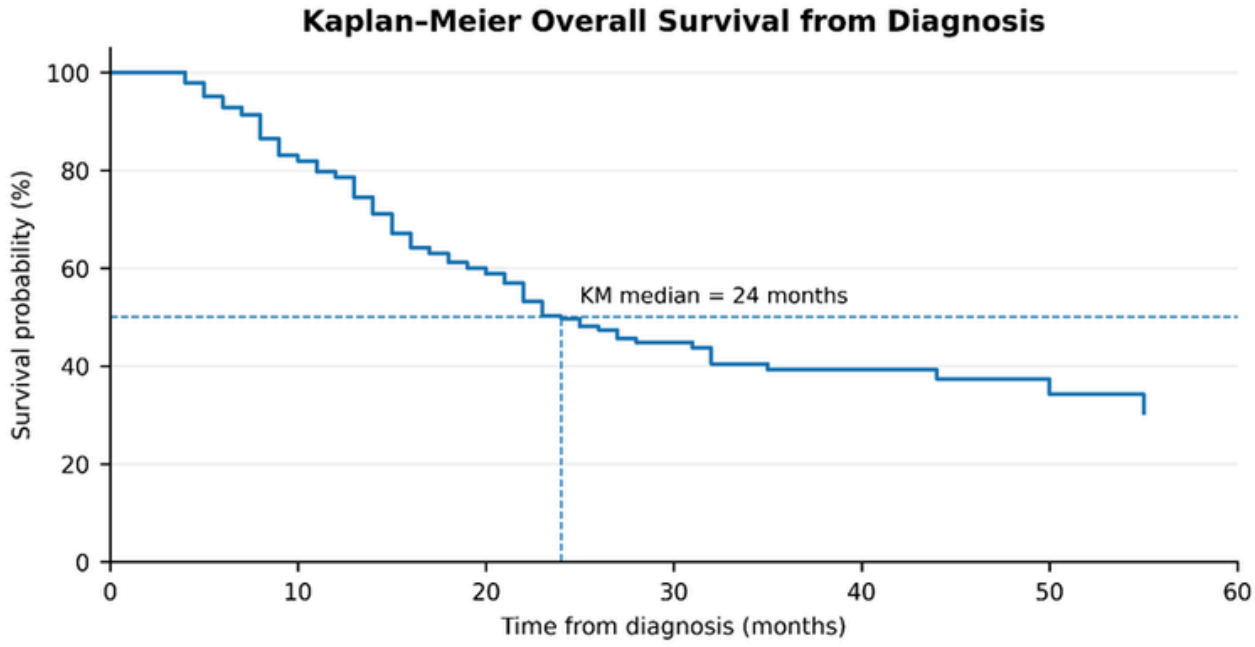


Figure 2: *Kaplan-Meier Progression-Free Survival from Diagnosis*

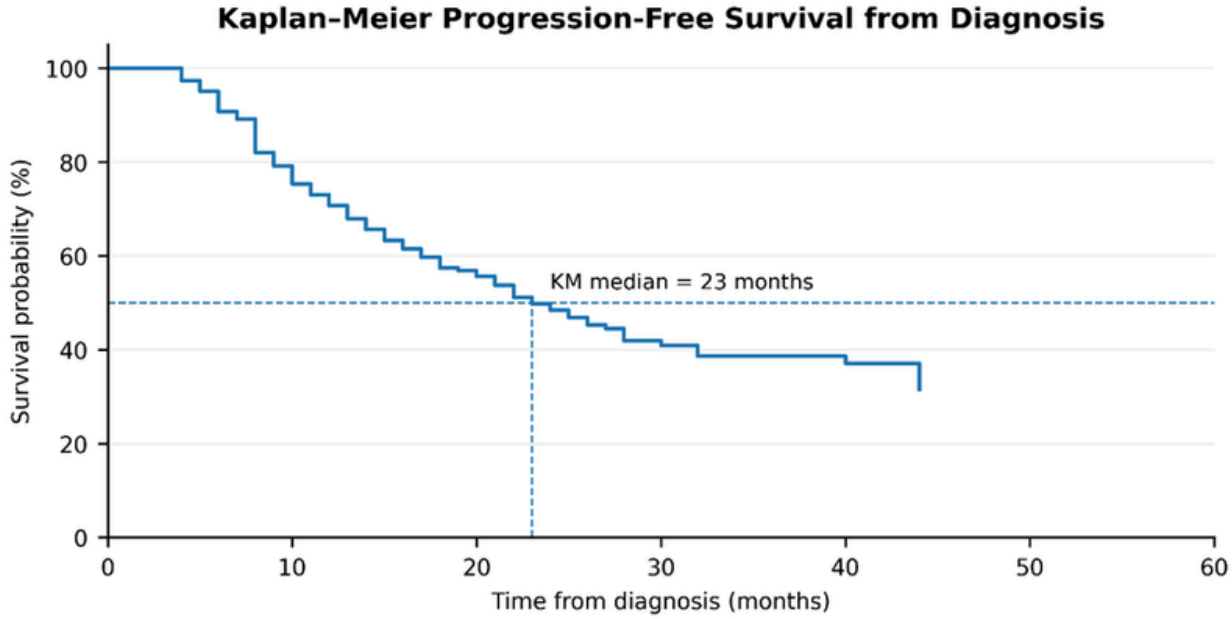


Table 4: *Bivariate Associations Between Study Variables and Achievement of Optimal RDI*

Variable	Category	Suboptimal RDI, n (%)	Optimal RDI, n (%)	Test statistic	p-value
Age group	18-40 years	3 (15.8)	16 (84.2)	Fisher-Freeman-Halton test	<0.001
	41-50 years	10 (31.3)	22 (68.8)		
	>50 years	89 (66.4)	45 (33.6)		
Gender	Male	66 (62.9)	39 (37.1)	$\chi^2 = 5.154$	0.023
	Female	36 (45.0)	44 (55.0)		
Stage at diagnosis	Stage I	1 (11.1)	8 (88.9)	$\chi^2 = 32.743$	<0.001
	Stage II	7 (21.9)	25 (78.1)		
	Stage III	46 (56.8)	35 (43.2)		
	Stage IV	48 (76.2)	15 (23.8)		
Metastasis	Present	40 (74.1)	14 (25.9)	$\chi^2 = 10.003$	0.002
	Absent	62 (47.3)	69 (52.7)		
Comorbidities	Present	61 (63.5)	35 (36.5)	$\chi^2 = 5.016$	0.025
	Absent	41 (46.1)	48 (53.9)		

Dose reduction/adjustment	Yes	62 (78.5)	17 (21.5)	$\chi^2 = 28.755$	<0.001
	No	40 (37.7)	66 (62.3)		
Treatment delay	Yes	102 (60.0)	68 (40.0)	$\chi^2 = 17.708$	<0.001
	No	0 (0.0)	15 (100.0)		

Percentages were calculated within each category. Pearson's chi-square was used for variables with more than two categories, except age group, for which the Fisher-Freeman-Halton test was used because of sparse cells after merging the 18-25, 26-30, and 31-40 years categories into 18-40 years. Continuity-corrected chi-square was used for 2×2 tables. Optimal RDI was defined as ≥85%. At bivariate analysis (Table 4), age group was associated with optimal RDI ($p < 0.001$), with 84.2% of participants aged 18-40 years, 68.8% aged 41-50 years, and 33.6% aged >50 years achieving optimal RDI. Gender ($p = 0.023$), stage ($p < 0.001$), metastasis ($p = 0.002$), and comorbidities ($p = 0.025$) were also associated. Dose reduction and treatment delay were significantly associated with RDI ($p < 0.001$).

Multivariable Analysis

The multivariable binary logistic regression model was statistically significant (omnibus $\chi^2 = 126.794$, $df = 18$, $p < 0.001$). Cox and Snell R^2 was 0.496 and Nagelkerke R^2 was 0.664. The Hosmer-Lemeshow test was not statistically significant ($\chi^2 = 9.812$, $df = 8$, $p = 0.278$), indicating no evidence of poor fit. Age group was independently associated with optimal RDI (overall $p = 0.021$). Dose reduction or adjustment was associated with lower odds of optimal RDI (AOR = 0.34, 95% CI 0.13-0.87; $p = 0.025$). Gender, BMI, metastasis, and comorbidities were not independently associated with optimal RDI after adjustment. Stage was not significant overall ($p = 0.141$), although stage II, compared with stage IV, the reference category, had an AOR of 12.52 (95% CI 1.48-105.76; $p = 0.020$). The full model estimates are shown in Table 5.

Table 5: *Predictors of Optimal Relative Dose Intensity (Binary Logistic Regression)*

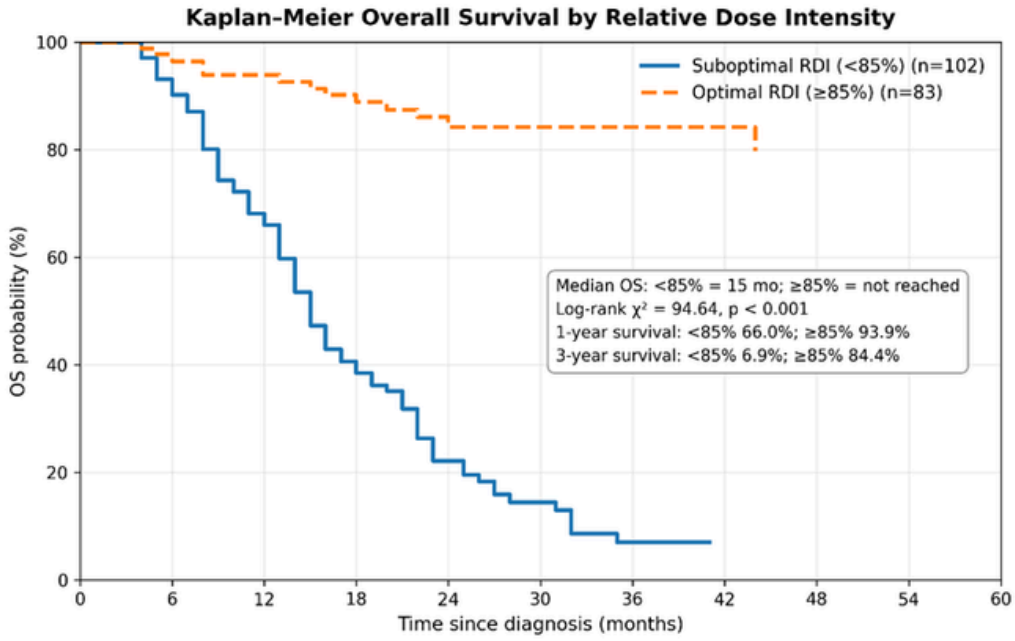
Predictor	Adjusted OR (95% CI)	p-value
Age group (overall)	—	0.021
Gender	0.60 (0.23-1.59)	0.303
BMI	1.04 (0.91-1.19)	0.549
Stage at diagnosis (overall)	—	0.141
Stage II vs reference	12.52 (1.48-105.76)	0.02
Stage III vs reference	3.18 (0.62-16.18)	0.164
Presence of metastasis	2.14 (0.40-11.46)	0.372
Presence of comorbidities	1.13 (0.44-2.89)	0.795
Dose reduction/adjustment	0.34 (0.13-0.87)	0.025
Response category 4	0.03 (0.001-0.51)	0.016
Disease recurrence	0.32 (0.08-1.23)	0.097

Note. AOR = adjusted odds ratio; CI = confidence interval; BMI = body mass index; RDI = relative dose intensity. Response category 4 was defined as refractory disease. The reference categories were >50 years for age, Stage IV for stage at diagnosis, and relapse (response category 5) for treatment response.

Relationship Between RDI and Survival

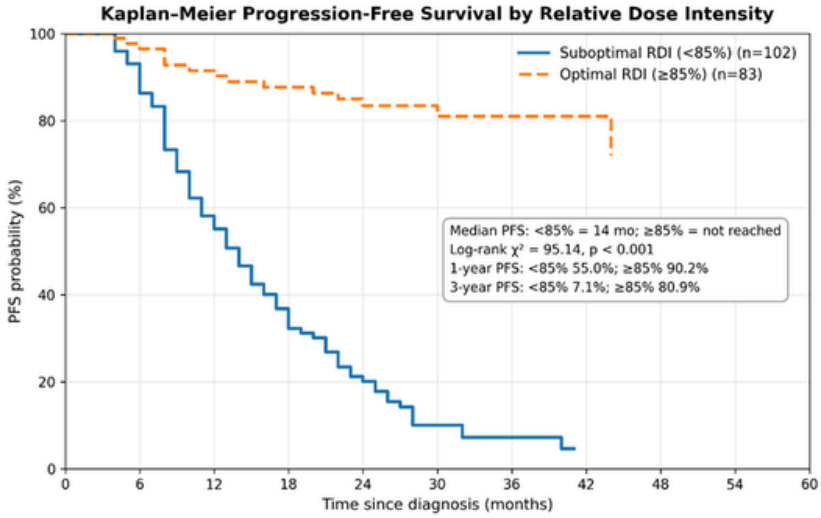
Overall survival differed between RDI categories (Figure 3). The suboptimal-RDI group included 102 participants, with 88 deaths and a median OS of 15 months. The optimal-RDI group included 83 participants, with 13 deaths and a median OS that was not reached. The log-rank test showed a difference between the survival curves ($\chi^2 = 94.64$, df = 1, $p < 0.001$), and unadjusted Cox regression estimated a lower hazard of death among participants with optimal RDI (HR = 0.093, 95% CI 0.052-0.168; $p < 0.001$) (Table 6). PFS showed a similar pattern (Figure 4). Median PFS was 14 months in the suboptimal-RDI group and was not reached in the optimal-RDI group. The log-rank test was significant ($\chi^2 = 95.14$, df = 1, $p < 0.001$), and the unadjusted Cox model showed a lower hazard of progression or death among participants with optimal RDI (HR = 0.103, 95% CI 0.060-0.179; $p < 0.001$) (Table 7).

Figure 3: *Overall Survival by Relative Dose Intensity*



Number at risk											
Suboptimal RDI (<85%)	102	94	66	37	19	10	3	3	3	2	1
Optimal RDI (≥85%)	83	81	75	69	53	35	27	19	12	9	3

Figure 4: *Progression-Free Survival by Relative Dose Intensity*



Number at risk											
Suboptimal RDI (<85%)	102	94	56	33	19	7	3	2	1	1	1
Optimal RDI (≥85%)	83	81	73	68	53	35	26	19	11	8	3

Table 6: *Overall Survival According to Relative Dose Intensity*

RDI category	N	Deaths	Censored	Median OS (months)
Suboptimal (<85%)	102	88	14	15
Optimal (≥85%)	83	13	70	Not reached
Total	185	101	84	24.0 overall

Table 7: *Progression-Free Survival According to Relative Dose Intensity*

RDI category	N	PFS events	Censored	Median PFS (months)
Suboptimal (<85%)	102	89	13	14
Optimal (≥85%)	83	16	67	Not reached
Total	185	105	80	23

Note. OS = overall survival; PFS = progression-free survival; RDI = relative dose intensity.

DISCUSSION

Summary of Main Findings

This study found that maintaining planned chemotherapy intensity was difficult in routine CRC care at a Kenyan county referral hospital. The mean RDI was 82.95%, below the predefined 85% threshold, and 55.1% of patients had suboptimal RDI. Treatment delays were documented in 91.9% and dose reductions or adjustments in 42.7%, with treatment toxicity the most frequently documented reason for delay. Median OS and PFS were 24 and 23 months, respectively, and optimal RDI was associated with longer observed OS and PFS.

RDI and Treatment Delivery

The proportion with suboptimal RDI is clinically relevant because RDI reflects both the quantity and timing of chemotherapy delivered. The finding is consistent with evidence that chemotherapy dose intensity can be compromised by dose modification and treatment interruption (Aspinall et al., 2015; Blazevic et al., 2020; Bylsma et al., 2021). Brown et al. (2024) reported poorer overall survival with lower postoperative RDI in colon cancer, while Hoba et al. (2025) evaluated RDI in first-line triplet chemotherapy for metastatic CRC. The present study extends this evidence to routine county-level oncology care in Kenya. The particularly high prevalence of treatment delays suggests that chemotherapy delivery problems may reflect not only planned clinical dose modifications but also broader health-system constraints, including barriers to cancer medicine availability and affordability in Kenya and other East African countries (Kizub et al., 2022).

Toxicity, Age, and Dose Modification

Treatment toxicity was the most frequently recorded reason for delay, and neutropenia was the most common documented toxicity. Previous work has identified chemotherapy toxicity and performance status as important considerations in treatment tolerance and chemotherapy delivery (Abdel-Rahman, 2019; Watanabe et al., 2017). The AOR of 0.34 for dose reduction or adjustment is expected because dose modification directly reduces the delivered dose relative to the planned regimen. However, dose reduction should not be interpreted as inappropriate care: clinical modification may be necessary to manage toxicity and preserve patient safety. The practical goal is therefore not to eliminate all dose reductions but to distinguish clinically necessary modifications from avoidable treatment interruptions.

Survival and the RDI-Outcome Relationship

The median OS of 24 months and the median PFS of 23 months were observed in a population in which 77.8% had stage III or IV disease. These findings are consistent with Kenyan and broader sub-Saharan African evidence showing substantial survival disadvantages associated with advanced presentation and health-system constraints (Hämmerl et al., 2023). The strong association between optimal RDI and survival is also consistent with the wider RDI literature. Zainal Abidin et al. (2022), Brown et al. (2024), Bylsma et al. (2021), Hoba et al. (2025), and Blazevic et al. (2020) reported associations between chemotherapy dose modification or intensity and survival outcomes.

The current study observed substantial differences in survival between RDI groups; however, these findings should be interpreted cautiously because the Cox models were unadjusted and may be affected by immortal time bias, and reverse causation, whereby poor early treatment outcomes may lead to reduced RDI rather than low RDI being solely responsible for poorer outcomes. Patients able to maintain optimal RDI may have been healthier, had less aggressive disease, experienced fewer complications, or had better access to treatment. Therefore, the findings support RDI as an important marker of chemotherapy delivery and a potential quality-of-care indicator, rather than as proof that increasing RDI alone improves survival.

Practical Implications

The findings support several feasible quality-improvement priorities. Oncology services should monitor treatment dates, dose changes, and toxicities prospectively enough to identify emerging reductions in RDI before treatment completion. Structured pre-treatment assessment and early management of clinically important toxicities may reduce avoidable delays, while medicine forecasting and stock monitoring may mitigate interruptions in drug availability. RDI should be interpreted alongside treatment intent, disease stage, performance status, toxicity, and response rather than used as an isolated treatment target. These priorities are consistent with evidence on chemotherapy dose intensity, treatment tolerance, and barriers to chemotherapy delivery (Kuderer et al., 2022; Ministry of Health, Kenya, 2023; Wonders et al., 2023).

Strengths and Limitations

A major strength was the use of a five-year clinical record cohort with 185 complete records and a detailed reconstruction of chemotherapy delivery. The study also incorporated RDI calculation, logistic regression, and time-to-event analyses, allowing the treatment-delivery and survival objectives to be examined within a single dataset. The use of clinician-reported responses and documented imaging or clinical information was appropriate for a retrospective study. Several limitations should nevertheless be considered. First, the single-facility retrospective design limits generalisability to other Kenyan oncology centres and introduces dependence on the completeness of routine documentation. Second, important prognostic factors, including molecular tumour characteristics, were only partially available and could not be fully incorporated. Third, the survival Cox analyses were unadjusted and are therefore vulnerable to confounding by stage, ECOG status, comorbidity, metastatic disease, and treatment tolerance. Fourth, causes of delay were based on documented records and may not capture all patient, financial, transport, or health-system barriers. Finally, the study did not independently reclassify responses using a standard radiological response system; it relied on clinician-reported responses as documented in the records.

Future Research

Future studies should use prospective, multicentre designs across county, regional, and national oncology facilities in Kenya. Prospective data collection would allow treatment delays, dose modifications, toxicity grades, drug availability, and patient-level barriers to be recorded as they occur. Future survival analyses should use adjusted Cox models incorporating stage, ECOG status, metastatic status, comorbidity, treatment regimen, treatment intent, and relevant tumour characteristics. Research should also clarify the temporal relationship between RDI and treatment response and examine which delays are avoidable. Implementation studies could test proactive toxicity monitoring, appointment reminders, supportive care pathways, real-time RDI dashboards, and chemotherapy supply management interventions.

CONCLUSION

Chemotherapy delivery among adults with colorectal cancer at the study hospital was characterised by frequent treatment interruptions and a mean RDI below the predefined optimal threshold. More than half of the participants had suboptimal RDI, while age group was associated with optimal RDI after adjustment. Median overall survival was 24 months and median progression-free survival was 23 months. Optimal RDI was associated with longer observed overall and progression-free survival, but the unadjusted survival models do not demonstrate a causal effect and the association is likely inflated by immortal time bias. The findings indicate that RDI is a useful indicator for monitoring the quality and continuity of chemotherapy delivery. Strengthening toxicity management, medicine availability, treatment scheduling, documentation, and routine RDI monitoring may support safer and more consistent cancer treatment in resource-constrained oncology settings.

RECOMMENDATIONS

Clinical practitioners

Implement structured toxicity assessment before each chemotherapy cycle and establish early management pathways for neutropenia, anaemia, diarrhoea, and other clinically important toxicities. Use RDI as a monitoring indicator alongside disease stage, treatment intent, ECOG performance status, and patient safety.

Hospital administrators and oncology services

Establish routine monitoring of planned and delivered chemotherapy dates and doses, with RDI reviewed at predefined treatment points. Develop appointment-tracking and reminder systems and document the reason for every treatment delay or dose modification.

County and national health authorities

Strengthen forecasting, procurement, stock monitoring, and distribution of essential chemotherapy and supportive medicines. Ensure county oncology services have adequate laboratory, infusion, diagnostic, and supportive care capacity to reduce avoidable interruptions.

Researchers

Conduct prospective multicentre studies with adjusted survival models and detailed recording of toxicity, treatment intent, drug availability, patient barriers, and tumour characteristics. Evaluate whether targeted interventions reduce avoidable treatment delays and increase the proportion of patients achieving clinically appropriate RDI.

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Competing Interests

The authors declare that they have no competing interests.

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Author Contributions

RMK conceptualized the study, performed data collection, cleaning and analysis. PKT and IWW contributed to the interpretation of the results and provided revisions to the manuscript. All authors read and approved the final manuscript.

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