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Effects of Treatment Delays on Colorectal Cancer Survival

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Abstract

Introduction: Colorectal cancer (CRC) is a leading cause of cancer-related deaths worldwide. Understanding the influence of patient characteristics and treatment modalities on delays in care and related outcomes is crucial for optimizing treatment strategies and improving patient survival. **Methods**: A retrospective analysis of 2359 CRC patients from the NCI PLCO trial was conducted to assess the relationships between treatment initiation delays (*i.e.*, waiting times from diagnosis to start of treatment) and mortality outcomes. Descriptive statistics, multivariable regression analyses, and Cox proportional hazards regression analyses were employed to analyze the data. **Results**: Patients who underwent resection with chemotherapy and those who received chemotherapy without resection, as well as patients with disabilities, exhibited a higher hazard ratio (HR) for mortality. Individuals who used ibuprofen showed a lower HR for mortality. Despite examining multiple waiting time predictors, no significant associations were found between these predictors and mortality risk. The model's non-significant likelihood ratio chi-square and log-likelihood value suggested that it did not provide an adequate fit to the data. **Discussion**: This study highlights the importance of understanding the relationships between patient characteristics, treatment modalities, and their impact on patient outcomes in CRC patients. The lack of association between waiting time predictors and mortality risk may reflect the short time between diagnosis and treatment initiation in this study cohort. **Conclusion**: Studies examining potential impacts of treatment initiation delays on CRC outcomes may need to utilize data from cohorts with broader ranges of delays. Further research is needed to identify additional factors that may influence mortality risk and to optimize treatment strategies for this patient population.

Keywords

Colorectal Cancer, Treatment Delay, Survival Analysis, PLCO Trial, Cox Regression

1. Introduction

CRC is among the most commonly diagnosed malignancies in the United States, with an estimated 154,270 new cases and 52,900 deaths projected in 2025 [1]. Survival outcomes vary markedly by stage at diagnosis: the five-year relative survival rate is approximately 91% for localized disease, declines to 73% for regional disease, and falls sharply to 13% for distant metastases [2].

Standard treatment for CRC typically involves surgical resection, particularly for patients with non-metastatic disease. Depending on tumor location and stage, treatment may also include adjuvant or neoadjuvant chemotherapy, other systemic therapies, and for rectal cancers, radiation therapy [3] [4]. Despite established treatment guidelines, delays in initiating treatment remain common, and their implications for patient survival are not fully understood [5]-[7].

Biologically, CRC exhibits a relatively slow tumor growth rate in its early stages. For example, Spratt *et al.* (2016) estimated that a CRC tumor may require up to 1000 days to grow from 10 mm to 20 mm. However, once established, tumor progression accelerates, with reported doubling times of 352 days for stage II - III tumors and just 85 days for metastatic lesions [8]. A separate study by Burke *et al.* (2021) reported that the transition from size T2 to T4 can occur within approximately 400 days [9].

The impact of treatment delays on survival remains a subject of debate. A systematic review by Whittaker *et al.* (2019) found mixed results: only 3 of 7 studies reported a statistically significant negative association between delay in resection and overall or disease-free survival [10]. In contrast, other large retrospective studies have found more consistent associations between treatment delays and adverse outcomes. For instance, Singh *et al.* (2020) identified a significant increase in recurrence and mortality among stage II - III CRC patients with delayed initiation of adjuvant chemotherapy [11]. Lash *et al.* (2018) and Wallace *et al.* (2020) similarly reported that longer wait times were associated with worse overall survival and higher risk of recurrence in their respective cohorts [12] [13].

Given these conflicting findings, further research is warranted to clarify the relationship between time from diagnosis to treatment initiation and survival in CRC. To address this gap, we conducted a retrospective analysis using data from the National Cancer Institute's Prostate, Lung, Colorectal and Ovarian (PLCO) Trial, a large, multicenter study with comprehensive information on treatment patterns, tumor staging, and survival outcomes. This study aimed to rigorously evaluate whether treatment delays are associated with mortality among CRC patients within this nationally representative cohort.

2. Methods

2.1. Study Population

Data for this study were obtained from the NCI PLCO Cancer Screening Trial. This trial examines patients who underwent periodic CRC screening using flexible sigmoidoscopy (flex sigmoidoscopy – intervention arm) versus usual care (control

arm) to determine whether these screenings could reduce cancer mortality. The study also collected information on treatment patterns, timing, and outcomes for participants diagnosed with cancer. Approximately 155,000 participants were enrolled in PLCO between November 1993 and July 2001 [14].

In this analysis, we included all patients diagnosed in the control arm and intervention arm with CRC from the PLCO trial except for those with stage 0 tumors (in situ) and individuals with missing dates of diagnosis or treatment initiation. This exclusion criterion ensured that only patients who were appropriate to receive treatment, such as surgery, chemotherapy, and/or radiation therapy, were included in the analysis. In addition, as participation in the PLCO intervention arm may affect the association between time from diagnosis to treatment initiation and survival, separate subgroup analyses of individuals in the control arm (usual care) and those in the intervention arm (flex sigmoidoscopy) were conducted. The study analyzed stage at diagnosis using AJCC 5th classifications (current classification system at the time of the PLCO study) [15]-[17].

Patients in the analysis were stratified into two groups based on stage at diagnosis: early-stage tumors (stage I - II) and advanced-stage tumors (stage III - IV). This stratification was important to account for the high incidence of endoscopic treatment, such as endoscopic resection of tumors, during the first (diagnostic) endoscopy for patients with early-stage CRC.

In subgroup analyses of time to treatment initiation, patients were further separated based on initial treatment modality: surgery without chemotherapy, surgery with chemotherapy, or chemotherapy alone. The groups receiving chemotherapy were further divided based on whether the patient received monotherapy or multitherapy (two or more systemic agents).

2.2. Patient Characteristics

Patient characteristics obtained from the PLCO dataset included age at diagnosis, sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, Hispanic, non-Hispanic other), marital status (married, widowed, divorced, other), employment status (paid employment, "houseworker", retired), occupation (homemaker, working, unemployed, retired, extended sick leave, disabled, other) smoking status, personal history of non-cancer colon disease (ulcerative colitis, Crohn's disease, and polyps), and family cancer history in first degree relatives. As the mean age of patients at diagnosis in the study sample was 64 years (range 55 - 78 years), patient age was stratified as <65 vs. ≥65 to reflect the standard age of Medicare enrollment. Clinical characteristics included CRC stage at diagnosis, colorectal tumor location, tumor grade, initial primary treatment modality (resection, radiation, or chemotherapy), and combined treatment modality (resection without chemotherapy, resection with chemotherapy, chemotherapy without resection, or missing).

2.3. Delay in Treatment Initiation

The PLCO dataset provided information on the time between cancer diagnosis

and the start of treatment. We classified this time period using seven different types of measures. The first category was based on weeks from diagnosis to treatment initiation, with intervals of one week (7 days) up to a maximum of 11 weeks (78 days or more). The second category was based on months, with intervals of one month (30 days) up to a maximum of 10 months. The third category was based on CRC doubling time reported by Spratt, which groups waiting times (*i.e.*, times from diagnosis to treatment initiation) into three categories: <100 days, 100-200 days, and >200 days. The fourth category simplified the Spratt CRC doubling time measure to <200 days vs >200 days. The fifth category was based on the mean time from diagnosis to receive treatment in the PLCO trial: ≤19 days and >20. The sixth measure was based on the 75th percentile of time from diagnosis to treatment initiation, ≤24 days vs. >24 days. Finally, the seventh categorization was based on the mean time between diagnosis and treatment dates. These categories allowed us to analyze the associations of different measures of waiting times for cancer treatment and patient outcomes.

2.4. Analyses

Correlation and chi-square analyses were conducted to examine associations between survival and the duration between diagnosis and initial treatment controlling for patient sociodemographic and clinical characteristics and treatment received. Multivariable linear, logistic, and proportional hazards regression analyses were performed to examine the association of time from diagnosis to treatment with survival while controlling for these other covariates. The analyses provided HR, standard errors (Std. Err.), z-scores, p-values, and 95% confidence intervals (CI). The PH model used the Breslow method for ties and accounted for the censoring of data at the end of the study period or loss to follow-up. The statistical significance of the predictors was determined by p-values less than 0.05. Multicollinearity was assessed prior to multivariable analysis. Data analysis was conducted using Microsoft Excel 97-2003, STATA 17, and IBM SPSS statistics software version 28.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Patient Characteristics

The study sample included 2359 individuals from the PLCO Trial who were diagnosed with CRC; 720 patients (30.5%) died during the follow-up period. **Table 1** presents the characteristics of the sample.

The age distribution was approximately even, with 1188 patients (50.4%) aged 65 years or older and 1171 patients (49.6%) under 65. A majority of patients were male (55.3%), non-Hispanic White (85.7%), married (71.4%), and never smokers (56.1%).

More than half of the sample (55.0%) were retired. Regarding comorbidities, 6.2% of patients had a personal history of diverticulitis, while 1.5% had active non-cancerous colonic diseases (e.g., ulcerative colitis, Crohn's disease, or polyps).

Table 1. Characteristics of study sample.

Characteristic	Frequency	Percentage
Study Cohort	2359	100%
Died during PLCO follow-up period	720	30.5%
Age		
<65 years	1171	49.6%
≥65 years	1188	50.4%
Sex		
Male	1307	55.3%
Female	1052	44.6%
Race/ethnicity		
Non-Hispanic White	2021	85.7%
Non-Hispanic Black	193	8.2%
Hispanic	85	3.6%
Asian/Pacific Islander	39	1.7%
American Indian/Alaska Native	21	0.9%
Marital status		
Married	1684	71.4%
Divorced/separated	269	11.4%
Widowed	208	8.8%
Never married	198	8.4%
Smoking status		
Never smoker	1324	56.1%
Former smoker	832	35.3%
Current smoker	203	8.6%
Retirement status		
Retired	1297	55.0%
Not retired	1062	45.0%
Personal history		
Diverticulitis	147	6.2%
Colonic diseases	35	1.5%
Family cancer history		
Yes	1382	58.6%
No	977	41.4%
Family history of CRC		
Yes	293	12.4%
No	2066	87.6%
Tumor location		
Sigmoid colon		21.6%
Cecum		19.5%

Continued

Rectum		18.8%
Transverse colon		7.6%
Ascending colon		16.5%
Descending colon		3.8%%
Hepatic flexure		6.1%
Splenic flexure		2.7%
Rectosigmoid junction		3.9%
AJCC 5TH stage at diagnosis		
I	769	32.6%
II	576	24.4%
III	594	25.2%
IV	361	15.3%
Missing data	59	2.5%
Grade		
Well differentiated		10.0%
Moderately differentiated		62.4%
Poorly differentiated		14.0%
Undifferentiated		0.8%
Unknown		12.7%

A family history of any cancer was reported by 58.6% of patients, and 12.4% had a family history specifically of CRC.

In terms of tumor location, the most frequent sites were the sigmoid colon (21.6%), cecum (19.5%), rectum (18.8%), ascending colon (16.5%), and transverse colon (7.6%). Other tumor sites included the hepatic flexure (6.1%), descending colon (3.89%), rectosigmoid junction (3.9%), and splenic flexure (2.7%).

Based on the AJCC 5th edition, 32.6% of patients were diagnosed at Stage I, 24.4% at Stage II, 25.2% at Stage III, and 15.3% at Stage IV, with 2.5% missing stage data.

Regarding tumor histological grade, the majority of tumors were moderately differentiated (62.4%), followed by poorly differentiated (14.0%), well differentiated (10.0%), undifferentiated (0.8%), and 12.7% of patients had unknown tumor grade.

3.2. Treatment Characteristics

Table 2 presents data on treatment patterns for patients in the study population. Of the total sample of 2359 patients, 93.3% (2209 patients) underwent resection at some point in their treatment protocol, either alone or in combination with chemotherapy or radiotherapy. Of this subgroup, 1252 patients (53.1%) received surgery alone (*i.e.*, without systemic therapy and/or radiation therapy), possibly

with curative intent. Only 26 patients (1.1%) received chemotherapy alone, possibly for palliative purposes. Regarding combination treatments, 957 patients (40.6%) received resection followed by adjuvant therapy (chemotherapy and/or radiation therapy). 79 patients (3.4%) underwent neoadjuvant therapy (chemotherapy and/or radiation therapy) followed by surgery, with or without additional adjuvant therapy. 45 patients (1.9%) received both chemotherapy and radiation therapy without surgery.

Table 2. Treatment characteristics by stage*.

	All Patients		**Patients with Stage I/II CRC**		**Patients with Stage III/IV CRC**		**Missing data**
	N = 2359 (100%)		N = 1345 (57%)		N = 946 (40%)		N = 68 (3%)
Treatment	**N**	**%**	**N**	**%**	**N**	**%**	**N (%)**
Resection only	1252	53.1	733	54.5	483	51.05	36 (52.9)
Resection and adjuvant therapy (chemotherapy and/or radiation therapy)	957	40.6	533	39.6	404	42.71	20 (29.4)
Chemotherapy only	26	1.1	16	1.2	11	1.17	(1.5)
Neo-adjuvant therapy (chemotherapy and/or radiation therapy) and subsequent surgery, with or without adjuvant therapy	79	3.4	42	3.1	35	3.69	0 (0)
Chemotherapy and radiation therapy without surgery	45	1.9	21	1.6	13	1.38	11 (16.2)
No Resection (any therapy or none)	150	6.4	57	4.2	93	9.8	0 (0)

***Note**: The AJCC 5th edition was used for staging in this table.

Table 3. Time intervals and patients' characteristics.

		Dx&Tx	Tx&Mx	Con.		Interv.	
				Dx&Tx	Tx&Mx	Dx&Tx	Tx&Mx
N	Valid	2288	2289	1281	1282	1007	1007
	Missing	71	70	40	39	31	31
Mean		**20**	**3340**	**19**	**3402**	**20**	**3269**
Median		10	3328	-	-	-	-
Std. Deviation		33	2390	33	2399	34	2359
Minimum		0	0	0	2	0	1
Maximum		365	8910	354	8910	365	8863
Percentiles	25	0	1095	0	1103	0	1080
	50	10	3328	10	3400	10	3258
	75	24	5207	24	5332	24	5067

Note: data are restricted to patients who died. **Dx&Tx**: days between diagnosis and treatment, **Tx&Mx**: days between treatment and mortality among patients who died during the study period. **Con.**: Control arm. **Interv.**: Flex sigmoidoscopy.

There were missing data on treatment modality for 68 patients (3.0%). Resection was not performed in 150 patients (6.4%), and among them, the majority (62.0%) had stage III or IV colorectal cancer at diagnosis. Among the small group who received chemotherapy only, 11 patients (42.3%) had stage III or IV disease at diagnosis.

Table 3 shows that the mean time between diagnosis and treatment was 19.95 days (SD = 33.71; median 10.0 days). Among individuals who died during the study period, the mean time between treatment and overall mortality was 3340 days (SD = 2390 median 3328 days).

3.3. Cox Regression

Table 4 presents the results from Cox proportional hazards regression models evaluating the association between time from diagnosis to treatment initiation and mortality, stratified by control arm, intervention arm, and all patients combined. Time to treatment was categorized using seven methods, as previously described in the Methods section.

Table 4. Cox proportional hazards regression analysis of association of time to treatment and mortality.

	HR	Std. Err.	z	P > z	95% CI
CONTROL ARM PATIENTS					
More vs less than 19 days	0.98	0.17	−0.13	0.9	0.70 - 1.37
Categorized by weeks	1.01	0.05	0.3	0.77	0.93 - 1.11
Categorized by months	1.05	0.13	0.4	0.69	0.82 - 1.34
Categorized into 3 categories*	0.58	0.22	−1.44	0.15	0.28 - 1.21
More and less than 200 days	2.43	1.78	1.22	0.22	0.58 - 10.19
Median (10 days)	0.92	0.12	−0.6	0.55	0.72 - 1.19
Percentile 75th (24 days)	0.96	0.19	−0.21	0.84	0.66 - 1.41
INTERVENTION ARM PATIENTS					
More vs less than 19 days	0.86	0.14	−0.96	0.34	0.62 - 1.17
Categorized by weeks	1.03	0.05	0.66	0.51	0.94 - 1.14
Categorized by months	0.93	0.13	−0.51	0.61	0.70 - 1.23
Categorized into 3 categories*	1.2	0.42	0.52	0.6	0.61 - 2.36
More and less than 200 days	0.52	0.36	−0.94	0.35	0.13 - 2.04
Median (10 days)	0.92	0.11	−0.65	0.52	0.73 - 1.17
Percentile 75th (24 days)	1.13	0.21	0.69	0.49	0.79 - 1.63
ALL PATIENTS COMBINED					
More vs less than 19 days	0.85	0.09	−1.54	0.12	0.70 - 1.04
Categorized by weeks	1.02	0.03	0.64	0.52	0.96 - 1.07
Categorized by months	1.05	0.09	0.53	0.59	0.89 - 1.24
Categorized into 3 categories*	0.84	0.19	−0.77	0.44	0.53 - 1.32

Continued

More and less than 200 days	1.36	0.61	0.69	0.49	0.57 - 3.26
Median (10 days)	0.95	0.05	−1.02	0.31	0.85 - 1.05
Percentile 75th (24 days)	1	0.06	0.06	0.96	0.89 - 1.13

HR = Hazard Ratio, **CI** = Confidence Interval, significant p-values are indicated by $p < 0.05$. LR chi2(4) = 3.61. Log likelihood = −10195.361. Prob > chi2 = 0.6075. *<100, 100-200, >200 days. **Control Arm:** This group did not receive the regular screenings provided to the screening arm. Instead, they received their usual medical care, which did not include the specific screening protocols used in the trial. Any screenings or tests performed in this group were based on standard medical practices and recommendations at the time, rather than the structured protocol of the study. **More and less than 200 days**: groups with more than 200 days versus less than 200 days. **Percentile 75th (24 days)**: group with a duration of 24 days, representing the 75th percentile. **Median (10 days)**: group with a duration of 10 days, representing the median. **_cons:** Represents the constant term in the regression model, providing the intercept value.

Across all models and categorizations, no statistically significant associations were found between time to treatment and mortality risk (all p-values > 0.05).

- Among control arm patients, the hazard ratios (HRs) for delayed treatment (e.g., >19 days: HR = 0.98, 95% CI: 0.70 - 1.37; >200 days: HR = 2.43, 95% CI: 0.58 - 10.19) were not statistically significant (all p > 0.15).
- In the intervention arm, results were similarly non-significant across all categorizations (e.g., >19 days: HR = 0.86, 95% CI: 0.62 - 1.17; categorized into 3 groups: HR = 1.20, 95% CI: 0.61 - 2.36).
- For all patients combined, none of the categorization methods yielded significant hazard ratios either (e.g., categorized by weeks: HR = 1.02, 95% CI: 0.96 - 1.07; by months: HR = 1.05, 95% CI: 0.89 - 1.24; 3-category model: HR = 0.84, 95% CI: 0.53 - 1.32).

The full model also demonstrated poor overall fit, with a likelihood ratio chi-square of 3.61 (p = 0.6075) and a log-likelihood of −10195.361, further suggesting that delays in treatment initiation were not significantly associated with mortality in this cohort. Other unmeasured clinical, biological, or socioeconomic variables may have a more substantial influence on patient outcomes.

Table 5 summarizes the results of the Cox proportional hazards regression analysis evaluating additional predictors of mortality.

Table 5. Cox proportional hazards regression analysis of predictors and mortality risk.

	HR	Std. Err.	z	P > z	95% CI	
Resection with chemotherapy	3.09	0.2655	13.15	0.000	2.61	3.66
Chemotherapy without resection	8.19	1.1878	14.52	0.000	6.17	10.89
Life-limiting conditions	2.36	0.0892	0.53	0.593	1.64	3.39
Ibuprofen Use	0.86	0.1938	−0.77	0.002	0.76	0.98

Note: HR = Hazard Ratio, CI = Confidence Interval, significant p-values are indicated by $p < 0.05$. LR chi2(4) = 3.61. Log likelihood = −10195.361. Prob > chi2 = 0.6075. **Regression model adjusted for** age, sex, cancer stage at diagnosis, race/ethnicity, and education level.

Patients who received resection with chemotherapy had a significantly higher risk of mortality compared to those who underwent resection alone (HR = 3.09; 95% CI: 2.61 - 3.66; $p < 0.001$). The mortality risk was even higher among patients who received chemotherapy without resection, with a hazard ratio of 8.19 (95% CI: 6.17 - 10.89; $p < 0.001$).

Although individuals with disabilities showed an increased hazard for mortality (HR = 2.36; 95% CI: 1.64 - 3.39), the association was not statistically significant ($p = 0.593$).

In contrast, ibuprofen use was associated with a significantly reduced risk of mortality (HR = 0.86; 95% CI: 0.76 - 0.98; $p = 0.002$), suggesting a possible protective effect.

4. Discussion

This study analyzed the association between treatment delays and mortality among 2359 individuals diagnosed with CRC in the PLCO Trial. The results demonstrated no statistically significant association between time from diagnosis to treatment initiation and mortality risk, across multiple categorizations and patient groups. This contrasts with findings from prior studies that reported adverse outcomes linked to treatment delays [11]-[13].

However, the discrepancy may be partially explained by the narrow distribution of wait times within the PLCO cohort: the median time to treatment was only 10 days, with a 75th percentile of 24 days, indicating that most patients-initiated treatment promptly. As such, the cohort may lack the variability needed to detect the adverse effects of longer delays. This limitation underscores the importance of including populations with a broader spectrum of delay durations in future studies.

Regarding treatment modality, Cox regression analysis revealed that patients who received resection with chemotherapy or chemotherapy alone exhibited significantly higher mortality risks compared to those treated with resection alone. These associations likely reflect disease severity and staging, as combination therapies are typically reserved for more advanced-stage cancers, which inherently carry a worse prognosis. Importantly, these findings do not suggest that chemotherapy increases mortality, but rather that it serves as a proxy for more aggressive disease.

In contrast, ibuprofen use was associated with a significantly reduced hazard of mortality. Although observational, this finding aligns with prior literature suggesting a possible protective role of NSAIDs in colorectal cancer survival, potentially due to anti-inflammatory or antitumor mechanisms [18]-[20].

Interestingly, some variables that are traditionally considered strong prognostic markers—such as AJCC stage at diagnosis, tumor location, and family history of CRC—did not show statistically significant associations with mortality in our multivariable model. This may be due to the close clinical alignment between treatment modality and disease stage, which may limit the ability to disentangle their individual effects in observational models. Moreover, the lack of data on

comorbidities and social determinants of health, both of which could influence treatment access and outcomes, further limits the interpretability of some results.

The study's strengths include a large, well-characterized cohort, detailed treatment data, and the use of multiple delay measures, allowing for robust exploratory modeling. However, limitations must be acknowledged: the retrospective nature, homogeneity of treatment timing, and the fact that PLCO participants may not reflect more vulnerable or underserved populations. These factors constrain generalizability and highlight the need for future studies across diverse healthcare settings.

5. Limitations

This study's interpretations are subject to several limitations that warrant careful consideration. First, the use of data from the PLCO Trial, which employed flexible sigmoidoscopy for CRC screening, introduces an important methodological constraint. Flexible sigmoidoscopy examines only the distal colon and may detect a different subset of tumors compared to colonoscopy, which visualizes the entire colon. This distinction is critical, as the biological behavior, stage at diagnosis, and growth patterns of tumors detected by each modality may differ, potentially influencing the observed relationship between treatment delays and survival. Therefore, the findings reported here may not be generalizable to populations screened with colonoscopy or other detection methods.

That said, the absence of significant associations between treatment delay and mortality in both the control and intervention arms—analyzed separately—suggests that the results are unlikely to be solely attributable to the screening method used.

Second, the retrospective nature of this study imposes inherent limitations, including possible misclassification, missing data, and lack of control over confounding variables. In particular, comorbid conditions, socio-economic status, access to care, and treatment adherence, which are known to influence cancer outcomes, were not comprehensively available in the dataset and therefore could not be included in the models.

Finally, the narrow distribution of treatment initiation times—with most patients starting therapy within a short window—limits the ability to detect differences attributable to longer delays. As such, our findings may underestimate the true effect of prolonged wait times on CRC outcomes.

Future studies should address these limitations by incorporating longer follow-up, varied screening approaches, more diverse populations, and detailed clinical and social determinants of health, to better understand the complex relationship between treatment timing and survival.

6. Conclusions

Our analysis of CRC patients from the PLCO Trial, where most individuals-initiated treatment rapidly after diagnosis, suggests that, within this short-delay win-

dow, treatment timing was not significantly associated with mortality. This finding may reflect the characteristics of slow-growing tumors typically detected via flexible sigmoidoscopy, the PLCO screening method. However, these results should be interpreted with caution and should not be extrapolated to settings where delays are longer or tumors are potentially more aggressive, such as those detected via colonoscopy.

Beyond treatment delay, the study identifies other predictors of mortality. Combination therapies (resection with chemotherapy or chemotherapy alone) were associated with higher mortality, likely reflecting advanced disease at presentation. Conversely, ibuprofen use was linked to improved survival, consistent with emerging literature on the potential antineoplastic effects of NSAIDs.

In conclusion, while our findings suggest that modest delays in treatment initiation may not adversely impact CRC survival in populations with timely care, further research is essential. Future studies should examine longer delays, incorporate more diverse screening strategies, and explore the role of inflammation, treatment intensity, and social factors in influencing CRC outcomes. These efforts will be critical for developing more nuanced, equitable, and effective approaches to CRC management and survivorship.

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Disclaimer

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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