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Adequacy of the National Quality Forum's Colon Cancer Adjuvant Chemotherapy Quality Metric: Is 4 Months Soon Enough?

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Abstract

Objective—To ascertain whether the National Quality Forum (NQF)-endorsed time interval for adjuvant chemotherapy (AC) initiation optimizes patient outcome.

Background—Delayed AC initiation for stage III colon cancer is associated with worse survival and the focus of an NQF quality metric (<4 months among patients aged <80 years).

Methods—Observational cohort study of stage III colon cancer patients aged <80 years within the National Cancer Data Base (2003–2010). The primary outcome was 5-year overall survival evaluated using multivariate Cox regression. Aggregate survival estimates for historical surgery-only controls from pooled National Surgical Adjuvant Breast and Bowel Project trial data were also used.

Results—Among 51,331 patients (60.8±11.6 years, 50.2% male, and 77.3% white), 76.3% received standard (<2 months) and 21.6% delayed (>2 and <4 months) AC. Earlier AC was associated with better five-year overall survival (standard, 69.8%; delayed, 62.0%; late [4–6 months], 51.4%; log-rank, $p<0.001$). Survival after late AC was similar to surgery alone (51.1%; Wilcoxon-rank sum, $p=0.10$). Compared with late AC, standard (Hazard Ratio [HR] 0.62; 95% CI 0.54–0.72) and delayed (HR 0.77; 95% CI 0.66–0.89) significantly decreased risk of death. Risk of death was also lower for standard AC compared to delayed (HR 0.81; 95% CI 0.77–0.86).

Conclusions—One in five stage III colon cancer patients initiates AC within the NQF-endorsed interval, but does not derive the full benefit. These data support strengthening current quality improvement initiatives and colon cancer treatment guidelines to encourage AC initiation within 2 months of resection when possible, but not beyond 4 months.

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Introduction

Adjuvant chemotherapy (AC) improves survival among patients with resected, lymph node positive (stage III) colon adenocarcinoma and is part of national treatment guidelines.¹⁻⁷ As metastatic disease in regional lymph nodes is an important predictor of systemic failure,⁸ there is reason to suspect early AC initiation in stage III patients may be beneficial. A recent meta-analysis demonstrated earlier administration was associated with better overall and disease-free survival.⁹ Although quality studies with little heterogeneity were analyzed, there were some important limitations. For example, both colon and rectal cancer patients were included. This is problematic because decisions about AC for colon cancer are generally based on post-operative pathology; whereas, decisions for rectal cancer are often based on pre-operative staging which could influence patient and provider expectations leading to fewer AC delays. Additionally, both stage II and III patients were included. As there remains controversy regarding which stage II patients are 'high risk' and firm recommendations regarding AC are lacking, this too could lead to variation in initiation.

Importantly, among patients for whom it is clearly indicated, the optimal time to AC initiation remains unclear. Minimizing practice variation by recommending a target time interval could offer patients more consistent expectations regarding care, optimize multidisciplinary colon cancer management, and provide clearly defined, uniform guidelines to inform quality improvement efforts aimed at standardizing cancer care pathways. For stage III colon cancer patients aged less than 80 years, the National Quality Forum (NQF) endorses AC initiation within 4 months as a quality metric.¹⁰ However, at least one other oncologic quality improvement initiative recommends an 8 week interval.¹¹ Furthermore, existing data suggest the full benefit of AC is realized at a time point far earlier than the NQF metric.^{9,12-14}

Using a primary data source with adequate sample size and not restricted to elderly Medicare beneficiaries, we sought to describe factors associated with delayed AC initiation and to ascertain the impact of early initiation among patients for whom it is clearly indicated. In so doing, we intend to evaluate the current NQF metric and delineate whether it represents the ideal time interval for optimizing patient outcome. Our main study hypothesis was AC initiation within the NQF 4 month metric improves patient outcome, but that this interval is too inclusive for ensuring all patients with stage III colon cancer receive optimal care.

Methods

Data

A prospectively maintained, hospital-based registry of cancer patients, the NCDB is a joint project of the American College of Surgeons Commission on Cancer (ACS CoC) and the American Cancer Society. It has accumulated over 25 million individual patient records and captures >70% of incident cancers in the US. Over 1,500 cancer centers participate, reflecting a range of patient care settings. Comprehensive discussions of the dataset have been published previously.¹⁵⁻¹⁷ National Surgical Adjuvant Breast and Bowel Project (NSABP) investigators were contacted and aggregate overall survival estimates from pooled

trial data for a historical, surgery-only control group of stage III patients (n=340) were obtained.¹⁸ This study was considered exempt by The University of Texas MD Anderson Cancer Center's Institutional Review Board.

Study Subjects

Figure 1 describes study exclusion criteria. Surgically resected stage III colon cancer patients (2003-2010) who subsequently received AC within 6 months were included. Patients diagnosed before 2003 were not included because comorbidity data were added to the dataset beginning that year. Patients initiating AC after 6 months were excluded to account for potential bias introduced by non-adjuvant utilization (e.g.: treating metastatic disease, locoregional recurrence, etc), patients with severe post-operative complications precluding earlier utilization, and patients who intentionally deferred earlier initiation. To be consistent with the NQF quality metric, the cohort was restricted to patients aged <80 years.

Variables

Demographic, clinical, and tumor data are provided in the NCDB. Indicators of income and education are provided (based on area of residence derived from Census 2000 data). A Charlson-Deyo comorbidity index is also provided. Time from resection to AC initiation was used to stratify into three groups: standard (< 2 months); delayed (>2 and <4 months); late (4-6 months). Since the NQF variably defines time to AC initiation as measured from diagnosis or resection,^{10,19,20} we evaluated the lag between diagnosis and resection and found it was relatively short (median 8 days; mean ~14 days) with similar time intervals across AC categories. Therefore, consistent with previous work, AC initiation was measured from surgical resection.²¹ Two month categorization intervals were selected because: previous data suggest no survival difference between 4 and 8 week time intervals;¹³ randomized data suggest an 8 week time window potentially represents an interval beyond which further delays adversely affect survival;¹² based on clinical experience, 2 months is a realistic and feasible time interval that not only allows patients adequate time to recover from surgery (accounting for delays due to minor complications), but also considers national waiting periods associated with chemotherapy initiation for colorectal cancer patients.²²

Analysis

Standard descriptive statistics were used to define distributions of categorical and continuous variables. The primary outcome was overall survival. For the survival analysis, the cohort was restricted to patients diagnosed through 2005 (n=18,290) because complete, long-term follow-up is only currently available for patients diagnosed through 2005. When modeling risk factors associated with delayed AC initiation, the whole cohort was included. The log-rank test was used to assess overall survival and the Wilcoxon rank sum test was used when comparing to surgery controls (as individual NSABP data were not provided).

The association between time to AC initiation and risk of death was evaluated using multivariate Cox hazard regression. The assumption of proportional hazards was verified using the Kolmogorov-type supremum test (p=0.19). An interaction between age and time to AC initiation was considered; however, it did not contribute to model performance and was therefore excluded from the final model. The survival analysis was repeated among patients

who had a short length of stay (LOS [7 days]) and no readmission (n=12,785) to represent patients for whom early AC initiation should have been possible (i.e.: no major post-operative complications that may have contraindicated early initiation). Logistic regression was utilized to examine factors associated with delayed AC initiation, defined as beyond 2 months (reference 2 months). Because the odds ratio approximation of the relative risk may be inaccurate as the outcome rate increases, odds ratios were converted and are presented as relative risk.²³ A non-parsimonious approach was used in model construction with sex, age, race, insurance status, income, education, comorbid conditions, extent of operation, positive resection margin, and pathologic grade included as model covariates. Length of stay and readmission were not included in the main Cox model as the analytic cohort evaluated in the subgroup model was restricted/stratified based on these variables. However, these were included in the logistic model as were rurality and type of institution.

We performed several additional sensitivity analyses to better delineate the robustness of our findings. With respect to the survival analysis, AC initiation was modeled as a continuous variable (by week) and categorized into one month time intervals. Additional time-dependent modeling using a single Heaviside function was also evaluated. But, the interaction between AC initiation interval and survival time was not significant; therefore, all analyses assume a baseline hazard. As cause of death is not available in the NCDB Participant User File, cancer-specific survival was assessed by modeling relative survival.²⁴ In evaluating factors associated with delayed AC, the definition of “delay” was changed to beyond 4 months (reference 4 months).

Within the cohort, 17.0% of patients were missing at least one covariate data point (standard, 16.8%; delayed, 17.5%; late, 17.8%). Differences in survival based on missing data were neither statistically significant nor clinically meaningful (standard: 69.7% missing vs 69.8% non-missing, log-rank p=0.43; delayed: 61.0% missing vs 62.3% non-missing, log-rank p=0.92; late: 49.5% missing vs 51.7% non-missing, log-rank p=0.72). To ensure model results were robust to varying assumptions about missing data, we performed a case-complete analysis followed by an imputed analysis using ten sets of data obtained through multiple imputation by chained equations.^{25,26} Point estimates and inference from both analyses were similar so imputed results are reported. Analyses were performed using SAS 9.3 (SAS Institute). Statistical comparisons were 2-sided and considered significant at the p<0.05 level.

Results

Among 51,331 patients, mean age was 60.8±11.6 years, 50.2% were male, and 77.3% were white. Overall, 76.3% and 21.6% of patients received standard and delayed AC, respectively, with similar proportions over the study period (74.2-80.5%, standard; 17.7-23.6%, delayed). Table 1 provides patient demographic and clinical characteristics. Median LOS for the cohort was 6 days. In the standard group, 90% of patients had a LOS of 9 days. Overall, 69.8% of patients had a LOS 7 days and no readmission and 83.1% had a LOS 10 days and no readmission.

Factors Associated with AC Delay

Several factors were associated with AC initiation beyond 2 months (Figure 2A), most notably LOS beyond 7 days (Relative Risk [RR] 1.89; 95% Confidence Interval [CI] 1.82-1.97) and readmission (RR 1.67; 95% CI 1.56-1.80). Compared to those with a Charlson of 0, greater comorbidity was associated with delayed AC (Charlson 1—RR 1.10; 95% CI 1.06-1.15; Charlson 2—RR 1.29; 95% CI 1.20-1.39). Younger age was associated with a lower likelihood of delayed initiation (<50 years—RR 0.78; 95% CI 0.73-0.83; 50-59 years—RR 0.87; 95% CI 0.82-0.92; 60-69 years—RR 0.95; 95% CI 0.91-1.00; 70-79 years—ref). As a sensitivity analysis, we varied the definition of ‘delay’ to beyond 4 months (reference <4 months). For many factors, the likelihood of delay was attenuated (Figure 2B). However, the magnitude of the effect for patients with LOS beyond 7 days (RR 2.24; 95% CI 1.98-2.54), readmission (RR 2.28; 95% CI 1.88-2.76), and greater comorbidity (Charlson 1—RR 1.20; 95% CI 1.04-1.39; Charlson 2—RR 1.75; 95% CI 1.42-2.15) remained significant and was accentuated.

Impact on AC Delays on Survival

Demographic and clinical characteristic distributions for patients evaluated in the survival analysis were similar to the overall cohort. Overall survival (Figure 3A) was significantly better with earlier AC (standard, 69.8%; delayed, 62.0%; late 51.4%; log-rank, $p<0.001$). Survival among patients receiving AC after 4 months was similar to historical surgery-only controls pooled from NSABP adjuvant therapy trials (51.1%; Wilcoxon rank sum, $p=0.10$). The effect was similar among patients with short LOS and no readmission (standard 72.9%; delayed 68.1%; late 59.7%; log-rank, $p<0.001$). When stratified into 1 month intervals (Figure 3B), survival resembled the 2 month categorization scheme (1 month, 69.8%; >1 and 2 months, 69.6%; >2 and 3 months, 61.2%; >3 and 4 months, 60.6%; 4-6 months, 51.4%; log-rank, $p<0.001$). After adjustment for demographic and clinical factors (Table 2), there was a significant benefit for standard (Hazard Ratio [HR] 0.62; 95% CI 0.54-0.72) and delayed (HR 0.77; 95% CI 0.66-0.89) as compared to late AC. Similarly, standard AC patients had a survival benefit compared with delayed (HR 0.81; 95% CI 0.54-0.72). When the analysis was restricted to patients with a short LOS and no readmission, the survival benefit persisted for standard AC as compared to delayed (HR 0.88; 95% CI 0.82-0.96) or late AC (HR 0.71; 95% CI 0.57-0.90). However, delayed AC offered no benefit over late.

Sensitivity Analyses

Demographic and clinical variables were compared between patients excluded versus included in the subgroup survival analysis. Characteristics of those excluded appeared to favor patients more likely to experience a post-operative complication—older, higher burden of comorbid conditions, and more likely to have undergone a total or complex colectomy. In additional sensitivity analyses, we modeled 1 month (4 week) time intervals to address potentially meaningful survival differences based on a shorter AC time interval in the multivariate model. Compared to those receiving AC within 1 month, there was no difference in risk of death for patients who received AC between 1 and 2 months (HR 1.00; 95% CI 0.94-1.06); however, differences were significant beyond 2 months (3 months, HR 1.26; 95% CI 1.16-1.37; 4 months, HR 1.18; 95% CI 1.03-1.35; 5 months, HR 1.48; 95% CI

1.22-1.79; 6 months, HR 1.91; 95% CI 1.46-2.51). Time to AC initiation was also modeled as a continuous variable, using one week time increments—with each additional week of delay, risk of death increased by 3% (HR 1.03; 95% CI 1.02-1.03). A relative survival model was constructed to evaluate cancer-specific risk of death, with generally similar findings to the overall survival model: compared to late AC, there was a significant benefit for standard (HR 0.54; 95% CI 0.45-0.65) and delayed (HR 0.70; 95% CI 0.58-0.85); standard AC also demonstrated a survival benefit compared with delayed (HR 0.77; 95% CI 0.0.72-0.84).

Discussion

The NQF endorses a 4 month interval to AC initiation as a quality metric for stage III colon cancer. While inclusive and implicitly emphasizes administration of adjuvant therapy, the current NQF metric neither stresses the importance of early AC initiation and its impact on patient outcome nor informs the multi-disciplinary care pathway such that all eligible patients derive the full benefits of systemic therapy.^{9,12-14} In this regard, our evaluation of the NQF metric supports several conclusions. First, earlier AC initiation is beneficial in stage III disease, but the benefit attenuates beyond 2 months. Second, compared to pooled NSABP trial historical surgery-only controls, any survival benefit associated with AC appears mitigated after 4 months. Thus, patients receiving late AC likely experience the toxicity with minimal if any benefit. Third, consistent with prior work,¹³ >75% of patients initiate AC within 2 months of surgical resection. Therefore, much of the care provided in the general community already exceeds this quality benchmark. More importantly, one in five stage III patients initiate AC within the NQF-endorsed time interval, but do not derive the full benefit. Thus, enhancing current national guidelines as well as strengthening the existing NQF quality metric to consistently recommend AC initiation within 2, but not beyond 4, months of resection could improve the multidisciplinary care provided to colon cancer patients.

The NQF is well-positioned to bridge the apparent existing gap between data and practice. The NQF's mission is to build consensus for and work towards achieving performance improvement, to endorse national consensus performance standards, and to attain goals through education and outreach.²⁷ Currently, 85% of quality measures used in federal programs are NQF-endorsed and 90% of NQF measures are in use.²⁸ Importantly, the NQF has demonstrated flexibility—augmenting, adding, and/or deleting metrics as data evolve.²⁹ A greater emphasis on early AC initiation, not simply receipt of AC, is needed to move the bar for defining and measuring quality colon cancer care in the general community forward. A modified and enhanced NQF metric could both set a higher benchmark and provide a uniform, data-driven colon cancer AC initiation guideline which could raise both patient and clinician awareness of the importance of timely therapy.

Post-operative complications are common following colorectal cancer surgery and may be associated with delayed or omitted chemotherapy.^{21,30-32} Since post-operative complications are not “never events”, it may be reasonable to include parameters around this metric. For example, 90% of patients in our standard group had a LOS of 9 days and >80% of patients overall had no readmission and a LOS 10 days. Additionally, AC is frequently

administered in the outpatient setting with a preponderance of care provided by private group practices.^{22,33} However, the NQF metric specifies this benchmark should be evaluated at the level of the treating facility. As the US healthcare system continues to evolve and Accountable Care Organizations become a more integral part, augmenting the quality metric to state AC should be initiated within 2 months for at least 80-90% of patients and tracking quality at the organizational, rather than the institutional, level may represent an equitable and actionable performance target.

Complications alone may not account for all AC delays. AC is omitted in one third of patients without a post-operative complication,³¹ suggesting clinical (e.g.: pre-existing comorbid conditions, patient frailty/deconditioning, etc.) and/or other patient factors (e.g.: lack of insurance, access to a medical oncologist, etc.) impact treatment decisions. Patients may delay AC initiation for personal reasons, particularly if not advised of the relationship between long-term outcome and earlier initiation.³⁴ Alternatively, a lack of unified recommendations/quality targets or a failure by providers to recognize unnecessary delays may completely mitigate therapeutic benefit may also play a role. Pragmatically, a simple calculation of the number needed to treat reveals very few patients are required for efforts aimed at earlier AC initiation to be beneficial (13 patients currently initiating AC in 2-4 months would need receive it within 2 months; 9 patients currently initiating AC in 4-6 months would need receive it within 2-4 months; 5 patients currently initiating AC in 4-6 months would need receive it within 2 months).

There are important limitations to consider when interpreting our results. Selection bias and the generalizability of our results to patients receiving care at non-CoC hospitals must be considered.^{35,36} NCDB does not specifically report post-operative complications. However, our subgroup analysis of patients with short LOS and no readmission represented patients unlikely to have experienced a major surgical complication. The data neither specify which chemotherapeutic regimen patients received nor how many patients completed a full course of AC. NCDB does not provide information on the indication for chemotherapy administration or the reason for delays in initiation; therefore, we restricted our cohort to patients who initiated AC within 6 months of resection in an effort to only capture adjuvant indications. The data do not provide information on geographic provider density, which would speak to issues of patient access. Important patient-level factors, such as treatment preferences and performance status, are not specified. Similarly, the data do not fully capture or explain clinical decision-making based on provider intent.

Finally, although we had aggregate survival estimates for NSABP historical surgery-only controls, we did not have individual patient data to allow multivariate modeling. As such, the comparison to patient receiving AC after 4 months could be subject to bias. Despite this, there have been improvements in surgical technique and additional emphasis on oncologic surgical principles since the NSABP data utilized in this study were collected. In addition, randomization of NSABP patients occurred after surgical resection, suggesting surgical technique was not standardized or subject to rigorous surgical quality control. However, this lack of surgical quality control likely biased the comparison in favor of the late AC group; yet, survival was similar compared to no chemotherapy. NSABP member institutions represent a varied cross-section of practice settings, including a large proportion of

community clinical oncology programs, similar to the majority of programs represented within the NCDB. Thus, although patients treated in randomized studies are often thought to have better outcomes than patients treated in the general community, we believe these factors support the generalizability of the NSABP data in this context and lend credence to the comparison in our study. Furthermore, because there is no longer equipoise with respect to the issue of systemic therapy administration for stage III colon cancer, there are unlikely to be future studies (randomized or not) where such patients are assigned to not receive chemotherapy. And, because systemic therapy is a standard part of treatment for stage III colon cancer patients in current practice (in large part because of data from the NSABP trials), a comparison to any contemporary cohort of patients who did not receive chemotherapy (but should have) would likely be inherently biased. For these reasons, although the NSABP data utilized in our work did not permit adjustment for all potential confounding variables, it likely represents the best available data to evaluate the important issue of a time threshold beyond which chemotherapy may not be effective.

Although the NQF metric provides a readily achievable target, it is suboptimal for ensuring all colon cancer patients receive the full benefit of AC. Our findings suggest a shorter interval (<2 months) would establish a higher bar for measuring quality and set a reasonable and actionable target. Our work also suggests a recommendation against AC initiation after 4 months could spare patients toxicity associated with seemingly non-beneficial therapy and reduce potentially unnecessary health care utilization and spending. Oncologic quality improvement initiatives should focus on enhancing multidisciplinary care coordination to facilitate referral to and consultation with medical oncologists and identifying perioperative processes that can minimize colorectal surgical complications. Benchmarking quality requires carefully chosen metrics that not only reflect attainable targets for care delivery, but also incorporate clinically meaningful care processes. Metrics not reflecting optimal care may cause providers to inadvertently miss opportunities to maximize the benefits of existing therapies.

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Figure 1.
Flow diagram of study design.

Figure 2.

Relative risk associated with chemotherapy initiation delayed beyond 2 months (reference 2 months) and 4 months (reference <4 months).

Figure 3.

Unadjusted overall survival stratified by time to AC initiation (A) and by 1 month time intervals (B). Log-rank, p-value<0.001 for both; Wilcoxon rank sum (surgery controls vs late AC), p=0.10.

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Table 1
Patient and Facility Characteristics Stratified by Time to Chemotherapy Initiation

	Time to Chemotherapy Initiation		
	Standard (n=39,141)	Delayed (n=11,095)	Late (n=1,095)
Demographic Characteristics			
Mean Age $\pm$ SD, years	60.4 $\pm$ 11.6	61.8 $\pm$ 11.4	62.1 $\pm$ 11.1
Age, years (%)			
50	17.9	14.6	14.2
50-59	26.5	24.1	23.3
60-69	30.2	32.0	33.2
70-79	25.4	29.4	29.3
Male sex (%)	50.2	50.0	50.3
Race (%)			
White	78.7	72.9	70.7
Black	12.2	16.4	17.4
Hispanic	4.8	5.9	8.2
Other	3.1	3.7	3.0
Missing	1.3	1.2	0.7
Insurance status (%)			
Private	52.5	42.6	40.4
Medicare	37.7	42.6	41.9
Medicaid	4.0	6.8	8.6
Other	0.7	0.9	0.9
Uninsured	3.7	5.6	6.6
Missing	1.3	1.5	1.6
*Income (%)			
\$46,000	37.9	34.7	33.8
Missing	5.9	5.7	4.6
*Education (%)			
29%	33.8	30.1	25.8
Missing	5.9	5.7	4.6
Rurality (%)			
Metropolitan	77.3	77.5	77.9
Suburban	14.1	14.3	14.7
Rural	2.1	1.8	1.9
Missing	6.5	6.4	5.5
Clinical Characteristics			
Comorbidity index (%)			
0	75.4	70.3	65.9

	Time to Chemotherapy Initiation		
	Standard (n=39,141)	Delayed (n=11,095)	Late (n=1,095)
1	19.9	22.7	24.0
2	4.8	7.1	10.1
Extent of Operation (%)			
<i>Partial colectomy</i>	90.4	88.0	88.3
<i>Total colectomy</i>	2.0	2.7	3.7
<i>Colectomy plus contiguous organ(s)</i>	6.8	8.5	7.3
<i>Colectomy, NOS</i>	0.8	0.8	0.6
Pathologic Margin Status (%)			
<i>Positive</i>	7.0	8.2	9.2
<i>Unknown</i>	0.8	1.2	1.1
Number of Lymph Nodes			
<i>12 nodes</i>	77.9	78.5	76.8
Pathologic Grade (%)			
<i>Well-differentiated</i>	6.5	6.4	6.6
<i>Moderately-differentiated</i>	66.3	67.3	65.9
<i>Poorly-differentiated</i>	23.3	22.4	22.9
<i>Undifferentiated</i>	2.0	1.9	1.9
<i>Missing</i>	1.9	2.0	2.7
Post-operative Length of Stay (%)			
<i>7 days</i>	79.3	63.7	55.5
30-day Readmission (%)			
<i>Yes</i>	4.1	7.4	11.4
<i>Unknown</i>	2.7	3.0	3.0
Time from diagnosis to surgery			
<i>Mean ± SD, days</i>	14.1 ± 20.9	14.9 ± 22.5	13.3 ± 19.7
Time from surgery to AC initiation			
<i>Mean ± SD, days</i>	51.5 ± 23.8	89.8 ± 27.7	156.2 ± 25.1
Facility Characteristics			
Hospital Type			
<i>Academic/Research</i>	23.2	30.9	27.7
<i>Comprehensive Community Cancer Center</i>	56.7	50.2	51.8
<i>Community Cancer Center</i>	19.0	18.0	19.8
<i>Other</i>	1.2	1.0	0.7
Region			
<i>West</i>	12.4	13.8	13.8
<i>Midwest</i>	29.0	25.6	20.8
<i>Northeast</i>	19.5	22.7	19.8
<i>South</i>	39.2	37.9	45.6

Column percentages may not add up to 100% due to rounding.

* Based on 2000 census data. For income, the percentage of patients whose area of residence (based on year 2000 Census data) had a median household income \$46,000 is presented. For education, the percentage of patients whose area of residence (based on year 2000 Census data) had 29% or more adults who did not attain a high school education is presented.

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Table 2

Association Between Time-to-Initiation of Adjuvant Chemotherapy and Overall Risk of Death.

	Hazard Ratio (95% Confidence Interval)	
	Overall cohort	LOS 7 days and no readmission
Chemotherapy Initiation		
<i>Late</i>	1.00	1.00
<i>Delayed</i>	0.77 (0.66-0.89)	0.81 (0.64-1.02)
<i>Standard</i>	0.62 (0.54-0.72)	0.71 (0.57-0.90)
<i>Standard vs Delayed (ref)</i>	0.81 (0.77-0.86)	0.88 (0.82-0.96)
Female Sex	0.87 (0.83-0.92)	0.89 (0.84-0.95)
Age, years		
50	0.67 (0.61-0.74)	0.63 (0.56-0.72)
50-59	0.69 (0.63-0.75)	0.67 (0.60-0.75)
60-69	0.76 (0.71-0.81)	0.72 (0.66-0.78)
70-79	1.00	1.00
Race		
<i>White</i>	1.00	1.00
<i>Black</i>	1.16 (1.08-1.24)	1.17 (1.07-1.29)
<i>Hispanic</i>	0.86 (0.75-0.97)	0.98 (0.84-1.14)
<i>Other</i>	0.83 (0.70-0.98)	0.86 (0.70-1.05)
Insurance status		
<i>Private</i>	1.00	1.00
<i>Medicare</i>	1.27 (1.19-1.36)	1.29 (1.17-1.41)
<i>Medicaid</i>	1.63 (1.44-1.85)	1.51 (1.27-1.80)
<i>Other</i>	1.01 (0.73-1.38)	0.96 (0.63-1.45)
<i>Uninsured</i>	1.36 (1.19-1.55)	1.39 (1.17-1.65)
Income \$46,000	1.06 (0.99-1.13)	1.05 (0.97-1.14)
Education	1.05 (0.99-1.13)	1.09 (1.00-1.18)
Comorbidity index		
0	1.00	1.00
1	1.21 (1.14-1.28)	1.19 (1.10-1.28)
2	1.75 (1.59-1.93)	1.75 (1.53-1.99)
Extent of Operation		
<i>Partial colectomy</i>	1.00	1.00
<i>Total colectomy</i>	1.21 (1.04-1.42)	1.25 (1.01-1.55)
<i>Colectomy plus contiguous organ(s)</i>	1.32 (1.22-1.44)	1.34 (1.20-1.50)
<i>Colectomy, NOS</i>	1.09 (0.86-1.39)	1.09 (0.80-1.50)
Positive Margin	2.08 (1.92-2.25)	2.20 (1.98-2.44)
Pathologic Grade		
<i>Well-differentiated</i>	0.54 (0.44-0.67)	0.49 (0.38-0.65)
<i>Moderately-differentiated</i>	0.63 (0.52-0.76)	0.65 (0.51-0.82)

	Hazard Ratio (95% Confidence Interval)	
	Overall cohort	LOS 7 days and no readmission
<i>Poorly-differentiated</i>	0.97 (0.80-1.17)	1.00 (0.78-1.27)
<i>Undifferentiated</i>	1.00	1.00